Evidence-based Guidelines for the use of Stem Cell Therapy

Cardiac Conditions Supplement

July 2025

Department of Health Research
Directorate General of Health Services

Ministry of Health & Family Welfare
Government of India

CONTENTS

ABBREVIATIONS

ABMMNCs	:	Autologous Bone Marrow Mononuclear Cells
AMI	:	Acute Myocardial Infarction
BMCs	:	Bone Marrow Cells
BMMNCs	:	Bone Marrow Mononuclear Cells
BMSCs	:	Bone Marrow Stem Cells
CABG	:	Coronary Artery Bypass Graft
CI	:	Confidence Interval
CK-MB	:	Creatine Phosphokinase-MB
CMR	:	Cardiovascular Magnetic Resonance
CVD	:	Cardiovascular Diseases
DCM	:	Dilated Cardiomyopathy
DoIs	:	Declaration of Interests
ECG	:	Electrocardiogram
EDV	:	End-Diastolic Volume
EF	:	Ejection Fraction
EtD	:	Evidence to Decision
ESV	:	End-Systolic Volume
EoI	:	Expression of Interest
G-CSF	:	Granulocyte Colony Stimulating Factor
GDG	:	Guideline Development Group
GDT	:	Guideline Development Tool
GMP	:	Good Manufacturing Practice
GRADE	:	Grading of Recommendations Assessment, Development and Evaluation
HF	:	Heart Failure
HFrEF	:	Heart Failure with Reduced Ejection Fraction
IC	:	Intracoronary
IDCM	:	Idiopathic Dilated Cardiomyopathy
IHF	:	Ischemic Heart Failure
ISCT	:	International Society for Cellular Therapy
KCCQ	:	Kansas City Cardiomyopathy Questionnaire
NIHF	:	Non-Ischemic Heart Failure
LVEDD	:	Left Ventricular End-Diastolic Diameter
LVEF	:	Left Ventricular Ejection Fraction
MACEs	:	Major Adverse Cardiovascular Events
MA	:	Meta-Analysis
MCID	:	Minimal Clinically Important Difference
MD	:	Mean Difference
MeSH	:	Medical Subject Heading
MLHFQ	:	Minnesota Living with Heart Failure Questionnaire
MI	:	Myocardial Infarction
MRI	:	Magnetic Resonance Imaging
6 MWT	:	6 Minute Walk Test
NICE	:	National Institute for Health and Care Excellence
NIDCM	:	Non-Ischemic Dilated Cardiomyopathy
NYHA	:	New York Heart Association

OIS	:	Optimal Information Size
PBMCs	:	Peripheral Blood Mononuclear Cells
PCI	:	Percutaneous Coronary Intervention
PICO	:	Population Intervention Comparison Outcome
PRISMA	:	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCTs	:	Randomized Controlled Trials
Re-MI	:	Recurrent-Myocardial Infarction
RoB2	:	Risk of Bias2
RR	:	Risk Ratio
SAEs	:	Serious Adverse Events
SCT	:	Stem Cell Transplantation
SD	:	Standard Deviation
SDF-1	:	Stromal Cell Derived Factor-1
SMD	:	Standard Mean Difference
SPECT	:	Single-Photon Emission Computed Tomography
SRs	:	Systematic Reviews
STEMI	:	ST-segment Elevation Myocardial Infarction
TIMI	:	Thrombolysis in Myocardial Infarction
UC-MSCs	:	Umbilical Cord-derived Mesenchymal Stem/Stromal Cells
WHO	:	World Health Organization

1. DILATED CARDIOMYOPATHY

i. **Key question in PICO format**

ii. **Search strategy**

iii. **PRISMA flow diagram**

iv. **Summary of included studies**

v. **Evidence to decision framework**

vi. **Data extraction**

vii. **List of excluded studies**

i. Key question in PICO format question:

Population: All patients with Dilated Cardiomyopathy Subgroup (pediatric/adults; Co-morbidities, Ischemic / non-ischemic)

Intervention: Any Stem cell and product derived from stem cells

Comparator: Usual Care/ Conventional Care

Outcome: Critical: mortality, Serious Adverse Events (safety), tumor formation

ii. Search Strategy:

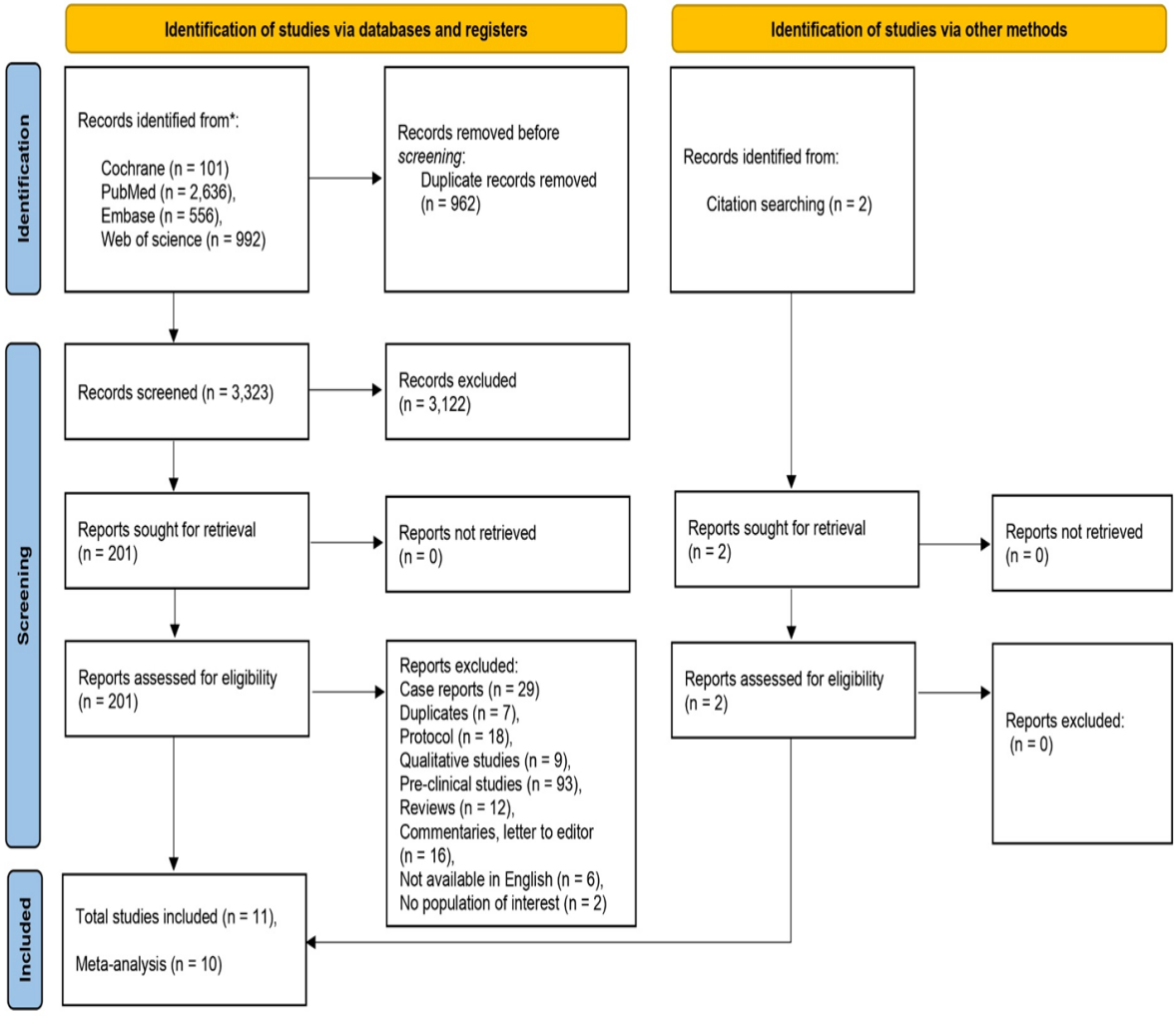
An electronic search was performed in PubMed, Embase, Web of Science, and Cochrane databases to identify relevant studies. MeSH terms and keywords related to stem cells and DCMP were used to build the search strategy. No restrictions were placed on the search regarding the year of publication, type of articles, or publication language.

Table 2: Search strategy

Database	No	Search Query	Results
Cochrane	#1	("stem cells":ti,ab OR "stromal cells":ti,ab OR "Wharton's Jelly cells":ti,ab OR "mother cell":ti,ab OR "mesenchymal stem cell":ti,ab OR "progenitor cells":ti,ab OR "bone marrow":ti,ab OR "umbilical cord":ti,ab OR "colony forming units":ti,ab)	21,274
	#2	("dilated cardiomyopathy":ti,ab OR "congestive cardiomyopathy":ti,ab OR "dilated":ti,ab OR "cardiac dilation":ti,ab OR "non-ischaemic cardiomyopathy":ti,ab OR "cardiac muscle distension":ti,ab OR "myocardial enlargement":ti,ab OR "cardiomegaly":ti,ab OR "hypertrophic cardiomyopathy":ti,ab)	34,515
	#3	#1AND#2	101
EMBASE	#1	'stem cells'/exp OR 'mesenchymal stem cells'/exp OR 'progenitor cells' OR 'bone marrow'/exp OR 'umbilical cord'/exp OR 'colony-forming units' OR 'stem cells':ab,ti OR 'stromal cells':ab,ti OR 'mother cell':ab,ti OR 'mesenchymal stem cell':ab,ti OR 'progenitor cells':ab,ti OR 'bone marrow':ab,ti OR 'umbilical cord':ab,ti OR 'colony forming units':ab,ti	1,036,152
	#2	'dilated cardiomyopathy'/exp OR 'dilated cardiomyopathy' OR 'cardiomegaly'/exp OR 'cardiomegaly' OR 'hypertrophic cardiomyopathy'/exp OR 'hypertrophic cardiomyopathy' OR 'dilated cardiomyopathy':ab,ti OR 'congestive cardiomyopathy':ab,ti OR 'dilated':ab,ti OR 'cardiac	629,510

		dilation':ab,tiOR 'non-ischaemic cardiomyopathy':ab,ti OR 'cardiac muscle distension':ab,ti OR 'myocardial enlargement':ab,ti OR 'cardiomegaly':ab,ti OR 'hypertrophic cardiomyopathy':ab,ti	
	#3	#1AND#2	556
Web of Science	#1	TS=((“stem cells” OR “stromal cells” OR “Wharton’s Jelly cells” OR “mother cell” OR "mesenchymal stem cell" OR “progenitor cells” OR “bone marrow” OR “umbilical cord” OR “colony forming units”))	688,798
	#2	TS=((“dilated cardiomyopathy” OR “Congestive cardiomyopathy” OR dilated OR “Cardiac dilation” OR “non-ischaemic cardiomyopathy” OR “Myocardial enlargement” OR “cardiomegaly” OR “hypertrophic cardiomyopathy”))	89,354
	#3	#1 AND#2 AND #3	992
PubMed	#1	("Stem Cells"[MeSH] OR "Mesenchymal Stem Cells"[MeSH] OR "Progenitor Cells"[Title/Abstract] OR "Bone Marrow"[MeSH] OR "Umbilical Cord"[MeSH] OR colony forming unit, hematopoietic[MeSH] OR "stem cells"[Title/Abstract] OR "stromal cells"[Title/Abstract] OR "Wharton's Jelly cells"[Title/Abstract] OR "mother cell"[Title/Abstract] OR "mesenchymal stem cell"[Title/Abstract] OR "progenitor cells"[Title/Abstract] OR "bone marrow"[Title/Abstract] OR "umbilical cord"[Title/Abstract] OR "colony forming units"[Title/Abstract])	658,864
	#2	(dilated Cardiomyopathy[MeSH] OR "Cardiomegaly"[MeSH] OR hypertrophic cardiomyopathy[MeSH] OR "dilated cardiomyopathy"[Title/Abstract] OR "congestive cardiomyopathy"[Title/Abstract] OR "dilated"[Title/Abstract] OR "cardiac dilation"[Title/Abstract] OR "non-ischaemic cardiomyopathy"[Title/Abstract] OR cardiac muscle distension[Title/Abstract] OR "myocardial enlargement"[Title/Abstract] OR "cardiomegaly"[Title/Abstract] OR "hypertrophic cardiomyopathy"[Title/Abstract])	331,389
	#3	#1AND#2	2,636

iii. PRISMA Flow Diagram:



iv. Summary of included studies:

Study	Population	Intervention	Comparison	Outcomes (including SAE)	Comments
Clinical trials					
Frljak et al. 2018[1]	Patients with non-ischemic DCMP, LVEF<40%, NYHA III	$CD34^+$ SCT	No intervention	All-cause mortality, LVEF %, LVEDD (cm), NYHA classification, 6-MWT	Results suggest that patients with DCM, changes in RV function correlate with changes of viability of interventricular septum. CD341 cell therapy appears to be associatedwith improved right ventricular function in this patient cohort
Hamshere et al. 2015[2]	Patients with DCMP, LVEF ≤45%, NYHA ≥2	BMC	Placebo	All-cause mortality, LVEF %	G-CSF and IC cell therapy demonstrated an improvement in cardiac function, symptoms, and biochemical parameters in patients with DCM.
Henry et al. 2014[3]	Patients with non-ischemic DCMP	BM-MNCs	No intervention	All-cause mortality, LVEF %, LVESV (ml), 6-MWT	Intramyocardial injection with ixmyelocel-T reduces major adverse cardiovascular event and improves symptoms in patients with ischemic DCMP but not in patients with nonischemic DCMP
Martino et al. 2015[4]	Patients with HF per Framingham, HF symptoms ≥1 year	NA	Placebo	All-cause mortality, LVEF %, 6-MWT	Intracoronary injection of autologous BMNC does not improve left ventricular function in patients with NIDCM
Sant et al. 2014[5]	Patients with non-ischemic DCM, LVEF <35%	BMNC	No intervention	All-cause mortality, LVEF %, NYHA classification	Direct intramyocardial application of bone marrow mononuclear cells in non-ischemic dilated cardiomyopathy was not associated with significant changes in left

					ventricular function
Seth et al. 2010[6]	Patients aged 15-70 with idiopathic DCMP, EF <40%	Autologous peripheral blood $CD34^+$ cells	Optimal medical care	All-cause mortality, LVEF %, NYHA classification	The clinical follow-up results of a first-in-man pilot study of stem cell therapy in patients with dilated cardiomyopathy at the completion of 3 years of follow-up demonstrate that the benefit is sustained and without any long-term side effects. is the effect is less in patients with more severely damaged myocardium
Vrtovec et al. 2011[7]	Patients with heart failure referred to Advanced Heart Failure	Autologous peripheral blood $CD34^+$ cells	Optimal medical care	All-cause mortality, LVEF %, LVEDD (cm), 6-MWT	Intracoronary stem cell transplantation may be associated with improved ventricular function, exercise tolerance, and long-term survival in patients with dilated cardiomyopathy. Higher intramyocardial homing is associated with better stem cell therapy response
Vrtovec et al. 2013[8]	Patients with heart failure referred to Advanced Heart Failure	G-CSF stimulated autologous $CD34^+$ PBMC	NA	All-cause mortality, 6-MWT	Intracoronary stem cell transplantation could lead to improved ventricular remodeling, better exercise tolerance and potentially improved survival in patients with DCMP.
Xiao et al. 2017[9]	Patients aged 18-75 with LVEF < 40%	BMMC	No intervention	All-cause mortality, LVEF %, LVEDD (cm), NYHA classification	Intracoronary bone marrow stem cell transplantation in DCM is safe and effective, while BMSC and BMMC infusion possess comparable effectiveness

v. Evidence to Decision Framework:

QUESTION

ISCHEMIC DILATED CARDIOMYOPATHY

In patients with ischemic dilated cardiomyopathy, what is the efficacy and safety of stem cell therapy as compared to usual care?	
POPULATION:	Ischemic Dilated Cardiomyopathy (IDCM)
INTERVENTION:	Stem cells therapy
COMPARISON:	Usual Care
MAIN OUTCOMES:	Mortality; MACE; Left ventricular ejection fraction; Left ventricular End diastolic volume; Left ventricular End systolic Diameter; Left ventricular End systolic volume; Left ventricular End diastolic Diameter; 6-minute walk test; NYHA; Adverse events (Other than Mortality and MACE)
SETTING:	Hospital setting
PERSPECTIVE:	
BACKGROUND:	Dilated cardiomyopathy is a chronic disorder that leads to enlargement of ventricles with impairment in contractility of cardiac muscle. It is one of the major causes of chronic heart failure and recurrent hospitalizations. It is multifactorial in etiology, major causes being genetic mutations, inflammation, autoimmune disorders& infections. Over the past decade the prevalence and mortality associated with has increased globally.
CONFLICT OF INTERESTS:	None

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○No	It is a disorder of the heart muscle with heart dilation (heart muscle becomes stretched)	

○Probably no ○Probably yes ● Yes ○Varies ○Don't know	and impaired contraction, in the absence of high blood pressure, damaged or diseased heart valves, or heart disease present at birth or related to myocardial infarction (heart attack). The current standard of treatment is based on medicines and cardiac devices. However, DCM is still one of the leading causes of heart transplantation in adults.	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○Trivial ● Small ○Moderate ○Large ○Varies ○Don't know	1. **All-cause mortality:** Two RCTs reported mortality with stem cell therapy in ischemic with 28 patients in the stem cell treatment group and 25 in the usual care group. For mortality at 6 months from one study, the RR was found to be 1.00 (95% CI: 0.112 to 8.94), and for mortality at 3 months from another study, the RR was found to be 0.394 (95% CI: 0.017 to 9.036). The pooled risk ratio (RR) for mortality was found to be 0.736 (95% CI: 0.003 to 191.20). The values were statistically non-significant. 2. **Left Ventricular Ejection Fraction (LVEF):** One RCT with 27 participants reported the change in LVEF% from baseline at the end of twelve months and showed a mean difference of 2.601 (95% CI: -6.546 to 11.747) between the stem cell arm and the usual care arm. The change was statistically non-significant. 3. **6-minute walk test (6-MWT):** Only one RCT with 27 participants reported the effect of stem cell therapy on the 6-minute walk test distance at the end of 12 months. The MD between the stem cell arm and the usual care arm was 151.98 meters (95% CI: 0.68 to 303.28). The difference was found to be statistically significant and clinically important (MCID 150 meters).	MCID considered: • 6-minute walk test: 150 meters • LVEF: 5%[10, 11]
Undesirable Effects How substantial are the undesirable anticipated effects?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○Small ○Moderate ○Large ○Varies ○Don't know	One RCT with a total of 12 participants reported the incidence of MACE at two time points. The risk ratio of MACE between the stem cell arm and the usual care arm was 0.167 (95% CI: 0.022 to 1.248) at 12 months, which was statistically non-significant.	
Certainty of Evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
● Very low ○Low ○Moderate ○High ○No included studies	The certainty of evidence is very low due to high risk of bias, inconsistency and imprecision in the effect shown by stem cell therapy.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○Important uncertainty or variability ○Possibly important uncertainty or variability	Most of HF patients attach more weight to quality of life over longevity.[12,13]	

● Probably no important uncertainty or variability ○No important uncertainty or variability		
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○Favors the comparison ○Probably favors the comparison ● Does not favor either the intervention or the comparison ○Probably favors the intervention ○Favors the intervention ○Varies ○Don't know	It is less clear if benefits of stem cell intervention outweigh the harms, based on limited evidence.	
Resources required How large are the resource requirements (costs)?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Large costs ○Moderate costs ○Negligible costs and savings ○Moderate savings ○Large savings ○Varies ○Don't know	The reported price to patients ranged from $6000 to $20,700 for 7 clinics willing to provide these data. The mean price for therapy utilizing adipose tissue-derived cells was $7742 (6 clinics) whereas the price for umbilical cord tissue-derived products was $12,162 (4 clinics). The mean price across 7 clinics was $9593, while the median price was $6500. These are costs when the stem cells have been infused intravenously. The costs are likely to be much higher for intra-coronary infusions. There are no studies evaluating the costs in an Indian setting.[14]	
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○Very low ○Low ● Moderate ○High ○No included studies	No research evidence was identified.	The GDG members were fairly certain that stem cell therapy requires large resources.
Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○Favors the comparison ● Probably favors the comparison ○Does not favor either the intervention or the comparison ○Probably favors the intervention ○Favors the intervention ○Varies ○No included studies	No direct research evidence was identified.	The intervention was not found to be effective and hence the committee deferred to comment on cost effectiveness.
Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○Reduced ● Probably reduced ○Probably no impact ○Probably increased ○Increased ○Varies ○Don't know	No research evidence was identified.	As stem cell therapy is an expensive treatment offered only at tertiary centers, it is likely to reduce equity.
Acceptability Is the intervention acceptable to key stakeholders?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○No ○Probably no ● Probably yes ○Yes ○Varies ○Don't know	No research evidence was identified.	Despite uncertainty regarding the medical risks and benefits associated with stem cell injections, stroke survivors may still consider undergoing treatment in private, unregulated clinics.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○No ○Probably no ● Probably yes ○Yes ○Varies ○Don't know	No research evidence was identified.	Feasible to implement in tertiary care centers.

NON-ISCHEMIC DILATED CARDIOMYOPATHY

In patients with non-ischemic dilated cardiomyopathy, what is the efficacy and safety of stem cell therapy as compared to usual care?	
POPULATION:	Non-Ischemic Dilated cardiomyopathy
INTERVENTION:	Stem cells therapy
COMPARISON:	Usual Care
MAIN OUTCOMES:	Mortality; MACE; Left ventricular ejection fraction; Left ventricular End diastolic volume; Left ventricular End systolic Diameter; Left ventricular End systolic volume; Left ventricular End diastolic Diameter; 6-minute walk test; NYHA; Adverse events (Other than Mortality and MACE).
SETTING:	Hospital setting
PERSPECTIVE:	
BACKGROUND:	Dilated cardiomyopathy is a chronic disorder that leads to enlargement of ventricles with impairment in contractility of cardiac muscle. It is one of the major causes of chronic heart failure and recurrent hospitalizations. It is multifactorial in etiology, major causes being genetic mutations, inflammation, autoimmune disorders and infections. Over the past decade the prevalence and mortality associated with has increased globally.
CONFLICT OF INTERESTS:	None

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○No ○Probably no ○Probably yes ● Yes ○Varies ○Don't know	It is a disorder of the heart muscle with heart dilation (heart muscle becomes stretched) and impaired contraction, in the absence of high blood pressure, damaged or diseased heart valves, or heart disease present at birth or related to myocardial infarction (heart attack). The current standard of treatment is based on medicines and cardiac devices. However, DCMP is still one of the leading causes of heart transplantation in adults.	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○Trivial ● Small ○Moderate ○Large ○Varies ○Don't know	1. **All-cause mortality:** Seven RCTs with a total of 382 participants (207 received stem cells and 175 were in the control group) reported all-cause mortality at one year. The pooled analysis yielded a risk ratio of 0.692 (95% CI: 0.32 to 1.48), which was statistically non-significant. 2. **LVEF:** Seven RCTs with a total of 394 participants (218 received stem cells and 176 were in the control group) reported change in ejection fraction from baseline in non-ischemic DCM. The mean difference was found to be 3.827 (95% CI: 1.042 to 6.612) between the stem cell arm and the usual; care arm. The difference was statistically significant but clinically unimportant (less than the MCID of 5%). 3. **6-MWT:** Four studies with a total of 294 participants (157 received stem cells and 137 were in the	MCID considered: 1. 6-minute walk test: 150 meters 2. LVEF: 5%[10]

	control group) reported a change in 6 MWT at the end of 12 months. The mean difference was found to be 46.69m (95% CI: -28.589 to 121.985; I^2 = 30%) between the stem cell arm and the usual care arm. The pooled estimate was statistically non-significant.	
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
● Trivial ○Small ○Moderate ○Large ○Varies ○Don't know	Three studies with a total of 83 participants (50 received stem cells and 33 were in the control group) reported MACE at the end of 12 months. The risk ratio of MACE between the stem cell arm and the usual care arm was 0.879 (95% CI: 0.433, 1.782) at 12 months. The ratio was statistically not significant.	
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
● Very low ○Low ○Moderate ○High ○No included studies	The certainty of evidence is very low due to high risk of bias, inconsistency and imprecision in the effect shown by stem cell therapy.	
Values		

Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○Important uncertainty or variability ○Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○No important uncertainty or variability	Most of HF patients attach more weight to quality of life over longevity.[12,13]	
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○Favors the comparison ○ Probably favors the comparison • Does not favor either the	It is less clear if benefits of stem cell intervention outweigh the harms, based on limited evidence.	

intervention or the comparison ○Probably favors the intervention ○Favors the intervention ○Varies ○Don't know		

Resources required How large are the resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Large costs ○Moderate costs ○Negligible costs and savings ○Moderate savings ○Large savings ○Varies ○Don't know	The reported price to patients ranged from $6000 to $20,700 for 7 clinics willing to provide these data. The mean price for therapy utilizing adipose tissue-derived cells was $7742 (6 clinics) while the price for umbilical cord tissue-derived products was $12,162 (4 clinics). The mean price across 7 clinics was $9593, while the median price was $6500.[14]	

Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○Very low ○Low ● Moderate ○High ○No included studies	No research evidence was identified.	The GDG members were fairly certain that stem cell therapy requires large resources.
Cost Effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○Favors the comparison ● Probably favors the comparison ○Does not favor either the intervention or the comparison ○Probably favors the intervention ○Favors the intervention ○Varies ○No included studies	No direct research evidence was identified	The intervention was not found to be effective and hence the committee deferred to comment on cost effectiveness.
Equity		

What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○Reduced ● Probably reduced ○Probably no impact ○Probably increased ○Increased ○Varies ○Don't know	No research evidence was identified.	As stem cell therapy is an expensive treatment offered only at tertiary centers, it is likely to reduce equity.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○No ○Probably no ● Probably yes ○Yes ○Varies ○Don't know	Despite uncertainty regarding the medical risks and benefits associated with stem cell injections, stroke survivors may still consider undergoing treatment in private, unregulated clinics.	
Feasibility Is the intervention feasible to implement?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○No ○Probably no ● Probably yes ○Yes ○Varies ○Don't know	No research evidence was identified.	Feasible to implement in tertiary care centers.

SUMMARY OF JUDGEMENTS (ISCHEMIC & NON ISCHEMIC DILATED CARDIOMYOPATHY):

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies

	JUDGEMENT						
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	**Large costs**	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	**Moderate**	High			No included studies
COST EFFECTIVENESS	Favors the comparison	**Probably favors the comparison**	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	**Probably reduced**	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the Intervention ○	Conditional recommendation against the Intervention ○	**Use only in the context of rigorously conducted RCTs** ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○

CONCLUSIONS

Recommendation

Stem Cell Therapy is **not recommended** in routine practice for the treatment of ischemic & non-ischemic dilated cardiomyopathy. It is recommended only in the context of rigorously conducted randomized controlled trials.

Justification

This recommendation has been made as there is very low certainty limited evidence of a trivial to small improvement in function and mortality. There is little or no difference in undesirable effects between stem cell therapy and usual care. Additionally, the follow up period is too small to comment on the side effect profile and long-term safety is also not known. Results should be interpreted with caution in view of few studies with low sample size and/or events.

vi. Data Extraction:

The data extraction process was conducted by two reviewers. Utilizing the tagging tool in the Nested Knowledge software, they systematically extracted relevant data, which was then exported to Microsoft Excel for further analysis. The extracted data included the first author's name, the country where the study was conducted, the year of publication, and the study design. Detailed information was also gathered about the number of participants in both the treatment and control groups, the type of intervention administered, and the specific outcomes assessed. The means and standard deviations (SD) in each group were recorded for continuous outcome variables. Additionally, the number of AEs reported in both control and experimental groups was carefully documented.

Data Extraction Sheet:

Study	**Frljak et al. 2018[1]**
Study type	Randomized controlled trial
Number of participants	60
Countries, setting and Funding	Slovenia: no funding details provided
Duration of study Follow up (post intervention)	3 months
Subgroup analysis within study	NA
Inclusion criteria	• Patients with non-ischemic DCMP, LVEF <40%, NYHA class III
Exclusion criteria	• Acute multiorgan failure, hematologic neoplasms, diminished capacity due to non-cardiac comorbidities, pregnancy.
Recruitment/selection of patients	Patients aged 18-70 years with non-ischemic DCMP, LVEF <40%, and NYHA functional class III, on optimal medical management for ≥3 months.
Intervention: Source and Type of stem cells	$CD34^+$ SCT (Stem Cell Transplantation)
Intervention: Method of their characterization	$CD341^+$ cells were characterized using immunomagnetic positive selection.
Intervention: Route of administration	Trans endocardial injection
Intervention: Dose	80 million $CD341^+$ cells injected.
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Not applicable
Efficacy Outcomes reported with time points	Improvement in right ventricular function measured by TAPSE, St, FAC at 6 months.
Safety Outcomes reported with time points- Serious AEs	One sudden cardiac death at 14 weeks, one urgent heart transplantation at 20 weeks, hospitalizations for heart failure (three in Control, one in SC Group).
Safety Outcomes reported with time points- Other Adverse Events	No acute adverse events reported post-infusion.

Study	**Hamshere et al. 2015[2]**
Study type	Randomized, single center, placebo-controlled Phase II trial
Number of participants	29
Countries, setting and Funding	UK; supported by unrestricted grants from the Heart Cells Foundation and Barts and the London Charity. Chugai Pharmaceutical donated supplies of G-CSF and pharmaceutical costs. Funding to pay the Open Access publication charges for the article provided by the Barts Cardiovascular Biomedical Research Unit
Duration of study Follow up (post intervention)	12 months
Subgroup analysis within study	NA
Inclusion criteria	• Diagnosis of NIDCM with no secondary cause found, LVEF < 45% (assessed by echocardiography at referral), symptoms classed as NYHA ≥ 2 and on optimal medical treatment (established for ≥ 6 months).
Exclusion criteria	• NYHA class <2, LVEF <10% or >45%, secondary causes of DCMP (like metabolic or infiltrative disorders), atrial fibrillation without permanent pacing, severe renal dysfunction (creatinine >200 mmol/L), and morbid obesity (weight >140 kg).
Recruitment/selection of patients	Patients with non-ischemic DCMP, LVEF ≤45%, NYHA class ≥2, and on stable optimal medical treatment for at least 6 months.
Intervention: Source and Type of stem cells	BMC (Bone Marrow Cells)
Intervention: Method of their characterization	Autologous bone marrow-derived cells (BMCs) characterized by $CD34^+$ cell count and granulocyte-macrophage colony-forming unit capacity.
Intervention: Route of administration	Intracoronary infusion of BMCs or serum, post G-CSF-induced mobilization.
Intervention: Dose	NA
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	NA
Efficacy Outcomes reported with time points	Improvement in LVEF, exercise capacity, and quality of life measured at 3 months and 1 year; changes in NYHA class and NT-proBNP levels

Safety Outcomes reported with time points- SAEs	Monitored through creatine kinase and Troponin T levels post-infusion; incidence of MACE reported at 1-year, All-cause mortality
Safety Outcomes reported with time points- Other Adverse Events	Common side effects included bone pain from G-CSF; procedural complications were minimal, with one instance of coronary dissection treated with stenting.

Study	**Henry et al. 2014[3]**
Study type	Prospective, randomized, open-label, multicenter, phase 2A trial
Number of participants	29
Countries, setting and Funding	USA; Aastrom Biosciences, Inc, Ann Arbor, MI, USA
Duration of study Follow up (post intervention)	12 months
Subgroup analysis within study	Patients stratified by ischemic and nonischemic dilated cardiomyopathy.
Inclusion criteria	• Symptomatic heart failure, NYHA class III or IV, LVEF ≤30%, ineligibility for revascularization, stable medical therapy for heart failure.
Exclusion criteria	• Severe valvular disease, severe chronic obstructive pulmonary disease, body mass index ≥40 kg/m^2, acute coronary syndrome, end-stage renal disease requiring dialysis, severe aortic disease, LV thrombus, uncontrolled atrial fibrillation.
Recruitment/selection of patients	High-risk population with ischaemic or NIDCM based on the following criteria: WHO definitions and classifications, symptomatic HF, NYHA class III or IV, LVEF ≤ 30% by echocardiogram, and ineligibility for percutaneous or surgical revascularization
Intervention: Source and Type of stem cells	BM-MNCs (Bone Marrow Mononuclear Cells) and Ixmyelocel-T, an expanded multicellular therapy cultured from autologous BMMCs that comprised myeloid cells and lymphoid cell types
Intervention: Method of their characterization	Ixmyelocel-T characterized by the presence of mesenchymal stromal cells ($CD90^+$) and macrophages ($CD14^+$Auto+).
Intervention: Route of administration	Intramyocardial via minithoracotomy (IMPACT-DCM) or intramyocardial catheter injections (Catheter-DCM)
Intervention: Dose	Mean volume/number administered: 35–295×10^6 cells
Intervention: Dose - If the trial has taken	Not applicable

multiple doses, then which dose values has been used for MA	
Efficacy Outcomes reported with time points	LVEF %, LVESV (ml), 6 MWT,Changes in NYHA class, 6-minute walk distance, and MLHFQ scores
Safety Outcomes reported with time points- SAEs	SAEs reported during the 6-month or 1-year follow-up, including heart failure exacerbation and ventricular arrhythmias during the surgical procedure.
Safety Outcomes reported with time points- Other Adverse Events	All-cause mortality, Common adverse events included hypotension, nausea, constipation, hyperglycemia, and hypertension during the initial 5 days post-procedure.

Study	**Martino et al. 2015[4]**
Study type	Randomized, double-blind, and placebo-controlled
Number of participants	160
Countries, setting and Funding	Brazil; Brazilian Ministry of Health, through the Brazilian Agency for Innovation (FINEP)
Duration of study Follow up (post intervention)	6 months (endpoint) and 12 months
Subgroup analysis within study	NA
Inclusion criteria	• Patients with HF according to Framingham criteria; heart failure symptoms for at least 1 year, with aetiological diagnosis of NIDCM according to WHO criteria; aged 18–75 years; NYHA functional class III or IV; appropriate drug therapy following the 4-week optimization period and an echocardiogram showing EF < 35%.
Exclusion criteria	• Valvular heart disease (other than functional mitral or tricuspid regurgitation), coronary artery disease with >50% lumen obstruction, systemic hypertension, Chagas disease, ventricular arrhythmias, substance abuse, pregnancy, cardiotoxic drug use, renal failure requiring dialysis, presence of pacemaker or defibrillator, co-morbidities affecting 2-year survival.
Recruitment/selection of patients	Patients recruited from heart failure clinics at specialized hospitals across Brazil, January 2006 to December 2012
Intervention: Source and Type of stem cells	Autologous bone marrow mononuclear cells (BMNCs).

Intervention: Method of their characterization	Cells characterized using flow cytometry with markers CD34, CD45, CD105, and CD133.
Intervention: Route of administration	Intracoronary (IC) using an angioplasty catheter without balloon inflation
Intervention: Dose	≥ 10^8 cells diluted in 20 mL of saline
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Not applicable
Efficacy Outcomes reported with time points	LVEF %, 6-MWT, Difference in change of LVEF between BMNC and placebo groups at 6 and 12 months. Secondary outcomes included changes in NYHA functional class, functional capacity (6-minute walk test and maximum oxygen consumption by ergospirometry), and quality of life (MLHFQ scores).
Safety Outcomes reported with time points- SAEs	Mortality rate was 20.37% in placebo and 21.31% in BMNC groups. No serious adverse events directly related to cell injection noted.
Safety Outcomes reported with time points- Other Adverse Events	All-cause mortality, CK-MB and troponin I levels measured post-procedure showed no significant increase suggesting no myocardial damage from the procedure. No increase in life-threatening arrhythmias detected by continuous ECG monitoring.

Study	**Sant' et al. 2014[5]**
Study type	Open, parallel-group, explanatory randomized trial
Number of participants	24
Countries, setting and Funding	Brazil; financial support from Brazilian government agencies National Council for Scientific and Technological Development, Committee for Postgraduate Courses in Higher Education, Ministry of Health, and FAPERGS
Duration of study Follow up (post intervention)	12 months
Subgroup analysis within study	NA
Inclusion criteria	• Patients with HF; LVEF < 35% by echocardiogram; NYHA functional class III or IV, despite full medical treatment; aged 20–65 years; diagnosis of NIDCM for ≥ 12 months before enrolment.

Exclusion criteria	• Episodes of ventricular tachycardia, moderate to severe mitral regurgitation, history of myocardial infarction, previous cardiac surgery, or other significant systemic diseases.
Recruitment/selection of patients	Recruitment started in 2005
Intervention: Source and Type of stem cells	Autologous; BMNC (Bone Marrow Nucleated Cells)
Intervention: Method of their characterization	Flow cytometry and immunohistochemistry were used to characterize the bone marrow cells.
Intervention: Route of administration	Intramyocardial (through a left mini thoracotomy)
Intervention: Dose	1.06×10^8 mononuclear cells per participant
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Not applicable
Efficacy Outcomes reported with time points	Change in LVEF %, NYHA classification, echocardiography
Safety Outcomes reported with time points- SAEs	Detailed adverse events and mortality rates
Safety Outcomes reported with time points- Other Adverse Events	Non-significant adverse effects such as transient procedural complications; no long-term detrimental effects directly attributed to the treatment were documented.

