SCE 0804 Public Evidence Appendix

Cardiovascular disease

Literature review date: September 13, 2026

Controlling principle. Cardiovascular evidence is indication-, product-, route-, and endpoint-specific. Mechanistic or surrogate signals must not be converted into claims of myocardial regeneration, limb salvage, or survival benefit without appropriate human clinical evidence.

Evidence map

Domain	Evidence posture	Interpretive boundary
Myocardial infarction	Investigational work examines cytoprotection, immunomodulation, angiogenic signaling, and remodeling after ischemic injury.	Not a substitute for reperfusion and established acute myocardial infarction care.
Ischemic cardiomyopathy	Studies evaluate perfusion, inflammation, fibrosis, viable myocardium, and ventricular remodeling.	Imaging or ejection-fraction changes do not establish myocardial regeneration, fewer hospitalizations, or survival benefit.
Heart failure	Cell and EV studies explore immunomodulation, vascular effects, antifibrotic signaling, and myocardial support.	Biomarker or ejection-fraction changes do not substitute for patient-important outcomes.
Peripheral arterial disease	Therapeutic angiogenesis, collateral development, endothelial signaling, and tissue repair have been studied.	Investigational biologic therapy should not replace risk reduction, exercise, foot care, or revascularization when indicated.
Critical limb ischemia	Research examines perfusion, wound healing, angiogenesis, and limb preservation in severe ischemia.	Limb salvage, amputation-free survival, function, wound healing, and survival are key clinical outcomes.
Endothelial dysfunction	Mechanistic studies assess nitric-oxide signaling, oxidative stress, inflammation, and vascular homeostasis.	Improved endothelial assays do not establish fewer cardiovascular events, better limb outcomes, or longer survival.

Key evidence conclusions

Cardiovascular conditions are not interchangeable. Acute myocardial infarction, chronic ischemic cardiomyopathy, heart failure, peripheral arterial disease, critical limb ischemia, and endothelial dysfunction require separate interpretation.

Mechanism is not regeneration. Anti-inflammatory, angiogenic, antifibrotic, or endothelial effects do not by themselves establish restoration of lost myocardium or durable limb benefit.

Surrogate changes must be separated from clinical outcomes. Ejection fraction, perfusion, scar imaging, or flow-mediated dilation can be informative without proving fewer admissions, amputations, or deaths.

Established cardiovascular care remains the comparator. Reperfusion, guideline-directed medical therapy, risk-factor treatment, rehabilitation, wound care, and revascularization should not be displaced by unproven biologic claims.

Principal references

1. Galipeau J, Sensebé L. Mesenchymal stromal cells: clinical challenges and therapeutic opportunities. Cell Stem Cell. 2018;22:824-833.

2. Pittenger MF, Discher DE, Péault BM, Phinney DG, Hare JM, Caplan AI. Mesenchymal stem cell perspective: cell biology to clinical progress. NPJ Regen Med. 2019;4:22.

3. Relevant contemporary clinical and translational literature concerning cell- and EV-based interventions after myocardial infarction, in ischemic cardiomyopathy, heart failure, peripheral arterial disease, chronic limb-threatening ischemia, and endothelial dysfunction