Study	**Seth et al. 2010[6]**
Study type	Open-label, randomized trial
Number of participants	81
Countries, setting and Funding	India; research funds from the All-India Institute of Medical Sciences (AIIMS) under the Stem Cell Research Program
Duration of study Follow up (post intervention)	36 months
Subgroup analysis within study	NA

Inclusion criteria	• Patients aged 15 to 70 years with idiopathic DCMP and normal coronary arteries, ejection fraction <40%.
Exclusion criteria	• Patients with severe comorbid conditions were excluded, though specific exclusions are not detailed beyond chronic renal failure.
Recruitment/selection of patients	Not reported
Intervention: Source and Type of stem cells	Autologous peripheral blood $CD34^+$ cells.
Intervention: Method of their characterization	Stem cells were characterized by their viability (92%) and proportion of $CD34^+$ cells after separation using the Ficoll density separation method.
Intervention: Route of administration	Intracoronary using a Swan-Ganz catheter to inject cells into both the left and right coronary arteries after slowing blood flow from the coronary sinus.
Intervention: Dose	28 (SD 16) × 10^6 cells/mL
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Not applicable
Efficacy Outcomes reported with time points	Change in LVEF %, NYHA classification, Quality of life as measured by KCCQ over a mean follow-up of 28 ± 9 months.
Safety Outcomes reported with time points- Serious AEs	Mortality rates and changes in NYHA functional class were monitored
Safety Outcomes reported with time points- Other Adverse Events	All-cause mortality

Study	**Vrtovec et al. 2011**[7]
Study type	Open-label, randomized trial
Number of participants	56
Countries, setting and Funding	Slovenia: No funding details provided
Duration of study Follow up (post intervention)	12 months

Subgroup analysis within study	NA
Inclusion criteria	• Patients aged ≥ 18 years, diagnosis of DCMP, optimal medical management for ≥ 6 months, marked ventricular systolic dysfunction (LVEF < 30%), and NYHA functional class III or IV for ≥ 3 months before referral. DCMP defined based on the absence of any stenotic lesions on coronary angiography, no congenital heart disease, no primary valve disease on echocardiography, and no history of hypertension or alcohol abuse.
Exclusion criteria	• Acute multiorgan failure and a history of hematologic neoplasms.
Recruitment/selection of patients	From advanced Heart Failure and Transplantation Center at University Medical Center Ljubljana and randomly allocated into the study from January 2008 to September 2008
Intervention: Source and Type of stem cells	Autologous peripheral blood $CD34^+$ cells
Intervention: Method of their characterization	Cells were characterized through viability assessments and quantified for the percentage of $CD34^+$ cells.
Intervention: Route of administration	Cells were injected intracoronarily into coronary arteries supplying the most perfused segments identified by myocardial scintigraphy.
Intervention: Dose	$123 \pm 23 \times 10^6$ cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Not applicable
Efficacy Outcomes reported with time points	Change in LVEF %, LVEDD (cm), 6-MWT
Safety Outcomes reported with time points- Serious AEs	Reported outcomes included total mortality, pump failure, and sudden cardiac death rates, with significant reductions in mortality and pump failure in the treatment group compared to controls.
Safety Outcomes reported with time points- Other Adverse Events	All-cause mortality, no significant adverse events like distal coronary artery occlusion or acute cardiac dysfunction were reported; transient increases in neutrophil counts.

Study	**Vrtovec et al. 2013[8]**

Study type	Open-label, randomized trial
Number of participants	110
Countries, setting and Funding	Slovenia: Ministry of Health, Republic of Slovenia, Tertiary Care Scientific grants (20110130 and 20100368), Slovenian Research Agency, Slovenian-US Collaborative Research grant (430-11/2009), and Stanford Cardiovascular Institute Seed grants (JCW, FH).
Duration of study Follow up (post intervention)	60 months
Subgroup analysis within study	NA
Inclusion criteria	• Patients aged 18-65 years, diagnosis of NIDCM according to European Society of Cardiology position statement, optimal medical management for ≥ 6 months, marked ventricular systolic dysfunction (LVEF < 30%), and NYHA functional class III for ≥ 3 months before referral
Exclusion criteria	• Secondary causes of cardiomyopathy based on certain diagnostic criteria (no significant coronary artery disease, no valvular heart disease, etc.).
Recruitment/selection of patients	January 2005 to May 2006
Intervention: Source and Type of stem cells	G-CSF stimulated autologous $CD34^+$ PBMC
Intervention: Method of their characterization	$CD34^+$ cells were characterized and quantified in the peripheral blood using flow cytometry before collection.
Intervention: Route of administration	Intracoronary delivery using a standard femoral approach with a microcatheter system
Intervention: Dose	$113 \pm 26 \times 10^6$ cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	Not applicable
Efficacy Outcomes reported with time points	LVEF, Increase in 6-minute walk test distance, NT-proBNP Levels
Safety Outcomes reported with time points- SAEs	Cardiac mortality/heart transplantation rate:

Safety Outcomes reported with time points- Other Adverse Events	All-cause mortality, Troponin I levels

Study	**Xiao et al. 2017[9]**
Study type	Randomized controlled trial
Number of participants	33
Countries, setting and Funding	China: no funding details provided
Duration of study Follow up (post intervention)	12 months
Method of assessment of disease condition	Echocardiography: Used for estimating left ventricular ejection fraction (LVEF) and measuring left ventricular end-diastolic diameter (LVEDd). NYHA classification: Used for assessing heart failure severity. Single-photon emission computed tomography (SPECT):
Subgroup analysis within study	NA
Inclusion criteria	• Patients aged 18–75 with LVEF < 40%, NYHA functional class II–IV, proportion of fixed defects < 40%, normal coronary arteries, and signed informed consent
Exclusion criteria	• Coronary artery disease based on coronary angiography prior to cell delivery, ventricular arrhythmias, and any comorbidities with an impact on survival
Recruitment/selection of patients	March 2010 through June 2011
Intervention: Source and Type of stem cells	BMMC (Bone Marrow Mononuclear Cells) (arm 1), BMSC (Bone Marrow Stem Cells) (arm 2)
Intervention: Method of their characterization	Cells were characterized by immunophenotyping using a panel of membrane markers (CD29, CD34, CD44, CD45, and CD166) and viability was determined by trypan blue exclusion test.
Intervention: Route of administration	Intracoronary (IC)
Intervention: Dose	BMMCs: 5.1 (SD 2.0) × 10^8 cells, BMSC: 4.9 (SD 1.7) × 10^8 cells
Intervention: Dose- If the trial has taken multiple doses, then which dose values has been used for MA	Not applicable

Efficacy Outcomes reported with time points	Change in LVEF %, LVEDD (cm), NYHA classification
Safety Outcomes reported with time points- Serious AEs	Procedural complications (defined as any new-onset ventricular arrhythmia, conduction disturbance, distal embolization, thrombus formation, and injury of the coronary artery related to the cell injection procedure)
Safety Outcomes reported with time points- Other Adverse Events	All-cause mortality

vii. List of excluded studies:

Study Title	Exclusion reason
Triple repeated fetal congenital heart disease linked to PLD1 mutation: a case report	Case reports
Bilateral central retinal vein occlusion as an initial presentation of Waldenström macroglobulinemia: a case report	Case reports
Hemangioma of the umbilical cord: A case report on a rare entity	Case reports
Case report: Cytokine therapy and an intracoronary autologous bone marrow-derived cell infusion with Impella support in a patient with dilated cardiomyopathy and a severely reduced ejection fraction	Case reports
Burkitt Lymphoma of the Appendix Presenting with Acute Appendicitis and Acute Kidney Injury: A Case Report and Review of Literature	Case reports
Berardinelli Seip Syndrome: A rare case report	Case reports
Disseminated histoplasmosis in a heart transplant recipient from Saudi Arabia: A case report	Case reports
Camptocormia and Other Orthopedic Compromise Dominating Mitochondrial Disorder: A Case Report	Case reports
Optical coherence tomography angiography characteristics in Waldenström macroglobulinemia retinopathy: A case report	Case reports
Severe fetal anemia as a consequence of extra-abdominal umbilical vein varix: A case report and review of the literature	Case reports
[Cell therapy in the multimodality treatment of a patient with dilated cardiomyopathy. A case report]	Case reports
Successful extraction of sperm cells after autologous bone marrow transplant: a case report	Case reports
A young female presenting with heart failure secondary to eosinophilic myocarditis: a case report and review of the literature	Case reports
A myeloid sarcoma involving the small intestine, kidneys, mesentery, and mesenteric lymph nodes: A case report and literature review	Case reports
Extensive Bone Marrow Necrosis: Initial Presentation in Sickle Cell Anemia-A Case Report and Review of the Literature	Case reports
Cytological features of atypical polypoid adenomyoma of the endometrium: A case report with literature review	Case reports
Concise Review: Stem Cell Trials Using Companion Animal Disease Models	Case reports

Severe fever with thrombocytopenia syndrome with myocardial dysfunction and encephalopathy: A case report	Case reports
Case Report: Congenital Erythroleukemia in a Premature Infant with Dysmorphic Features	Case reports
Anemia in a middle-aged female with aortitis: a case report	Case reports
Massive ovarian edema associated with a broad ligament leiomyoma: a case report and review	Case reports
Precursor T-cell acute lymphoblastic leukemia presenting with bone marrow necrosis: a case report	Case reports
Is a red umbilical cord a sign of umbilical venous congestion?a case report	Case reports
Localized lymphedema (elephantiasis): a case series and review of the literature	Case series
Sarcoidosis and immunoglobulin lambda II light-chain amyloidosis diagnosed after orthotopic heart transplantation: a case report and review of the literature	Case reports
Phyllodes tumor of the seminal vesicle: case report and literature review	Case reports
Peliosis hepatis associated with lymphoplasmacytic lymphoma: an autopsy case report	Case reports
Pulmonary veno-occlusive disease after autologous bone marrow transplant in a child with stage IV neuroblastoma: case report and literature review	Case reports
Dysregulated Cell Homeostasis and miRNAs in Human iPSC-Derived Cardiomyocytes from a Propionic Acidemia Patient with Cardiomyopathy	Duplicates
Esophageal Squamous Cell Carcinoma in Cats	Duplicates
Long-term results of intracoronary transplantation of autologous bone marrow cells in dilated cardiomyopathy	Duplicates
In vitro cardiac modeling of desmin-related myofibrillar myopathy and deep learning-based image analysis to develop a high-content screening assay	Duplicates
Study of peripheral stem cells mobilization as a treatment line of pediatric dilated cardiomyopathy.	Duplicates
A randomized comparative study on the efficacy of intracoronary infusion of autologous bone marrow mononuclear cells and mesenchymal stem cells in patients with dilated cardiomyopathy	Duplicates
Safety and efficacy of direct cardiac shockwave therapy in patients with ischemic cardiomyopathy undergoing coronary artery bypass grafting (the CAST-HF trial): study protocol for a	Protocol

randomized controlled trial-an update	
Safety and efficacy of direct Cardiac Shockwave Therapy in patients with ischemic cardiomyopathy undergoing coronary artery bypass grafting (the CAST-HF trial): study protocol for a randomized controlled trial	Protocol
An Upgrade on the Rabbit Model of Anthracycline-Induced Cardiomyopathy: Shorter Protocol, Reduced Mortality, and Higher Incidence of Overt Dilated Cardiomyopathy	Protocol
Validating intramyocardial bone marrow stem cell therapy in combination with coronary artery bypass grafting, the PERFECT Phase III randomized multicenter trial: study protocol for a randomized controlled trial	Protocol
Protocol for the Stimulating Î² (3)-Adrenergic Receptors for Peripheral Artery Disease (STAR-PAD) trial: a double-blinded, randomised, placebo-controlled study evaluating the effects of mirabegron on functional performance in patients with peripheral arterial disease.	Protocol
INtimalhyPerplasiaevAluated by oCT in de novo COROnary lesions treated by drug-eluting balloon and bare-metal stent (IN-PACT CORO): study protocol for a randomized controlled trial.	Protocol
Clinical protocol for angiogenesis by intramyocardial injection of autologous bone marrow mononuclear cells in patients with severe coronary artery disease - TACT-NAGOYA-HEART	Protocol
VascuFit: vascular effects of non-linear periodized exercise training in sedentary adults with elevated cardiovascular risk - protocol for a randomized controlled trial.	Protocol
Evaluation of a Protocol Postural changes in Women Giving Birth with Epidural Analgesia. Clinical Trial	Protocol
Effect of oral intake of royal jelly on endothelium function in hemodialysis patients: study protocol for multicenter, double-blind, randomized control trial.	Protocol
Study of endothelial function response to exercise training in hypertensive individuals (SEFRET): study protocol for a randomized controlled trial.	Protocol
Randomised, double-blind, placebo-controlled clinical trial for evaluating the efficacy of intracoronary injection of autologous bone marrow mononuclear cells in the improvement of the ventricular function in patients with idiopathic dilated myocardiopathy: a study protocol	Protocol
Myocardial regeneration protocols towards the routine clinical	Protocol

scenario: An unseemly path from bench to bedside	
An upgrade on the rabbit model of anthracycline-induced cardiomyopathy: shorter protocol, reduced mortality, and higher incidence of overt dilated cardiomyopathy	Protocol
Development of a robust induced pluripotent stem cell atrial cardiomyocyte differentiation protocol to model atrial arrhythmia	Protocol
Preventing the adverse cardiovascular consequences of allogeneic stem cell transplantation with a multi-faceted exercise intervention: the ALLO-Active trial protocol	Protocol
Epicardial injection of allogeneic human-induced-pluripotent stem cell-derived cardiomyocytes in patients with advanced heart failure: protocol for a phase I/IIa dose-escalation clinical trial	Protocol
Replating Protocol for Human Induced Pluripotent Stem Cell-Derived Cardiomyocytes	Protocol
Qualitative and Quantitative Analysis of Cardiac Progenitor Cells in Cases of Myocarditis and Cardiomyopathy	Qualitative study
Megaesophagus microbiota: a qualitative and quantitative analysis	Qualitative studies
Acute leukemic cells. Qualitative and quantitative electron microscopy	Qualitative studies
Head-to-head Comparison of Qualitative Radiologist Assessment with Automated Quantitative Computed Tomography Analysis for Bronchiolitis Obliterans Syndrome After Hematopoietic Cell Transplantation	Qualitative studies
Acute leukemic cells. Qualitative and quantitative electron microscopy	Qualitative studies
Prevalence of congenital malformations at the "les Orangers" maternity and reproductive health Hospital of Rabat: Descriptive study of 470 anomalies	Qualitative studies
Primiparas with or without oxytocin augmentation: a prospective descriptive study	Qualitative studies
Delayed Clamping of the Umbilical Cord: A Review with Implications for Practice	Qualitative studies
Social stress up-regulates inflammatory gene expression in the leukocyte transcriptome via Î²-adrenergic induction of myelopoiesis	Qualitative studies
Advances in Hypertrophic Cardiomyopathy Disease Modeling using Human iPSC-derived Cardiomyocytes	Pre-clinical study

Living myocardial slices for the study of nucleic acid-based therapies	Pre-clinical studies
Human engineered cardiac tissue model of hypertrophic cardiomyopathy recapitulates key hallmarks of the disease and the effect of chronic mavacamten treatment	Pre-clinical studies
Enhanced Angiogenesis in HUVECs Preconditioned with Media from Adipocytes Differentiated from Lipedema Adipose Stem Cells In Vitro	Pre-clinical studies
Maturation of iPSC-derived cardiomyocytes in a heart-on-a-chip device enables modeling of dilated cardiomyopathy caused by R222Q-SCN5A mutation	Pre-clinical studies
Paradigm shift in myocarditis treatment	Pre-clinical studies
A spatially resolved timeline of the human maternal-fetal interface	Pre-clinical studies
Advancing Treatments for Feline Hypertrophic Cardiomyopathy: The Role of Animal Models and Targeted Therapeutics	Pre-clinical studies
Molecular and cellular evidence for the impact of a hypertrophic cardiomyopathy-associated RAF1 variant on the structure and function of contractile machinery in bioartificial cardiac tissues	Pre-clinical studies
An Alternative Mechanism of Subcellular Iron Uptake Deficiency in Cardiomyocytes	Pre-clinical studies
Human umbilical cord mesenchymal stem cell exosomes alleviate acute kidney injury by inhibiting pyroptosis in rats and NRK-52E cells	Pre-clinical studies
Modeling Duchenne Muscular Dystrophy Cardiomyopathy with Patients' Induced Pluripotent Stem-Cell-Derived Cardiomyocytes	Pre-clinical studies
TRPA1 deficiency aggravates dilated cardiomyopathy by promoting S100A8 expression to induce M1 macrophage polarization in rats	Pre-clinical studies
1-Deoxynojirimycin promotes cardiac function and rescues mitochondrial cristae in mitochondrial hypertrophic cardiomyopathy	Pre-clinical studies
The SHH-GLI1 pathway is required in skin expansion and angiogenesis	Pre-clinical studies
Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) in cardiovascular disease: A Comprehensive Clinical Review on Dilated Cardiomyopathy	Pre-clinical studies
CRaTER enrichment for on-target gene editing enables generation of variant libraries in hiPSCs	Pre-clinical studies
Impaired Reorganization of Centrosome Structure Underlies	Pre-clinical studies

Human Infantile Dilated Cardiomyopathy	
Cardiomyocyte Apoptosis Is Associated with Contractile Dysfunction in Stem Cell Model of MYH7 E848G Hypertrophic Cardiomyopathy	Pre-clinical studies
Cardiomyocyte apoptosis contributes to contractile dysfunction in stem cell model of MYH7 E848G hypertrophic cardiomyopathy	Pre-clinical studies
Prominin-1 promotes restitution of the murine extrahepatic biliary luminal epithelium following cholestatic liver injury	Pre-clinical studies
Therapeutic Angiogenesis Using Autologous CD34-Positive Cells for Vascular Diseases	Pre-clinical studies
Absence of early platelet increment in healthy mice during decitabine treatment	Pre-clinical studies
Multiple Myeloma with Aberrant CD3 Expression in a Red-Lored Amazon Parrot (Amazona autumnalis)	Pre-clinical studies
NLRP3 Inflammasome Activation Through Heart-Brain Interaction Initiates Cardiac Inflammation and Hypertrophy During Pressure Overload	Pre-clinical studies
Calcium handling maturation and adaptation to increased substrate stiffness in human iPSC-derived cardiomyocytes: The impact of full-length dystrophin deficiency	Pre-clinical studies
Mutant Phosphodiesterase 3A Protects from Hypertension-Induced Cardiac Damage	Pre-clinical studies
Generation of two induced pluripotent stem cell lines from dilated cardiomyopathy patients carrying heterozygous FLNC mutations	Pre-clinical studies
Burkitt Lymphoma of the Appendix Presenting with Acute Appendicitis and Acute Kidney Injury: A Case Report and Review of Literature	Pre-clinical studies
Ventricular arrhythmia and sudden cardiac death in hypertrophic cardiomyopathy: From bench to bedside	Pre-clinical studies
Long-term culture of patient-derived cardiac organoids recapitulated Duchenne muscular dystrophy cardiomyopathy and disease progression	Pre-clinical studies
Infusion of two-dose mesenchymal stem cells is more effective than a single dose in a dilated cardiomyopathy rat model by upregulating indoleamine 2,3-dioxygenase expression	Pre-clinical studies
Transcription Factor GATA4 Regulates Cell Type-Specific Splicing Through Direct Interaction with RNA in Human Induced Pluripotent Stem Cell-Derived Cardiac Progenitors	Pre-clinical studies
Ligamentum arteriosum and its telocytes: An ultrastructure	Pre-clinical studies

description	
Characterization of cardiac metabolism in iPSC-derived cardiomyocytes: lessons from maturation and disease modeling	Pre-clinical studies
Human-Induced Pluripotent Stem Cell-Derived Cardiomyocyte Model for TNNT2 Δ160E-Induced Cardiomyopathy	Pre-clinical studies
Genetic Basis of Dilated Cardiomyopathy in Dogs and Its Potential as a Bidirectional Model	Pre-clinical studies
Myogenic Determination and Differentiation of Chicken Bone Marrow-Derived Mesenchymal Stem Cells under Different Inductive Agents	Pre-clinical studies
Serine biosynthesis as a novel therapeutic target for dilated cardiomyopathy	Pre-clinical studies
Wnt Signaling Interactor WTIP (Wilms Tumor Interacting Protein) Underlies Novel Mechanism for Cardiac Hypertrophy	Pre-clinical studies
Modeling hypertrophic cardiomyopathy with human cardiomyocytes derived from induced pluripotent stem cells	Pre-clinical studies
MED1 Deficiency in Macrophages Aggravates Isoproterenol-Induced Cardiac Fibrosis in Mice	Pre-clinical studies
Generation of two iPSC lines from hypertrophic cardiomyopathy patients carrying MYBPC3 and PRKAG2 variants	Pre-clinical studies
Generation of two human iPSC lines, HMGUi003-A and MRIi028-A, carrying pathogenic biallelic variants in the PPCS gene	Pre-clinical studies
Muscle LIM Protein Force-Sensing Mediates Sarcomeric Biomechanical Signaling in Human Familial Hypertrophic Cardiomyopathy	Pre-clinical studies
Liver progenitor cells may construct cysts having heterogeneous gene expression of liver-enriched transcription factors in mice with conditional knockout of the Hhex gene	Pre-clinical studies
Effects of Sarcomere Activators and Inhibitors Targeting Myosin Cross-Bridges on $Ca^{(2+)}$-Activation of Mature and Immature Mouse Cardiac Myofilaments	Pre-clinical studies
Intracellular virus sensor MDA5 mutation develops autoimmune myocarditis and nephritis	Pre-clinical studies
The effects of extracellular vesicles derived from Krüppel-Like Factor 2 overexpressing endothelial cells on the regulation of cardiac inflammation in the dilated cardiomyopathy	Pre-clinical studies
Biosensor-based profiling to track cellular signalling in patient-derived models of dilated cardiomyopathy	Pre-clinical studies
Cell cycle defects underlie childhood-onset cardiomyopathy associated with Noonan syndrome	Pre-clinical studies

Mechanisms of Arrhythmogenicity of Hypertrophic Cardiomyopathy-Associated Troponin T (TNNT2) Variant I79N	Pre-clinical studies
A homozygous CAP2 pathogenic variant in a neonate presenting with rapidly progressive cardiomyopathy and nemaline rods	Pre-clinical studies
Morphology of the Myocardium after Experimental Bone Tissue Trauma and the Use of Extracellular Vesicles Derived from Mesenchymal Multipotent Stromal Cells	Pre-clinical studies
Transcriptomic Analysis of Cardiomyocyte Extracellular Vesicles in Hypertrophic Cardiomyopathy Reveals Differential snoRNA Cargo	Pre-clinical studies
A transcriptome atlas of the mouse iris at single-cell resolution defines cell types and the genomic response to pupil dilation	Pre-clinical studies
Interplay of Genotype and Substrate Stiffness in Driving the Hypertrophic Cardiomyopathy Phenotype in iPSC-Micro-Heart Muscle Arrays	Pre-clinical studies
Protein tyrosine phosphatase receptor-ζ1 deletion triggers defective heart morphogenesis in mice and zebrafish	Pre-clinical studies
Neuronal and cardiac toxicity of pharmacological compounds identified through transcriptomic analysis of human pluripotent stem cell-derived embryoid bodies	Pre-clinical studies
Clinical features of Danon disease and insights gained from LAMP-2 deficiency models	Pre-clinical studies
Generation and genetic repair of two human induced pluripotent cell lines from patients with Epidermolysis Bullosa simplex and dilated cardiomyopathy associated with a heterozygous mutation in the translation initiation codon of KLHL24	Pre-clinical studies
Ion Channel Impairment and Myofilament $Ca^{(2+)}$ Sensitization: Two Parallel Mechanisms Underlying Arrhythmogenesis in Hypertrophic Cardiomyopathy	Pre-clinical studies
Extracorporeal Shock Wave Enhanced Exogenous Mitochondria into Adipose-Derived Mesenchymal Stem Cells and Further Preserved Heart Function in Rat Dilated Cardiomyopathy	Pre-clinical studies
RBM20-Related Cardiomyopathy: Current Understanding and Future Options	Pre-clinical studies
On computational classification of genetic cardiac diseases applying iPSC cardiomyocytes	Pre-clinical studies
3D models of dilated cardiomyopathy: Shaping the chemical, physical and topographical properties of biomaterials to mimic the cardiac extracellular matrix	Pre-clinical studies
Isolation and morphological characterization of equine	Pre-clinical studies

mesenchymal stem cells from harvested adipose tissue and bone marrow and stably transfected with green fluorescent protein	
What Is the Status of Regenerative Therapy in Heart Failure?	Pre-clinical studies
Actinin BioID reveals sarcomere crosstalk with oxidative metabolism through interactions with IGF2BP2	Pre-clinical studies
Generation of three induced pluripotent stem cell lines from hypertrophic cardiomyopathy patients carrying MYH7 mutations	Pre-clinical studies
Adipose-derived mesenchymal stem cells preserve cardiac function via ANT-1 in dilated cardiomyopathy hamster model	Pre-clinical studies
Toxocaracanis Infection Alters lncRNA and mRNA Expression Profiles of Dog Bone Marrow	Pre-clinical studies
Double overexpression of miR-19a and miR-20a in induced pluripotent stem cell-derived mesenchymal stem cells effectively preserves the left ventricular function in dilated cardiomyopathic rat	Pre-clinical studies
Single-cell transcriptomic analyses of cardiac immune cells reveal that Rel-driven CD72-positive macrophages induce cardiomyocyte injury	Pre-clinical studies
Exosomally derived Y RNA fragment alleviates hypertrophic cardiomyopathy in transgenic mice	Pre-clinical studies
Generation of three human induced pluripotent stem cell lines, LUMCi024-A, LUMCi025-A, and LUMCi026-A, from two patients with combined oxidative phosphorylation deficiency 8 and a related control	Pre-clinical studies
An induced pluripotent stem cell line (EHTJUi003-A) generated from a neonate with c.1377delC mutation in the gene MYBPC3 causing hypertrophic cardiomyopathy	Pre-clinical studies
Dystrophin Deficiency Causes Progressive Depletion of Cardiovascular Progenitor Cells in the Heart	Pre-clinical studies
Translational investigation of electrophysiology in hypertrophic cardiomyopathy	Pre-clinical studies
Unfolded Protein Response as a Compensatory Mechanism and Potential Therapeutic Target in PLN R14del Cardiomyopathy	Pre-clinical studies
Drinking Molecular Hydrogen Water Is Beneficial to Cardiovascular Function in Diet-Induced Obesity Mice	Pre-clinical studies
Role of Cdkn2a in the Emery-Dreifuss Muscular Dystrophy Cardiac Phenotype	Pre-clinical studies
CD24 for Cardiovascular Researchers: A Key Molecule in Cardiac Immunology, Marker of Stem Cells and Target for Drug Development	Pre-clinical studies

Establishment of an iPSC line (JSPHi001-A) from a patient with familial dilated cardiomyopathy and atrial fibrillation caused by LMNA missense mutation (c.1003C>T)	Pre-clinical studies
Genetic Cardiomyopathies: The Lesson Learned from hiPSCs	Pre-clinical studies
Angiotensin II receptor 1 controls profibrotic Wnt/β-catenin signalling in experimental autoimmune myocarditis	Pre-clinical studies
Long-Term Effects of Sulfadiazine-Trimethoprim Medicated Diet on Cardiac Function, Hematology, and Weight Gain in Hsd:ICR (CD1) and Tac:SW Mice	Pre-clinical studies
Cardiomyocytes Derived from Induced Pluripotent Stem Cells as a Disease Model for Propionic Acidemia	Pre-clinical studies
Targeting the histone demethylase LSD1 prevents cardiomyopathy in a mouse model of laminopathy	Pre-clinical studies
Generation of an induced pluripotential stem cell (iPSC) line from a patient with hypertrophic cardiomyopathy carrying myosin binding protein C (MYBPC3) c.3369-3370 insC mutation	Pre-clinical studies
Pathology of macrophage activation syndrome in humanized NSGS mice	Pre-clinical studies
Trophoblast Stem-Cell-Derived Exosomes Improve Doxorubicin-Induced Dilated Cardiomyopathy by Modulating the let-7i/YAP Pathway	Pre-clinical studies
Double overexpression of miR-19a and miR-20a in induced pluripotent stem cell-derived mesenchymal stem cells effectively preserves the left ventricular function in dilated cardiomyopathic rat	Pre-clinical studies
Efficacy and Mode of Action of Mesenchymal Stem Cells in Non-Ischemic Dilated Cardiomyopathy: A Systematic Review	Review
Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) in cardiovascular disease: A Comprehensive Clinical Review on Dilated Cardiomyopathy	Review
Burkitt Lymphoma of the Appendix Presenting with Acute Appendicitis and Acute Kidney Injury: A Case Report and Review of Literature	Reviews
Cell therapy in patients with heart failure: a comprehensive review and emerging concepts	Reviews
Dysostosis in mucopolysaccharidosis type 2: A case of longitudinal follow up and literature review	Reviews
Severe fetal anemia as a consequence of extra-abdominal umbilical vein varix: A case report and review of the literature	Reviews
Umbilical cord-derived mesenchymal stromal cells in	Reviews

cardiovascular disease: review of preclinical and clinical data	
Concise Review: The Current State of Human In Vitro Cardiac Disease Modeling: A Focus on Gene Editing and Tissue Engineering	Reviews
A young female presenting with heart failure secondary to eosinophilic myocarditis: a case report and review of the literature	Reviews
A myeloid sarcoma involving the small intestine, kidneys, mesentery, and mesenteric lymph nodes: A case report and literature review	Reviews
Cytological features of atypical polypoid adenomyoma of the endometrium: A case report with literature review	Reviews
Angiectatic nasal polyps that clinically simulate a malignant process: report of 2 cases and review of the literature	Reviews
Modeling Human Dilated Cardiomyopathy Using Humans	Commentary, editorial
Optimizing Cardiovascular Care in Children with Acute Myeloid Leukemia to Improve Cancer-Related Outcomes	Commentries, editorials
Disease modelling and drug discovery for hypertrophic cardiomyopathy using pluripotent stem cells: how far have we come?	Commentries, editorials
Hematopoietic Id Deletion Triggers Endomyocardial Fibrotic and Vascular Defects in the Adult Heart	Commentries, editorials
Stem cells: Allogenic mesenchymal stem cells for dilated cardiomyopathy	Commentries, editorials
The Cutaneous Telocytes	Commentries, editorials
Mesenchymal Stem Cells Drive Cardiac Stem Cell Chemotaxis, Proliferation, and Phenotype via CXCR4 and cKit Signaling	Commentries, editorials
The esophageal mucosa and submucosa: immunohistology in GERD and Barrett's esophagus	Commentries, editorials
Early cardiac retention of administered stem cells determines clinical efficacy of cell therapy in patients with dilated cardiomyopathy	Commentries, editorials
Granulocyte colony-stimulating factor-induced blood stem cell mobilisation in patients with chronic heart failure--Feasibility, safety and effects on exercise tolerance and cardiac function	Commentries, editorials
A perspective on Notch signalling in progression and arrhythmogenesis in familial hypertrophic and dilated cardiomyopathies	Commentries, editorials
Kulikova O	Commentries, editorials
Cardiovascular Precision Medicine in the Genomics Era	Commentries, editorials

Rare presentation of four primary pediatric cardiac tumors	Commentries, editorials
The hippo pathway in heart development, regeneration, and diseases	Commentries, editorials
Intracoronary autologous myeloid stem cells transplantation in the treatment of dilated cardiomyopathy	Not available in English
Intracoronary transplantation of autologous bone marrow mesenchymal stem cells for ischemic cardiomyopathy due to isolated chronic occluded left anterior descending artery	Not available in engllish
Effects of intracoronary autologous bone marrow mononuclear cells transplantation in patients with dilated cardiomyopathy. Zhonghua Xin Xue Guan Bing Za Zhi. 2008; 36:1087	Not available in engllish
A prospective, randomized, controlled trial of autologous mesenchymal stem cells transplantation for dilated cardiomyopathy. Chung Hua Hsin Hsueh Kuan Ping Tsa Chih 2006;34 (2):107-10	Not available in engllish
Effect and security of intracoronary transplantation of autologous bone marrow stem cells on patients with dilated cardiomyopathy. Chinese J Cardiovasc Rehabil Med. 2008; 17:348-50	Not available in engllish
Autologous bone marrow mesenchymal stem cells transplantation for dilated cardiomyopathy. J Chinese Pract Diagnosis Therapy. 2012; 26:544-46	Not available in engllish
Triple repeated fetal congenital heart disease linked to PLD1 mutation: a case report	Case report
Safety and Efficacy of the Intravenous Infusion of Umbilical Cord Mesenchymal Stem Cells in Patients with Heart Failure A Phase 1/2 Randomized Controlled Trial (RIMECARD Trial [Randomized Clinical Trial of Intravenous Infusion Umbilical Cord Mesenchymal Stem Cells on Cardiopathy])	Not mentioned DCMP
Granulocyte-colony stimulating factor or granulocyte-colony stimulating factor associated to stem cell intracoronary infusion effects in non ischemic refractory heart failure	The results presented in the paper compared SCT vs a non-randomized external control group.
Intravenous Allogeneic Mesenchymal Stem Cells for Non-Ischemic Cardiomyopathy: Safety and Efficacy Results of a Phase II-A Randomized Trial	Not mentioned DCMP
Therapeutic Role of Mobilized Bone Marrow Cells in Children with Nonischemic Dilated Cardiomyopathy	Observational study
Randomized Comparison of Allogeneic Versus Autologous Mesenchymal Stem Cells for Nonischemic Dilated	Comparing autologous vs allogenic, without control group

Cardiomyopathy POSEIDON-DCMP Trial (hare)	
Transendocardial Mesenchymal Stem Cells and MononuclearBone Marrow Cells for Ischemic Cardiomyopathy: The TAC-HFT Randomized Trial	Not mentioned DCM
Isolated Coronary Artery Bypass Graft Combined with Bone Marrow Mononuclear Cells Delivered Through a Graft Vessel for Patients with Previous Myocardial Infarction and Chronic Heart Failure	Not mentioned DCMP
REVIVE Trial: Retrograde Delivery of Autologous Bone Marrow in Patients with Heart Failure	Not mentioned DCMP
A Phase II Dose-Escalation Study of Allogeneic Mesenchymal Precursor Cells in Patients with Ischemic or Nonischemic Heart Failure	Not mentioned DCMP
Improved Exercise Capacity and Ischemia 6 and 12 Months After Transendocardial Injection of Autologous Bone Marrow Mononuclear Cells for Ischemic Cardiomyopathy	Not mentioned DCMP and non-randomized
Comparison of Mesenchymal Stem Cell Efficacy in Ischemic Versus Nonischemic Dilated Cardiomyopathy	Pooled sub-analysis from already included duplicated trials

REFERENCES:

1. Frljak S, Jaklic M, Zemljic G, Cerar A, Poglajen G, Vrtovec B. CD34+ cell transplantation improves right ventricular function in patients with non-ischemic dilated cardiomyopathy. Stem Cells Translational Medicine. 2018; 7(2):168-72.
2. Hamshere S, Arnous S, Choudhury T, Choudry F, Mozid A, Yeo C, et al. Randomized trial of combination cytokine and adult autologous bone marrow progenitor cell administration in patients with non-ischaemic dilated cardiomyopathy: the Regenerate -DCM clinical trial. European Heart Journal. 2015; 36(44):3061-9.
3. Henry TD, Traverse JH, Hammon BL, East CA, Bruckner B, Remmers AE, et al. Safety and efficacy of ixmyelocel-T: an expanded, autologous multi-cellular therapy, in dilated cardiomyopathy. Circulation research. 2014; 115(8):730-7.
4. Martino H, Brofman P, Greco O, Bueno R, Bodanese L, Clausell N, et al. Multicentre, randomized, double-blind trial of intracoronary autologous mononuclear bone marrow cell injection in non-ischaemic dilated cardiomyopathy (the dilated cardiomyopathy arm of the MiHeart study). European Heart Journal. 2015; 36(42):2898-904.
5. Sant'Anna RT, Fracasso J, Valle FH, Castro I, Nardi NB, Sant'Anna JR, et al. Direct intramyocardial transthoracic transplantation of bone marrow mononuclear cells for non-ischemic dilated cardiomyopathy: Intraell, a prospective randomized controlled trial. Rev Bras Cir Cardiovasc. 2014; 29(3):437-47.
6. Seth S, Bhargava B, Narang R, Ray R, Mohanty S, Gulati G, et al. The ABCD (Autologous Bone Marrow Cells in Dilated Cardiomyopathy) trial: a long-term follow-up study. Journal of the American College of Cardiology. 2010; 55(15):1643-4.
7. Vrtovec B, Poglajen G, Sever M, Lezaic L, Domanovic D, Cernelc P, et al. Effects of intracoronary stem cell transplantation in patients with dilated cardiomyopathy. Journal of Cardiac Failure. 2011; 17(4):272-81.
8. Vrtovec B, Poglajen G, Lezaic L, Sever M, Socan A, Domanovic D, et al. Comparison of transendocardial and intracoronary CD34+ cell transplantation in patients with nonischemic dilated cardiomyopathy. Circulation. 2013; 128 (11_suppl_1):S42-S9.
9. Xiao W, Guo S, Gao C, Dai G, Gao Y, Li M, et al. A randomized comparative study on the efficacy of intracoronary infusion of autologous bone marrow mononuclear cells and mesenchymal stem cells in patients with dilated cardiomyopathy. International Heart Journal. 2017; 58(2):238-44.
10. Kramer DG, Trikalinos TA, Kent DM, Antonopoulos GV, Konstam MA, Udelson JE. Quantitative evaluation of drug or device effects on ventricular remodeling as predictors of therapeutic effects on mortality in patients with heart failure and reduced ejection fraction: a meta-analytic approach. J Am Coll Cardiol. 2010 Jul 27; 56(5):392-406.
11. Stanek EJ, Oates MB, McGhan WF, Denofrio D, Loh E. Preferences for treatment outcomes in patients with heart failure: symptoms versus survival. J Card Fail. 2000 Sep; 6(3):225-32.
12. Lindeman, A., Pepine, C.J. & March, K.L. Cardiac stem cell therapy among Clinics of Uncertain Regulatory Status (COURS): under-regulated, under-observed, incompletely understood. J Transl Med. 2020; 18, 285. https://doi.org/10.1186/s12967-020-02425-6 (https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-020-02425-6).

13. DeVore AD, Hellkamp AS, Thomas L, Albert NM, Butler J, Patterson JH, Spertus JA, Williams FB, Duffy CI, Hernandez AF, Fonarow GC. Improvement in Left Ventricular Ejection Fraction in Outpatients with Heart Failure With Reduced Ejection Fraction: Data From CHAMP-HF. Circ Heart Fail. 2020 Jul; 13(7): e006833.
14. Kraai IH, Vermeulen KM, Luttik ML, Hoekstra T, Jaarsma T, Hillege HL. Preferences of heart failure patients in daily clinical practice: quality of life or longevity? Eur J Heart Fail. 2013 Oct; 15(10):1113-21.

2. MYOCARDIAL INFARCTION (MI)

i. **Key question in PICO format**

ii. **Search strategy**

iii. **PRISMA flow diagram**

iv. **Summary of included studies.**

v. **Evidence to decision framework**

vi. **Data extraction**

vii. **Publication bias**

viii. **List of excluded studies**

i. Key Question in PICO format:

In patients with myocardial infarction, what is the efficacy and safety of stem cell therapy as compared to usual care?

Population: All patients with Myocardial infarction (upto 3-Months) Co-morbidities, anterior/inferior MI

Intervention: Any Stem cell and product derived from stem cells

Comparator: Usual Care/ Conventional Care

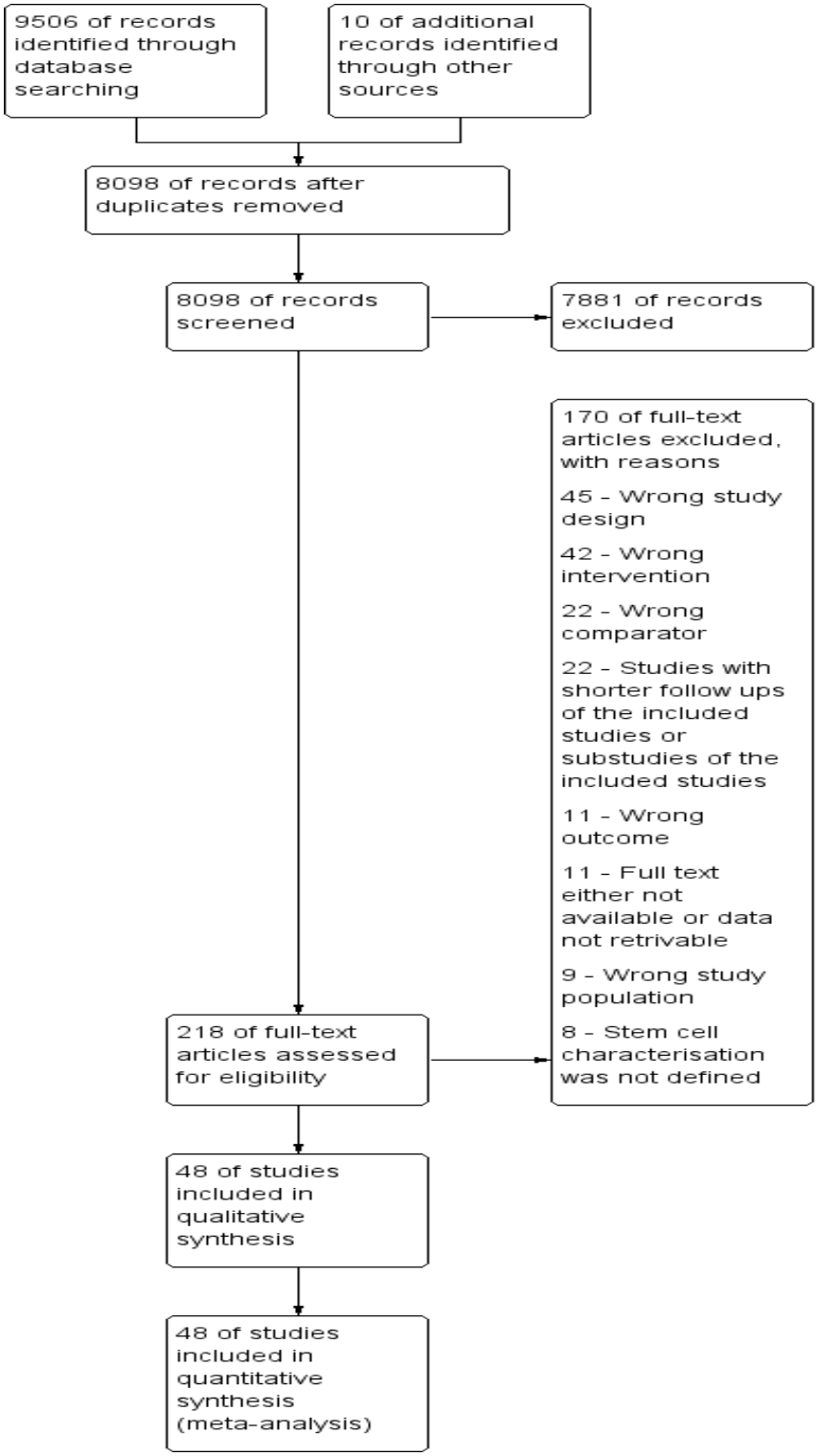
Outcome: Critical: Mortality (6 mo,1Y, 3Y) Serious Adverse Events (e.g. Recurrent MI) (safety), tumor formation; Important outcomes- Re-Myocardial Infarction, incidence of stroke, hospitalization due to heart failure, left ventricular ejection fraction (LVEF)

ii. Search Strategy:

Based on previously published reviews and discussion amongst the investigators, authors have used same search strategy used by Cochrane review entitled "Stem cell treatment for acute myocardial infarction" (Zwetsloot et al. 2024).

Risk of Bias Assessment (RoB-2)**:** Risk of bias assessment was done based on the (RoB-2) tool mentioned in Cochrane Handbook of Systematic Review of Interventions. All the included clinical trials were assessed based on the various questions and algorithm mentioned in the RoB-2 into low, high risk or some concern.

iii. PRISMA Flow Diagram:



iv. Summary of Included Studies:

Study	Patient population	Intervention cell type	Comparator arm (placebo or control)	Outcomes (including SAEs)
Angeli et al. 2012[1]	STEMI, LVEF<45%	BMMNCs	Medium	LVEF (2D ECHO) End of the study, LVEF (SPECT) End of the study, LVEF (%) End of the study echo, LVEF (%) End of the study SPECT
Assmus et al. 2014[2]	Acute STEMI, LVEF<45%	BMMNCs	Patient's own serum	Cancer incidence, Cardiovascular mortality Mortality, Hospitalization due to heart failure, Recurrent MI, SAEs Arrhythmia frequency Revascularization frequency Stroke frequency
Attar et al. 2023[3]	STEMI, LVEF < 40%	HWJMSC allogeneic	Standard treatment	LVEF MRI, LVEF ECHO, LVEF (2D ECHO) End of the study, LVEF (ECHO) difference between groups, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, EDV (ECHO) End of the study, EDV (ECHO) difference between the groups, LVEF (%) End of the study echo, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups Echocardiography,

				LVEF (%) Difference between the groups MRI, EDV (MRI) End of the study, EDV (MRI) difference between the groups, EDV (ml) End of the study Echocardiography, EDV (ml) End of the study MRI, EDV (ml) Difference between the groups Echocardiography, EDV (ml) Difference between the groups MRI, ESV (ml) End of the study Echocardiography, ESV (ml) End of the study MRI, ESV (ECHO) End of the study, ESV (ECHO) difference between groups, ESV (ml) Difference between the groups Echocardiography, ESV (ml) Difference between the groups MRI, ESV (MRI) End of the study, ESV (MRI) difference between the groups, Infarct size (MRI) difference between the groups, LVEDD (Echo) difference between the groups, LVESD (echo) difference between the groups
Cao et al. 2009[4]	STEMI	BMMNCs	Heparinized saline	Mortality, Hospitalization due to heart failure, LVEF ECHO LVEF (2D ECHO) End of the study LVEF (ECHO) difference between groups, EDV (ECHO) End of the study, EDV (ECHO) difference between the groups, LVEF (%) End of the study echo, LVEF (%) Difference between the groups

				Echocardiography, EDV (ml) End of the study Echocardiography, EDV (ml) Difference between the groups Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study, ESV (ECHO) difference between groups, ESV (ml) Difference between the groups Echocardiography, Infarct size (SPECT) End of the study, WMSI (ECHO) End of the study, WMSI (ECHO) Difference between the group Restenosis
Chen et al. 2004[5]	Acute MI	BMMSCs	Heparinized saline	LVEF (Angiography) End of the study, EDV (ECHO) End of the study, LVEF (%) End of the study Angiography, EDV (ml) End of the study Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study, Perfusion defect end of the study (cm2))
Choudry et al. 2016[6]	Acute AMI	BMMNCs	10 ml sterile NaCl 0.9% with 33 ml autologous whole BM	Mortality, SAEs, Recurrent MI, LVEF MRI Difference, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV (MRI) End of the study,

				EDV (MRI) difference between the groups, EDV (ml) End of the study MRI, EDV (ml) Difference between the groups MRI, ESV (ml) End of the study MRI, ESV (ml) Difference between the groups MRI, ESV (MRI) End of the study, ESV (MRI) difference between the groups, ESV (MRI) difference between the groups, Infarct size (MRI) end of the study, Infarct size (MRI) difference between the groups, Quality of life (VAS) difference between the groups, Quality of life (VAS) End of the study, Quality of life (EQ5D) difference between the groups, Quality of life (European quality of life dimension) End of study, Revascularization frequency
Chullikana et al. 2015[7]	STEMI, LVEF 30-50%	BM-MSC allogeneic	Multiple electrolytes injection (PLASMA-LYTE A)	Mortality, SAE, LVEF (2D ECHO) End of the study, LVEF (2D ECHO) Difference of Difference from baseline, LVEF (SPECT) End of the study, LVEF (%) End of the study echo, LVEF (%) End of the study SPECT, Volume of infarct (MRI) mm end of study
Colombo et al. 2011[8]	STEMI, LVEF < 45	CD133+ cells	Standard treatment	Hospitalization due to heart failure, LVEF (2D ECHO) End of the study, EDV (ECHO) End of the study, LVEF (%) End of the study echo, EDV (ml) End of the study Echocardiography,

				Infarct size (SPECT) End of the study, WMSI (ECHO) End of the study Arrhythmia frequency
Delewi et al. 2015[9]	STEMI	BMMNC	Standard treatment	Mortality, Hospitalization due to heart failure, Recurrent MI, LVEF MRI Difference, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups, Arrhythmia frequency, Revascularization frequency Stroke frequency
Dill et al. 2009[10]		BMMNC	Standard treatment	LVEF MRI Difference, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV (MRI) End of the study, EDV (MRI) difference between the groups, EDV (ml) End of the study MRI, EDV (ml) Difference between the groups MRI, ESV (ml) End of the study MRI, ESV (ml) Difference between the groups MRI, ESV (MRI) End of the study,

				ESV (MRI) difference between the groups, ESV (MRI) difference between the groups, WMSI (MRI) end of the study, WMSI (MRI) difference between groups
Fernandez-Aviles et al. 2018[11]	STEMI, LVEF ≤45%	Cardiac stem cells- Allogenic	Standard treatment	Cancer incidence, LVEF MRI Difference, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups, Infarct size (MRI) end of the study, Infarct size (MRI) difference between the groups, WMSI (MRI) end of the study, WMSI (MRI) difference between groups
Gao et al. 2013[12]	STEMI	BM-MSC	Standard treatment	Mortality, Hospitalization due to heart failure, Recurrent MI, LVEF ECHO, LVEF (2D ECHO) End of the study, LVEF (2D ECHO) Difference of Difference from baseline, LVEF (ECHO) difference between groups, EDV (ECHO) End of the study, EDV (ECHO) difference between the groups, LVEF (%) End of the study echo, LVEF (%) Difference between the groups

				Echocardiography, EDV (ml) End of the study Echocardiography, EDV (ml) Difference between the groups Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study, ESV (ECHO) difference between groups, ESV (ml) Difference between the groups Echocardiography, WMSI (ECHO) End of the study, WMSI (ECHO) Difference between the group
Gao et al. 2015[13]	Acute STEMI	WJ-MSCS	Placebo	Cancer incidence, Mortality, Hospitalization due to heart failure, LVEF ECHO LVEF (2D ECHO) End of the study LVEF (2D ECHO) Difference of Difference from baseline LVEF (ECHO) difference between groups, EDV (ECHO) End of the study, EDV (ECHO) difference between the groups, LVEF (%) End of the study echo, LVEF (%) Difference between the groups Echocardiography, EDV (ml) End of the study Echocardiography, EDV (ml) Difference between the groups Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study, ESV (ECHO) difference between groups,

				ESV (ml) Difference between the groups Echocardiography, WMSI (ECHO) End of the study, WMSI (ECHO) Difference between the group Revascularisation
Ge et al. 2006[14]	STEMI	BMMNC	Placebo, BM supernatant mixed with heparinized saline	LVEF (2D ECHO) End of the study, LVEF (%) End of the study echo, Perfusion defect score, LVEDD (ECHO) End of the study
Grajek et al. 2010[15]	Anterior AMI	BMMNC	Standard treatment	Mortality, Recurrent MI, SAEs LVEF (2D ECHO) End of the study, LVEF (Radionucleotide ventriculography) end of the study, EDV (ECHO) End of the study, LVEF (%) End of the study echo, LVEF (%) End of the study Radionucleotide Angiography, EDV (ml) End of the study Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study, WMSI (ECHO) End of the study Restenosis
Haddad et al. 2020[16]	Acute STEMI, LVEF 25% - 50%	CD133+	Placebo	Cancer incidence, Mortality, Hospitalization due to heart failure Recurrent MI, LVEF MRI Difference,

				LVEF (MRI) difference between the groups, LVEF (%) Difference between the groups MRI, Arrhythmia frequency, Revascularization frequency, Stroke frequency
Hare et al. 2009[17]	MI; LVEF 30-60%	Hmsc- allogenic	Solution of 1.9% human serum albumin with 3.8% dimethyl sulfoxide in plasmalyte A.	SAE, LVEF MRI Difference, LVEF (2D ECHO) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study echo, LVEF (%) Difference between the groups MRI, EDV (MRI) difference between the groups, EDV (ml) Difference between the groups MRI, ESV (ml) Difference between the groups MRI, ESV (MRI) difference between the groups, ESV (MRI) difference between the groups, Arrhythmia frequency
Huikuri et al. 2008[18]	STEMI	BMMNCs	Placebo (heparinised saline and 50% autologous serum)	Mortality, Recurrent MI, SAE, LVEF ECHO, LVEF (2D ECHO) End of the study, LVEF (2D ECHO) Difference of Difference from baseline, LVEF (ECHO) difference between groups, LVEF (Angiography) difference between groups, EDV (ECHO) End of the study, EDV (ECHO) difference between the groups, LVEF (%) End of the study echo, LVEF (%) Difference between the groups

				Echocardiography, LVEF (%) Difference between the groups Angiography, EDV (ml) End of the study Echocardiography, EDV (ml) End of the study Angiography, EDV (Angiography) end of the study, EDV (Angiography) difference between the groups, EDV (ml) Difference between the groups Echocardiography, EDV (ml) Difference between the groups Angiography, ESV (ml) End of the study Echocardiography, ESV (ml) End of the study Angiography, ESV (ECHO) End of the study, ESV (ECHO) difference between groups, ESV (ml) Difference between the groups Echocardiography, ESV (ml) Difference between the groups Angiography, ESV (Angiography) end of the study, ESV (Angiography) difference between group
Janssens et al. 2006[19]	STEMI	BMMNC	Placebo heparinised saline and 50% autologous serum	Mortality, SAE, LVEF MRI Difference, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups,

				Arrhythmia frequency Restenosis
Kaminek et al. 2008[20]	Acute STEMI	BMMNC	Control	LVEF (2D ECHO) End of the study, EDV (ECHO) End of the study, LVEF (%) End of the study echo, EDV (ml) End of the study Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study
Kim et al. 2018[21]	Anterior MI, LVEF ≤ 40%	BM-MSC	Standard treatment	LVEF ECHO LVEF (2D ECHO) End of the study, LVEF (ECHO) difference between groups, LVEF (SPECT) End of the study, LVEF (SPECT) difference between the groups, EDV (ECHO) End of the study, EDV (ECHO) difference between the groups, LVEF (%) End of the study echo, LVEF (%) End of the study SPECT, LVEF (%) Difference between the groups Echocardiography, LVEF (%) Difference between the groups SPECT, EDV (SPECT) End of the study, EDV (SPECT) difference between the groups, EDV (ml) End of the study Echocardiography, EDV (ml) End of the study SPECT, EDV (ml) Difference between the groups Echocardiography, EDV (ml) Difference between the groups SPECT, ESV (ml) End of the study Echocardiography, ESV (ml) End of the study SPECT,

				ESV (ECHO) End of the study, ESV (ECHO) difference between groups, ESV (ml) Difference between the groups Echocardiography, ESV (ml) Difference between the groups SPECT, ESV (SPECT) End of the study, ESV (SPECT) difference between the groups Arrhythmia frequency
Laguna et al. 2018[22]	AMI, LVEF < 50%	BMMNCs	Saline and CABG	Mortality, SAEs, LVEF MRI Difference, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV (MRI) End of the study, EDV (MRI) difference between the groups, EDV (ml) End of the study MRI, EDV (ml) Difference between the groups MRI, ESV (ml) End of the study MRI, ESV (ml) Difference between the groups MRI, ESV (MRI) End of the study, ESV (MRI) difference between the groups, ESV (MRI) difference between the groups, WMSI (MRI) end of the study, WMSI (MRI) difference between groups, Arrhythmia frequency, Stroke frequency,

Lezo et al. 2007[23]	Anterior STEMI	BMMNCs	Heparinised saline	LVEF (Angiography) End of the study, LVEF (%) End of the study Angiography, EDV Index (Angiography) End of the study, ESV Index (Angiography)
Lee et al. 2014[24]	STEMI	BM-MSCs	Standard treatment	LVEF ECHO LVEF (2D ECHO) End of the study LVEF (2D ECHO) Difference of Difference from baseline LVEF (ECHO) difference between groups, LVEF (SPECT) End of the study, LVEF (SPECT) difference between the groups, EDV (ECHO) End of the study, EDV (ECHO) difference between the groups, LVEF (%) End of the study echo, LVEF (%) End of the study SPECT, LVEF (%) Difference between the groups Echocardiography, LVEF (%) Difference between the groups SPECT, EDV (SPECT) End of the study, EDV (SPECT) difference between the groups, EDV (ml) End of the study Echocardiography, EDV (ml) End of the study SPECT, EDV (ml) Difference between the groups Echocardiography, EDV (ml) Difference between the groups SPECT, ESV (ml) End of the study Echocardiography, ESV (ml) End of the study SPECT, ESV (ECHO) End of the study, ESV (ECHO) difference between groups, ESV (ml) Difference between the groups

				Echocardiography, ESV (ml) Difference between the groups SPECT, ESV (SPECT) End of the study, ESV (SPECT) difference between the groups, WMSI (ECHO) End of the study, WMSI (ECHO) Difference between the group
Lunde et al. 2007[25]	Ant. STEMI	BMMNCs	Standard treatment	Quality of life
Mathur et al. 2020[26]	STEMI, LVEF <45%	BMMNCs	Standard treatment	Cancer incidence, Mortality, Recurrent MI, SAE, Cardiovascular mortality Arrhythmia frequency, Revascularization frequency Stroke frequency
Meyer et al. 2009[27]	STEMI	BMMNCs	Standard treatment	Cardiovascular mortality, Mortality, Hospitalization due to heart failure Recurrent MI, LVEF MRI Difference, LVEF (%) End of the study MRI LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups,

				NYHA FCI end of the study. Arrhythmia frequency, Revascularization frequency
Naseri et al. 2018[28]	STEMI, LVEF: 20-45%	BMMNCs; $CD133^{+}$	2 ml normal saline supplemented with 2% autologous serum.	Mortality, Hospitalization due to heart failure Recurrent MI, LVEF (SPECT) End of the study, LVEF (SPECT) difference between the groups, LVEF (%) End of the study SPECT, LVEF (%) Difference between the groups SPECT, WMS (SPECT) End of the study
Ostovaneh et al. 2021[29]	MI, LVEF <45%	Allogeneic cardiosphere-derived cells (cdcs) [CAP-1002]		LVEF MRI Difference LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups
Penicka et al. 2007[30]	Anterior STEMI, LVEF < 50%	BMMNCs	Standard treatment	Cancer incidence, Mortality, RECURRENT MI LVEF (2D ECHO) End of the study, EDV (ECHO) End of the study, LVEF (%) End of the study echo, EDV (ml) End of the study Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study,

				Infarct size (SPECT) End of the study
Piepoli et al. 2010[31]	STEMI	BMMNCs	Control	Cardiovascular mortality Mortality, Hospitalization due to heart failure, SAEs, LVEF (SPECT) difference between the groups, LVEF (%) Difference between the groups SPECT, EDV (SPECT) difference between the groups, EDV (ml) Difference between the groups SPECT, ESV (ml) Difference between the groups SPECT, ESV (SPECT) difference between the groups, LVEDD (Echo) difference between the groups, LVESD (echo) difference between the groups
Plewka et al. 2009[32]	STEMI, LVEF <40%	BMMNCs	Standard treatment	Mortality, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study, WMSI (ECHO) End of the study
Quyyumi et al. 2011[33]	Acute STEMI and LVEF ≤ 50%	$CD34^+$ cells	Standard treatment	Mortality, LVEF MRI Difference, Hospitalization due to heart failure, SAE LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV (MRI) End of the study, EDV (MRI) difference between the groups, EDV (ml) End of the study MRI, EDV (ml) Difference between the groups MRI,

				ESV (ml) End of the study MRI, ESV (ml) Difference between the groups MRI, ESV (MRI) End of the study, ESV (MRI) difference between the groups, ESV (MRI) difference between the groups, Infarct size (MRI) end of the study, Infarct size (MRI) difference between the groups, Revascularization frequency Stroke frequency.
Quyyumi et al. 2017[34]	STEMI LVEF ≤48%	$CD34^+$ cells	Phosphate buffered saline, autologous serum and HAS without cells.	Mortality, LVEF MRI Difference, LVEF (MRI) difference between the groups, LVEF (%) Difference between the groups MRI
San Roman et al. 2015[35]	AMI	BMMNCs		Mortality Hospitalization due to heart failure Recurrent MI SAEs LVEF (MRI) End of the study LVEF (MRI) difference between the groups LVEF (Angiography) End of the study, LVEF (Angiography) difference between groups, LVEF (%) End of the study MRI, LVEF (%) End of the study Angiography, LVEF (%) Difference between the groups MRI, LVEF (%) Difference between the groups Angiography, EDV (MRI) End of the study, EDV (MRI) difference between the groups, EDV (ml) End of the study MRI, EDV (ml) End of the study Angiography,

				EDV (Angiography) end of the study, EDV (Angiography) difference between the groups, EDV (ml) Difference between the groups MRI, EDV (ml) Difference between the groups Angiography, ESV (ml) End of the study MRI, ESV (ml) End of the study Angiography, ESV (ml) Difference between the groups MRI, ESV (ml) Difference between the groups Angiography, ESV (MRI) End of the study, ESV (MRI) difference between the groups, ESV (MRI) difference between the groups, ESV (Angiography) end of the study, ESV (Angiography) difference between group, Infarct size (MRI) end of the study, Infarct size (MRI) difference between the groups, WMSI (MRI) end of the study, WMSI (MRI) difference between groups Arrhythmia frequency
Roncalli et al. 2011[36]	Acute STEMI, LVEF ≤ 45%;	BMMNCs	Standard treatment	Mortality, Hospitalization due to heart failure, SAE LVEF (2D ECHO) End of the study LVEF (MRI) End of the study, LVEF (Radionucleotide ventriculography) end of the study, LVEF (%) End of the study echo, LVEF (%) End of the study MRI, LVEF (%) End of the study Radionucleotide Angiography,

				EDV Index (MRI) End of the study, ESV Index (MRI) End of the study, Infarct size (MRI) end of the study Arrhythmia frequency Restenosis
Srimahachota et al. 2011[37]	STEMI, LVEF < 50%	BMMNCs	Standard treatment	LVEF MRI Difference, LVEF ECHO LVEF (2D ECHO) End of the study LVEF (2D ECHO) Difference of Difference from baseline, LVEF (ECHO) difference between groups, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (Angiography) difference between groups, LVEF (%) End of the study echo, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups Echocardiography, LVEF (%) Difference between the groups MRI, LVEF (%) Difference between the groups Angiography, WMSI (ECHO) End of the study, WMSI (ECHO) Difference between the group, NYHAFCI end of the study, NYHA FCI difference between the groups
Surder et al. 2016[38]	STEMI, LVEF <45%	BMMNCs	Standard treatment	Mortality SAEs Hospitalization due to heart failure Recurrent MI LVEF MRI Difference, LVEF (MRI) difference between the groups,

				LVEF (%) Difference between the groups MRI, EDV (MRI) difference between the groups, EDV (ml) Difference between the groups MRI, ESV (ml) Difference between the groups MRI, ESV (MRI) difference between the groups, ESV (MRI) difference between the groups, Revascularization frequency Stroke frequency.
Tendra et al. 2009[39]	Anterior AMI, LVEF ≤ 40%	Selected cells (S): $CD34^+/CXCR4^+$ cells Unselected cells (U): BMMNC	Standard treatment	Mortality, Recurrent MI, LVEF (MRI) End of the study, LVEF (%) End of the study MRI, EDV (MRI) End of the study, EDV (ml) End of the study MRI, ESV (ml) End of the study MRI, ESV (MRI) End of the study, Revascularization frequency
Traverse et al. 2010[40]	STEMI; LVEF <50%	BMMNCs	0.9% saline solution and 5% human serum albumin	LVEF MRI Difference, Recurrent MI, LVEF (MRI) difference between the groups, LVEF (%) Difference between the groups MRI, EDV Index (MRI) difference between the groups, ESV (ml) Difference between the groups MRI, ESV (MRI) difference between the groups, ESV (MRI) difference between the groups, Revascularization frequency
Traverse et al. 2011[41]	STEMI, LVEF ≤ 45%; PCI	BMMNCs	0.9% saline solution and 5% human serum albumin	Mortality, hospitalization due to heart failure, Recurrent MI,

				LVEF MRI Difference, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups, Infarct size (MRI) end of the study, Infarct size (MRI) difference between the groups, Revascularization frequency
Traverse et al. 2018[42]	Anterior STEMI, LVEF ≤45%	BMMNCs	5% ALBUMIN IN NS with 100 ml of whole blood	Mortality, hospitalization due to heart failure, Recurrent MI, LVEF MRI Difference, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups, Infarct size (MRI) end of the study, Infarct size (MRI) difference between the groups, Revascularization frequency, Stroke frequency.
Wang et al.	Acute STEMI	BM-MSCs	Heparinized saline	Mortality, LVEF (Angiography) End of the study,

2014[43]				LVEF (%) End of the study Angiography, Infarction region % (Ventriculography), Left ventricular diameter (Ventriculography)
Wen-tao et al. 2012[44]	AMI	BM-MSCs	Heparinised saline	LVEF (2D ECHO) End of the study, LVEF (%) End of the study echo, LVEDD (ECHO) End of the study
Wohrle et al. 2010[45]	AMI	BMMNCs	0.9% saline solution, 2% human serum albumin and 0.1% autologous erythrocytes	Mortality, Hospitalization due to heart failure, LVEF MRI Difference, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups, Infarct size (MRI) end of the study, Infarct size (MRI) difference between the groups Restenosis.
Wollert et al. 2017[46]	STEMI LVEF < 52%	BMMNCs	Pure red blood cell suspension	Mortality, hospitalization due to heart failure, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study,

				ESV Index (MRI) difference between the groups, Volume of infarct (MRI) ml end of the study, Volume of infaract (MRI) ml difference between groups
Yao et al. 2009[47]	STEMI, LVEF 20-39%	BMMNCs	Heparinised plasma	Recurrent MI, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV (MRI) End of the study, EDV (ml) End of the study MRI, ESV (ml) End of the study MRI, ESV (MRI) End of the study, Infarct size (MRI) end of the study Perfusion defect % (SPECT) End of study
Zhang et al. 2021[48]	STEMI	BM-MSCs		Mortality, Hospitalization due to heart failure LVEF (2D ECHO) End of the study, EDV (ECHO) End of the study, LVEF (%) End of the study echo, EDV (ml) End of the study Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study, NYHA FCI end of the study, Revascularization frequency, Perfusion defect % (SPECT) End of study

v. Evidence to Decision Framework:

QUESTION

In patients with myocardial infarction, what is the efficacy and safety of stem cell therapy as compared to usual care?	
POPULATION:	Myocardial Infarction
INTERVENTION:	Stem cell therapy
COMPARISON:	Usual care
MAIN OUTCOMES:	Mortality; SAEs frequency; Re MI frequency; Heart Failure Frequency; Stroke frequency; Cancer incidence; LVEF (ECHO) difference between groups; LVEF (2D ECHO) End of the study; LVEF (MRI) difference between the groups; LVEF (MRI) End of the study
SETTING:	Hospital
PERSPECTIVE:	
BACKGROUND:	Myocardial infarction is a major cause of cardiovascular mortality and morbidity, wherein the blood flow to one or more of the coronary arteries supplying the cardiac muscle is blocked. The cardiovascular disease epidemic in Indians is characterized by a higher relative risk burden, an earlier age of onset, higher case fatality and higher premature deaths.[1] Myocardial injury during the episode is not fully reversible by the available treatment options and there is an unmet need for developing novel methods or interventions for reversing the ischemic damage.
CONFLICT OF INTERESTS:	None

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL**

		CONSIDERATIONS
○No ○Probably no ○Probably yes ● Yes ○Varies ○Don't know	Cardiovascular disease, and specifically acute myocardial infarction (AMI), is the leading cause of morbidity and mortality worldwide. While the advent of reperfusion therapy, especially primary percutaneous coronary intervention (PCI), has dramatically improved survival rates in patients with AMI, a significant percentage of patients still develop post-myocardial infarction (MI) ischemic heart failure, leading to adverse long-term clinical outcomes.	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○Small ○Moderate ○Large ○Varies ○Don't know	1. **Mortality:** All-cause mortality was reported by 30 RCTs with 2879 participants (1633 participants in the stem cell group and 1246 participants in the control group) at the end of follow up (< than 6 months to > 12 months). Pooled analysis revealed a risk ratio of 0.73 (95% CI: 0.50 to 1.05) which was statistically non-significant. The subgroup analysis based on cell type, route of administration and source (autogenic vs allogenic) were all statistically non-significant. 2. **Recurrent-myocardial infarction:** Eighteen RCTs with 1981 participants (1158 in the stem cell group and 823 in the control group) reported the incidence of re-myocardial infarction at the end of follow up (< than 6 months to > 12 months). Pooled analysis revealed a risk ratio of 0.67 (95% CI: 0.43 to 1.05), which was statistically non-significant. 3. **Hospitalization due to heart failure:** Nineteen RCTs with 1641 participants (928 in the stem cell group vs. 713 in the control group) reported the incidence of hospitalization due to heart failure at the end of follow up (< than 6 months to > 12 months). Pooled analysis comparing hospitalization due to heart failure between the stem cells and the control group yielded a risk ratio of 0.79 (95% CI: 0.52 to 1.20), which was statistically non-significant.	The MCID for change in LVEF was decided as 5% by the committee.[49]

	4. **Stroke incidence:** Eight RCTs with 1121 participants (610 in stem cell group and 511 in the control group) reported the incidence of stroke at the end of follow up (< than 6 months to > 12 months). Pooled analysis revealed a risk ratio of 0.81 (95% CI: 0.41 to 1.60), which was statistically non-significant. 5. **Cancer incidence:** Six RCTs with 807 participants (411 in stem cell group Vs 396 in control group) reported the incidence of cancer at the end of follow up (< than 6 months to > 12 months). Pooled analysis revealed a risk ratio of 0.82 (95% CI: 0.43 to 1.55), which was statistically non-significant. 6. **Left ventricular ejection fraction (LVEF):** Nineteen RCTs with 20 comparisons (909 participants, 480 in the stem cell group, and 429 in the control group) reported the LVEF (%) measured by echocardiography at the end of follow up (< than 6 months to > 12 months. The mean difference in LVEF was 2.53% (95% CI: 0.95 to 4.10), which was statistically significant but unimportant clinically as it was less than the MCID.	
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
● Trivial ○Small ○Moderate ○Large ○Varies ○Don't know	Twelve RCTs with 1161 participants (571participants in the stem cell group and 590 participants in the control group) reported SAEs at the end of follow up (< than 6 months to > 12 months). Pooled analysis revealed a risk ratio of 0.93 (95% CI: 0.76 to 1.14), which was statistically non-significant.	

Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
● Very low ○Low ○Moderate ○High ○No included studies	The certainty of evidence is very low due to high risk of bias, inconsistency and imprecision in the effect shown by stem cell therapy.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○Important uncertainty or variability ○Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○No important uncertainty or	Main outcome is clinical improvement in the form of decreased mortality and reduced complications which are likely to be highly valued by most patients.[50]	

variability		
Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○Favors the comparison ○Probably favors the comparison ● Does not favor either the intervention or the comparison ○Probably favors the intervention ○Favors the intervention ○Varies ○Don't know	It is not clear whether the benefits of stem cell therapy outweigh the harms.	
Resources required How large are the resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

● Large costs ○Moderate costs ○Negligible costs and savings ○Moderate savings ○Large savings ○Varies ○Don't know	The reported price to patients ranged from $6000 to $20,700 for 7 clinics willing to provide these data. The mean price for therapy utilizing adipose tissue-derived cells was $7742 (6 clinics) whereas the price for umbilical cord tissue-derived products was $12,162 (4 clinics). The mean price across 7 clinics was $9593, while the median price was $6500.[51]	
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○Very low ○Low ● Moderate ○High ○No included studies	No direct research evidence was identified	The GDG members were fairlycertain that stem cell therapy requires large resources.
Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○Favors the comparison ● Probably favors the comparison ○Does not favor either the intervention or the comparison ○Probably favors the intervention ○Favors the intervention ○Varies ○No included studies	No direct research evidence was identified.	The intervention was not found to be effective and hence the committee deferred to comment on cost effectiveness.
Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○Reduced ● Probably reduced ○Probably no impact ○Probably increased ○Increased ○Varies ○Don't know	No research evidence was identified.	As stem cell therapy is an expensive treatment offered only at tertiary centers, it is likely to reduce equity.
Acceptability		

Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○No ○Probably no ● Probably yes ○Yes ○Varies ○Don't know	No direct evidence was identified.	Despite uncertainty regarding the medical risks and benefits associated with stem cell injections, stroke survivors may still consider undergoing treatment in private, unregulated clinics.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○No ○Probably no ● Probably yes ○Yes ○Varies ○Don't know	No direct evidence was identified.	Feasible to implement in tertiary care centers.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	**Large costs**	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	**Moderate**	High			No included studies
COST EFFECTIVENESS	Favors the comparison	**Probably favors the comparison**	Does not favor either the intervention or	Probably favors the intervention	Favors the intervention	Varies	No included studies

	JUDGEMENT						
			the comparison				
EQUITY	Reduced	**Probably reduced**	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	**Use only in the context of rigorously conducted RCTs**	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	●	○	○	○

CONCLUSIONS

Recommendation
Stem Cell Therapy is **not recommended** in routine practice for the treatment of myocardial infarction. It may be used only in the context of rigorously conducted randomized controlled trials. Strength: Conditional Certainty of Evidence: Very Low

Justification

Overall justification

This recommendation has been made as there is very low certainty evidence of improvement in function and mortality. There is little or no difference in undesirable effects between stem cell therapy and usual care. In addition, the follow up period is too small to comment fully on the side effect profile and long-term safety is not known. Results should be interpreted with caution in view of studies with high risk of bias and/or fewer events.

Detailed justification

Desirable effects:

This judgment was made as there is very low certainty evidence of trivial improvement in function and mortality.

Undesirable effects:

This judgment was made as there is little or no difference in undesirable effects between stem cell therapy and usual care.

Resources required:

The committee opined that stem cell treatment is associated with large costs.

vi. Data Extraction:

All randomized controlled trials having patients with MI with or without other co-morbidities and treated with any stem cell product in comparison with placebo or no treatment with standard of care were included in this study. After the electronic search, the duplicates were removed and abstracts were assessed for inclusion by two reviewers independently. The full text articles for the selected abstracts were collected along with the supplementary material and protocols and were again assessed by both the reviewers independently. The reasons for the exclusions of studies were noted down. Any disagreements for inclusion at the first screen (Title and Abstract) or second screen (Full text) was resolved after discussion with the third reviewers. Data extraction was done in the excel sheet by one reviewer and verified by another reviewer independently. Data related to trial characteristics e.g. Title of the article, authors, setting of research, date of publication, study participants' characteristics, details of intervention and comparison and details of outcome was extracted and utilized

during the analysis to assess the reasons for different direction in results. The outcome data has been extracted based on the nature of data. For dichotomous data, number of events and for the continuous data, mean and standard deviation were extracted. The data originally extracted from the studies was converted into the suitable forms for analysis. Median and range mentioned in few studies were converted into the mean and SD based on the method given by Hozo et al. 2005. In the case of missing data, the corresponding author of the paper was contacted.to prevent any unit of analysis issue, each trial was included only once in the analysis. Longest follow up for each trial was considered for the analysis.

RevMen Version 5.4.1 (Review Manager 5.4.1) was used for the analysis. Heterogeneity was assessed by I^2 value. Fixed effect model was used when heterogeneity based on I^2 value was < 50%. In the case of heterogeneity > 50%, PICO for heterogeneity was checked and finally random effect model was used for those outcomes where heterogeneity could not be explained based on PICO. Risk ratio with confidence interval was used to pool dichotomous data while mean and standard deviation was used for the continuous data. Summary of finding table was produced using GRADEpro GDT software. The summary of finding table was based on most important seven outcomes i.e. all-cause mortality, Re-Myocardial Infarction, Serious Adverse Events, Hospitalization due to heart failure, Cancer incidence, stroke incidence and Left ventricular ejection fraction measured by echocardiography.

Study	**Angeli et al. 2012[1]**
Study type:	Randomized Controlled Trial
Number of participants:	22
Countries, setting and Funding:	Brazil
Duration of study Follow up (post intervention):	12 Months
Subgroup analysis within study	-
Inclusion criteria:	• Assess the efficacy of bmcs therapy 5-9 days post symptoms onset in patients with AMI successfully treated with PCI, and with LVEF≤45%.
Exclusion criteria:	-
Recruitment/selection of patients:	• A randomized, placebo-controlled, double blind PILOT study aiming to assess the efficacy of BMCs therapy 5-9 days post symptoms onset in patients with AMI successfully treated with PCI, and with LVEF≤45%.
Intervention: Source and Type of stem cells	NR, BMMNCs
Intervention: Method of their characterization	-
Intervention: Route of administration	Injection intracoronary through balloon

Intervention: Dose	260 (160) million BMMNCs; 1.4 (1.5) % $CD34^+$
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF (2D ECHO) End of the study, LVEF (SPECT) End of the study, LVEF (%) End of the study echo, LVEF (%) End of the study SPECT,
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	-

Study	**Assmus et al. 2014[2]**
Study type:	Randomized Controlled Trial
Number of participants:	204
Countries, setting and Funding:	Germany, Guidant, Inc. Guidant provided balloon catheters, and Eli Lilly provided the abciximab
Duration of study Follow up (post intervention):	60 Months
Subgroup analysis within study	-
Inclusion criteria:	• Patients aged 18–80 years were eligible for inclusion into the study, if they had an acute ST elevation myocardial infarction successfully reperfused with stent implantation with a residual significant LV regional wall motion abnormality (EF <45% by visual estimate).
Exclusion criteria:	-
Recruitment/selection of patients:	In this double-blind, placebo-controlled, randomized trial, performed in 17 centres, at a median of 4 days after AMI reperfusion therapy, bone marrow aspiration was performed in 204 patients, and the aspirate was sent to a central cell processing laboratory (Institute for Transfusion Medicine, Frankfurt, Germany), where patients were randomized to placebo medium or BMC receiving

	groups.
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	After Ficoll density gradient centrifugation, BMC subpopulations were quantified by fluorescence-activated cell sorting ($CD34^+/CD45^+$, $CD133^+/CD45^+$, and $CD45^+/KDR^+$ cells). Gating was performed according to the international society of hematotherapy and graft engineering guideline. The migratory capacity of isolated BMC was assessed in a modified Boyden chamber assay. In brief, a total of 1×10^6 BMCs were resuspended in 250 ml X-vivo 10 medium and placed in the upper chamber of a modified Boyden chamber filled with Matrigel (biocoat invasion assay, 8 mm pore size, Becton Dickinson). Then, the chamber was placed in a 24-well culture dish containing 500 ml of endothelial basal medium. For stimulation of invasion, 100 ng/ml of stromal cell derived factor-1 (SDF-1) was added in the lower chamber. After incubation for 24 h at 37^0C, transmigrated cells were counted by independent investigators. Invasion assays were run in duplicates. Migration was assessed under basal conditions and after stimulation with SDF-1.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	236 (174) million
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	-
Safety Outcomes reported with time points- Serious AEs	SAEs 60 months Intervention (Total = 9- ACS 8, Pacemaker implantation 1 Control (Total = 11 - ACS 10, Pacemaker implantation 1)
Safety Outcomes reported with time points- Other Adverse Events	Cancer incidence, 60 months, Cardiovascular mortality, Mortality, Hospitalization due to heart failure, Recurrent MI, Arrhythmia frequency,

	Revascularization frequency, Stroke frequency

Study	**Attar et al. 2023[3]**
Study type:	Randomized Controlled Trial
Number of participants:	75
Countries, setting and Funding:	Iran, Clinician-scientist program of Iran's Ministry of Health and Medical Education and by the Vice-Chancellery for Research of Shiraz University of Medical Sciences (Grants No. SG-98-5, SG-98-94, and SG-96-86).
Duration of study Follow up (post intervention):	6 Months
Subgroup analysis within study:	-
Inclusion criteria:	Inclusion criteria consisted of • Age of patients were 20-60 years old, • had their MI 3–7 days earlier, • had an echocardiographic LVEF<40%
Exclusion criteria:	Exclusion criteria were: • prior history of an anterior MI, • regional wall motion abnormalities in the non-infarct region, • history of coronary artery bypass graft (CABG) surgery, • significant valve disease (stenosis/regurgitation grade≥2), • alternative etiology of LV dysfunction (non-ischemic cardiomyopathy, • anthracycline therapy, • regular ethanol abuse>6 oz. Ethanol/day), • poor echocardiography window, • active syphilis, • hepatitis B, hepatitis C, HIV or HTLV-1, • terminal disease or cancer, • history of a bone marrow transplant, or an autoimmune disease, • being pregnant.

Recruitment/selection of patients:	Patients were randomized using a web-based randomization service into three groups with a 1:1:1 allocation ratio via permuted block randomization with a block size of 6.
Intervention: Source and Type of stem cells	BM Aspiration, HWJMSCs allogeneic
Intervention: Method of their characterization	
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	10 million
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points: 6 months	LVEF MRI, LVEF ECHO, LVEF (2D ECHO) End of the study, LVEF (ECHO) difference between groups, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, EDV (ECHO) End of the study, EDV (ECHO) difference between the groups, LVEF (%) End of the study echo, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups Echocardiography, LVEF (%) Difference between the groups MRI, EDV (MRI) End of the study, EDV (MRI) difference between the groups, EDV (ml) End of the study Echocardiography, EDV (ml) End of the study MRI, EDV (ml) Difference between the groups Echocardiography, EDV (ml) Difference between the groups MRI, ESV (ml) End of the study Echocardiography, ESV (ml) End of the study MRI, ESV (ECHO) End of the study,

	ESV (ECHO) difference between groups, ESV (ml) Difference between the groups Echocardiography, ESV (ml) Difference between the groups MRI, ESV (MRI) End of the study, ESV (MRI) difference between the groups, Infarct size (MRI) difference between the groups, LVEDD (Echo) difference between the groups, LVESD (echo) difference between the groups,
Safety Outcomes reported with time points- SAEs:	-
Safety Outcomes reported with time points- Other Adverse Events:	-

Study	**Cao et al. 2009[4]**
Study type:	Randomized Controlled Trial
Number of participants:	86
Countries, setting and Funding:	China, Xijing Research Boosting Program on Stem Cell Research (No. XJZT08Z04), Xijing Research Boosting Program on Cardiac Microvascular Formation Research (No. XJZT07Z05)
Duration of study Follow up (post intervention):	48 MONTHS
Subgroup analysis within study	-
Inclusion criteria:	• Age between 40 and 65 years old, STEMI according to the WHO definition, PCI, 12 h from the onset of symptoms, one vessel disease with an open infarct related artery amenable to cell therapy
Exclusion criteria:	• Previous MI, cardiomyopathy, atrial fibrillation or flutter, previous heart surgery, severe valvular heart disease, disease of the haematopoietic system, NYHA functional class IV heart failure at baseline, severe renal, lung and liver disease or cancer, significant coronary lesion in one or more major coronary vessels, intracardiac thrombus, and bone marrow disease.
Recruitment/selection of patients:	Eighty-six STEMI patients with the culprit lesion in the left anterior descending artery proximal to the two diagonal branches were enrolled consecutively between July

	2003 and March 2004. Patients were treated by acute PCI successfully within 12 h of the onset of symptoms.
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	Bone marrow (40 ml) aspiration was conducted 7 days after successful PCI under local anaesthesia. Density gradient centrifugation was used to isolate BMMNC. In brief, the bone marrow solution was gently added onto 10 ml Ficoll (lymphopreptm, Axis-Shield, Norway, density 1.073) and centrifuged at 900g for 30 min at room temperature. The mononuclear cell layer was harvested and washed three times before final resuspension in 10 ml heparinized saline. The final preparation of the injected cells contained 5±1.2 x 10^7 mononuclear cells per milliliter. Cell viability was 96±3.2% and $CD34^+$ cell fraction was 1.8±0.6%.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	50 (12) million BMMNCs; 1.8 (0.6) % $CD34^+$
Intervention: Dose- If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF ECHO LVEF (2D ECHO) End of the study, LVEF (ECHO) difference between groups, EDV (ECHO) End of the study, EDV (ECHO) difference between the groups, LVEF (%) End of the study echo, LVEF (%) Difference between the groups Echocardiography, EDV (ml) End of the study Echocardiography, EDV (ml) Difference between the groups Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study, ESV (ECHO) difference between groups, ESV (ml) Difference between the groups Echocardiography, Infarct size (SPECT) End of the study, WMSI (ECHO) End of the study,

	WMSI (ECHO) Difference between the group
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Mortality, Hospitalization due to heart failure, Restenosis

Study	**Chen et al. 2004[5]**
Study type:	Randomized controlled trial
Number of participants:	69
Countries, setting and Funding:	China
Duration of study Follow up (post intervention):	6 Months
Subgroup analysis within study:	
Inclusion criteria:	• Age <70 years, without cardiac shock and cardiac block, stable haemodynamics and no severe comorbidity
Exclusion criteria:	-
Recruitment/selection of patients:	Rom November 2002 to May 2003, 78 patients with acute transmural myocardial infarction, according to WHO criteria, within twelve hours from the onset of continuous chest pain were enrolled and underwent emergency angiography/ angioplasty. The mean time from onset of myocardial infarction (MI) to angiography and angioplasty was (8.0±3.7) hours.
Intervention: Source and Type of stem cells	BM Aspiration, BMMSCs
Intervention: Method of their characterization	Sixty milliliters of autologous bone marrow were aspirated under local anaesthesia from ileum of all the 69 patients during the morning of the 8th day after the PCI procedure and cultured for 7 days to 10 days. BMSCs was cultured and harvested by the method of Jaiswal et al, 2000. Several attempts were used to control BMSCs under 15 generations. BMSCs was harvested and washed three or four times with heparinized saline. The BMSCs suspension was mixed with heparin, filtered and prepared for implantation just two hours before implantation. Each milliliter of the final BMSCs suspension had over 8×10^9 cells.

	The infarct-related coronary artery was occluded just at the proximal edge of former angioplasty as described by Strauer et al. Each milliliter of the BMSCs suspension containing 8×10^9-10×10^9 cells was directly injected through an inflated over-the-wire (OTW) balloon catheter central lumen at high pressure (1 Mpa) into the target coronary artery. The balloon was inflated for at least two minutes continuously to occlude the anterior blood flow just before the beginning of BMSCs injection.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	48,000 (60,000) million
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points: 6 months	LVEF (Angiography) End of the study, EDV (ECHO) End of the study, LVEF (%) End of the study Angiography, EDV (ml) End of the study Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study, Perfusion defect end of the study (cm^2)
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	-

Study	**Choudry et al. 2016[6]**
Study type:	Randomized controlled trial
Number of participants:	100
Countries, setting and Funding:	Multicentre, no role of sponsor/funders in design or conduct of study.
Duration of study Follow up (post intervention):	12 Months
Subgroup analysis within study:	-
Inclusion criteria:	• Patients presenting with acute anterior myocardial infarction (ST elevation in at

	least; contiguous anterior leads ≥0.2 mv) and treated with acute percutaneous coronary intervention (PCI) with stent implantation within 24 h after symptom onset; Acute PCI/stent implantation has been successful (residual stenosis visually).
Exclusion criteria:	• Regional wall motion abnormality not consistent with culprit vessel; Need to revascularise additional vessels, outside the infarct artery as a planned procedure (these vessels can be treated at baseline); Arteriovenous malformations or aneurysms; Active infection, or fever or diarrhoea within the past 4 weeks; Chronic inflammatory disease; Known HIV infection or active hepatitis; Neoplastic disease without documented remission within the past 5 years; Cerebrovascular insult within 3 months; Impaired renal function (creatinine >200 mmol) at the time of cell therapy; Significant liver disease (gamma-glutamyl trasferase>2× upper limit) or spontaneous International Normalised Ratio >1.5); Anemia.
Recruitment/selection of patients:	Patients will be randomised to receive autologous BMCbmcs or matching placebo (in a 1:1 block randomisation allocation) with the patient and treating clinicians blinded to the assignment (double-blind).
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	Following consent, patients will undergo bone marrow aspiration performed by a trained member of the research team. The patient will be rolled onto their side and local anaesthetic administered into the posterior superior iliac spine. One hundred millilitres of bone marrow will be aspirated into heparinised syringes and the contents transferred to a specimen bag for transport to the stem cell unit. The bone marrow is passed to the cell culture laboratory of the hospital where the bone marrow aspiration has been performed. The progenitor cells will be isolated using Ficoll-Hypaque centrifugation. The autologous BMCs or placebo will be placed in identical sterile syringes and transferred back to the cardiac catheter laboratories for the infusion procedure (Heparin will not be included in the final solution for reinfusion).
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	59.8 (59.9) million BMMNCs; 1.9(1.5) million $CD34^{+}$

Intervention: Dose- If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF MRI Difference LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV (MRI) End of the study, EDV (MRI) difference between the groups, EDV (ml) End of the study MRI, EDV (ml) Difference between the groups MRI, ESV (ml) End of the study MRI, ESV (ml) Difference between the groups MRI, ESV (MRI) End of the study, ESV (MRI) difference between the groups, ESV (MRI) difference between the groups, Infarct size (MRI) end of the study, Infarct size (MRI) difference between the groups, Quality of life (VAS) difference between the groups, Quality of life (VAS) End of the study, Quality of life (EQ5D) difference between the groups, Quality of life (European quality of life dimension) End of study,
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Mortality, Recurrent MI, Revascularization frequency,

Study	**Chullikana et al. 2015[7]**
Study type:	Randomized controlled trial
Number of participants:	20

Countries, setting and Funding:	India, Stempeutics Research Private limited
Duration of study Follow up (post intervention):	24 Months
Subgroup analysis within study:	-
Inclusion criteria:	• Patients with STEMI ages between 20 and 70 years, either men or women with none child-bearing potential, after 2 days of successful PCI. Patient has global left ventricular systolic dysfunction with an ejection fraction of 30%. Electrocardiogram with sign of acute anterior MI with stelevation 2 mm in at least two of the following: leads I, AVL or V1-V6 or electrocardiogram with sign of acute inferoposterior MI with ST-elevation 1 mm on all of the following leads: II, III and V5-V6 or ST-elevation 2 mm in at least two of the leads. Target lesion islocatedin the proximal section of the left anterior descending, left circumflex or right coronary artery. Patient with AMI within 10 days before intraperitoneal administration. Normal liver and renal function. Able to understand study information provided. Able to give voluntary written consent.
Exclusion criteria:	• History of acute/chronic inflammatory condition or severe aortic stenosis or insufficiency; severe mitral stenosis or severe mitral insufficiency. Severe co-morbidity associated with a reduction in life expectancy of <1 year. Advanced renal dysfunction and creatinine 2 mg%. Advanced hepatic dysfunction. Clinically serious and/or unstable intercurrent infection, medical illnesses or conditions that are uncontrolled or whose control, in the opinion of the investigator, may be jeopardized by participation in this study or by the complications of this therapy. Previous MI. Patients already enrolled in another investigational drug trial. History of severe alcohol or drug abuse within 3 months of screening. Women with child-bearing potential or who are pregnant or lactating. Positive test for human immunodeficiency virus 1, hepatitis C virus, hepatitis B virus, syphilis and cytomegalovirus (immunoglobulin M). Patients contraindicated for MRI.
Recruitment/selection of patients:	Thirty patients were screened after written informed consent was obtained. Computer generated block randomization was performed centrally to randomly assign 20 patients to Stempeucel or to the placebo group in a 1:1 ratio. An independent data safety monitoring board (DSMB), which consisted of safety

	physicians and biostatisticians, was established to assess the progress of this study.
Intervention: Source and Type of stem cells	BM Aspiration, BM-MSCs allogeneic
Intervention: Method of their characterization	Stempeucel showed more than 90% expression of CD73 (99.04%), CD90 (94.00%) and CD166 (98.38%) and less than 5% expression of CD34 (0.14%), CD45 (0.06%) and HLA-DR (0.18%).
Intervention: Route of administration	Antecubital vein of forearm
Intervention: Dose	2 million cells/kg body weight; 0.14% $CD34^+$
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF (2D ECHO) End of the study, LVEF (2D ECHO) Difference of Difference from baseline, LVEF (SPECT) End of the study, LVEF (%) End of the study echo, LVEF (%) End of the study SPECT, Volume of infarct (MRI) mm end of study
Safety Outcomes reported with time points- SAEs	SAEs, 3 IN Control (Ventricular Tacycardia, Pericardial Effusion And AMI)
Safety Outcomes reported with time points- Other Adverse Events	Mortality

Study	**Colombo et al. 2011[8]**
Study type:	Randomized controlled trial
Number of participants:	10
Countries, setting and Funding:	Italy, Grants from the Italian Ministry of Health (Progetto Ricerca Finalizzata 2002 and 2005. Progetto ex art. 56 2007); the Italian Ministry of University and Research (Progetto FIRB 2002), the Istituto Superiore di Sanità (project title "Transplantation of hematopoietic CD133 stem cells to reconstitute infarcted myocardium', 2003) and the 6FP EU Project-THERCORD. Materials for CD133 cell separations were kindly provided by Miltenyi Biotec.

Duration of study Follow up (post intervention):	12 Months
Subgroup analysis within study	-
Inclusion criteria:	• Age between 18 and 65 years; anterior infarction with more than 2 mm ST-segment elevation in at least five ECG chest leads due to single-vessel thrombotic occlusion of the proximal left anterior descending artery; successful coronary stenting within 12 h of symptom onset with final thrombolysis in myocardial infarction (TIMI) 3 flow; myocardial blush 0 or 1 at the end of the procedure; ST-segment recovery less than 50% 1 hour after PCI, as estimated by the formula: ½S ST after PCI=S ST before PCI 100 where SST is the sum of ST-segment elevation 80 ms after the J point in all six chest leads, and 6) echocardiographic left ventricular ejection fraction 45% or less 24 h after PCI.
Exclusion criteria:	• The exclusion criteria were pregnancy, previous myocardial infarction, scheduled aortocoronary bypass grafting, previous or current neoplasia, primary bone marrow diseases, diabetes, immunosuppressive therapy, deficiencies in protein S, protein C, antithrombin or fibrinogen, factor V or II mutation, hyperhomocysteinemia and severe comorbidity.
Recruitment/selection of patients:	Echocardiographic left ventricular ejection fraction 45% or less 24 h after PCI.
Intervention: Source and Type of stem cells	BM aspiration, selection to isolate CD133-positive cells, CD133+ cells
Intervention: Method of their characterization	The bone marrow was processed immediately after harvesting; the peripheral blood was stored overnight at 4±2^{0}C and processed within 24 h of collection. The cells were produced in a class B room under a class A biosafety cabinet, with a closed automated system (Miltenyiclinimacs System; MiltenyiBiotec, Bergisch Gladbach, Germany) being used to select the cells immunomagnetically, which were then resuspended in 10 ml (±2) of normal saline solution (0.9% NaCl) with 10% human serum albumin. The final cell product underwent quality controls, including sterility tests for aerobic and anaerobic bacteria and fungi, CD133^{+} cell count and viability by flow cytometry.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	Median (range): 5.9 (4.9 to 13.5) million
Intervention: Dose- If the trial has taken multiple doses, then which dose values has been used for MA	-

Efficacy Outcomes reported with time points:	LVEF (2D ECHO) End of the study, EDV (ECHO) End of the study, LVEF (%) End of the study echo, EDV (ml) End of the study Echocardiography, Infarct size (SPECT) End of the study, WMSI (ECHO) End of the study
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Arrhythmia frequency Hospitalization due to heart failure
Study	**Delewi et al. 2015[9]**
Study type:	Randomised controlled trial
Number of participants:	134
Countries, Setting and Funding:	Netherlands, Not commissioned
Duration of study follow up (post intervention):	60 Months
Subgroup analysis within study:	-
Inclusion criteria:	-
Exclusion criteria:	-
Recruitment/selection of patients:	Briefly, 200 patients with first ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention (PCI) were enrolled in this study. After cardiac MRI (CMR), on day 2–7, patients were randomly assigned in a 1:1:1 ratio to either intracoronary infusion of autologous mononuclear bmmcs (n=69), intracoronary infusion of peripheral blood mononuclear cells (PBMCs) (n=66) or standard therapy (without placebo infusion) (n=65).
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	Collection of cells for intracoronary infusion is performed within 24 hours of the anticipated time of cell infusion and only when tests for HIV, hepatitis B virus, and hepatitis C virus infection are known to be negative. Either 60 mL of bone marrow is aspirated from the iliac crest under local anesthesia or 150 mL of venous blood is

	collected, after which, it is transported to the local stem cell facility. Mononuclear bone marrow cells or peripheral mononuclear blood cells are isolated by density gradient centrifugation, and 15 mL of cell suspension is transported back for intracoronary infusion. The local stem cell facility forwards a small volume of the final cell suspension to a central laboratory for further characterization and analysis. Intracoronary cell infusion was performed between 3 and 8 days after PCI with a median of 6 days in the BM group and 5 days in the peripheral blood group. The median time from cell harvesting to cell infusion was 6.3 h (IQR 5.7–6.9) in the BM group and 6.3 (IQR 5.8 –7.0) in the peripheral blood group. The total number of cells was comparable in the BM and peripheral blood group (296±164 × 10^6 vs. 287±137 × 10^6). This is a long-term study of HEBE trial; the original HEBE trial- ref 10, 11 mention stem cell characterization: the number of nucleated blood cells was measured, and the number of $CD34^+$cells and $CD14^+$cells was determined according to the ISHAGE protocol.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	296 (164) million cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points: 60 months	GLOBAL LVEF LVEF MRI Difference, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups,
Safety Outcomes reported with time points- SAEs	
Safety Outcomes reported with time points- Other	Mortality,

Adverse Events	Hospitalization due to heart failure, Recurrent MI, Arrhythmia frequency, Revascularization frequency, Stroke frequency

Study	**Dill et al. 2009[10]**
Study type:	Randomized clinical trial
Number of participants:	204
Countries, setting and Funding:	Germany
Duration of study Follow up (post intervention):	24 months
Subgroup analysis within study:	-
Inclusion criteria:	-
Exclusion criteria:	-
Recruitment/selection of patients:	204 patients undergoing bone marrow aspiration, 103 were randomly assigned to receive an infusion of placebo medium and 101 to receive a BMC infusion into the infarct-related coronary artery. The two groups were well matched with respect to baseline characteristics and procedural characteristics of the reperfusion therapy and concomitant pharmacologic therapy during the study.
Intervention: Source and Type of stem cells	BM Aspiration, BMMNC
Intervention: Method of their characterization	A total of 50 ml of bone marrow was aspirated into heparin-treated syringes from the iliac crest with the use of local anesthesia. The bone marrow aspirate was shipped at room temperature together with 20 ml of venous blood used to produce patients' own serum to the central cell-processing laboratory. Progenitor cells were isolated and enriched with the use of Ficoll–Hypaque centrifugation procedures. The cell suspension consisted of a heterogeneous cell population including hematopoietic, mesenchymal, and other progenitor cells, as well as mononuclear cells. The cells were suspended in 10ml of X VIVO 10 medium (a serum-free medium containing pharmaceutical-grade human components, Cambrex), including 2ml of the patient's

	own serum. The placebo medium consisted of the 10 ml of X VIVO 10 medium, including 2ml of the patient's own serum (without BMC).
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	236(174) million
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points: 24 months	GLOBAL LVEF LVEF MRI Difference LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV (MRI) End of the study, EDV (MRI) difference between the groups, EDV (ml) End of the study MRI, EDV (ml) Difference between the groups MRI, ESV (ml) End of the study MRI, ESV (ml) Difference between the groups MRI, ESV (MRI) End of the study, ESV (MRI) difference between the groups, ESV (MRI) difference between the groups, WMSI (MRI) end of the study, WMSI (MRI) difference between groups
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	-

Study	**Fernandez-Aviles et al. 2018[11]**
Study type:	Randomized controlled trial
Number of participants:	49

Countries, setting and Funding:	SPAIN, Belgium, Tigenix S.A.U. (Madrid, Spain) and partially funded by the European FP7-HEALTH-2009-1.4-3 program (Grant 242038) and by the Spanish Cardiovascular Research Network (Red de Investigación Cardiovascular—RIC, RD12/0042/0025).
Duration of study Follow up (post intervention):	12 Months
Subgroup analysis within study	-
Inclusion criteria:	• Patients were eligible for enrollment if they were between 18 and 80 years old, presented with STEMI and had a medium-high risk of developing chronic HF. The latter was defined as LV ejection fraction (EF) ≤45% and infarct size ≥25% of LV mass in the screening MR scan performed 3 to 5 days after STEMI onset. Successful revascularization by percutaneous coronary intervention, within 12 hours after symptom onset with stent implantation and Thrombolysis in Myocardial Infarction flow grade 3, had to be achieved. All critical, non–infarct-related artery lesions should have been treated percutaneously at least 24 hours before MR evaluation. Patients were recruited in 8 participating tertiary academic hospitals.
Exclusion criteria:	-
Recruitment/selection of patients:	Patients were randomly allocated 2:1 to receive allocsc-01 (35×10^6) or placebo.
Intervention: Source and Type of stem cells	Human heart biopsies, Cardiac stem cells- Allogenic
Intervention: Method of their characterization	In the dose-escalation phase, all patients received active treatment at increasing doses of allocsc-01. The target dose was 35×10^6 cells, based on preclinical experiments.10 The first dose to be tested was 10×10^6 cells and the dose-escalation process comprised 3 steps (10×10^6, 20×10^6, and 35×10^6) with a primary follow-up of 7 days for each group of 2 patients before the next escalation step was initiated. Once the dose-escalation short-term safety data were analyzed by the Data and Safety Monitoring Board, patients were randomly allocated 2:1 to receive allocsc-01 (35×10^6) or placebo.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	35 million

Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF MRI Difference, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups, Infarct size (MRI) end of the study, Infarct size (MRI) difference between the groups, WMSI (MRI) end of the study, WMSI (MRI) difference between groups
Safety Outcomes reported with time points- SAEs	
Safety Outcomes reported with time points- Other Adverse Events	Cancer incidence,

Study	**Gao et al. 2013[12]**
Study type:	Randomized controlled trial
Number of participants:	43
Countries, setting and Funding:	China, Funded by a grant from the National Advanced Technology Development Project of China (863 Project).
Duration of study Follow up (post intervention):	24 Months
Subgroup analysis within study	-
Inclusion criteria:	• Between May 2008 and November 2009, patients at 18–80 years with acute STEMI were recruited into this single-blind, randomized control, open-labeled, multicenter exploratory study, who had been successfully reperfused within 12

	hours by means of stent implantation and had a substantial residual left ventricular regional wall motion abnormality on echocardiography, as well as a creatine kinase MB level more than three times the upper reference value.
Exclusion criteria:	• > Previous Q-wave myocardial infarction, 2 > cardiogenic shock, and 3 > severe coexisting conditions (such as advanced renal or hepatic dysfunction or documented terminal illness or cancer) that will influence the patients' compliance with the protocol.
Recruitment/selection of patients:	Randomization and baseline examination: Patients were randomly allocated at the ratio of 1:1 to either the BMSCs or control group (standard medication after primary PCI), with use of sequential numbers.
Intervention: Source and Type of stem cells	BM Aspiration, BM-MSCs
Intervention: Method of their characterization	Cell surface phenotype was determined by flow cytometry. Bmscs were stained with saturating amounts of monoclonal antibodies conjugated with fluorescein isothiocyanate for CD44, CD70, CD90, CD105, CD31, CD34, and CD45, testing procedures for mycoplasma, sterility, endotoxin, identity, and purity were consistent with the International Society for Cellular Therapy (ISCT) criteria.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	3.08 (0.52) million cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF ECHO LVEF (2D ECHO) End of the study, LVEF (2D ECHO) Difference of Difference from baseline, LVEF (ECHO) difference between groups, EDV (ECHO) End of the study, EDV (ECHO) difference between the groups, LVEF (%) End of the study echo, LVEF (%) Difference between the groups Echocardiography, EDV (ml) End of the study Echocardiography,

	EDV (ml) Difference between the groups Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study, ESV (ECHO) difference between groups, ESV (ml) Difference between the groups Echocardiography, WMSI (ECHO) End of the study, WMSI (ECHO) Difference between the group
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Mortality, Hospitalization due to heart failure, Recurrent-MI,

Study	**Gao et al. 2015[13]**
Study type:	Randomized clinical trial
Number of participants:	116
Countries, setting and Funding:	China, Funded by a grant from the National Advanced Technology Development Project of China (863 Project), (2006AA02Z469), (2011AA020102), (2013AA020101)
Duration of study Follow up (post intervention):	18 Months
Subgroup analysis within study:	-
Inclusion criteria:	• Patients had to satisfy the following eligibility criteria: 18- to 80-years old; a first ST segment elevation MI; successful reperfusion with stent implantation of the infarct-related artery within 12 hours after the onset of symptoms; a substantial residual LV regional wall-motion abnormality (three or more hypokinetic LV segments observed on an echocardiograph after percutaneous coronary intervention, PCI); and creatine kinase (CK)- MB levels over three-fold the upper limit of the reference values.
Exclusion criteria:	• Previous Q-wave MI and severe coexisting conditions, such as advanced renal or hepatic dysfunction, and documented terminal illness or cancer. All subjects were administered medications according to the current updated ACC/AHA/SCAI

	guidelines along with standard rehabilitation programs for MI.
Recruitment/selection of patients:	The eligible patients were assigned randomly to each of two groups (WJ_MSCS or placebo control) in a 1:1 fashion using a computer-generated randomization of sequence numbers.
Intervention: Source and Type of stem cells	Umbilical cord, WJ-MSCS
Intervention: Method of their characterization	The infused WJ-MSCS were harvested at passage 3, during which ≥95% of cells expressed CD29, CD73, CD90 and CD105, while the expression of CD45, CD34, CD14, CD79 and HLA-DR was 2% or less.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	6 million
Intervention: Dose- If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF ECHO LVEF (2D ECHO) End of the study LVEF (2D ECHO) Difference of Difference from baseline LVEF (ECHO) difference between groups, EDV (ECHO) End of the study, EDV (ECHO) difference between the groups, LVEF (%) End of the study echo, LVEF (%) Difference between the groups Echocardiography, EDV (ml) End of the study Echocardiography, EDV (ml) Difference between the groups Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study, ESV (ECHO) difference between groups, ESV (ml) Difference between the groups Echocardiography, WMSI (ECHO) End of the study, WMSI (ECHO) Difference between the group
Safety Outcomes reported with time points- SAEs	-

Safety Outcomes reported with time points- Other Adverse Events	Cancer incidence, Mortality, Hospitalization due to heart failure

Study	**Ge et al. 2006[14]**
Study type:	Randomized controlled trial
Number of participants:	20
Countries, setting and Funding:	China, Shangai Scientific Research Fund
Duration of study Follow up (post intervention):	6 Months
Subgroup analysis within study	-
Inclusion criteria:	• Only patients who were admitted within 24 h after the onset of symptoms of a first ST segment elevation myocardial infarction and had successfully undergone PCI with stent implantation in the infarct-related artery were included in this study.
Exclusion criteria:	• With cardiogenic shock, cardioversion, bleeding, leucopenia, thrombocytopenia, hepatic or renal failure, documented terminal illness, HIV, hepatitis or cancer.
Recruitment/selection of patients:	Eligible patients (n = 20) were randomly allocated at a 1:1 ratio
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	BM-MNCs in the BMT group were prepared by ficoll hypaque gradient centrifugation (Lymphoprep; Axis-Shield poc, Oslo, Norway). BM-MNCs were suspended in 16 ml cold heparinised saline at a density of 2.42 (1.35) x 10^6 cells/ml and kept on ice before transplantation. An equal volume of bone marrow supernatant mixed with heparinised saline was used for patients in the control group. To ensure that a certain percentage of stem cells were present in the infused mononuclear cells, 1 ml BM-MNCs was analysed by fluorescence-activated cell sorter (FACS) after incubation with antihuman monoclonal antibodies: anti-human CD34 (CALTAG Laboratories, Burlingame, California, USA and Coulter Comp) or CD133 (MiltenyiBiotec) antibodies conjugated with fluorescein isothiocyanate (FITC). An FITC-conjugated isotopic serum was used as the isotype control. FACS analysis showed that BM-MNCs were

	4.7% positive for CD34 and 0.79% positive for CD133.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	40 million cells; 4.7% $CD34^{+}$
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF (2D ECHO) End of the study, LVEF (%) End of the study echo, Perfusion defect score, LVEDD (ECHO) End of the study
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	-

Study	**Grajek et al. 2010[15]**
Study type:	Randomized controlled trial
Number of participants:	45
Countries, setting and Funding:	Poland, Grant from the Polish Cardiac Society sponsored by Servier Polska and by a grant from the Polish Committee for Scientific Research (Komitet Badan Naukowych) PBZ-KBN-099/ P05/03.
Duration of study Follow up (post intervention):	12 Months
Subgroup analysis within study	-
Inclusion criteria:	• First AMI of anterior wall with ST elevation within 12 h from symptom onset; age between 35 and 70, and; the absence of critical stenosis in other than left anterior descending (LAD), which was infarct-related artery (IRA).
Exclusion criteria:	• Previous MI, insulin-dependent diabetes mellitus, cardiogenic shock, pulmonary oedema, renal or hepatic dysfunction, and other severe disease or suspected inability to comply with the study protocol. Patients underwent immediate primary angioplasty with bare metal stent implantation
Recruitment/selection of patients:	Patients having numbers 1-4 were allocated to the treatment group, whereas patients

	having numbers 5 or 6 were allocated to the control group (2:1 ratio).
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	Bone marrow from the pelvic bones was collected to phosphate buffered saline (PBS) with heparin (50 U/ml) from 31 patients under local anaesthesia. Total volume of aspirates ranged from 50 to150 ml, mean 80 ml. The material was diluted 1:2 with PBS and then centrifuged on Ficoll gradient (400g, 30 min, 18^{o}C). Mononuclear cells were removed from the interphase between the red cells and the Ficoll. After washing in PBS with heparin (200g, 10 min, 18^{o}C), cells were resuspended in a few millilitres of X-vivo 15 medium (biowhittaker, USA) with 2% heat-inactivated autologous plasma. The cells were counted automatically using Micros 60 (ABX, Germany). The haematopoietic cells were identified by three-colour immunofluorescence using FACS scan flow cytometry (Becton-Dickinson, USA). The following antibodies were used: CD34-FITC, CD133-PE, CD45-API. Mononuclear cells (1 106 in 1 ml) were placed in Teflon bags (Vuelife, Cell Genix, USA) and overnight cultivated (5% CO^{2}, 37^{o}C, 100% humidity) in X-vivo 15 medium with 2% heat-inactivated autologous plasma. The next day, cells were harvested and washed three times with heparinized PBS. Viability with the use of trypan blue test was 94+3%. Microbiological tests of the clinically used cell preparations were negative.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	410 (180) million
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF (2D ECHO) End of the study, LVEF (Radionucleotide ventriculography) end of the study, EDV (ECHO) End of the study, LVEF (%) End of the study echo, LVEF (%) End of the study Radionucleotide Angiography, EDV (ml) End of the study Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study,

	WMSI (ECHO) End of the study
Safety Outcomes reported with time points- SAEs	SAEs Unstable Angina (1 in each group)
Safety Outcomes reported with time points- Other Adverse Events	Restenosis Mortality, Recurrent-MI,
Study	**Haddad et al. 2020[16]**
Study type:	Randomized controlled trial
Number of participants:	37
Countries, setting and Funding:	Canada, Samer Mansour and Nicolas Noiseux received financial support from Fonds de la recherche en santé du Québec, MiltenyiBiotec, Inc. And Boston Scientific in Canada.
Duration of study Follow up (post intervention):	8.5 Years
Subgroup analysis within study	-
Inclusion criteria:	• Age between 30 and 75 years, chest pain for more than 30 min and less than 24 h, electrocardiography ST segment elevation >1 mm in two consecutive leads in the limb leads or >2 mm in the precordial leads, and an increase in creatine kinase (CK) or CK-muscle and brain types (CK-MB). Patients need to be 25%, and significant regional wall motion abnormalities in at least two adjacent segments on the resting echocardiography.
Exclusion criteria:	• Patients with known previous MI, those who presented with cardiogenic shock, chronic cardiomyopathy, liver disease, renal failure, concomitant disease with a life expectancy of less than 1 year, alcohol or drug dependency, and contraindication for bone marrow aspiration are excluded from our trial. Other exclusion criteria include blood transfusion in the previous 24 h, hematopoietic disease, chronic inflammatory disease, malignancy, stroke in the previous 3 months or transient ischemic attack in the previous 24 h, or extended ongoing myocardial infarction as evidenced by a new episode of chest pain with new ST segment elevations and a new CK/CK-MB peak.

Recruitment/selection of patients:	Patients are randomized either to the $CD133^+$ cells treatment or placebo group.
Intervention: Source and Type of stem cells	BM Aspiration, $CD133^+$
Intervention: Method of their characterization	Bone marrow-derived $CD133^+$ autologous progenitor cells for this trial are immunomagnetically selected using the clinimacs® system (Miltenyi Biotec gmbh) at the HMR Cellular Therapy Laboratory. Briefly, immunomagnetic particles composed of iron oxide and dextran conjugated to monoclonal antibodies bind to target cells expressing the $CD133^+$ cell surface antigen. When exposed to a magnetic field, labeled cells are retained within the column and separated from unlabeled cells.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	10 million cells except in one patient (5.2 million)
Intervention: Dose- If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF MRI Difference, LVEF (MRI) difference between the groups, LVEF (%) Difference between the groups MRI,
Safety Outcomes reported with time points- Serious AEs	
Safety Outcomes reported with time points- Other Adverse Events	Cancer incidence, Mortality, Hospitalization due to heart failure Recurrent-MI, Arrhythmia frequency, Revascularization frequency Stroke frequency

Study	**Hare et al. 2009[17]**
Study type:	Randomized controlled trial
Number of participants:	60
Countries, setting and Funding:	USA, Drs. Hare, Gerstenblith, and Schulman also received support from the Johns

	Hopkins University School of Medicine General Clinical Research Center and National Institutes of Health Specialized Center for Cell-based Therapy (SCCT) grant U54 HL081028. Dr. Demaria has received research funding/grants from Lantheus, Acusphere, CV Therapeutics, Cardiovascular Biotherapeutics, Angioblast Systems, Inc., Philips Medical Systems
Duration of study Follow up (post intervention):	12 Months
Subgroup analysis within study	-
Inclusion criteria:	• Patients must have had a first MI (either ST-segment elevation or non–ST-segment elevation) 1 to 10 days before randomization. All patients were required to have a patent infarct related artery on coronary angiography at the time of randomization. Angiographic measures included epicardial blood flow and myocardial perfusion, as assessed by Thrombolysis in Myocardial Infarction (TIMI) flow grade and TIMI myocardial perfusion grade respectively. • The index MI for all patients enrolled met the following criteria: elevation of >2X upper limit of normal of creatine kinase-MB or troponin; presence of regional wall motion abnormality; an; global left ventricular ejection fraction (LVEF) of ≤60% and ≥30% as determined by 16-segment echocardiogram or ventriculogram.
Exclusion criteria:	• Patients were not enrolled in the trial if revascularization via coronary artery bypass surgery was required or if the physician anticipated further coronary revascularization procedures during the 6-month study period. Patients with clinically significant primary valvular heart disease or evidence of life-threatening arrhythmia on baseline electrocardiogram (ECG) were also excluded.
Recruitment/selection of patients:	Patients were enrolled by study investigators. Randomization, stratified by dose cohort, was conducted in a centralized manner and communicated to cellular therapy laboratory personnel. Subjects were randomly assigned to either Prochymal or placebo in a 2:1 ratio within each cohort.
Intervention: Source and Type of stem cells	BM Aspiration, HMSC- allogenic
Intervention: Method of their characterization	The phenotype of the HMSC population was characterized by a cell-surface profile of $CD10^{+}$, $CD166^{+}$, and $CD45^{-}$. The infused Prochymal formulation consists of 2.5x 10^{6} HMSCs/ml, 1.9% human serum albumin, and 3.8% dimethyl sulfoxide in plasmalyte A

	(Baxter, Deerfield, Illinois). Patients assigned to placebo groups received a solution of 1.9% human serum albumin with 3.8% dimethyl sulfoxide in PlasmaLyte A. Release testing of the cells included measurement of cell-surface markers CD105 and CD166, absence of CD45, testing for mycoplasma, sterility, endotoxin, identity, purity, and viability and karyotyping to exclude chromosomal abnormalities.
Intervention: Route of administration	Intravenous
Intervention: Dose	5 million HMSCs/kg body weight
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF MRI Difference LVEF (2D ECHO) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study echo, LVEF (%) Difference between the groups MRI, EDV (MRI) difference between the groups, EDV (ml) Difference between the groups MRI, ESV (ml) Difference between the groups MRI, ESV (MRI) difference between the groups, ESV (MRI) difference between the groups,
Safety Outcomes reported with time points- Serious AEs	SAEs, Events Name Not Mentioned, Only Number Mentioned
Safety outcomes reported with time points- Other Adverse Events	Arrhythmia frequency

Study	**Huikuri et al. 2008[18]**
Study type:	Randomized clinical trial
Number of participants:	80
Countries, setting and Funding:	Finland, Grants from the Medical Council of the Academy of Finland. Helsinki, Finland, from the Finnish Foundation for Cardiovascular Research, Helsinki, Finland, and the

	Foundation for the Northern Health Support, Boston Scientific Sverige AB. Stockholm, Sweden.
Duration of study Follow up (post intervention):	6 Months
Subgroup analysis within study	-
Inclusion criteria:	-
Exclusion criteria:	-
Recruitment/selection of patients:	The randomization code for each patient using a computer-generated random-permuted block design with variable block sizes and selected on the basis of whether suspension containing BMCs or placebo medium was given to each patient.
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	To assess the validity of our cell preparation system, we assessed the BMCs function and viability using a colony-forming unit assay as follows: The BM-MNCS (including $2x10^3$ $CD34^+$ cells per plate) were seeded in methylcellulose plates in triplicate (Methocult GF H84434, Stem Cell Technologies, Vancouver, Canada), with PHA-stimulated human leucocyte-conditioned medium and foetal bovine serum as growth factors. Culture plates were incubated at 37^0C in a humidified atmosphere with 5% CO^2 for 14 days. Thereafter, the granulocyte macrophage colony-forming units (CFU-GM, colonies .50 cells) were classified and counted under phase-contrast microscopy and the mean colony number calculated. In these analyses, a mean of 450 CFUs were formed per plate, indicating a high functional activity of the isolated BMCs.
Intervention: Route of administration	Injected intracoronary through balloon
Intervention: Dose	402 (196) million cells; 2.6(1.6) million $CD34^+$
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF ECHO LVEF (2D ECHO) End of the study, LVEF (2D ECHO) Difference of Difference from baseline, LVEF (ECHO) difference between groups, LVEF (Angiography) difference between groups,

	EDV (ECHO) End of the study, EDV (ECHO) difference between the groups, LVEF (%) End of the study echo, LVEF (%) Difference between the groups Echocardiography, LVEF (%) Difference between the groups Angiography, EDV (ml) End of the study Echocardiography, EDV (ml) End of the study Angiography, EDV (Angiography) end of the study, EDV (Angiography) difference between the groups, EDV (ml) Difference between the groups Echocardiography, EDV (ml) Difference between the groups Angiography, ESV (ml) End of the study Echocardiography, ESV (ml) End of the study Angiography, ESV (ECHO) End of the study, ESV (ECHO) difference between groups, ESV (ml) Difference between the groups Echocardiography, ESV (ml) Difference between the groups Angiography, ESV (Angiography) end of the study, ESV (Angiography) difference between group
Safety Outcomes reported with time points- Serious AEs	SAEs, Major Bledding, No Reflow To Infarct Artery After PCI, Stent Thrombosis, CABG During Follow Up
Safety Outcomes reported with time points- Other Adverse Events	Mortality, Recurrent-MI

Study	**Janssens et al. 2006[19]**
Study type:	Randomized clinical trial
Number of participants:	67
Countries, setting and Funding:	Belgium, Academic trial, no external sponsor
Duration of study Follow up (post intervention):	4 Months

Subgroup analysis within study:	-
Inclusion criteria:	• Aged 18–75 years, with acute myocardial infarction with cumulative ST-segment elevation of 6 mm or more, successful epicardial reperfusion after percutaneous coronary intervention with stent replacement, and significant LV dysfunction (hypokinesia or akinesia, involving more than half of the anterior, septal, or inferior wall, using angiography, or involving three contiguous segments or more out of 17, using echocardiography.
Exclusion criteria:	• To avoid dilution of any treatment effect, resulting from aborted infarctions, we excluded patients who presented within 2h of symptom onset. We also excluded those who had had a previous coronary artery bypass graft, or who had pulmonary oedema, cardiogenic shock, or major co-morbidities.
Recruitment/selection of patients:	We assigned patients, according to a computer generated randomisation list, in a one-to-one ratio, using sequentially numbered sealed envelopes.
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	With respect to cell transfer, centrifugation and resuspension reduced cell volume from the bone marrow harvest (mean 130 ml, SD 22) to a final volume of 10 ml, which we injected into the infarct-related coronary artery, and which contained 304106 (SD 128106) nucleated cells and 172*10*6 (72106) mononuclear cells. FACS analysis revealed 2·8*10*6 (1·7*10*6 $CD34^+$, 2·0*10*6 (1·3*10*6) $CD133^+$, 0·2 10*6 (0·15106) CD90/Thy1, 2·5106 (2·0*10*6) CD105/endoglin, 7·0106 (3·9106) CD117/c-kit, and 32106 (20106) CD73cells.
Intervention: Route of administration	Injected intracoronary through balloon
Intervention: Dose	172(72) million cells; 2(1.3) million $CD34^+$
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF MRI Difference LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI,

	LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups
Safety Outcomes reported with time points- SAEs	SAEs, In Stent thrombosis, Reangina
Safety Outcomes reported with time points- Other Adverse Events	Arrhythmia frequency, Restenosis, Mortality

Study	**Kaminek et al. 2008[20]**
Study type:	
Number of participants:	62
Countries, setting and Funding:	Czech Republic.
Duration of study Follow up (post intervention):	12 Months
Subgroup analysis within study	-
Inclusion criteria:	• Successful recanalization of the infarct related artery thrombolysis in MH flow grade 3; a significant increase in cardiac enzymes, i.e., creatine kinase (CK) more than 20 kat/L or CK-MB over 3 kat/L or troponin I over 20 g/L (the normal upper limits in our laboratories are 2.85 kat/L, 0.42 kat/L, and 2.0 g/L, respectively); and; irreversible damage of at least 2 akinetic or dyskinetic myocardial segments identified by dobutamine echocardiography and confirmed by at least rest-gated MIB SPECT. In patients, who underwent fluorodeoxyglucose PET (95% of patients), the PET evidence of non-viability of the infarcted myocardium was also required.
Exclusion criteria:	-
Recruitment/selection of patients:	The patients were initially randomized in a 1:1:1 ratio into 3 categories: (1) a treatment group (autologous BMC transplantation) treated with the lower dose of cells ($1x10^7$ cells), (2) a treatment group treated with a higher cell dose ($1x10^8$ cells), and (3) a control group without the cell transplantation therapy.

Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	-
Intervention: Route of administration	Injected intracoronary through balloon
Intervention: Dose	100 million
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	100 million
Efficacy Outcomes reported with time points:	LVEF (2D ECHO) End of the study, EDV (ECHO) End of the study, LVEF (%) End of the study echo, EDV (ml) End of the study Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	-

Study	**Kim et al. 2018[21]**
Study type:	Randomized clinical trial
Number of participants:	26
Countries, setting and Funding:	SOUTH KOREA, no funding received
Duration of study Follow up (post intervention):	12 Months
Subgroup analysis within study	-
Inclusion criteria:	• Patients were eligible if they were admitted to the hospital less than 24 h after the onset of chest pain; presented an electrocardiography (ECG) showing ST-segment elevation greater than 1 mm in two consecutive leads, greater than 2 mm in the precordial leads; and could be enrolled in the study less than 72 h after successful revascularization of anterior AMI (defined as residual stenosis less than 30% of left anterior descending artery [LAD] infarction) and EF ≤ 40%.
Exclusion criteria:	• Patients excluded with non-LAD infarction, cardiogenic shock, life-threatening

	arrhythmia, advanced renal or hepatic dysfunction, history of previous coronary artery bypass graft, history of hematologic disease and malignancy, major bleeding requiring blood transfusion, stroke or transient ischemic attack in the previous 6 months, use of corticosteroids or antibiotics during the previous month, major surgical procedure in the previous 3 months, cardiopulmonary resuscitation for more than 10 min within the previous 2 weeks, positive results for viral markers [human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), and Venereal Disease Research Laboratory (VDRL) test], and pregnancy or possible pregnancy.
Recruitment/selection of patients:	-
Intervention: Source and Type of stem cells	BM Aspiration, BM-MSCs
Intervention: Method of their characterization	We excluded patients with non-LAD infarction, cardiogenic shock, life-threatening arrhythmia, advanced renal or hepatic dysfunction, history of previous coronary artery bypass graft, history of hematologic disease and malignancy, major bleeding requiring blood transfusion, stroke or transient ischemic attack in the previous 6 months, use of corticosteroids or antibiotics during the previous month, major surgical procedure in the previous 3 months, cardiopulmonary resuscitation for more than 10 min within the previous 2 weeks, positive results for viral markers [human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), and Venereal Disease Research Laboratory (VDRL) test], and pregnancy or possible pregnancy.
Intervention: Route of administration	Injected intracoronary through balloon
Intervention: Dose	72 (9) million
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF ECHO LVEF (2D ECHO) End of the study, LVEF (ECHO) difference between groups, LVEF (SPECT) End of the study,

	LVEF (SPECT) difference between the groups, EDV (ECHO) End of the study, EDV (ECHO) difference between the groups, LVEF (%) End of the study echo, LVEF (%) End of the study SPECT, LVEF (%) Difference between the groups Echocardiography, LVEF (%) Difference between the groups SPECT, EDV (SPECT) End of the study, EDV (SPECT) difference between the groups, EDV (ml) End of the study Echocardiography, EDV (ml) End of the study SPECT, EDV (ml) Difference between the groups Echocardiography, EDV (ml) Difference between the groups SPECT, ESV (ml) End of the study Echocardiography, ESV (ml) End of the study SPECT, ESV (ECHO) End of the study, ESV (ECHO) difference between groups, ESV (ml) Difference between the groups Echocardiography, ESV (ml) Difference between the groups SPECT, ESV (SPECT) End of the study, ESV (SPECT) difference between the groups
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Arrhythmia frequency

Study	**Laguna et al. 2018[22]**
Study type:	Randomized, controlled clinical trial
Number of participants:	20
Countries, setting and Funding:	SPAIN, No financial support
Duration of study Follow up (post intervention):	9 Months

Subgroup analysis within study	-
Inclusion criteria:	-
Exclusion criteria:	-
Recruitment/selection of patients:	LVEF lower than 50% assessed by ventriculography from 2007 to 2015 were included. Patients were randomized into two groups within 10 days of transmural AMI
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	Bone marrow (50 ml) was obtained 24 hours before surgery under local anesthesia by puncture of the iliac crest of the patient. The mononuclear fraction of the bone marrow diluted in phosphate-buffered saline (PBS)/heparin was prepared using Ficoll medium. The final product was resuspended in heparinized Ringer's lactate solution prepared for its infusion. A cell suspension with a final volume of 10 ml in 1% albumin diluted in physiological serum was prepared for intramyocardial injection. The cell count was adjusted to 1 million cells per milliliter Stem cells were typed using an immunoassay to assess the percentage of $CD34^+$, $CD117^+$ and $CD133^+$ cells grafted in each patient
Intervention: Route of administration	Direct intramyocardial injection
Intervention: Dose	1 million cells per millilitre
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF MRI Difference LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV (MRI) End of the study, EDV (MRI) difference between the groups, EDV (ml) End of the study MRI, EDV (ml) Difference between the groups MRI, ESV (ml) End of the study MRI,

	ESV (ml) Difference between the groups MRI, ESV (MRI) End of the study, ESV (MRI) difference between the groups, ESV (MRI) difference between the groups, WMSI (MRI) end of the study, WMSI (MRI) difference between groups
Safety Outcomes reported with time points- Serious AE	SAEs DVT (1) AND DEFIB IMPLANTATION (1)
Safety Outcomes reported with time points- Other Adverse Events	Arrhythmia frequency Stroke frequency Mortality

Study	**Lezo et al. 2007[23]**
Study type:	Randomized clinical trial
Number of participants:	20
Countries, setting and Funding:	Spain
Duration of study Follow up (post intervention):	3 Months
Subgroup analysis within study	-
Inclusion criteria:	• patients with anferior wall AMI arriving at the hospital within 12 hours of the onset of symptoms; Poor LV-function (angiographic EF <45%); Early reperfusion of the left anterior descending artery, by intravenous administration of fibrinolytics or by rescue percutaneous coronary intervention; and in all instances, full stent revascularization of the left anterior descending artery supplying the anterior wall was mandatory to enter the study.
Exclusion criteria:	• Age >80 years; mechanical complications of AMI or cardiogenic shock; hematologic disorders: and; concomitant malignant or pre-malignant systemic disease.
Recruitment/selection of patients:	3 groups im 1:1:1
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs

Intervention: Method of their characterization	-
Intervention: Route of administration	Injected intracoronary through balloon
Intervention: Dose	900 (300) million; 17(13) million $CD34^+$
Intervention: Dose- If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF (Angiography) End of the study, LVEF (%) End of the study Angiography, EDV Index (Angiography) End of the study, ESV Index (Angiography)
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	-

Study	**Lee et al. 2014[24]**
Study type:	Randomized clinical trial
Number of participants:	80
Countries, setting and Funding:	South Korea, FCB-Pharmicell Company Limited (Seongnam, Korea) supported this study
Duration of study Follow up (post intervention):	6 Months
Subgroup analysis within study	-
Inclusion criteria:	• Aged 18-70 yr; they had ischemic chest pain for > 30 min; they were admitted to hospital < 24 hr after the onset of chest pain; electrocardiography (ECG) showed ST segment elevation >1 mm in two consecutive leads in the limb leads or > 2 mm in the precordial leads; and they could be enrolled in the study < 72 hr after successful revascularization (defined as residual stenosis < 30% of the infarct-related artery [IRA]).
Exclusion criteria:	• patients with cardiogenic shock, life-threatening arrhythmia, advanced renal or hepatic dysfunction, history of previous coronary artery bypass graft, history of hematologic disease and malignancy, major bleeding requiring blood transfusion,

	stroke or transient ischemic attack in the previous 6 months, use of corticosteroids or antibiotics during the previous month, major surgical procedure in the previous 3 months, cardiopulmonary resuscitation for >10 min within the previous 2 weeks, positive skin test for penicillin, positive result for viral markers (human immunodeficiency virus [HIV], hepatitis B virus [HBV], hepatitis C virus [HCV] and Venereal Disease Research Laboratory [VDRL] test), pregnant woman and possible candidate for pregnancy.
Recruitment/selection of patients:	1:1
Intervention: Source and Type of stem cells	BM Aspiration, BM-MSCs
Intervention: Method of their characterization	On the day of administration, MSCs were harvested using trypsin and EDTA, washed twice with PBS and once with saline solution, and resuspended to a final concentration of $1x10^6$ cells/kg. The criteria for the release of MSCs for clinical use included viability > 80%, absence of microbial contamination (bacteria, fungus, virus, and mycoplasma) if undertaken 3-4 days before administration, and expression of CD73 and CD105 by > 90% of cells and absence of CD14, CD34, and CD45 by < 3% of cells as assessed by flow cytometry (data not shown). Also, the in vitro osteogenic and cardiomyogenic differentiation potential of MSCs in passage 0 or 1 was tested before release as a potency test.
Intervention: Route of administration	Injected intracoronary through balloon
Intervention: Dose	72 (9) million cells
Intervention: Dose- If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF ECHO, LVEF (2D ECHO) End of the study, LVEF (2D ECHO) Difference of Difference from baseline, LVEF (ECHO) difference between groups, LVEF (SPECT) End of the study, LVEF (SPECT) difference between the groups, EDV (ECHO) End of the study,

	EDV (ECHO) difference between the groups, LVEF (%) End of the study echo, LVEF (%) End of the study SPECT, LVEF (%) Difference between the groups Echocardiography, LVEF (%) Difference between the groups SPECT, EDV (SPECT) End of the study, EDV (SPECT) difference between the groups, EDV (ml) End of the study Echocardiography, EDV (ml) End of the study SPECT, EDV (ml) Difference between the groups Echocardiography, EDV (ml) Difference between the groups SPECT, ESV (ml) End of the study Echocardiography, ESV (ml) End of the study SPECT, ESV (ECHO) End of the study, ESV (ECHO) difference between groups, ESV (ml) Difference between the groups Echocardiography, ESV (ml) Difference between the groups SPECT, ESV (SPECT) End of the study, ESV (SPECT) difference between the groups, WMSI (ECHO) End of the study, WMSI (ECHO) Difference between the group
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	-

Study	**Lunde et al. 2007[25]**
Study type:	Randomized clinical trial
Number of participants:	100
Countries, setting and Funding:	Norway, NOT FUNDED
Duration of study Follow up (post intervention):	6 Months

Subgroup analysis within study:	-
Inclusion criteria:	• Age 40–75 years; anterior wall AMI with 120–720 min from onset of symptoms to PCI; ST-elevation on ECG according to WHO criteria; angiographically significant stenosis on LAD proximal to the second diagonal branch; successful PCI with stenting of culprit lesion; ≥3 hypokinetic, akinetic or dyskinetic segments assessed by echocardiography in a standard 16 segment model and; creatine kinase MB (CK-MB) above three times upper reference value.
Exclusion criteria:	• Previous MI with established significant Q-waves on ECG cardiogenic shock; permanent pacemaker or other contraindication to MRI; stroke with significant sequela; short life expectancy due to extra cardiac reason; uncontrolled endocrinological disturbance; HIV and/or HBV/HCV positive serology and; mental disorder or other condition which interferes with patient possibility to comply with the protocol. A patient is included in the study if eligible and after giving written informed consent.
Recruitment/selection of patients:	Patients are included and randomized in a 1:1 way to either intracoronary transplantation of autologous BMC or control.
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	The bone marrow aspirate is diluted in 75 ml NaCl, and is gradient centrifuged on Lymphoprep (Axis-Shield, Oslo, Norway). The MBMCs are washed three times with NaCl containing 5% autologous plasma prior to resuspension in 11 ml NaCl with 20% plasma for overnight storage. The next day, the MBMCs suspension is filtered through a 70 µm sieve prior to quality control analysis and intracoronary transplantation. All cell preparation takes place in a laboratory approved according to good manufacturing practice (GMP) by the Norwegian Medicines Agency for ex vivo cell manipulation. Samples are tested for bacterial contamination, cell yield, viability, aggregate count and content of $CD34^+$ cells and $CD34^+$ cell subpopulations. Cell viability has to be above 90%, bacterial specimens should be negative and the proportion of cell aggregates ≥3 cells should be less than 10% of all cells to permit intracoronary transplantation.
Intervention: Route of administration	Injected intracoronary through balloon

Intervention: Dose	68 (IQR 54-130) million
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	Quality of life
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	-

Study	**Mathur et al. 2020[26]**
Study type:	Randomized clinical trial
Number of participants:	375
Countries, setting and Funding:	Multicentre, UK Stem Cell Foundation, the Heart Cells Foundation and Barts and the London Charity.
Duration of study Follow up (post intervention):	24 Months
Method of assessment of disease condition:	Patients 18 years of age or older with an acute ST-elevation myocardial infarction (as defined by the universal definition of AMI) undergoing acute revascularization (i.e. Either acute percutaneous coronary intervention (PCI) within 24 h of symptom onset or thrombolysis within 12 h, followed by acute PCI within 24 h after thrombolysis).
Subgroup analysis within study	-
Inclusion criteria:	• Signed and dated informed consent; Men and women of any ethnic origin aged ≥ 18 years; Patients with acute ST-elevation myocardial infarction as defined by the universal definition of AMI (including new LBBB); Successful acute reperfusion therapy (residual stenosis visually <50% and TIMI flow ≥2) within 24 hours of symptom onset or thrombolysis within 12 hours of symptom onset followed by successful percutaneous coronary intervention (PCI) within 24 hours after thrombolysis; Left ventricular ejection fraction ≤ 45% with significant regional wall motion abnormality assessed by quantitative echocardiography (central, independent core lab analysis) 2 to 6 days after reperfusion therapy; Open coronary artery suitable for cell infusion supplying the target area of abnormal

	wall motion.
Exclusion criteria:	• Participation in another clinical trial within 30 days prior to randomisation unless non interventional trials or trials where patients are randomised to only standard care and this has been discussed and agreed with the CI/sponsor prior to consenting; Previously received stem/progenitor cell therapy; Pregnant or nursing women; Mental condition rendering the patient unable to understand the nature, scope and possible consequences of the study or to follow the protocol ; Necessity to revascularise additional vessels, outside the target coronary artery at the time of BM-MNC infusion (additional revascularisations after primary PCI and before BM-MNC cell infusion are allowed), unless clinically indicated and according to latest guidelines. This decision should be made at the time of the index procedure and explicitly stated at that time; Cardiogenic shock requiring mechanical support; Platelet count <100,000/µl, or hemoglobin<8.5 g/dl; Impaired renal function, i.e. Serum creatinine>2.5 mg/dl; Persistent fever or diarrhoea not responsive to treatment within 4 weeks prior screening ; Clinically significant bleeding within 3 months prior screening ; Uncontrolled hypertension (systolic >180 mmhg and diastolic >120 mmhg); Life expectancy of less than 2 years from any non-cardiac cause or neoplastic disease
Recruitment/selection of patients:	Eligible patients were randomized to the control arm or treatment arm in a 1:1 ratio
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	For patients randomized to the treatment arm, a bone marrow aspirate was performed under local anaesthesia within 2–8 days of the primary PCI. Fifty millilitres of bone marrow was drawn into 5-10 ml heparinized syringes. The aspirates were immediately transported to a dedicated cell processing facility where the bone marrow-derived mononuclear cells (BM-MNCs) were isolated using a Ficoll density gradient as per the t2cure method. Following separation, the BM-MNCs was re-suspended in X-Vivo 10 medium and returned to the source site in a cryocytevr bag. The BM-MNCs (range 25–500x10^6 as per protocol) were infused into the culprit coronary artery that was treated with primary PCI at the index admission, using an over-the-wire balloon that matched the

	vessel dimensions. Infusion used the stop-flow technique: 3 min of balloon inflation with cells delivered through the central lumen of the catheter, followed by 3 min of flow with the balloon down. This cycle was repeated three times to deliver the full 10 ml of cells—3 stop-flow cycles of 3.3 ml each. Patients randomized to the treatment arm were infused with BM-MNCs 2–8 days following the primary PCI. Procedural anticoagulation was performed with bivalirudin not heparin due to the possible interaction between the latter and the BM-MNCs.
Intervention: Route of administration	Injected intracoronary through balloon
Intervention: Dose	25-500 million
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	-
Safety Outcomes reported with time points- SAEs	SAEs, ONLY NUMBER MENTIONED, DEFINATION OF SAEs IN SUPPLEMENT
Safety Outcomes reported with time points- Other Adverse Events	Cancer incidence, Mortality, Recurrent-MI, Cardiovascular mortality, Arrhythmia frequency, Revascularization frequency, Stroke frequency
Study	**Meyer et al. 2009[27]**
Study type:	Randomized clinical trial
Number of participants:	60
Countries, setting and Funding:	Germany, Hannover Medical School
Duration of study Follow up (post intervention):	5 Years
Subgroup analysis within study	-
Inclusion criteria:	• Patients were eligible if they were admitted within 5 days of the onset of symptoms of a first ST-segment elevation myocardial infarction, had undergone

	successful PCI with stent implantation in the infarctrelated artery, and had hypokinesia or akinesia involving more than two thirds of the left-ventricular anteroseptal, lateral, and/or inferior wall, as shown by angiography done immediately after PCI.
Exclusion criteria:	• We excluded patients who had multivessel coronary artery disease, pulmonary oedema, cardiogenic shock, advanced renal or hepatic dysfunction, or documented terminal illness or cancer.
Recruitment/selection of patients:	Patients were randomly allocated in a 1:1 ratio to either the control or bone-marrow-cell groups,
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	6–8 h after bone-marrow harvest, the final preparation of bone-marrow cells was infused into the infarct-related artery via the central lumen of an over-the-wire balloon catheter (Concerto, Occam International, Eindhoven, Netherlands). To allow bone-marrow cells maximum contact time with the microcirculation of the infarct-related artery, the balloon was inflated inside the stent to transiently interrupt antegrade blood flow during infusions. The entire bone-marrow cell preparation was infused during four to five coronary occlusions, each lasting 2·5–4 min. Between occlusions, the coronary artery was reperfused for 3 min.
Intervention: Route of administration	Injected intracoronary through balloon
Intervention: Dose	2460 (940) million, 9.5 (6.3) million $CD34^+$
Intervention: Dose- If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF MRI Difference, LVEF (%) End of the study MRI, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups,

	ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups, NYHA FCI end of the study
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Cardiovascular mortality, Mortality, Hospitalization due to heart failure, Recurrent-MI, Arrhythmia frequency, Revascularization frequency

Study	**Naseri et al. 2018[28]**
Study type:	Randomized clinical trial
Number of participants:	Tehran, Iran Financially supported in part by a grant from Royan Institute, the Iran Industrial Development and Renovation Organization (IDRO), and the Small Business Development Center (SBDC).
Countries, setting and Funding:	77
Duration of study Follow up (post intervention):	18 Months
Subgroup analysis within study:	-
Inclusion criteria:	• Age: 18-75 years; First ST elevation myocardial infarction (STEMI) 10 days-3 months; post-acute myocardial infarction (AMI) left ventricular ejection fraction (LVEF) as assessed by echocardiography: 20-45%; Target lesion must be in the left anterior descending (LAD) section; Coronary artery bypass graft (CABG) candidate; At least 4 akinetic segments (assessed by stress echocardiography).
Exclusion criteria:	• History of prior AMI; Active infection history of recurrent infection positive test for syphilis (RPR), hepatitis B and C (HBsAg, anti- HBc, anti-HCV), HIV or HTLV-1; Documented terminal illness or malignancy; Documented autoimmune disease, ; Pulmonary edema; Urgent or emergency; CABG Systolic blood

	pressure<80mmHg; 4000>leukocytes (µl)>15000; AST>100 IU/L or ALT>100 IU/L; Hemoglobin10g/dL; platelets<100,000 l, (12) INR>1.8
Recruitment/selection of patients:	We randomized 77 eligible patients via a computer-generated randomization sequence in a 1:1:1 ratio between the $CD133^+$, the MNC, and placebo groups
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs; $CD133^+$
Intervention: Method of their characterization	Patients underwent bone marrow aspiration 24 hours before CABG. MNCs and $CD133^+$ cells were isolated by Ficoll density gradient and a CliniMACS machine. Isolated cells were analyzed by flow cytometry before intramyocardial injection. Bone marrow MNCs (150 ml) were isolated under Good Manufacturing Practice (GMP) conditions by centrifuging the resultant bone marrow through a low-density gradient using Ficoll-Paque PREMIUM (Lymphodex, Inno-train, 002041600) according to the manufacturer's protocol. Briefly, bone marrow samples [diluted 1:1 in phosphate buffered saline (PBS)] were subsequently loaded over a Ficoll-Paque at a 3:1 ratio and centrifuged for 30 minutes at 400 g with no brake. Cells were collected at the interface and washed in PBS buffer (1:1; Milteny Biotech GmbH, 700-25). Cell viability and counts were determined by trypan blue exclusion staining and a Nucleo Counter. Bone marrow MNCs were counted by a Nucleo Counter instrument (Chemo Metec A/S, Denmark). $CD133^+$ cells were isolated by a CliniMACS automated machine. The bone marrow cell suspension was filtered through a 200 µm filter (Baxter S.A, RMC 5849). We used a 10% Gamunex reagent as the blocking antibody (100 mg/ml, Talecris Biotherapeutics, Inc.). A monoclonal magnetic micro-bead antibody that had the capability to detect $CD133^+$ cells (Milteny Biotech GmbH, 172-01) was applied. The magnetically labeled cell bags were subsequently attached to a CliniMACS tubing set LS (Milltenyi Biotec GmbH) and sorted by a CliniMACS instrument. We assessed cell count, viability, and sterility, after which the positive fractions were centrifuged for 5 minutes at 350 g. We assessed for cell specific marker expressions in the cell populations by flow cytometry. Cells were stained with phycoerythrin (PE) or fluorescein isothiocyanate (FITC) conjugated antihuman CD133 (293C3, Milteny Biotech GmbH, 130- 090-853),

	hVEGFR2/KDR (R&D Systems, FAB357P), CD31 (BD Biosciences, 555445), CD45/34 (BD Biosciences, 341071), and CD44 (BD Biosciences, 555479) antibodies, IgG2b/RPE (BD Biosciences, 556656), and IgG1FITC/IgG1RPE (Dako, X0932). Next, they were analyzed with a BD FACSCalibur flow cytometry system (BD Biosciences, San Jose, CA, USA) and software version 2.5.1 (BD Biosciences) by gating at 2% of the isotype control. A total of 100,000 events were acquired for each marker and isotype.
Intervention: Route of administration	Direct intramyocardial injection
Intervention: Dose	564.63 million (± 69.35) MNC cells; 8.19 million (± 4.26) $CD133^+$ cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF (SPECT) End of the study, LVEF (SPECT) difference between the groups, LVEF (%) End of the study SPECT, LVEF (%) Difference between the groups SPECT, WMS (SPECT) End of the study
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Mortality, Hospitalization due to heart failure Recurrent MI,

Study	**Ostovaneh et al. 2021[29]**
Study type:	Randomized clinical trial
Number of participants:	142
Countries, setting and Funding:	Supported by the California Institute of Regenerative Medicine and Capricor Therapeutics
Duration of study Follow up (post intervention):	12 Months
Subgroup analysis within study	-
Inclusion criteria:	• History of MI due to atherosclerotic coronary artery disease within the prior 4

	weeks to 12 months; History of percutaneous coronary intervention with stent placement resulting in TIMI 3 flow in the coronary artery supplying the infarcted, dysfunctional territory and through which the treatment will be infused; Left ventricular ejection function ≤45%†‡; Left ventricular infarct size ≥15% of left ventricular mass as determined by screening MRI, with associated thinning and/or hypokinesis, akinesis, or dyskinesis, with no large aneurysmal area in the infarcted regions; No further revascularization clinically indicated at the time the subject is assessed for participation in the clinical trial; Ability to provide informed consent and follow-up with protocol procedures; Age ≥18 years.
Exclusion criteria:	• History of coronary artery bypass surgery and a graft (arterial or venous) attached to the coronary artery to be infused; Diagnosed or suspected myocarditis; History of cardiac tumor or cardiac tumor demonstrated on screening MRI; History of previous stem cell therapy; History of radiation treatment to the chest or thorax; Current or history (within the previous 5 years) of systematic auto-immune or connective tissue disease; History of or current treatment with immunosuppressive, anti-inflammatory, or other agents to treat manifestations of systemic immunologic reactions; Prior ICD and/or pacemaker placement, where study imaging site has not been trained and certified specifically for this protocol to conduct cardiac MRI in patients with ICD and/or pacemaker placement; The presence of a pacemaker and/or ICD generator with any of the following limitations/conditions are excluded; Manufactured before the year 2000; Leads implanted <6 weeks prior to signing informed consent; Nontransvenous epicardial, abandoned, or no-fixation leads; Subcutaneous ICDs; Leadless pacemakers; Any other condition that, in the judgement of device-trained staff, would deem an MRI contraindicated. • Pacemaker dependence with an ICD (note: pacemaker-dependent candidates without an ICD are not excluded); A cardiac resynchronization therapy (CRT) device implanted <3 months prior to signing informed consent; Non-cardiovascular disease with life expectancy of <3 years; Participation in an ongoing protocol studying an experimental drug or device or participation in an

	interventional clinical trial within the last 30 days; Diagnosis of arrhythmogenic right ventricular cardiomyopathy. • Current alcohol or drug abuse or an inability to comply with protocol-related procedures; Pregnant/nursing women and women of child-bearing potential without use of active and highly reliable contraception; Human immunodeficiency virus infection; Viral hepatitis; Uncontrolled diabetes (hba1c >9%); Abnormal liver function (SGPT >3 times the upper reference range) and/or abnormal hematology (hematocrit <25%, WBC <3,000 µl, platelets <100,000 µl) studies without a reversible, identifiable cause; Sustained ventricular tachycardia or non sustained ventricular tachycardia >30 beats, not associated with the acute phase of a previous MI (>48 h after the MI onset) or a new acute ischemic episode; Ventricular fibrillation not associated with a new acute ischemic episode; New York Heart Association class IV congestive heart failure. • Evidence of tumor on screening chest/abdominal/pelvic (body) CT scan; Any prior transplant; Known hypersensitivity to dimethyl sulfoxide (DMSO); Known hypersensitivity to bovine products; Any malignancy within past 5 years (except for in situ non-melanoma skin cancer and in situ cervical cancer).
Recruitment/selection of patients:	The randomisation for phase II trial was performed with 2:1 ratio
Intervention: Source and Type of stem cells	Donor hearts at the time of cardiac transplantation, allogeneic cardiosphere-derived cells (CDCs) [CAP-1002]
Intervention: Method of their characterization	On the morning of the cell transplantation, under both local and light general anaesthesia (midazolam), an average of 100 mL (range 80–140 mL) of BM were harvested from the posterior – superior iliac crest by multiple aspirations into heparinized syringes. The procedure was performed in about 15 min. All patients received prophylaxis with moxifloxacin, to avoid the risk of infection induced by the iliac puncture. Ten ml of NaCl 0.9% solution containing 250 U of heparin (0.005) was added to the marrow in 50 mL Falcon tubes to prevent coagulation. Progenitor cells were isolated and enriched using Ficoll Hypaque centrifugation procedures. This procedure allowed the depletion of myeloid cells from the harvest. The cell suspension consisted of a heterogeneous cell population including haematopoietic,

	mesenchymal, and other progenitor cells, as well as mononuclear cells. The cells were suspended in 7 mL of PBS-EDTA buffer containing 3 mL of human albumin 5% W/V. The mononuclear cell fraction was concentrated into a final volume of 25–30 ml. Finally, before intracoronary injection, the cells were subjected to quality control procedures (i.e. sterility test for aerobic and anaerobic bacteria, ELISA test for HCV, HBV, HIV viruses) which excluded any contamination. In addition, full blood count and immune-phenotype analyses of the cell suspension were performed, including absolute CD34 and CD45 positive cell count and five colour MoAb panel for the identification of the cellular subpopulation CD66b/CD33/CD45/CD11b/CD34, CD31/CD133/CD45/CD117/CD34, and CD71/CD105/CD45/CD38/ CD41.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	25 million
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF MRI Difference LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	-

Study	**Penicka et al. 2007[30]**
Study type:	Randomized clinical trial

Number of participants:	27
Countries, setting and Funding:	Czech Republic, Research grant and by the CHARLES University Prague Research Project
Duration of study Follow up (post intervention):	24 Months
Subgroup analysis within study	-
Inclusion criteria:	-
Exclusion criteria:	-
Recruitment/selection of patients:	Eligible patients were randomly assigned in a 2:1 ratio either to intracoronary BMNCs injection (n=17) or standard medical therapy (n=10).
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	On average, 171±48 ml of bone marrow blood was harvested and processed to a final volume of 27±7 ml. The median number of injected BMNCs and $CD34^{+}$ cells was $26.4x10^{8}$ (IQR $19.6x10^{8}$ to $33.0x10^{8}$) and $1.3x10^{6}$ (IQR $1.1x10^{6}$ to $1.4x10^{6}$) respectively. The viability of bmncs ranged from 94% to 99%.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	2640 (IQR 1960-3300) million
Intervention: Dose- If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF (2D ECHO) End of the study, EDV (ECHO) End of the study, LVEF (%) End of the study echo, EDV (ml) End of the study Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study, Infarct size (SPECT) End of the study
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Cancer incidence, Mortality,

	RECURRENT MI

Study	**Piepoli et al. 2010[31]**
Study type:	Randomized controlled trial
Number of participants:	38
Countries, setting and Funding:	Italy
Duration of study Follow up (post intervention):	12 Months
Subgroup analysis within study:	-
Inclusion criteria:	• Age 18–80 years, the presence of ST elevation MI of the anterior wall (positive ECG, troponin level, and symptoms, according to the WHO criteria), PCI treatment 2–6 h after the onset of symptoms, successful PCI with stent implantation performed on the culprit lesion in the left anterior descending coronary artery proximal to the second diagonal branch, and three or more hypokinetic LV segments observed on echocardiography with global LV dysfunction.
Exclusion criteria:	• Previous Q-wave MI, cardiogenic shock, or any severe coexisting conditions that interfered with the patient's ability to comply with the protocol. All patients received medication according to current guidelines, followed the standard rehabilitation programmes for MI, and were given general advice on diet, smoking, and lifestyle changes.
Recruitment/selection of patients:	Subjects giving their informed consent were randomly assigned by uneven vs. Even numbers in 1:1 fashion into two parallel groups.
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	Immunophenotype Finally, before intracoronary injection, the cells were subjected to quality control procedures (i.e. Sterility test for aerobic and anaerobic bacteria, ELISA test for HCV, HBV, HIV viruses) which excluded any contamination. In addition, full blood count and immune-phenotype analyses of the cell suspension were performed, including absolute CD34 and CD45 positive cell count and five colourmoab panel for the identification of the cellular subpopulation CD66b/CD33/CD45/CD11b/CD34,

	CD31/CD133/CD45/CD117/CD34, and CD71/CD105/CD45/CD38/ CD41
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	248 million BMMNC, 2 million $CD34^+$
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF (SPECT) difference between the groups, LVEF (%) Difference between the groups SPECT, EDV (SPECT) difference between the groups, EDV (ml) Difference between the groups SPECT, ESV (ml) Difference between the groups SPECT, ESV (SPECT) difference between the groups, LVEDD (Echo) difference between the groups, LVESD (echo) difference between the groups
Safety Outcomes reported with time points- SAEs	SAEs, Cardiac hospitalization and instent thrombosis
Safety Outcomes reported with time points- Other Adverse Events	Cardiovascular mortality Mortality, Hospitalization due to heart failure,

Study	**Plewka et al. 2009[32]**
Study type:	Randomized clinical trial
Number of participants:	60
Countries, setting and Funding:	Poland, Polish Ministry of Sciences and Higher Education
Duration of study Follow up (post intervention):	24 Months
Subgroup analysis within study:	-
Inclusion criteria:	• A total of 60 patients with a first anterior wall STEMI (18 women and 42 men, age 56± 9 years, range 34 to 72) and a baseline LVEF <40%, were included in the present study. All the patients were successfully treated with primary PCI within

	12 hours after the onset of symptoms. The STEMI diagnosis was determined from the findings of typical chest pain, the presence of ST elevations on a standard 12-lead electrocardiogram, and a significant increase in the serum markers of myocardial infarction. The symptom-to-balloon time did not differ between the treatment (7±2 hours) and control (8±3 hours, p=NS) groups.
Exclusion criteria:	• Previous myocardial infarction, significant stenosis in a nonculprit coronary vessel, clinical and hemodynamic instability, current infection, neoplasm, and other severe coexisting conditions that could influence a patient's compliance to the protocol or a patient's 1year prognosis.
Recruitment/selection of patients:	The patients were randomly assigned to the treatment group (BMSC group) or the control group in a 2:1 ratio.
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	A total of 100 ml of bone marrow was aspirated from the iliac crest using local anesthesia 3 to 11 days after STEMI. The cell preparation and administration protocol has previously been described in detail. In brief, bone marrow aspirates were diluted with 20 ml of 0.9% NaCl, filtrated, and mononuclear cells ($CD34^+$ and $CD133^+$) were isolated by density gradient centrifugation (Ficoll-Paque Plus, 15°C, 20 minutes). The mononuclear cells were then washed 2 times with 0.9% NaCl, filtered, and subjected to quality and quantity control. Within 2 hours after the bone marrow harvest, a volume of 20 ml of mononuclear cell suspension was infused into the infarct-related artery distally to the inflated over-the-wire balloon catheter (Ninja, Cordis, Miami, Florida). The balloon was inflated with low pressure to completely block blood flow for 2 minutes, and 5 ml of the BMSC suspension was infused distally to the occluding balloon through the central port of the balloon catheter. This maneuver was repeated 4 times, interrupted by 2 minutes of reflow by deflating the balloon to minimize ischemia. After completion of the intracoronary cell transplantation, coronary angiography was repeated to ascertain vessel patency. The mean radiation exposure was 975±154 □Gy/m^2.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	144 (49) million cells

Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study, WMSI (ECHO) End of the study
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Mortality

Study	**Quyyumi et al. 2011[33]**
Study type:	Randomized clinical trial
Number of participants:	31
Countries, setting and Funding:	USA
Duration of study Follow up (post intervention):	12 Months
Subgroup analysis within study	-
Inclusion criteria:	• Subjects with acute STEMI treated with intracoronary stent implantation within 3 days of AMI and an LVEF ≤50% by echocardiography with a regional wall motion abnormality in the distribution of the IRA ≥4 days after stenting were enrolled after providing institutional review board–approved informed written consent.
Exclusion criteria:	-
Recruitment/selection of patients:	Subjects were enrolled randomly at each site as controls (n = 15), receiving the standard of care, or to a dose-escalation, open-label cell therapy group, assigned prospectively in cohorts of 5 patients each, sequentially with a 2-week interval between dose escalations (5, 10, and then 15 million $CD34^+$ cells).
Intervention: Source and Type of stem cells	BM aspiration, selection to isolate $CD34^+$ cells, $CD34^+$ cells
Intervention: Method of their characterization	Mini–bone marrow harvest of 320 ml (median 402 ± 17 ml including heparin) was free of significant complications (Table II). Total harvested nucleated cells (mean 7.8 × 10^9, range 3.8-14 × 10^9), percentage of CD34+ cells (mean 0.75%, range 0.2%-

	1.9%), and $CD34^+$ cells preselection (mean 5.9×10^7, range $1.6\text{-}14.8\times10^7$) did not differ significantly between cohorts. Post selection, the mean total CD34+ cells available for infusion were 2.1×10^7 (range, $0.84\text{-}4.9\times10^7$ cells), reflecting a mean 38% $CD34^+$ selection efficiency (range 25%-50%). Cells were 98%±1% viable; achieved 86.5% ± 5.8% purity; and had negative sterility, endotoxin, and gram stain test results in all dose groups. $CD34^+$ cells were infused a mean of 199 ± 22 hours (range 6.3-9.8 days) after stenting, with the lowest time interval in the 5 million dose cohort. Mean SDF-1 migratory capacity were similar in the 5 and 10 million cohorts but was lower in the 15 million cohort.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	LD: 4.8 (0.4) million cells MD: 9.9 (0.7) million cells HD: 14.3 (1.6) million cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	LD: 4.8 (0.4) million cells MD: 9.9 (0.7) million cells HD: 14.3 (1.6) million cells
Efficacy Outcomes reported with time points:	LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV (MRI) End of the study, EDV (MRI) difference between the groups, EDV (ml) End of the study MRI, EDV (ml) Difference between the groups MRI, ESV (ml) End of the study MRI, ESV (ml) Difference between the groups MRI, ESV (MRI) End of the study, ESV (MRI) difference between the groups, ESV (MRI) difference between the groups, Infarct size (MRI) end of the study,

	Infarct size (MRI) difference between the groups,
Safety Outcomes reported with time points- SAEs	SAEs INTERVENTION = ACUTE STENT THROMBOSIS (1), CHEST PAIN (1), IN STENT RESTENOSIS (2) CONTROL = IN STENT RESTENOSIS (1), SEPTIC THROMBO(1)
Safety Outcomes reported with time points- Other Adverse Events	Mortality, LVEF MRI Difference, Hospitalization due to heart failure, Revascularization frequency, Stroke frequency

Study	**Quyyumi et al. 2017[34]**
Study type:	Randomized clinical trial
Number of participants:	195
Countries, setting and Funding:	USA, Caladrius Biosciences
Duration of study Follow up (post intervention):	6 Months
Method of assessment of disease condition:	Patients with LVD (EF≤48% by CMR imaging) ≥4 days after coronary artery stenting
Subgroup analysis within study:	
Inclusion criteria:	• Age 18 years or older; Acute ST elevation myocardial infarction meeting ACC/AHA criteria, with symptoms of chest pain within 3 days of admission. Criteria include (ST elevation > 1mm in limb leads or 2 mm in two or more precordial leads, and increased levels of troponin, CPK MB or both). Chest pain syndrome can extend to more than 3 days prior to admission if its course is consistent with transient/intermittent ischemia rather than symptoms that are continuous suggesting ongoing infarction extending beyond 3 days; Successful stent placement and reperfusion within 3 days of chest pain onset and with TIMI Flow score of 2 or 3 and infarct related artery (IRA) with < 20% stenosis after revascularization; Wall motion abnormality associated with the target lesion; NYHA heart failure class I, II or III; Study entry LVEF< 48% determined by CMR no sooner than 96 hours from stent placement; Able to provide informed written

	consent and willing to participate in all required study follow-up assessments; Subjects must have an INR ≤ 2.0 within 2 days of the bone marrow collection; Subjects must have a Hgb ≥ 10 grams/dl, WBC ≥ 3500 cells/mm3, a platelet count ≥ 100,000 cells/mm3, serum creatinine ≤ 2.5, and total bilirubin ≤ 2.0 within 7 days of the bone marrow collection or by end of screening phase; Expected survival of at least one year; Females of child bearing potential agree to use birth control (barrier method accepted) for one month post bone marrow harvest;
Exclusion criteria:	• Continuous/ongoing chest pain – unremitting and unresponsive to nitroglycerin or rest – persisting 4 or more days before stent placement. If the chest pain syndrome is transient and/or intermittent – even if it began more than 3 days prior to admission – the patient is not excluded; Subjects in cardiogenic shock (systolic pressure < 80mm/Hg, on vasopressors, or intra-aortic counterpulsation) at the time of consenting. Subjects who recover from cardiogenic shock by the time of consenting are eligible; Subjects unable to receive antiplatelet agents (e.g. Aspirin, clopidogrel, ticlopidine, prasugrel, etc); Subjects receiving warfarin who have an INR >2 or with major bleeding requiring active transfusion support; Subjects who require continuous anticoagulation during the time when the bone marrow harvest is scheduled, as heparin must be discontinued for 4 hours prior to and 24 hours after bone marrow harvest procedure. (See Appendix VII.); Subjects with severe cardiac valvular disease expected to undergo surgery within 1 year; Subjects with known severe immunodeficiency states (AIDS); Cirrhosis requiring active medical management; Malignancy requiring active treatment (except basal cell skin cancer); Subjects with documented active alcohol and /or other substance abuse; Females of child bearing potential unless a pregnancy test is negative within 7 days of the mini-bone marrow harvest; Re-occlusion of the IRA prior to the infusion procedure; Planned revascularization intervention during the next 6 months (A second PCI can be performed if done prior to qualifying CMR at least 96 hours post primary PCI); Participation in an ongoing investigational trial; Active or suspected bacterial infection requiring systemic intravenous antibiotics; Post Randomization Criteria to Receive Infusion of

	Investigational Product: Bone marrow harvest should be terminated for patients who become sufficiently unstable that vasopressors(s) (or more aggressive therapy) is (are) required, and subject can continue to participate in trial only if the bone marrow harvested prior to the initiation of vasopressors proves sufficient .to manufacture AMR-001/placebo. Even when patients are stabilized and weaned from vasopressors, no further bone marrow can be harvested.
Recruitment/selection of patients:	Were randomized 1:1 to receive either autologous $CD34^+$ cells (minimum dose of 10 million (±20%) $CD34^+$ cells in autologous serum) or autologous serum by intracoronary infusion
Intervention: Source and Type of stem cells	BM aspiration, selection to isolate $CD34^+$ cells, $CD34^+$ cells
Intervention: Method of their characterization	Bone marrow aspiration was performed in all subjects randomized to either $CD34^+$ cells or placebo between 4 and 9 days after stent implantation using conscious sedation and local anesthesia (supplemental materials). $CD34^+$ cells were selected from the harvested cells using the clinimacs system. $CD34^+$ cell enumeration, purity, and viability were assayed by flow cytometry (Stem-Kit reagents; Beckman Coulter, Brea, CA). Endotoxin levels were determined using Limulus test kits (Lonza, Allendale, NJ). The $CD34^+$ cell product was suspended in 10 ml phosphate buffered saline supplemented with autologous serum and human serum albumin (HSA). All treatment subjects received a minimum dose of ≥ 10 million (±20%) $CD34^+$ cells as defined in release criteria. The cell dose in each subject was the total dose of $CD34^+$ cells produced from their bone marrow aspirate. Control subjects received 10 ml phosphate buffered saline supplemented with autologous serum and HSA without cells
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	14.9 ± 8 million cells (range 8 to 43.8)
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF MRI Difference, LVEF (MRI) difference between the groups, LVEF (%) Difference between the groups MRI

Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Mortality,

Study	**San Roman et al. 2015[35]**
Study type:	Randomized clinical trial
Number of participants:	120
Countries, setting and Funding:	Spain, Grants PI04/1078, PI051770, and Red Cardiovascular (RIC) from the Plan Nacional de InvestigaciónCientífica, Desarrollo e InnovaciónTecnológica, Instituto de Salud Carlos III–Ministerio de Economía y Competitividad, Spain; HUV02A05 and HUV308A11-2 from the Junta de Castilla y León; CACL from the Cajas de Ahorro Castilla y León; and from Fundación Mutua Madrileña.
Duration of study Follow up (post intervention):	12 Months
Subgroup analysis within study	-
Inclusion criteria:	• Age ≥18 years, AMI diagnosis with cardiac enzyme release and total summed ST-segment elevation ≥6 mm, akinesis or hypokinesis in the infarct-related artery area, successful reperfusion either with primary percutaneous coronary intervention (PCI) or post-fibrinolysis PCI with a final Thrombolysis In Myocardial Infarction 3 grade flow, rapamycin drug-eluting stent (DES) implantation in the infract-related artery, and adequate revascularization of the remaining coronary arteries before stem cell therapy.
Exclusion criteria:	• Cardiogenic shock; suspicion or evidence of infarct mechanical complication; history of sustained ventricular tachycardia or atrial fibrillation; patient with cardiac defibrillator or candidate for its potential implantation; investigational drug treatment in the previous 4 weeks; actual or potential use of antineoplastic drugs; oncology antecedents in the last 5 years; previous treatment with transmyocardial laser revascularization; women of childbearing potential; severe concomitant disease-modifying patient's survival during the study; active bleeding or major surgery within 2 weeks forbidding the use of heparin,

	abciximab, or antiplatelet therapy; previous malignant hematology disease or hypercoagulability disorders; previous known renal failure (creatinine >2.5 mg/dl); any kind of stroke in the previous year or any episode ever of hemorrhagic stroke; major surgery pending in the next year; previously known vascular disease that prevents catheterization; evidence of hypersensitivity to G-CSF treatment (filgrastim); or inability to give written informed consent.
Recruitment/selection of patients:	The TECAM (Trial of Hematopoietic Stem Cells in Acute Myocardial Infarction) study was a randomized (1:1:1:1), From November 2005 to January 2010, patients were enrolled from 8 Spanish hospitals. The patients were enrolled from the following institutions: Instituto de Ciencias del Corazón (n ¼ 81), Hospital General Universitario Gregorio Marañón (n ¼ 21), Hospital Universitario de Salamanca (n ¼ 5), Hospital Río Hortega (n ¼ 4), ComplejoHospitalario de León (n ¼ 4), Hospital Río Carrión de Palencia (n ¼ 3), Hospital de Segovia (n ¼ 1), and Hospital General Yague de Burgos (n = 1).
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	A total of 50 ml of bone marrow was aspirated under local anesthesia from the iliac crest. The aspirate was filtered and centrifuged and isolated by Ficoll density separation. The interface was collected and washed twice with heparinized phosphate-buffered saline and resuspended at approximately $5x10^6$ cells/ml in the heparinized saline. Just before intracoronary injection, a small BMMC sample was collected for cytometry studies (facscalibur, BD Biosciences, San Jose, California) for cluster of differentiation (CD) 34^+, $CD117^+$, $CD133^+$, and cell viability analyzed using trypan blue reagent. An over-the-wire balloon catheter positioned at the site of stent implantation was inflated at 2 to 4 atm until complete block of blood flow. Then, the guidewire was retired and the BMMC suspension was infused with a pump at 1 to 2 ml/min during 3-minute periods of inflation and cell infusion alternating with 1 minute of de inflation and reperfusion until the total BMMC dose was given.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	560 million
Intervention: Dose - If the trial has taken multiple	-

doses, then which dose values has been used for MA	
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF MRI Difference, LVEF (MRI) difference between the groups, LVEF (%) Difference between the groups MRI
Safety Outcomes reported with time points- SAEs	SAEs RE-HOSPITALIZATION
Safety Outcomes reported with time points- Other Adverse Events	Mortality

Study	**Roncalli et al. 2011[36]**
Study type:	Randomised clinical trial
Number of participants:	101
Countries, setting and Funding:	France, this work was supported in part by a PHRC (Programme Hospitalier de Recherche Clinique) from the French Department of Health, and grants from the Association Française contre les Myopathies and the Fondation de France.
Duration of study Follow up (post intervention):	3 Months
Subgroup analysis within study:	-
Inclusion criteria:	• Patients admitted to the University Hospitals of Cre´teil, Grenoble, Lille, Montpellier, Nantes, and Toulouse, between December 2004 and January 2007, with an ST-segment elevation myocardial infarction (STEMI) were screened for inclusion in the BONAMI trial. Screening criteria were age 18–75 years, a successful percutaneous coronary intervention (PCI) with bare metal stent implantation performed on the culprit lesion during the 24 h after the onset of symptoms, and LVEF, 50% assessed by echocardiography.
Exclusion criteria:	Main exclusion criteria were • age >75 years; previous myocardial infarction; patient instability after myocardial infarction; cardiac disease except ischemic heart disease; multivessel coronary artery disease; need for coronary revascularization in the future; pulmonary

	edema and cardiogenic shock; advanced renal or hepatic failure; non-cardiac disease adversely affecting prognosis; coagulopathy, thrombocytopenia, and leukopenia.
Recruitment/selection of patients:	Patients were randomly assigned in a 1:1 ratio Patients admitted to the University Hospitals of Cre´teil, Grenoble, Lille, Montpellier, Nantes, and Toulouse, between December 2004 and January 2007, with an ST-segment elevation myocardial infarction (STEMI) were screened for inclusion in the BONAMI trial. Screening criteria were age 18–75 years, a successful percutaneous coronary intervention (PCI) with bare metal stent implantation performed on the culprit lesion during the 24 h after the onset of symptoms, and LVEF, 50% assessed by echocardiography.
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	A total of 50 ml of bone marrow was aspirated into heparin-treated syringes from the iliac crest under local anesthesia. The aspirate was shipped at room temperature to the cell processing laboratory of each local center. Progenitor cells were isolated and enriched using lymphocyte preparation medium centrifugation procedures (Ficoll, Eurobio). The cell suspension consisted of a heterogeneous cell population including hematopoietic, endothelial, and other progenitor cells, as well as mononuclear cells. A single syringe of $100x10^6$ BMCs were prepared in 10 ml 4% human albumin; all safety analyses were performed before release of the final cell therapy product in accordance with the French regulations.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	98.3 (8.7) million cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF (2D ECHO) End of the study, LVEF (MRI) End of the study, LVEF (Radionucleotide ventriculography) end of the study, LVEF (%) End of the study echo,

	LVEF (%) End of the study MRI, LVEF (%) End of the study Radionucleotide Angiography, EDV Index (MRI) End of the study, ESV Index (MRI) End of the study, Infarct size (MRI) end of the study
Safety Outcomes reported with time points- SAEs	SAEs Restenosis, Ischemic Events, Thrombosis, Pericarditis, Other Cardiac Event, Iplantable Cardio DEF
Safety Outcomes reported with time points-Other Adverse Events	Mortality, Hospitalization due to heart failure, Arrhythmia frequency Restenosis

Study	**Srimahachota et al. 2011[37]**
Study type:	Randomized clinical trial
Number of participants:	23
Countries, setting and Funding:	Thailand
Duration of study Follow up (post intervention):	6 Months
Subgroup analysis within study	-
Inclusion criteria:	• Enrolled the patients who had a history of STEMI with LVEF less than 50% and demonstrated regional wall motion abnormality by echocardiography. The patient had to have successful angioplasty with or without stent implantation for infarct related artery
Exclusion criteria:	• Excluded the patients who had cardiogenic shock, severe congestive heart failure (function class 4), impaired renal function (creatinine > 1.8 mg/dl), pregnancy, and other severe co-morbid disease with life expectancy less than one year.
Recruitment/selection of patients:	Enrolled the patients who had a history of STEMI with LVEF less than 50% and demonstrated regional wall motion abnormality by echocardiography. The patient had to have successful angioplasty with or without stent implantation for infarct related artery

Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	One hundred ml of bone marrow from the iliac crest was harvested in the morning under local anesthesia with conscious sedation and sent immediately to the cell-processing laboratory at the National Blood Centre, the Thai Red Cross Society. Mononuclear cells were isolated by density gradient centrifugation (Isoprep®). After two washing steps with saline+2% autologous serum, cells were suspended in 10 ml of saline+2% autologous serum. Cells population including total mononuclear cells, $CD34^{+}$ cells, and $CD133^{+}$ cells were analyzed using flow cytometer as well as the cell viability study before transplantation.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	420 (221) MILLION CELLS
Intervention: Dose- If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF MRI Difference, LVEF ECHO LVEF (2D ECHO) End of the study LVEF (2D ECHO) Difference of Difference from baseline, LVEF (ECHO) difference between groups, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (Angiography) difference between groups, LVEF (%) End of the study echo, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups Echocardiography, LVEF (%) Difference between the groups MRI, LVEF (%) Difference between the groups Angiography, WMSI (ECHO) End of the study,

	WMSI (ECHO) Difference between the group, NYHA FCI end of the study, NYHA FCI difference between the groups
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	-

Study	**Surder et al. 2016[38]**
Study type:	Randomized clinical trial
Number of participants:	200
Countries, setting and Funding:	Switzerland Research grants of the Foundation for Cardiovascular Research-Zurich Heart House, Zurich, Switzerland; the Fondazione Cardiocentro Ticino, Lugano, Switzerland;
Duration of study Follow up (post intervention):	12 Months
Subgroup analysis within study:	-
Inclusion criteria:	• Patients with acute ST-segment–elevation myocardial infarction (STEMI) and successful PCI within 24 hours after symptom onset were eligible for enrollment into this multicenter, randomized, controlled trial (RCT) provided they presented with an LVEF of <45% as assessed by an LV angiogram or transthoracic echocardiography the day of or after the AMI.
Exclusion criteria:	• Abnormal regional wall motion outside the infarct region Known previous myocardial infarction in the same target vessel Known preexisting LV dysfunction (ejection fraction b 45% before admission). Need for revascularization in the non–infarct-related coronary within 4 m Preexisting symptoms of heart failure or known cardiomyopathy Known active infection or chronic infection with HIV, hepatitis B virus, or hepatitis C virus Chronic inflammatory disease Serious concomitant disease with a life expectancy of b1 y Follow-up unlikely (no fixed abode, and others) Contraindication for CMR (ie,

	pacemaker, neurostimulator, severe claustrophobia) Severe renal failure (creatinine level N250 mmol/L) Relevant liver disease (aspartate aminotransferase N2× norm or spontaneous international normalized ratio N1.5) Anemia (hemoglobin level b 8.5 mg/dl), thrombocytopenia (b100,000/μl) Pregnancy Participation at a clinical trial in the last 30 d
Recruitment/selection of patients:	Patients were randomly assigned in a 1:1:1 fashion to 1 open-labeled control and 2 BMMNCs treatment groups.
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	Cell viability, functional testing, characterization of the product, and sterility were assessed from an aliquot of the cell suspension. An aliquot of cell suspension was utilized for fluorescence-activated cell sorting analysis with the use of fluorochrome conjugated antibodies against anti-human CD34 and CD133; cell viability was assessed by 7-AAD cell uptake, and sterility was assessed by the Bact/Alert rapid method.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	E: 159.7 (125.8) million cells; L: 139.5 (120.5) million cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	E: 159.7 (125.8) million cells; L: 139.5 (120.5) million cells
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF MRI Difference, LVEF (MRI) difference between the groups, LVEF (%) Difference between the groups MRI, EDV (MRI) difference between the groups, EDV (ml) Difference between the groups MRI, ESV (ml) Difference between the groups MRI, ESV (MRI) difference between the groups, ESV (MRI) difference between the groups,
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Mortality Hospitalization due to heart failure

	Recurrent MI Revascularization frequency Stroke frequency.

Study	**Tendra et al. 2009[39]**
Study type:	Randomized clinical trial
Number of participants:	200
Countries, setting and Funding:	Multicentre Polish Ministry of Science and Higher Education
Duration of study Follow up (post intervention):	6 Months
Subgroup analysis within study	-
Inclusion criteria:	• Anterior AMI, successful PCI with stent implantation in the infarct-related left anterior descending (LAD) artery within 12 h after the symptom onset, reduced LVEF ≤40% in qualifying echocardiogram, and age 18–75 years.
Exclusion criteria:	• Prior MI, presence of significant stenoses in other coronary vessels requiring revascularization, cardiogenic shock, renal failure, past or present malignancy, pregnancy, lactation and contraindications for magnetic resonance imaging (MRI).
Recruitment/selection of patients:	Study population consisted of 200 patients with AMI treated with primary percutaneous coronary intervention (PCI). Patients were enrolled in five centres in Poland between March 2005 and September 2007, and 6-month follow-up was completed in March 2008.
Intervention: Source and Type of stem cells	BM aspiration; Selected cells: immunomagnetic selection to isolate $CD34^+/CXCR4^+$ cells, Selected cells (S): $CD34^+/CXCR4^+$ cells Unselected cells (U): BMMNCs
Intervention: Method of their characterization	Bone marrow aspiration was performed under sterile conditions in patients randomly assigned to the BM-MNCs treatment arms with negative serological testing for hepatitis B, hepatitis C, and HIV either 5 to 7 days or 3 to 4 weeks after AMI. The cell processing was done in a centralized, good manufacturing practice–

	certified facility (Cell Therapy Unit, Cardiocentro Ticino, Lugano, Switzerland). Between 60 and 80 mL of bone marrow was collected from the iliac crest under local anesthesia. Then 1 mL of a solution containing 1000 IU heparin was added to each 10 mL of bone marrow aspirate to prevent clotting. Then the aspirate and 20 mL of the patient's serum were sent at room temperature by courier to the cell-processing center. The BM-MNC cell suspension was shipped back to the participating hospital within 24 hours. Shipping protocols as well as the isolation of the mononuclear cell fraction were performed according to a standard protocol according to previous studies with minor modifications as described. Briefly, with the use of density gradient centrifugation, the mononuclear cell fraction was resuspended in 10mL of serum-free medium with 20% of autologous serum added without any additional heparin. An aliquot of cell suspension was utilized for fluorescence activated cell sorting analysis with the use of fluorochrome conjugated antibodies against anti-human CD34 and CD133; cell viability was assessed by 7-AAD cell uptake, and sterility was assessed by the Bact/Alert rapid method. Release criteria of the BMMNCs were product sterility, cell count between 5×10^7 and 5×10^8, and cell viability of ≥80%. Migration capacity of BM-MNCs was measured in a modified Boyden chamber as described previously. This parameter was expressed as percentage of mononuclear cells able to actively cross a membrane coated with extracellular matrix proteins and, with the use of an invasion index, indicating the ratio between the latter and the percentage of cells passively crossing the same membrane when uncoated.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	S: 1.9 million cells U: 178 million cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	S: 1.9 million cells U: 178 million cells
Efficacy Outcomes reported with time points:	LVEF (MRI) End of the study, LVEF (%) End of the study MRI, EDV (MRI) End of the study,

	EDV (ml) End of the study MRI, ESV (ml) End of the study MRI, ESV (MRI) End of the study
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Mortality, Recurrent MI, Revascularization frequency

Study	**Traverse et al. 2010[40]**
Study type:	Randomized clinical trial
Number of participants:	40
Countries, setting and Funding:	USA Jon Holden Dehaan Foundation
Duration of study Follow up (post intervention):	15 Months
Subgroup analysis within study:	-
Inclusion criteria:	• Eligible patients included those who presented with their first anterior STEMI who underwent successful angioplasty and stenting (percutaneous coronary intervention [PCI]) of the left anterior descending (LAD) coronary artery. Enrolled patients were required to have at least 2 hours of chest pain and electrocardiographic changes consistent with anterior STEMI or new left bundle branch block and an initial ejection fraction <50% by echocardiography following PCI. We included patients with cardiac arrest or cardiogenic shock
Exclusion criteria:	• Key exclusions included history of coronary artery bypass graft (CABG) or significant comorbidities.
Recruitment/selection of patients:	Forty patients consented to participate in the study and were randomized in a 3:1 ratio to 100 million autologous BMCs versus placebo. Forty patients (31 male, 9 female) were enrolled in this single center phase I trial beginning in December 2005 following Food and Drug Administration approval.

Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	Lot release criteria included >90% viability by trypan blue exclusion, negative gram stain, and endotoxin <5.0 EU/kg. Routine infectious disease testing included anaerobic, aerobic, and fungal cultures and virology assays for detection of HIV, hepatitis C virus, and hepatitis B. Flow cytometry for measurement of CD34, CD45, and CD133 was performed in all samples.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	100 million cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF (MRI) difference between the groups, LVEF (%) Difference between the groups MRI, EDV Index (MRI) difference between the groups, ESV (ml) Difference between the groups MRI, ESV (MRI) difference between the groups, ESV (MRI) difference between the groups,
Safety Outcomes reported with time points- Serious AEs	-
Safety Outcomes reported with time points- Other Adverse Events	LVEF MRI Difference, Recurrent MI, Revascularization frequency

Study	**Traverse et al. 2011[41]**
Study type:	Randomized clinical trial
Number of participants:	87
Countries, setting and Funding:	USA National Heart, Lung, and Blood Institute (NHLBI) under the cooperative agreement 5 U01 HL087318-04 and in part by the NHLBI contracts N01-HB-37164 and HHSN268201000008C to the Molecular and Cellular Therapeutics Facility, University of Minnesota, and N01-HB-37163 and HHSN268201000007C

	to the Cell Processing Facility, Baylor College of Medicine
Duration of study Follow up (post intervention):	6 Months
Subgroup analysis within study:	-
Inclusion criteria:	• Patients with an LVEF of 45% or less by echocardiography post-PCI were randomized in a 2:1 ratio of BMC to placebo following successful stenting of the infarct-related coronary artery.
Exclusion criteria:	-
Recruitment/selection of patients:	A randomized, double-blind, placebo-controlled trial (late time) of the National Heart, Lung, and Blood Institute–sponsored Cardiovascular Cell Therapy Research Network of 87 patients with significant LV dysfunction (LV ejection fraction [LVEF] 45%) following successful primary percutaneous coronary intervention (PCI) between July 8, 2008, and February 28, 2011. O (BMC: placebo, 2:1)
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	Bone marrow aspiration and intracoronary infusion of BMCs or cell-free solution (placebo). All caregivers and patients were blinded to treatment. Approximately 80 to 90 ml of bone marrow were aspirated from the iliac crest using standard techniques. The aspirate was processed at all sites with a closed, automated cell processing system (Sepax, Biosafe SA) 15 to ensure a uniform cellular product. After BMC enrichment, cells were washed 3 times and suspended in 5% human serum albumin/saline solution. The composition of CD34 and CD133 cells was determined by fluorescent activated cell sorting. After the cells passed stipulated lot release criteria, including viability (>70%) and sterility, randomization was performed by the data coordinating center. Treatment assignment was masked to all but 1 designated cell processing team member at each of the 5 centers who was not involved in patient care. The target dose for the treatment group was $150x10^6$ total nucleated cells. Patients randomized to placebo received 5% human serum albumin/saline solution to which 100 µl of autologous blood was added to ensure that the color and consistency of the solution matched that of the BMC product.

Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	147 (17) million cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF MRI Difference LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups, Infarct size (MRI) end of the study, Infarct size (MRI) difference between the groups,
Safety Outcomes reported with time points- SAEs	
Safety Outcomes reported with time points- Other Adverse Events	Mortality, hospitalization due to heart failure Recurrent MI Revascularization frequency

Study	**Traverse et al. 2018[42]**
Study type:	Randomized clinical trial
Number of participants:	120
Countries, setting and Funding:	USA Grant number UM1 HL087318.
Duration of study Follow up (post intervention):	12 Months
Subgroup analysis within study:	-

Inclusion criteria:	• Patients at least 21 years of age; Patients with first acute anterior MI with successful primary percutaneous coronary intervention (PCI) in the LAD artery at least 2.5 mm in diameter within 24 hours of onset of symptoms; Hemodynamic stability as defined as no requirement for IABP, inotropic or blood pressure supporting medications; Ejection fraction following reperfusion with PCI ≤45% as assessed by echocardiography; Consent to protocol and agree to comply with all follow-up visits and studies; Women of child-bearing potential willing to use an active form of birth control.
Exclusion criteria:	• History of sustained ventricular arrythmias not related to their AMI (evidenced by previous Holter monitoring and/or medication history for sustained ventricular arrhythmias in patient's medication chart). • Requires CABG or PCI due to the presence of residual coronary stenosis >70% luminal obstruction in the non-infarct related vessel (Additionally PCI of non-culprit vessels may be performed prior to enrollment). • History of any malignancy within the past five years excluding non-melanoma skin cancer or cervical cancer in-situ. • History of chronic anemia (hemoglobin (Hb) <9.0 mg/dl). • History of thrombocytosis (platelets >500k). • Baseline platelet count (prior to revascularization) < 120,000 or known history of thrombocytopenia. • Known history of elevated INR (PT) or PTT. • Life expectancy less than one year. • History of untreated alcohol or drug abuse. • Currently enrolled in another investigational drug or device trial. • Previous CABG. • Previous MI or history of non-ischemic cardiomyopathy resulting in LV

	dysfunction (LVEF <55%). • History of stroke or transient ischemic attack (TIA) within the past six months. • History of severe valvular heart disease (aortic valve area < 1.0 cm^2 or > 3+ mitral regurgitation). • Pregnancy or breast feeding. • Subjects with a known history of HIV, hepatitis B or C infection, or TB positive therapy. • Patients with active inflammatory or autoimmune disease on chronic immunosuppressive therapy. • Contraindications to cMRI. • Previous radiation to the pelvis with white blood cell count (WBC) and platelet counts below hospital specific normal values. • Women of child-bearing potential not willing to practice an active form of birth control. • Hepatic dysfunction as defined by: Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥3 times the upper limit of normal (ULN); or Total bilirubin ≥2 times ULN with AST or ALT ≥2 times ULN. • Chronic renal insufficiency as defined by a creatinine ≥ 2.0 mg/dl or requires chronic dialysis. • The revascularized vessel is not patent at the time cell administration is to be attempted. • Patient with two or more of the following criteria will be excluded from the trial, unless the LVEF is less than 30%: • Onset of symptoms to treatment PCI< 2 hours • Peak CK < 1500 IU/ml • Absence of q-wave on Day 1 EKG (post stenting).

	• Age < 45 years
Recruitment/selection of patients:	Patients were randomized (1:1) to study product delivery on day 3 or day 7 post-PCI.
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	Cells will be harvested and washed three times in heparinized phosphate buffered saline (PBS) before resuspension in PBS supplemented with 5% human albumin. The composition of $CD34^+$, $CD45^+$ and $CD133^+$ cells will be determined by fluorescent activated cell sorting (FACS) analysis. Viability of the cells will be determined by Trypan Blue exclusion; and ≥70% viability will be required before transplantation.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	146.1(20.1) million
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF MRI Difference, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups, Infarct size (MRI) end of the study, Infarct size (MRI) difference between the groups
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Revascularization frequency Stroke frequency

	Mortality, hospitalization due to heart failure Recurrent MI

Study	**Wang et al. 2014[43]**
Study type:	Randomized clinical trial
Number of participants:	58
Countries, setting and Funding:	China
Duration of study Follow up (post intervention):	6 Months
Subgroup analysis within study	-
Inclusion criteria:	Patients were included in the study if • They had a primary documented STEMI, and were scheduled undergo primary PCI within 8 h of the onset of ischemic symptoms
Exclusion criteria:	The major exclusion criteria were • Hemodynamic or electrical instability, cardiogenic shock, severe bradycardia, pre-existing chronic heart failure, renal impairment, or left bundle branch block pattern on electrocardiography (ECG).
Recruitment/selection of patients:	Fifty-eight patients fulfilling the inclusion criteria for this study were enrolled between July 2008 and October 2009.
Intervention: Source and Type of stem cells	BM aspiration and culture of MSC, BMMSCs
Intervention: Method of their characterization	MSCs were also tested for their ability to differentiate into adipocytes and osteoblasts. Adipocytic differentiation was induced by DMEM containing 10% (v/v) FBS, 0.5 mm isobutylmethylxanthine, 5 lg insulin/ml, 1 lm dexamethasone, and 60 lm indomethacin. For osteoblastic differentiation, 1 mm b-glycerol phosphate, 0.1 lm dexamethasone, and 50 lm ascorbate were used. Oil Red O and von Kossa dyes were used to identify adipocytes and osteoblasts, respectively. The identity of MSCs was confirmed by immunophenotyping based on the expression of CD73 and CD105, and the absence of hematopoietic (with anti-CD45, -CD14, -CD34 antibodies) and endothelial cell (with anti-CD31 antibodies) markers. All the chemical reagents used here were from Sigma - Aldrich and the

	antibodies were from Becton - Dickinson Co.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	100 million cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF (Angiography) End of the study, LVEF (%) End of the study Angiography, Infarction region % (Ventriculography), Left ventricular diameter (Ventriculography)
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Mortality,

Study	**Wen et al. 2012[44]**
Study type:	Randomized clinical trial
Number of participants:	38
Countries, setting and Funding:	China The major public scientific research program of henan province 091100910800
Duration of study Follow up (post intervention):	3 Months
Subgroup analysis within study	-
Inclusion criteria:	• Age 18-75 years old, no gender limit. Ÿnyha cardiac function classification: Class II-IV. Left ventricular ejection fraction <40%. Those with myocardial perfusion defect confirmed by 997cm SPECT (an area where the radiation count is lower than 40% of the normal myocardial radiation count.
Exclusion criteria:	• Bleeding disorders, leukemia, severe liver disease; Patients with renal insufficiency and tumors.
Recruitment/selection of patients:	Left ventricular ejection fraction <40%
Intervention: Source and Type of stem cells	BM Aspiration, BMMSCs
Intervention: Method of their characterization	Obtained cells were counted, and their components were identified using a flow

	cytometer. Before transplantation, 80-100 mL of bone marrow was extracted from patients in the test group in the laboratory through the 6-point method on the bilateral posterior superior iliac spines and separated. A bone marrow mesenchymal stem cell suspension (1-10) $\times 10^8$ L^{-1} was obtained by culturing and amplifying it in vitro. The obtained cells were counted, and their components were identified using a flow cytometer. Trial Group A in percutaneous coronary After interventional treatment, inject into the infarction-related blood vessels through a large-lumen catheter Bone marrow mesenchymal stem cells, test group B injected 2/3 and 1/3 of the bone marrow mesenchymal stem cells into the left and right coronary, respectively; the control group injected an equal amount of normal saline into the corresponding blood vessel, Use heparinized saline after transplantation. Rinse the angiography tube twice and review the angiography immediately to determine whether the cells are injected whether with intracoronary thrombosis or distal micro embolism, postoperative bedside ECG monitoring Nursing for 24 hours, liver and kidney Rinckom and myocardial enzyme spectrum were rechecked on the second day.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	460 (160) million cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF (2D ECHO) End of the study, LVEF (%) End of the study echo, LVEDD (ECHO) End of the study
Safety Outcomes reported with time points- Serious AEs	-
Safety Outcomes reported with time points- Other Adverse Events	-
Study	**Wohrle et al. 2010[45]**
Study type:	Randomized clinical trial

Number of participants:	42
Countries, setting and Funding:	Germany
Duration of study Follow up (post intervention):	36 Months
Subgroup analysis within study	Age <60 or ≥60 years, anterior versus nonanterior AMI, and a reduction in LVEF (severe vs non-severe) as visually assessed by echocardiography
Inclusion criteria:	• Patients aged 35 to 75 years with AMI. The inclusion criteria were AMI with 6 to 48 hours between symptom onset to successful percutaneous coronary intervention, a proximal lesion, creatine kinase level 1,000 U/L, and infarct size of 10% of the LV muscle mass, as determined by CMRI.
Exclusion criteria:	• A history of myocardial infarction, cardiogenic shock, contraindications to CMRI or 12 months of dual antiplatelet therapy, a history of hematologic disease, chemotherapy, previous stem cell therapy or treatment with granulocyte colony stimulating factor, severe renal dysfunction, or documented terminal illness.
Recruitment/selection of patients:	Patients with reperfusion >6 hours after symptom onset were randomly assigned in a 2:1. The patients were randomly assigned in a 2:1 ratio to either the mononuclear BMC group or the placebo group by external randomization.
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	With the patient under local anesthesia, the bone marrow was aspirated from the iliac crest into 20-ml syringes containing 500 IU heparin, 0.04 mg gentamicin, and 3,000 IU penicillin in 3-ml 0.9% NaCl. The aspirate was shipped at room temperature between the catheter laboratory and cell-processing laboratory within about 15 minutes. The cells were morphologically checked to exclude any subclinical hematologic disease. Mononuclear cells were isolated with Ficoll density gradient centrifugation (Cambrex, Belgium, same charge as in REPAIR-AMI, 823 g, 20 minutes, without a brake), washed, and resuspended in 15 ml 0.9% NaCl with 2% human albumin. The placebo syringes also contained 15 ml 0.9% NaCl with 2% human albumin and autologous erythrocytes with a hematocrit of 0.1% without BMC.
Intervention: Route of administration	Injection intracoronary through balloon

Intervention: Dose	381 (130) million cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF MRI Difference, LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups, Infarct size (MRI) end of the study, Infarct size (MRI) difference between the groups
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Restenosis Mortality, Hospitalization due to heart failure
Study	**Wollert et al. 2017[46]**
Study type:	Randomized clinical trial
Number of participants:	127
Countries, setting and Funding:	Germany, Norway German Research Foundation
Duration of study Follow up (post intervention):	6 Months
Subgroup analysis within study:	-
Inclusion criteria:	-
Exclusion criteria:	-
Recruitment/selection of patients:	Patients were recruited from 10 centres and were randomly allocated to 6 groups

	in a 1:1:2:2:2:2 ratio
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	Cells were harvested 7.1 ± 2.6 days after PCI (Table 1). The cell product in the hiBMCi group had a volume of 36 ± 5ml. The product contained 20.6 ± 7.7108 nucleated cells and 8.2 ± 5.3x10^6 $CD34^+$cellsand displayed in vitro colony-forming activity. Cell viability was 99 ± 1%. The lobmc product contained approximately one-third of the nucleated and $CD34^+$ cells in the hibmcproduct, but was comparable in terms of volume and haematocrit. C-irradiation abolished colony forming activity in the lobmci and hibmci products but did not affect cell numbers, cell viability, and paracrine potential. Cell characteristics of the hibmc product matched well with those of the BMC product used in BOOST.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	loBMCi (Nucleated cells - 700 ± 290 million; CD34 cells - 2.9 ± 2.1 million); hibmc (Nucleated cells - 2060 ± 770 million; CD34 cells - 8.2 ± 5.3 million)
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV Index (MRI) End of the study, EDV Index (MRI) difference between the groups, ESV Index (MRI) End of the study, ESV Index (MRI) difference between the groups, Volume of infarct (MRI) ml end of the study, Volume of infaract (MRI) ml difference between groups
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Mortality, hospitalization due to heart failure,
Study	**Yao et al. 2009[47]**

Study type:	Randomized clinical trial
Number of participants:	39
Countries, setting and Funding:	China Shanghai Scientific Research Fund, Program for Shanghai Outstanding Medical Academic Leader, National Basic Research Program of China & Science Foundation for Youth of Shanghai Medical Administrative Bureau
Duration of study Follow up (post intervention):	12 Months
Subgroup analysis within study	-
Inclusion criteria:	• Patients aged 18–74 years, admitted within 12 h after symptom onset of a first ST-elevation MI of the anterior wall, who had undergone successful percutaneous coronary intervention (PCI), with reduced LV function (LVEF 20–39%) on LV angiography, were eligible to participate. Patients with lower LV function (LVEF, 40%) as revealed by LV angiography were selected as large myocardial infarction.
Exclusion criteria:	• Previous Q-wave myocardial infarction, cardiogenic shock, or severe coexisting conditions that interfered with the ability of the patients to comply with the protocol. Figure 1 illustrates the study design.
Recruitment/selection of patients:	-
Intervention: Source and Type of stem cells	BM Aspiration, BMMNCs
Intervention: Method of their characterization	Bone marrow mononuclear cells were isolated and enriched using Ficoll-Hypaque gradient centrifugation procedures as previously reported. Briefly, bone marrow aspirates were diluted with 0.9% NaCl (1:5) and mononuclear cells were isolated by density gradient centrifugation using Ficoll (Sigma, 800g x 25 min). Mononuclear cells were washed (800g x 5min) three times with PBS and then suspended in 16 ml heparin-treated plasma at a density of (1.3±1.0) x 10^7 cells/ml at room temperature. Placebo solution consisted of 0.9% nacl containing heparin. All microbiological tests of the cell preparations proved negative. To ensure that a certain percentage of stem cells was present in the infused mononuclear cells, 1 ml suspension was subjected to FACS analysis after

	incubation with anti-human monoclonal antibodies: anti-human CD34 (BD Pharmingen) conjugated with FITC or CD133 (MiltenyiBiotec.) Antibodies conjugated with APC. An isotopic serum conjugated to FITC and APC was used as isotype control. The FACS analysis revealed that 2.4±0.9% of BMCs were positive for CD34 and 0.75±0.20% for CD133.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	SD: 410 million cells; DD: 190 (SE 120) million cells
Intervention: Dose- If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	GLOBAL LVEF LVEF (MRI) End of the study, LVEF (MRI) difference between the groups, LVEF (%) End of the study MRI, LVEF (%) Difference between the groups MRI, EDV (MRI) End of the study, EDV (ml) End of the study MRI, ESV (ml) End of the study MRI, ESV (MRI) End of the study, Infarct size (MRI) end of the study Perfusion defect % (SPECT) End of study
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Recurrent MI
Study	**Zhang et al. 2021[48]**
Study type:	Randomized clinical trial
Number of participants:	43
Countries, setting and Funding:	China Scientific Research Projects of Sichuan Medical Planning Commission: Heart transplantation effect of stem cells—Study on Paracrine Mechanism
Duration of study Follow up (post intervention):	12 Months

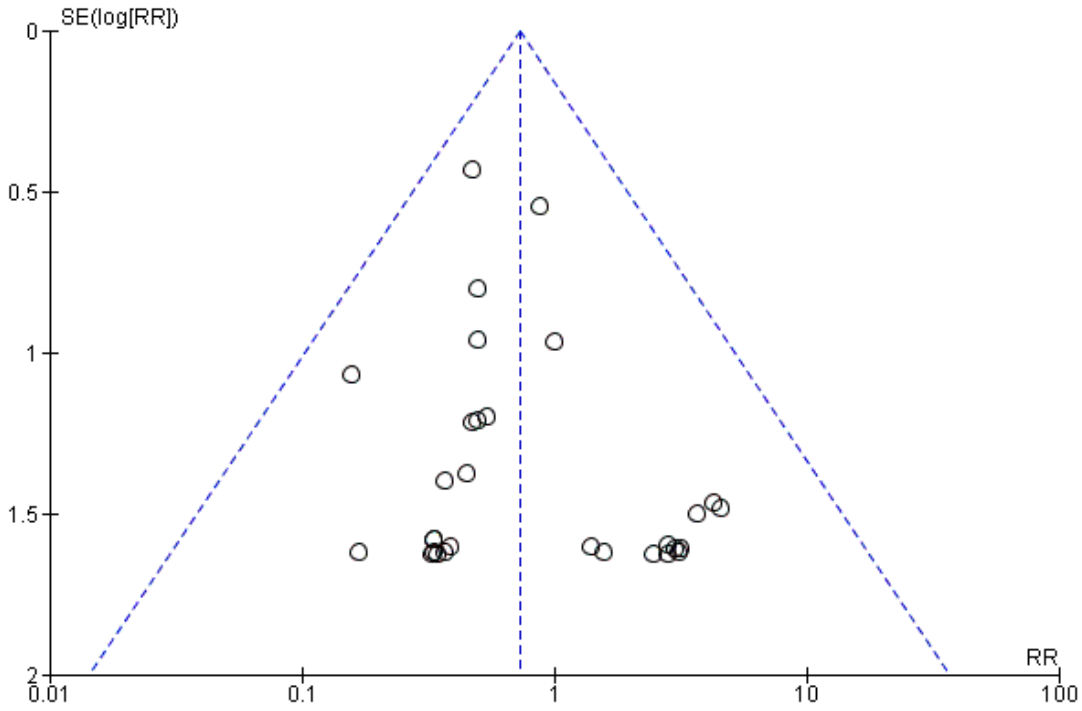
Method of assessment of disease condition:	STEMI patients
Subgroup analysis within study	-
Inclusion criteria:	• The standards of getting enrolled are STEMI patients, older than 18 years, who had an onset time of less than 1 month and was successfully revascularized with infarct-related vascular blood flow returning to TIMI level 3. All patients enrolled in the study signed an informed consent form and promised to complete all follow-up plans.
Exclusion criteria:	• Exclusion criteria include the following eight items: • Patients with refractory persistent ventricular tachycardia; • Patients with high heart block and not controlled by pacemaker; • patients with hepatic or kidney dysfunction (ALT> 80 U/L, creatinine (Cr) > 440 mmol/L); • patients with bleeding disorders or malignant tumors; • patients with autoimmune diseases or any serious fatal disease; • patients with contraindications for coronary intervention; • patients with the following other heart diseases: congenital heart disease (such as ventricular defect, atrial defect, patent ductus arteriosus), primary heart valve disease, active myocarditis, pulmonary heart disease, hyperthyroid heart disease, mucoedema heart disease, etc.; and • patients with mental illness, no self awareness, and no precise expression and cooperation.
Recruitment/selection of patients:	The 43 patients were randomly divided into a cell transplantation group (BM-MSCs injection via coronary artery perfusion, n = 21) and a control group
Intervention: Source and Type of stem cells	BM Aspiration, BM-MSCs
Intervention: Method of their characterization	Then, mononuclear cells were cultured in DMEM medium with 10% fetal bovine serum to obtain BM-MSCs, and they were sub-cultured when the stem cells grew to 80% confluence. Next, take the cells after the 2–3 subculture and expansion for 72h, and at the same time, take the culture supernatant for bacteria, mold, and mycoplasma identification tests. The next step was to digest the cells with 0.25%

	trypsin at 37°C. After repeated washing with normal saline for 3 times, we then calculated the cell concentration, the ratio of living cells, and verified the cell phenotype. Finally, resuspend the cells with 2 ml of normal saline for injection, place them in a 2-ml vial, and mark the patient's name and product number to ready for transplantation. The specification of this product was 1.0~2.5 × 10^6 BM-MSCs/2 ml, 2.0 ml/bottle. During the operation, 4ml of BM-MSC injection was diluted to 10 ml.
Intervention: Route of administration	Injection intracoronary through balloon
Intervention: Dose	2-5 million cells
Intervention: Dose - If the trial has taken multiple doses, then which dose values has been used for MA	-
Efficacy Outcomes reported with time points:	LVEF (2D ECHO) End of the study, EDV (ECHO) End of the study, LVEF (%) End of the study echo, EDV (ml) End of the study Echocardiography, ESV (ml) End of the study Echocardiography, ESV (ECHO) End of the study, NYHA FCI end of the study, Perfusion defect % (SPECT) End of study
Safety Outcomes reported with time points- SAEs	-
Safety Outcomes reported with time points- Other Adverse Events	Mortality, Hospitalization due to heart failure, Revascularization frequency,

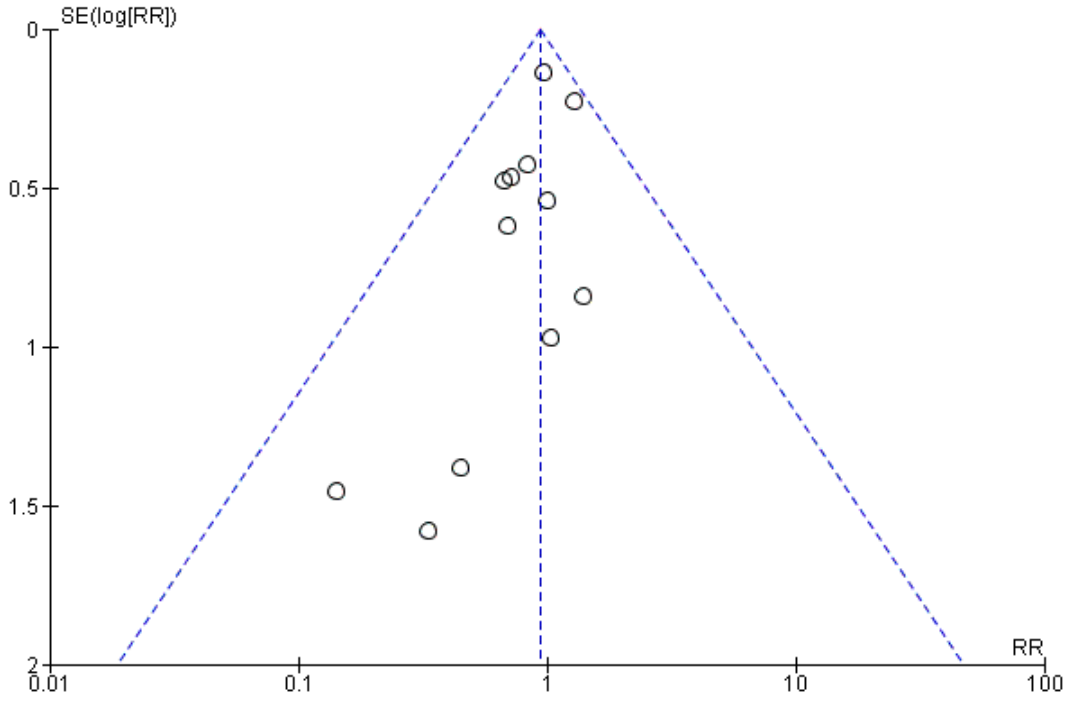
vii. Publication bias:

Outcomes having less than 10 trials are not eligible for publication bias.

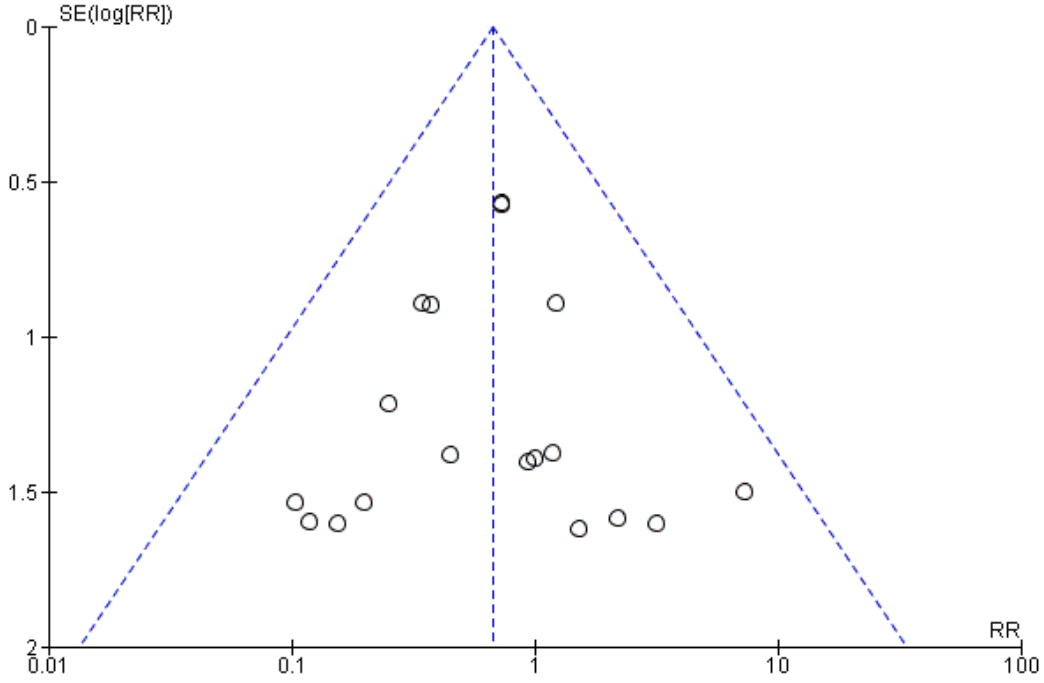
MORTALITY



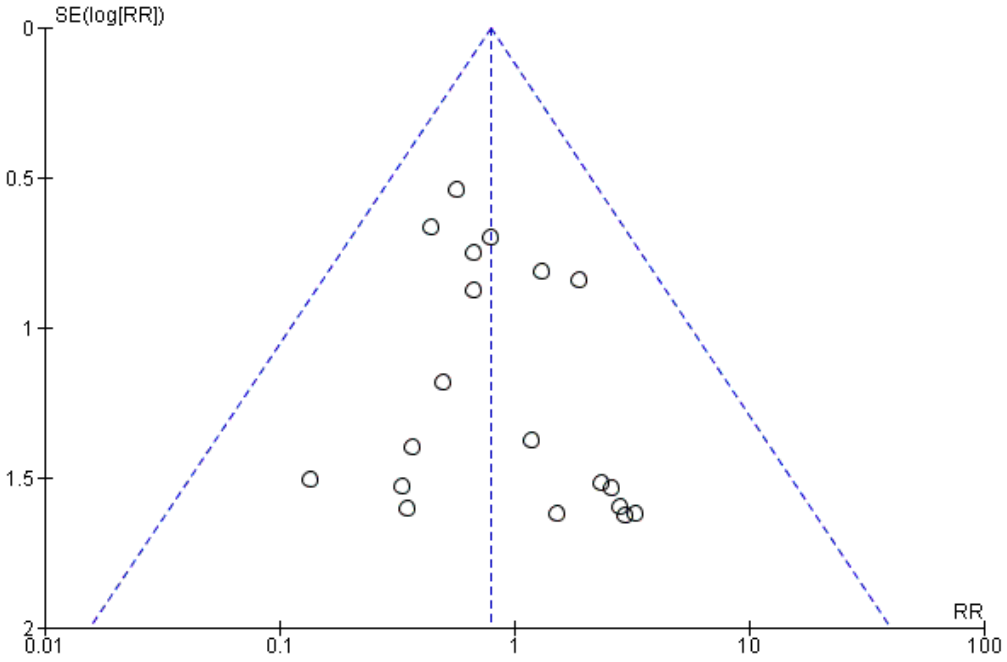
Serious Adverse Events



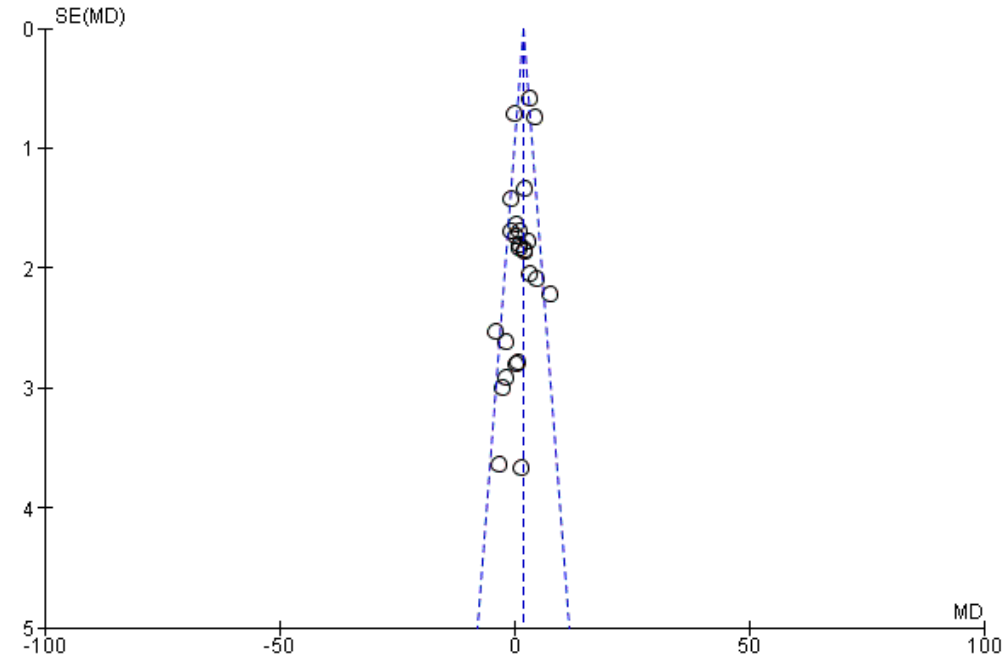
RECURRENT MI



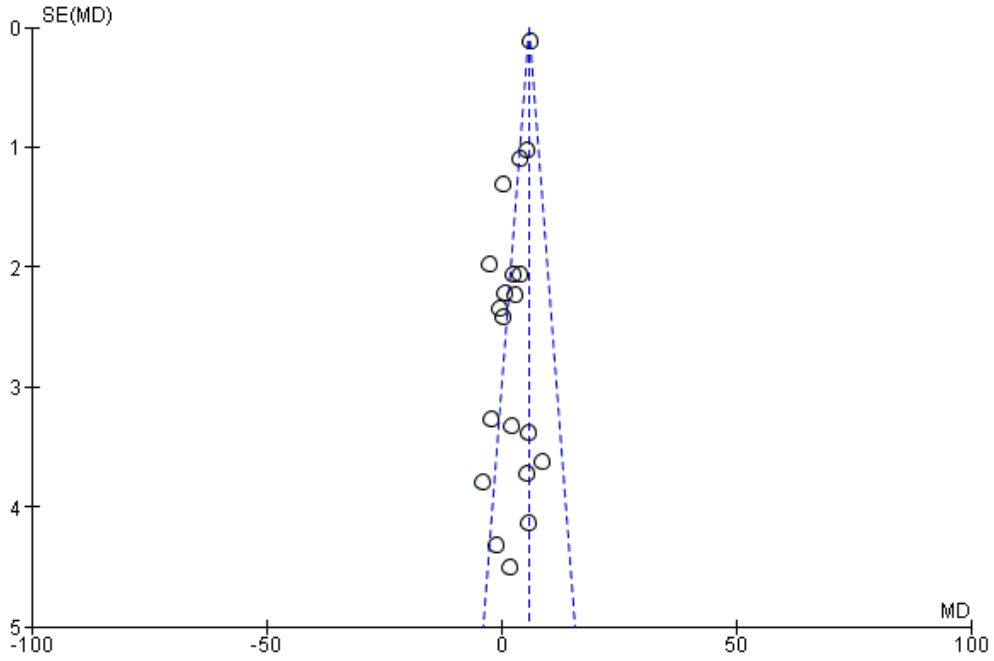
HEART FAILURE



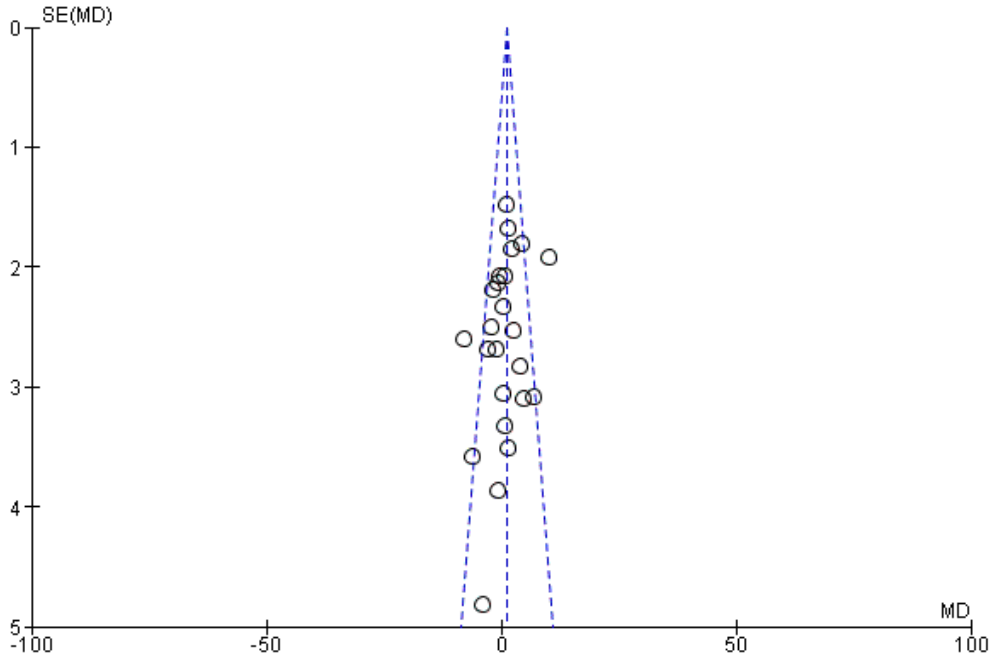
LVEF MRI DIFFERENCE BETWEEN THE GROUPS



LVEF ECHO END OF THE STUDY



LVEF MRI END OF THE STUDY



viii. List of Excluded Studies:

STUDY	Author Name	Reason
A multicenter, prospective, randomized, controlled trial evaluating the safety and efficacy of intracoronary cell infusion mobilized with granulocyte colony-stimulating factor and darbepoetin after acute myocardial infarction: study design and rationale of the 'MAGIC cell-5-combination cytokine trial'	Kang 2004	Wrong Intervention
A multicenter, prospective, randomized, open-labeled, trial comparing different bone-marrow-derived stem cell approaches in patients with reperfused ST-elevation myocardial infarction	Roman 2013	Wrong Study Design
A Phase II Randomized, Double-blind, Controlled Trial of Combined Mesenchymal Stromal Cells and C-kit+ Cardiac Progenitor Cells in Ischemic Heart Failure: The CCTRN CONCERT-HF Trial	Bolli 2020	Wrong Population
A pilot trial of autologous bone marrow mononuclear cell transplantation through grafting artery: A sub-study focused on segmental left ventricular function recovery and scar reduction	Lu M 2013	Wrong Population
A placebo controlled, dose-ranging, safety study of allogenic mesenchymal stem cells injected by endomyocardial delivery after an acute myocardial infarction	Hashemi Sm 2008	Wrong Population
A prospective, multicenter randomized, placebo-controlled trial of autologous bone marrow-derived progenitor cells in patients with acute myocardial infarction: 1year clinical results		Not Retrieved
A randomized, open-labeled, multicenter trial for safety and efficacy of intracoronary adult human mesenchymal stem cells after acute	Lee 2013	Short Term Follow-up of already included studies

myocardial infarction		
Absence of accelerated atherosclerotic disease progression after intracoronary infusion of bone marrow derived mononuclear cells in patients with acute myocardial infarction--angiographic and intravascular ultrasound--results from the TErapia Celular Aplicada al Miocardio Pilot study	Arnold 2010	Wrong Study Design
Acute myocardial infarction reparation/regeneration strategy using Wharton's jelly multipotent stem cells as an 'unlimited' therapeutic agent: 3-year outcomes in a pilot cohort of the CIRCULATE-AMI trial	Kwiecien 2022	Wrong Study Design
Acute myocardial infarction: Long term echocardiographic remodeling after bone marrow cell transplantation	Malagoli A 2010	Wrong Study Design
Adjunctive laser-stimulated stem-cells therapy to primary reperfusion in acute myocardial infarction in humans: Safety and feasibility study	Greener 2018	Wrong Intervention
Adventitial delivery of an allogeneic bone marrow-derived adherent stem cell in acute myocardial infarction: Phase i clinical study	Penn 2012	Wrong Study Design
Allogeneic cardio-reparative cell therapy for acute myocardial infarction Preliminary results of the CAREMI clinical trial	Fernandez Aviles F 2018	Wrong Study Design
Autologous bone marrow stem cell mobilization induced by granulocyte colony-stimulating factor after subacute ST-segment elevation myocardial infarction undergoing late revascularization - Final results from the G-CSF-STEMI (Granulocyte colony-stimulating factor ST-Segment elevation myocardial infarction) trial	Engelmann 2006	Wrong Comparator
Autologous bone-marrow mononuclear cell	Silva 2009	Wrong Comparator

transplantation after acute myocardial infarction: Comparison of two delivery techniques		
Autologous peripheral blood stem cell transplantation via coronary artery for acute myocardial infarction: A follow-up of short-term curative effect	Zhang	Short Term Follow-up of already included studies
Autologous stem cell transplantation in acute myocardial infarction: The ASTAMI randomized controlled trial. Intracoronary transplantation of autologous mononuclear bone marrow cells, study design and safety aspects	Lunde 2005	Short Term Follow-up of already included studies
Bone marrow cell transplantation in patients after acute myocardial infarction and left ventricular dysfunction: Long term effects on heart function and remodeling	Malagoli A 2010	Wrong Study Design
Bone Marrow Mononuclear Cell Transplantation Restores Inflammatory Balance of Cytokines after ST Segment Elevation Myocardial Infarction	Estalo 2015	Wrong Outcome
Bone marrow stem cell transplantation for myocardial regeneration after myocardial infarction: A clinical phase-I trial.	Stamm 2003	Wrong Study Design
Bone marrow-derived mesenchymal cell mobilization by granulocyte-colony stimulating factor after acute myocardial infarction: Results from the Stem Cells in Myocardial Infarction (STEMMI) trial	Ripa 2007	Wrong Intervention
Cardiac contractility after transplantation of autologous mononuclear bone marrow cells in patients with myocardial infarction	Ryabov 2006	Not Retrieved
Cardiac Function Improvement and Bone Marrow Response â€“: Outcome Analysis of the Randomized PERFECT Phase III Clinical Trial of Intramyocardial CD133(+) Application	Steinhoff 2017	Wrong Outcome

After Myocardial Infarction		
Cell Functionality of Administered Antologous Bone Marrow-Derived Mononuclear Cells Predicts 5-Year Clinical Outcome in Patients with Acute Myocardial Infarction - Results of the REPAIR-AMI Trial	Assmus 2012	wrong study design
Cell-based therapy for myocardial repair in patients with acute myocardial infarcion: rationale and study design of the SWiss multicenter Intracoronary Stem cells Study in Acute Myocardial Infarction (SWISS-AMI)	Surder 2010	Short Term Follow-up of already included studies
Clinical outcome 2 years after intracoronary administration of bone marrow-derived progenitor cells in acute myocardial infarction	Assmus 2010	Substudy of already included studies
Clinical outcome after stem cell mobilization with granulocyte-colony-stimulating factor after acute ST-elevation myocardial infarction: 5-year results of the STEMMI trial.	Ripa 2013	Wrong Intervention
Combined delivery approach of bone marrow mononuclear stem cells early and late after myocardial infarction: the MYSTAR prospective, randomized study	Gyongyosi 2009	Wrong Comparator
Combined therapy with sitagliptin plus granulocyte-colony stimulating factor in patients with acute myocardial infarction-Long-term results of the SITAGRAMI trial	Gross 2016	Wrong Intervention
Cotreatment with darbepoetin and granulocyte colony-stimulating factor is efficient to recruit proangiogenic cell populations in patients with acute myocardial infarction	Kang 2012	Wrong Intervention
Design and implementation of the TRACIA: Intracoronary autologous transplant of bone marrow-derived stem cells for acute ST elevation myocardial infarction	Deque 2011	Wrong Study Design

Design and rationale for the Myocardial Stem Cell Administration After Acute Myocardial Infarction (MYSTAR) Study: A multicenter, prospective, randomized, single-blind trial comparing early and late intracoronary or combined (percutaneous intramyocardial and intracoronary) administration of nonselected autologous bone marrow cells to patients after acute myocardial infarction	Nyolczas	Wrong Study Design
Design and rationale of the Reduction of Infarct Expansion and Ventricular Remodeling with Erythropoietin after Large Myocardial Infarction (REVEAL) trial	Melloni 2010	Wrong Study Design
Determinants of functional recovery after myocardial infarction of patients treated with bone marrow-derived stem cells after thrombolytic therapy	Miettinen 2010	Wrong Study Design
Differential effect of intracoronary infusion of mobilized peripheral blood stem cells by granulocyte colony-stimulating factor on left ventricular function and remodeling in patients with acute myocardial infarction versus old myocardial infarction: The MAGIC cell-3-DES randomized, controlled trial	Kang 2006	Wrong Outcome
Double-Blind, Placebo-Controlled, Randomized Trial of Stem Cell Therapy Combined with Bypass Surgery - The MiHeart Trial	Gowdak 2018	Wrong Study Design
Effect of Erythropoietin in patients with acute myocardial infarction: five-year results of the REVIVAL-3 trial	Steppich 2017	Wrong Intervention
Effect of granulocyte colony stimulating EPC on cardiac function and myocardial energy expenditure in patients with heart failure after myocardial infarction	Zhao 2015	Wrong Intervention
Effect of granulocyte colony stimulating factor EPC on cardiac function in patients with heart	Zhao 2011	Not Retrieved

failure after myocardial infarction		
Effect of granulocyte colony-stimulating factor treatment at a low dose but for a long duration in patients with coronary heart disease - A pilot study	Suzuki 2006	Wrong Intervention
Effect of intramyocardial delivery of autologous bone marrow mononuclear stem cells on the regional myocardial perfusion. NOGA-guided subanalysis of the MYSTAR prospective randomised study	Charwat S 2010	Wrong Study Design
Effect of self-marrow stem cell transplantation in situ on the size of infarct area and cardiac functions after acute myocardium infarction	Chen 2004	Wrong Intervention
Effect of the Use and Timing of Bone Marrow Mononuclear Cell Delivery on Left Ventricular Function After Acute Myocardial Infarction The TIME Randomized Trial	Traverse 2012	Short Term Follow-up of already included studies
Effect on heart rate variability of autologous bone marrow mesenchymal stem cell in patients with ST segment elevation myocardial infarction		Not Retrieved
Effects of erythropoietin after an acute myocardial infarction: Rationale and study design of a prospective, randomized, clinical trial (HEBE III)	Belonje 2008	Wrong Study Design
Effects of G-CSF on systemic inflammation, coagulation and platelet activation in patients with acute myocardial infarction	Steppich 2011	Wrong Intervention
Effects of GM-CSF on the stem cells mobilization and plasma C-reactive protein levels in patients with acute myocardial infarction	Deng 2006	Wrong Comparator
Effects of granulocyte-colony-stimulating factor on mobilization of bone-marrow-derived stem cells after myocardial infarction	Nienaber 2006	Wrong Comparator

in humans		
Effects of intracoronary infusion of bone marrow-derived stem cells on pulmonary artery pressure and diastolic function after myocardial infarction	Miettinen 2010	Short Term Follow-up of already included studies
Effects of intracoronary infusion of peripheral blood stem-cells mobilised with granulocyte-colony stimulating factor on left ventricular systolic function and restenosis after coronary stenting in myocardial infarction: The MAGIC cell randomised clinical trial	Kang 2004	Wrong Intervention
Effects of intracoronary injection of autologous bone marrow-derived stem cells on natriuretic peptides and inflammatory markers in patients with acute ST-elevation myocardial infarction	Miettinen 2011	Wrong Outcome
Effects of recombinant human erythropoietin on platelet activation in acute myocardial infarction: Results of a double-blind, placebo-controlled, randomized trial	Tang 2009	Wrong Intervention
Effects of stem cell therapy with G-CSF on coronary artery after drug-eluting stent implantation in patients with acute myocardial infarction	Kang 2008	Wrong Comparator
Endothelial progenitor cell captures stent implantation in patients with ST-segment elevation acute myocardial infarction: One year follow-up	Lee 2010	Wrong Study Design
Edothelial Progenitor Cells Overexpressing Endothelial No-Synthase May Improve Infarct Healing: Results From The Enhanced Angiogenic Cell Therapy â€“Acute Myocardial Infarction (Enact-AMI) Trial	Stewart 2021	Wrong Outcome
Enhanced mobilization of the bone marrow-derived circulating progenitor cells by intracoronary freshly isolated bone marrow	Turan 2012	Wrong Study Design

cells transplantation in patients with acute myocardial infarction		
Erythropoietin-induced progenitor cell mobilisation in patients with acute ST-segment-elevation myocardial infarction and restenosis	Stein 2012	Wrong Intervention
Exercise capacity, arrhythmic risk profile, and pulmonary function is not influenced by intracoronary injection of Bone Marrow Stem Cells in patients with acute myocardial infarction	Migaj 2012	Wrong Outcome
First-in-human pilot trial of combined intracoronary and intravenous mesenchymal stem cell therapy in acute myocardial infarction	Hsiao 2022	Wrong Study Design
Five-year results of intracoronary infusion of the mobilized peripheral blood stem cells by granulocyte colony-stimulating factor in patients with myocardial infarction	Kang 2012	Wrong Comparator
Functional and structural benefits after therapy with autologous GCSF-mobilized peripheral blood progenitor cells in subacute myocardial infarction: A prospective, randomized, controlled study		Not Retrieved
G-CSF in patients suffering from late revascularized ST elevation myocardial infarction: Analysis on the timing of G-CSF administration	Engelmann 2008	Wrong Intervention
G-CSF induced arteriogenesis in humans: Molecular insights into a randomized controlled trial	Meier 2013	Wrong Study Design
Granulocyte colony stimulating factor in patients with large acute myocardial infarction: Results of a pilot dose-escalation randomized trial	Ellis 2006	Wrong Intervention

Granulocyte colony-stimulating factor attenuates left ventricular remodelling after acute anterior STEMI: results of the single-blind, randomized, placebo-controlled multicentreSTemcEll Mobilization in Acute Myocardial Infarction (STEM-AMI) Trial	Achilli 2010	Wrong Comparator
Granulocyte colony-stimulating factor therapy for stem cell mobilization following anterior wall myocardial infarction: The CAPITAL STEM MI randomized trial	Hibbert 2014	Wrong Intervention
Granulocyte-colony stimulating factor for large anterior ST-elevation myocardial infarction: Rationale and design of the prospective randomized phase III STEM-AMI OUTCOME trial	Achilli 2015	Wrong Study Design
Immunomodulatory effect of first-in-human PeriCord cardiac bioimplant: Preliminary data of the PERISCOPE clinical trial	Tortajada 2022	Wrong Intervention
Impact of intracoronary injection of mononuclear bone marrow cells in acute myocardial infarction on left ventricular perfusion and function: a 6-month follow-up gated ^{99m}Tc-MIBI single-photon emission computed tomography study	Plewka 2009	Short Term Follow-up of already included studies
Improved clinical outcome after intracoronary administration of bone-marrow-derived progenitor cells in acute myocardial infarction: final 1year results of the REPAIR-AMI trial	Assmus 2007	Short Term Follow-up of already included studies
Improved regional function after autologous bone marrow-derived stem cell transfer in patients with acute myocardial infarction: A randomized, double-blind strain rate imaging study	Janssens 2009	Short Term Follow-up of already included studies
Infused CD34 cell dose, not bone marrow $CD34^+$ cell content, improves clinical outcomes and lvef in patients with left ventricular	Quyyumi A 2017	Wrong Study Design

dysfunction post stemi: Results of the preserve-AMI trial		
Instent neointimal hyperplasia after percutaneous intervention for ST-elevation myocardial infarction and treatment with granulocyte-colony stimulating factor. Results from the stem cells in myocardial infarction (STEMMI) trial	Jorgensen 2010	Wrong Intervention
In-stent neo-intimal hyperplasia after stem cell mobilization by granulocyte-colony stimulating factor. Preliminary intracoronary ultrasound results from a double-blind randomized placebo-controlled study of patients treated with percutaneous coronary intervention for ST-elevation myocardial infarction (STEMMI Trial)	Deng 2006	Wrong Comparator
Intracoronary ALLogeneic heart STem cells to Achieve myocardial Regeneration (ALLSTAR): a randomized, placebo-controlled, double-blinded trial	Makkar 2020	Wrong Population
Intracoronary autologous bone-marrow cell transfer after myocardial infarction: the BOOST randomised controlled clinical trial	Wollert 2004	Short Term Follow-up of already included studies
Intracoronary bone marrow-derived progenitor cells in acute myocardial infarction	Assmus 2006	Short Term Follow-up of already included studies
Intracoronary cardiosphere-derived cells after myocardial infarction: Evidence of therapeutic regeneration in the final 1-year results of the CADUCEUS trial (CArdiosphere-derived aUtologous stem CElls to reverse ventricular dysfunction)	Malliaras 2014	Wrong Intervention
Intracoronary cardiosphere-derived cells for heart regeneration after myocardial infarction (CADUCEUS): A prospective, randomised phase 1 trial	Makkar 2013	Wrong Intervention

Intracoronary cardiosphere-derived cells for heart regeneration after myocardial infarction: Determinants of regenerative efficacy in the final 1-year results of the caduceus trial	Makkar 2013	Wrong Intervention
Intracoronary infusion of autologous mononuclear bone marrow cells in patients with acute myocardial infarction treated with primary PCI: Pilot study of the multicenter HEBE trial	Hirsch 2011	Substudy of already included studies
Intracoronary infusion of bone marrow mesenchymal stem cells in acute myocardial infarction-a critical challenge for dosage-related efficacy and safety	Gao 2013	Short Term Follow-up of already included studies
Intracoronary infusion of bone marrow-derived mononuclear cells in acute myocardial infarction: 5-year clinical outcome and MRI data of the randomized, Double-blind, Placebo-controlled repair-ami trial	Assmus 2011	Short Term Follow-up of already included studies
Intracoronary infusion of bone-marrow-derived progenitor cells is associated with improved clinical outcome in patients with acute myocardial infarction: 12 months follow up of the REPAIR-AMI trial	Assmus 2006	Short Term Follow-up of already included studies
Intracoronary infusion of the mobilized peripheral blood stem cell by G-CSF is better than mobilization alone by G-CSF for improvement of cardiac function and remodeling: 2-Year follow-up results of the Myocardial Regeneration and Angiogenesis in Myocardial Infarction with G-CSF and Intra-Coronary Stem Cell Infusion (MAGIC Cell) 1 trial	Kang 2007	Wrong Outcome
Intracoronary Injection of Bone Marrow-Derived Mononuclear Cells Early or Late After Acute Myocardial Infarction Effects on Global Left Ventricular Function	Surder 2013	Short Term Follow-up of already included studies

Intracoronary injection of mononuclear bone marrow cells in acute myocardial infarction	Lunde 2006	Short Term Follow-up of already included studies
Intracoronary stem cell therapy in patients with acute myocardial infarction-36months results of a randomized, double blind, placebo controlled trial	Whorle 2012	Wrong Study Design
Intracoronary stem-cell injection after myocardial infarction: Microcirculation sub-study	Moreira 2011	Wrong Study Design
Intracoronary transplantation of autologous peripheral blood stem cells in old patients with acute myocardial infarction: 5-year postoperative evaluation of cardiac function		Not Retrieved
Intramyocardial injection of autologous bone marrow-derived ex vivo expanded mesenchymal stem cells in acute myocardial infarction patients is feasible and safe up to 5-years of follow-up	Rodrigo 2013	Wrong Study Design
Isolated Coronary Artery Bypass Graft Combined with Bone Marrow Mononuclear Cells Delivered Through a Graft Vessel for Patients with Previous Myocardial Infarction and Chronic Heart Failure A Single-Center, Randomized, Double-Blind, Placebo-Controlled Clinical Trial	Hu 2011	Wrong Population
Lack of beneficial eff ects of granulocyte colony-stimulating factor in patients with subacute myocardial infarction undergoing late revascularization: A double-blind, randomized, placebo-controlled clinical trial	Karimabad 2011	Wrong Comparator
LateTIME: A Phase-II, randomized, double-blinded, placebo-controlled, pilot trial evaluating the safety and effect of administration of bone marrow mononuclear cells 2 to 3 weeks after acute myocardial	Traverse 2010	Short Term Follow-up of already included studies

infarction		
Left ventricular function after intracoronary infusion of bone marrow-derived progenitor cells after acute STEMI: MRI substudy of the double-blind, randomized, placebo-controlled multicenter REPAIR-AMI trial	Assmus 2006	Short Term Follow-up of already included studies
Left ventricular systolic and diastolic function improve after acute myocardial infarction treated with acute percutaneous coronary intervention, but are not influenced by intracoronary injection of autologous mononuclear bone marrow cells: a 3-year serial echocardiographic sub-study of the randomized-controlled ASTAMI study	Lunde 2011	Short Term Follow-up of already included studies
Long-term follow-up of stem cell therapy after acute myocardial infarction	Forrester 2009	Wrong Study Design
Long-Term Outcome of Combined (Percutaneous Intramyocardial and Intracoronary) Application of Autologous Bone Marrow Mononuclear Cells Post Myocardial Infarction: The 5-year MYSTAR Study	Gyongyosi 2016	Wrong Comparator
Long-term safety and clinical outcome after intracoronary progenitor cell transplantation in patients with acute myocardial infarction: 1 year follow-up analysis of the TOPGARE-AMI trial	Schachinger 2004	Wrong Comparator
Multicenter double-blind trial of autologous bone marrow mononuclear cell transplantation through intracoronary injection post acute myocardium infarction - MiHeart/AMI study	Nogueira 2008	Short Term Follow-up of already included studies
Myocardial regeneration strategy using Wharton's jelly multipotent stem cells as an â€œunlimitedâ€ therapeutic agent: 3-year outcomes in a pilot cohort of circulate-acute	Kwiecien 2022	Wrong Study Design

myocardial infarction trial		
Normalization of coronary microvascular function in the infarct artery by bone marrow-derived progenitor cells after acute myocardial infarction: Results from the double-blind, placebo-controlled Repair-AMI trial	Assmus 2006	Short Term Follow-up of already included studies
Observation on the safety: clinical trail on intracoronary autologous bone marrow mononuclear cells transplantation for acute myocardial infarction	Yao 2006	Not Retrieved
One year follow-up of left ventricular function and remodeling after intracoronary infusion of bone marrow - Derived progenitor cells after acute stemi: MRI substudy of the double-blind, randomized, placebo-controlled multicenter Repair-AMI trial.	Assmus 2007	Short Term Follow-up of already included studies
One year follow-up results from preserve-AMI: A randomized, double-blind, placebo controlled clinical trial of intracoronary infusion of autologous $CD34^+$ cells in patients with left ventricular dysfunction post stemi	Qyummi 2015	Wrong Study Design
One-year follow-up of intracoronary stem cell delivery on left ventricular function following ST-elevation myocardial infarction	Traverse 2014	Wrong Study Design
Paclitaxel-eluting balloon versus conventional balloon predilatation in acute myocardial infarction undergoing endothelial progenitor cell-capture stent implantation: the DEBORA 2 randomised multicentre trial	Kim 2020	Wrong Intervention
Percutaneous, trans endocardial injection of bone marrow-derived mononuclear cells in heart failure patients following acute ST-elevation myocardial infarction: ALSTER-Stem Cell trial	Heeger 2012	Wrong Population
Phase 2 study of intramyocardial injection of	Livingston 2009	Wrong Intervention

autologous CD34+ cells to treat subjects with refractory chronic myocardial ischemia (CMI): Factors influencing mobilization and apheresis		
Phase iii randomized clinical trial comparing the effects of autologous bone marrow derived mnc and cd133 cells transplantation in AMI patients during cabg	Nasseri 2013	Wrong Study Design
Pluripotent stem cell-derived mesenchymal stromal cells improve cardiac function and vascularity after myocardial infarction	Thavapalachandran S 2021	Wrong Population
Predictors of ventricular remodelling in patients with reperfused acute myocardial infarction and left ventricular dysfunction candidates for bone marrow cell therapy: insights from the BONAMI trial	Manrique 2016	Wrong Study Design
Preservation from left ventricular remodeling by front-integrated revascularization and stem cell liberation in evolving acute myocardial infarction by use of granulocyte-colony-stimulating factor (FIRSTLINE-AMI)	Ince 2005	Wrong Comparator
Prevention of left ventricular remodeling with granulocyte colony-stimulating factor after acute myocardial infarction: Final 1-year results of the front-integrated revascularization and stem cell liberation in evolving acute myocardial infarction by granulocyte colony-stimulating factor (FIRSTLINE-AMI) trial	Ince 2005	Wrong Comparator
Randomized Comparison of Endothelial Progenitor Cells Capture Stent Versus Cobalt-Chromium Stent for Treatment of ST-Elevation Myocardial Infarction. Six-Month Clinical, Angiographic, and IVUS Follow-Up	Bystron 2010	Wrong Intervention
Randomized transcoronary delivery of CD34(+) cells with perfusion versus stop-flow method in patients with recent myocardial	Musialek 2011	Wrong Intervention

infarction: Early cardiac retention of (99m)Tc-labeled cells activity		
Rationale and design for TIME: A phase II, randomized, double-blind, placebo-controlled pilot trial evaluating the safety and effect of timing of administration of bone marrow mononuclear cells after acute myocardial infarction	Traverse 2009	Wrong Study Design
Rationale and design of the trans endocardial injection of autologous human cells (bone marrow or mesenchymal) in chronic ischemic left ventricular dysfunction and heart failure secondary to myocardial infarction (TAC-HFT) trial: A randomized, double-blind, placebo-controlled study of safety and efficacy	Trachtenberg 2011	Wrong Study Design
Recovery of regional but not global contractile function by the direct intramyocardial autologous bone marrow transplantation - Results from a randomized controlled clinical trial	Hendrikx 2006	Wrong Study Design
Red Ginseng Extract Improves Coronary Flow Reserve and Increases Absolute Numbers of Various Circulating Angiogenic Cells in Patients with First ST-Segment Elevation Acute Myocardial Infarction	Ahn 2011	Wrong Intervention
REPAIR-AMI: Stem cells for acute myocardial infarction	Mills 2007	Short Term Follow-up of already included studies
Residual Viability Is a Predictor of the Perfusion Enhancement Obtained with the Cell Therapy of Chronic Myocardial Infarction A Pilot Multimodal Imaging Study	Maureira 2012	Wrong Population
Restoration of coronary microvascular function in the infarct-related artery by bone marrow-derived progenitor cells after acute MI: Results from the double-blind, placebo-	Assmus 2006	Short Term Follow-up of already included studies

controlled REPAIR-AMI trial		
Restoration of left ventricular synchronous contraction after acute myocardial infarction by stem cell therapy: new insights into the therapeutic implication of stem cell therapy for acute myocardial infarction	Chang 2008	Wrong Comparator
Restoration of microvascular function in the infarct-related artery by intracoronary transplantation of bone marrow progenitor cells in patients with acute myocardial infarction: the Doppler Sub study of the Reinfusion of Enriched Progenitor Cells and Infarct Remodeling in Acute Myocardial Infarction (REPAIR-AMI) trial	Assmus 2007	Short Term Follow-up of already included studies
Results from Late TIME: A Randomized, Placebo Controlled Trial of Intracoronary Stem Cell Delivery Two to Three Weeks Following Acute Myocardial Infarction from the Cardiovascular Cell Therapy Research Network	Traverse 2011	Short Term Follow-up of already included studies
Results of the swiss multicenter intracoronary stem cells study in acute myocardial infarction (Swiss AMI) trial	Surder 2013	Short Term Follow-up of already included studies
Safety and efficacy of intracoronary hypoxia-preconditioned bone marrow mononuclear cell administration for acute myocardial infarction patients: The CHINA-AMI randomized controlled trial	Hu 2015	Wrong Study Design
Safety and efficacy of intracoronary infusion of mobilized peripheral blood stem cell in patients with myocardial infarction: MAGIC Cell-1 and MAGIC Cell-3-DES-trials	Kang 2008	Wrong Study Design
Safety and efficacy of intracoronary transplantation of G-CSF mobilized autologous peripheral blood stem cells in patients with acute myocardial infarction	Li 2006	Wrong Comparator

Safety and efficacy of sitagliptin plus granulocyte-colony stimulating factor in patients suffering from acute myocardial infarction - Sitagrami trial	Theiss 2010	Wrong Intervention
Safety and efficacy of sitagliptin plus granulocyte-colony stimulating factor in patients suffering from acute myocardial infarction (sitagrami trial)-primary and secondary analyses	Theiss 2010	Wrong Intervention
Safety and feasibility of combined granulocyte colony stimulating factor and erythropoetin based-stem cell therapy using intracoronary infusion of peripheral blood stem cells in patients with recent anterior myocardial infarction: one-year follow-up of a phase 1 study.	Santoso 2011	Wrong Study Design
Safety of bone marrow stem cell mobilization induced by granulocyte-colony stimulating factor: 30 Days blinded clinical results from the Stem Cells in Myocardial Infarction (STEMMI) trial	Engelmann 2006	Wrong Study Design
Single-Dose Intravenous Administration of Recombinant Human Erythropoietin Is a Promising Treatment for Patients with Acute Myocardial Infarction - Randomized Controlled Pilot Trial of EPO/AMI-1 Study	Ozawa 2009	Wrong Intervention
Six months follow up results of "granulocytes-colony stimulating factor" based stem cell therapy in patients with myocardial infarction: MAGIC cell randomized controlled trial	Kang 2006	Wrong Intervention
Stem cell mobilisation by granulocyte-colony stimulating factor in patients with acute myocardial infarction: Long-term results of the REVIVAL-2 trial	Steppich 2016	Wrong Comparator
STEM cell mobilization by Granulocyte colony stimulating factor post myocardial infarction	Zohlnhofer 2006	Wrong Intervention

to promote myocyte repair		
Stem cell mobilization by granulocyte colony-stimulating factor in patients with acute myocardial infarction: A randomized controlled trial	Zohlnhofer 2006	Wrong Comparator
Stem cell mobilization by granulocyte-colony-stimulating factor in acute myocardial infarction: lessons from the REVIVAL-2 trial	Zohlnhofer 2007	Wrong Study Design
Stem cell mobilization induced by subcutaneous granulocyte-colony stimulating factor to improve cardiac regeneration after acute ST-elevation myocardial infarction - Result of the double-blind, randomized, placebo-controlled stem cells in myocardial infarction (STEMMI) trial	Ripa 2066	Wrong Comparator
Stem cells mobilization in acute myocardial infarction (stem-AMI trial): preliminary data of a perspective, randomized, single blind trial	Kang 2004	Wrong Intervention
Sustained improvement in left ventricular function after bone marrow derived cell therapy in patients with acute ST elevation myocardial infarction. A 5-year follow-up from the Stem Cell Transplantation in Ischaemic Myocardium Study.	Moccetti 2012	Wrong Study Design
The clinical study of autologous peripheral blood stem cell transplantation by intracoronary infusion in patients with acute myocardial infarction (AMI)	Li ZQ 2007	Wrong Intervention
The combined effect of subcutaneous granulocyte- colony stimulating factor and myocardial contrast echocardiography with intravenous infusion of sulfur hexafluoride on post-infarction left ventricular function, the RIGENERA 2.0 trial: study protocol for a randomized controlled trial	Leone 2016	Wrong Intervention

The Effect of Intracoronary Infusion of Autologous Bone Marrow-Derived Lineage-Negative Stem/Progenitor Cells on Remodeling of Post-Infarcted Heart in Patient with Acute Myocardial Infarction	Peregud-Pogorzelska 2020	Wrong Study Design
The effect of intracoronary stem cell injection on markers of leukocyte activation in acute myocardial infarction	Helseth 2015	Wrong Outcome
The effect of timing of stem cell delivery following acute myocardial infarction: The NHLBI and CCTRN TIME trial	Traverse 2012	Wrong Study Design
The effects of intracoronary delivery of mononuclear bone marrow cells in patients with myocardial infarction: A two-year follow-up results	Plewka 2011	Short Term Follow-up of already included studies
The improvement of myocardial function by granulocyte colony stimulating factor following acute anterior myocardial infarction: A double-blind placebo controlled study	Kojuri 2011	Wrong Intervention
The Influence of Autologous Bone Marrow Stem Cell Transplantation on Matrix Metalloproteinases in Patients Treated for Acute ST-Elevation Myocardial Infarction	Furenes 2014	Wrong Outcome
The influence of intracoronary injection of bone marrow cells on prothrombotic markers in patients with acute myocardial infarction	Solheim 2012	Wrong Outcome
Timing for intracoronary administration of bone marrow mononuclear cells after acute ST-elevation myocardial infarction: A pilot study	Huang 2015	Wrong Study Design
Transcoronary stem cell delivery using physiological endothelium-targeting perfusion technique: The rationale and a pilot study involving a comparison with conventional over-the-wire balloon coronary occlusions in	Musialek 2006	Wrong Study Design

patients after recent myocardial infarction		
Transcoronary transplantation of progenitor cells after myocardial infarction	Assmus 2006	Wrong Population
Transplantation efficacy of autologous bone marrow mesenchymal stem cells combined with atorvastatin for acute myocardial infarction (TEAM-AMI): rationale and design of a randomized, double-blind, placebo-controlled, multi-center, Phase II TEAM-AMI trial	Xu 2019	Wrong Study Design
Transplantation of progenitor cells and regeneration enhancement in acute myocardial infarction (TOPCARE-AMI): final 5-year results suggest long-term safety and efficacy	Leistner 2011	Wrong Comparator
Two-year follow-up results of the CARDIAC (CARDIomyoplasty by Autologous intraCoronary bone marrow in acute myocardial infarction) randomised controlled trial.	Piepolli 2013	Short Term Follow-up of already included studies
Use of granulocyte-colony stimulating factor during acute myocardial infarction to enhance bone marrow stem cell mobilization in humans: Clinical and angiographic safety profile	Valgimigli 2005	Wrong Study Design
Usefulness of granulocyte colony-stimulating factor in patients with a large anterior wall acute myocardial infarction to prevent left ventricular remodeling (the rigenera study)	Leone 2007	Wrong Comparator
Value of a single bolus erythopoetin in STEMI patients treated with the Genous endothelial progenitor cell capture stent	Suryapranata 2019	Wrong Intervention
Long-term results after intracoronary injection of autologous mononuclear bone marrow cells in acute myocardial infarction: the ASTAMI randomised, controlled study	Beitnes Jo 2009	Stem cell characterization not defined

Initial clinical outcomes of intracoronary infusion of autologous progenitor cells in patients with acute myocardial infarction	Jazi 2012	Stem cell characterization not defined
Autologous mononuclear bone marrow cells during reparative regeneration after acute myocardial infarction	Karpov 2005	Stem cell characterization not defined
Efficacy of stem cell in improvement of left ventricular function in acute myocardial infarction--MI3 Trial	Nair 2015	Stem cell characterization not defined
Stem-cell therapy in ST-segment elevation myocardial infarction with reduced ejection fraction: A multicenter, double-blind randomized trial	Nicolau 2018	Stem cell characterization not defined
Systolic function of patients with myocardial infarction undergoing autologous bone marrow transplantation	Nogueira 2009	Stem cell characterization not defined
Effect of Autologous Bone Marrow Cell Transplantation Combined with Off-Pump Coronary Artery Bypass Grafting on Cardiac Function in Patients with Chronic Myocardial Infarction	Wang 2015	Stem cell characterization not defined
Assessment of left ventricular segmental function after autologous bone marrow stem cells transplantation in patients with acute myocardial infarction by tissue tracking and strain imaging	Wen R 2005	Stem cell characterization not defined

REFERENCES:

1. Angeli FS, Caramori PR, da Costa Escobar Piccoli J, Danzmann LC, Magedanz E, Bertaso A, et al. Autologus transplantation of mononuclear bone marrow cells after acute myocardial infarction: a PILOT study. International Journal of Cardiology 2012; 158:449-50.
2. Assmus B, Leistner DM, Schächinger V, Erbs S, Elsässer A, Haberbosch W, et al. Long-term clinical outcome after intracoronary application of bone marrow-derived mononuclear cells for acute myocardial infarction: migratory capacity of administered cells determines event-free survival. Eur Heart J 2014; 14:1275-83.
3. Attar A, Farjoud Kouhanjani M, Hessami K, Vosough M, Kojuri J, Ramzi M, et al. Effect of once versus twice intracoronary injection of allogeneic-derived mesenchymal stromal cells after acute myocardial infarction: BOOSTER-TAHA7 randomized clinical trial.Stem Cell Res Ther 2023; 14:264.
4. Cao F, Sun D, Li C, Narsinh K, Zhao L, Li X, et al. Long-term myocardial functional improvement after autologous bone marrow mononuclear cells transplantation in patients with ST-segment elevation myocardial infarction: 4 years follow-up, European Heart Journal, Volume 30, Issue 16, August 2009; Pages 1986–1994, https://doi.org/10.1093/eurheartj/ehp220.
5. Chen SL, Fang WW, Qian J, Ye F, Liu YH, Shan SJ, et al. Improvement of cardiac function after transplantation of autologous bone marrow mesenchymal stem cells in patients with acute myocardial infarction. Chinese Medical Journal 2004; 117:1443-8.
6. Choudry F et al. A randomized double blind control study of early intra-coronary autologous bone marrow cell infusion in acute myocardial infarction: the Regenerate AMI clinical trial. European Heart Journal 2016; 37:256-263.
7. Chullikana A, Majumdar AS, Gottipamula S, Krishnamurthy S, Kumar AS, Prakash VS. Randomized, double-blind, phase I/II study of intravenous allogeneic mesenchymal stromal cells in acute myocardial infarction. Cytotherapy 2015-03-01; 17:250-261.
8. Colombo A, Castellani M, Piccaluga E, Pusineri E, Palatresi S, Longari V, et al. Myocardial blood flow and infarct size after $CD133^{+}$ cell injection in large myocardial infarction with good recanalization and poor reperfusion: results from a randomized controlled trial. Journal of Cardiovascular Medicine 2011; 12:239-48.
9. Delewi R, van der Laan AM, Robbers LF, Hirsch A, Nijveldt R, van der Vleuten PA, et al. Long term outcome after mononuclear bone marrow or peripheral blood cells infusion after myocardial infarction. Heart 2015; 101:363-8.
10. Dill T, Schächinger V, Rolf A, Möllmann S, Thiele H, Tillmanns H, et al. Intracoronary administration of bone marrow-derived progenitor cells improves left ventricular function in patients at risk for adverse remodeling after acute ST-segment elevation myocardial infarction: Results of the Reinfusion of Enriched Progenitor cells And Infarct Remodeling in Acute Myocardial Infarction study (REPAIR-AMI) cardiac Magnetic Resonance Imaging substudy. Am Heart J 2009; 157:541-7.
11. Fernández-Avilés F, Sanz-Ruiz R, Bogaert J, Casado Plasencia A, Gilaberte I. Safety and Efficacy of Intracoronary Infusion of Allogeneic Human Cardiac Stem Cells in Patients with

ST-Segment Elevation Myocardial Infarction and Left Ventricular Dysfunction. Circ Res 2018 Aug 17; 123:579-589.

12. Gao LR, Pei XT, Ding QA, Chen Y, Zhang NK, Chen HY, et al.A critical challenge: dosage-related efficacy and acute complication intracoronary injection of autologous bone marrow mesenchymal stem cells in acute myocardial infarction. International Journal of Cardiology 2013; 168:3191-9.
13. Gao LR, Chen Y, Zhang Xi, Liu HL, Wang ZG, Yan Xiao. Intracoronary infusion of whartons jelly derived mesenchymal stem cells in acute myocardial infarction: doble blind randomized controlled trial. BMC Medicine 2015; 13:10.1186/s12916-015-0399-z.
14. Ge J, Li Y, Qian J, Shi J, Wang Q, Niu Y, et al. Efficacy of emergent transcatheter transplantation of stem cells for treatment of acute myocardial infarction (TCT-STAMI). Heart 2006; 92:1764-7.
15. Grajek S, Popiel M, Gil L, Breborowicz P, Lesiak M, Czepczynski R, et al. Influence of bone marrow stem cells on left ventricle perfusion and ejection fraction in patients with acute myocardial infarction of anterior wall: randomized clinical trial: Impact of bone marrow stem cell intracoronary infusion on improvement of microcirculation. European Heart Journal 2010; 31:691-702.
16. Haddad K, Potter BJ, Matteau A, et al. Analysis of the COMPARE-AMI trial: First report of long term safety of CD133 cells. International Journal of Cardiology 2020; 319:32-35.
17. Hare JM, Traverse JH, Henry TD, Dib N, Strumpf RK, Schulman SP, GerstenblithG. A randomized, double-blind, placebo-controlled, dose-escalation study of intravenous adult human mesenchymal stem cells (prochymal) after acute myocardial infarction. J Am Coll Cardiol 2009; 54:2277-86.
18. Huikuri HV, Kervinen K, Niemela M, Ylitalo K, Saily M, Koistinen P, et al. Effects of intracoronary injection of mononuclear bone marrow cells on left ventricular function, arrhythmia risk profile and restenosis after thrombolytic therapy of acute myocardial infarction. European Heart Journal 2008; 29:2723-32.
19. Janssens S, Dubois C, Bogaert J, Theunissen K, Deroose C, Desmet W, et al. Autologous bone marrow-derived stem-cell transfer in patients with ST-segment elevation myocardial infarction: double-blind, randomised controlled trial. Lancet 2006; 367:113-21.
20. Kaminek, M, Meluzin, J, Panovsky, R.et al.Individual differences in the effectiveness of intracoronary bone marrow cell transplantation assessed by gated sestamibi SPECT/FDG PET imaging. J Nucl Cardiol 2008; 15 392-399. https://doi.org/10.1016/j.nuclcard.2008.02.016.
21. Kim SH, Cho JH, Lee YH, Lee JH, Kim SS, Kim MY, et al. Improvement in Left Ventricular Function with Intracoronary Mesenchymal Stem Cell Therapy in a Patient with Anterior Wall ST-Segment Elevation Myocardial Infarction. Cardiovasc Drugs Ther2018; 32:329-338.
22. Laguna et al. Effect of direct intramyocardial autologous stem cell grafting in the sub-acute phase after myocardial infraction. 2018; 59:259-67.
23. Lezo JSD, Herrera C, Pan M, Romero M, Pavlovic D, Segura et al. Regenerative therapy in patients with a revascularized acute anterior myocardial infarction and depressed ventricular function. Rev Esp Cardiol2007;60:357-65

24. Lee JW, Lee SH, Youn YJ, Ahn MS, Kim JY, Yoo BS, et al. A randomized, open-label, multicenter trial for the safety and efficacy of adult mesenchymal stem cells after acute myocardial infarction. Journal of Korean Medical Science 2014; 29:23-31.
25. Lunde K, Solheim S, Aakhus S, Arnesen H, Moum T, Abdelnoor M, et al. Exercise capacity and quality of life after intracoronary injection of autologous mononuclear bone marrow cells in acute myocardial infarction: results from the Autologous Stem cell Transplantation in Acute Myocardial Infarction (ASTAMI) randomized controlled trial. Am Heart J 2007; 154:e1-8. doi: 10.1016/j.ahj.2007.07.003.
26. Mathur A, Fernandez Aviles F, Bartunek J, Belmans A, Crea F, et al. The effect of intracoronary infusion of bone marrow-derived mononuclear cells on all-cause mortality in acute myocardial infarction: the BAMI trial. European Heart Journal 2020; 41:3702-3710.
27. Meyer GP, Wollert KC, Lotz J, Pirr J, Rager U, Lippolt P, et al. Intracoronary bone marrow cell transfer after myocardial infarction: 5-year follow-up from the randomized-controlled BOOST trial. European Heart Journal 2009; 30:2978-2984.
28. Naseri MH, Madani H, Ahmadi Tafti SH, Moshkani Farahani M, et al. COMPARE CPM-RMI Trial: Intramyocardial Transplantation of Autologous Bone Marrow-Derived $CD133^+$ Cells and MNCs during CABG in Patients with Recent MI: A Phase II/III, Multicenter, Placebo-Controlled, Randomized, Double-Blind Clinical Trial. Cell J 2018; 20:267-277.
29. Ostovaneh MR, Makkar RR, Ambale-Venkatesh B, Ascheim D, Chakravarty T, Henry TD, et al. Effect of cardiosphere-derived cells on segmental myocardial function after myocardial infarction: ALLSTAR randomised clinical trial. Open Heart 2021; 8:10.1136/openhrt-2021-001614.
30. Penicka M, Horak J, Kobylka P, Pytlik R, Kozak T, Belohlavek O, et al. Intracoronary injection of autologous bone marrow-derived mononuclear cells in patients with large anterior acute myocardial infarction. A prematurely terminated randomised study. Journal of the American College of Cardiology 2007; 49:2373-4.
31. Piepoli MF, Vallisa D, Arbasi M, et al. Bone marrow cell transplantation improvescardiac, autonomic, and functional indexes inacute anterior myocardial infarction patients(Cardiac Study. European Journal of Heart Failur2010; 12:172-180.
32. Plewka M, Krzemińska-Pakuła M, Lipiec P, Peruga JZ, Jezewski T, Kidawa M, et al. Effect of Intracoronary injection of mononuclear bone marrow stem cells on left ventricular functions in patients with acute myocardial infarction. The American Journal of Cardiology 2009; 104:1336-1342.
33. Quyyumi AA, Waller EK, Murrow J, Esteves F, Galt J, Oshinski J, et al. CD 34 cell infusion after ST elevation myocardial infarction in associated with improved perfusion and is dose dependent. Am Heart J 2011; 161:98-105.
34. Quyyumi AA, Vasquez A, Kereiakes DJ, Klapholz M, Schaer GL, Abdel-Latif A, Frohwein S,PreSERVE-AMI: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial of Intracoronary Administration of Autologous $CD34^+$ Cells in Patients With Left Ventricular Dysfunction Post STEMI. Circ Res 2017; 120:324-331.
35. San Roman JA, Sánchez PL, Villa A, Sanz-Ruiz R, Fernandez-Santos ME, Gimeno F, et al. Comparison of Different Bone Marrow-Derived Stem Cell Approaches in Reperfused STEMI.

A Multicenter, Prospective, Randomized, Open-Labeled TECAM Trial. J Am Coll Cardiol 2015; 65:2372-82.

36. Roncalli J, Mouquet F, Piot C, Trochu JN, Le Corvoisier P, Neuder Y, et al. Intracoronary autologous mononucleated bone marrow cell infusion for acute myocardial infarction: results of the randomized multicenter BONAMI trial. Eur Heart J 2011; 32:1748-57.
37. Srimahachota S, Boonyaratavej S, Rerkpattanapipat P, Wangsupachart S, Tumkosit M, Bunworasate U, et al. Intra-coronary Bone Marrow Mononuclear Cell Transplantation in Patients with ST-Elevation Myocardial Infarction: A Randomized Controlled Study. J Med Assoc Thai 2011; 94:657-63.
38. Sürder D, Manka R, Moccetti T, Lo Cicero V, Emmert MY, Klersy C, et al. Effect of Bone Marrow-Derived Mononuclear Cell Treatment, Early or Late After Acute Myocardial Infarction: Twelve Months CMR and Long-Term Clinical Results. Circ Res 2016; 119:481-90.
39. Tendera M, Wojakowski W, Ruzyłło W, Chojnowska L, Kepka C, Tracz W,et al. Intracoronary infusion of bone marrow-derivedselected CD341CXCR41 cells and non-selected mononuclear cells in patients with acute STEMIand reduced left ventricular ejection fraction:results of randomized, multicentre Myocardial Regeneration by Intracoronary Infusion of Selected Population of Stem Cells in Acute Myocardial Infarction (REGENT) Trial. European Heart Journal 2009; 30:1313-1321.
40. Traverse JH, McKenna DH, Harvey K, Jorgenso BC, Olson RE, Bostrom N, et al. Results of a phase 1, randomized, double-blind,placebo-controlled trial of bone marrow mononuclearstem cell administration in patients following ST-elevation myocardial infarction. Am Heart J 2010; 160:428-34.
41. Traverse JH, Henry TD, Ellis SG, Pepine CJ, Willerson JT, Zhao DX, et al. Effect of Intracoronary Delivery ofAutologous Bone Marrow Mononuclear Cells 2 to 3 Weeks Following Acute MyocardialInfarction on Left Ventricular Function. The Late TIME Randomized Trial. JAMA 2011; 306:2110-2119.
42. Traverse JH, Henry TD, Pepine CJ, Willerson JT, Chugh A, Yang PC, et al. TIME Trial: Effect of Timing of Stem Cell Delivery Following ST-Elevation Myocardial Infarction on the Recovery of Global and Regional Left Ventricular Function: Final 2-Year Analysis. Circ Res 2018; 122:479-488.
43. Wang X, Xi WC, Wang F. The beneficial effects of intracoronary autologous bone marrow stem cell transfer as an adjunct to percutaneous coronary intervention in patients with acute myocardial infarction. Biotechnollett 2014; 36:2163-2168.
44. Wen-tao X, Chuan-yu G, Guo-you D, Mu-wei L, Xian-pei W, et al. Autologous bone marrow mesenchymal stem cells for myocardial renewal and repair. Chinese Journal of Tissue Engineering Research. 2012; (27): 5081-5086. DOI: 10.3969/j.issn.2095-4344.2012.27.027.
45. Wohrle J, Merkle N, Mailander V, Nusser T, Schauwecker P, von Scheidt F, et al. Results of the intracoronary stem cell therapy after acute myocardial infarction. American Journal of Cardiology 2010; 105:804-12.
46. Wollert et al. Intracoronary autologous bone marrow cell transfer after myocardial infarction: the BOOST-2 randomized placebo controlled clinical trial. European Heart Journal 2017; 38:2936-2943.

47. Yao K, Huang R, Sun A, Qian J, Liu X, GeL, et al. Repeated autologous bone marrow mononuclear cell therapy in patients with large myocardial infarction. European Journal Heart Failure 2009; 11:691-8.
48. Zhang R, Yu J, Zhang N, Li W, Wang J, Cai G, et al. Bone marrow mesenchymal stem cells transfer in patients with ST-segment elevation myocardial infarction: single-blind, multicenter, randomized controlled trial.Stem Cell Res Ther 2021;12:33.
49. De Vore AD, Hellkamp AS, Thomas L, Albert NM, Butler J, Patterson JH, Spertus JA, Williams FB, Duffy CI, Hernandez AF, Fonarow GC. Improvement in Left Ventricular Ejection Fraction in Outpatients with Heart Failure with Reduced Ejection Fraction: Data From CHAMP-HF. Circ Heart Fail. 2020 Jul; 13 (7): e006833.
50. Dai, W, Liu, C, Liu, J et al. Preference of individuals in the treatment strategies of acute myocardial infarction in China: a discrete choice experiment. Dai et al. Health and Quality of Life Outcomes (2020) 18:217 https://doi.org/10.1186/s12955-020-01466-1.
51. Lindeman et al. 2020. https://doi.org/10.1186/s12967-020-02425-6 (https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-020-02425-6).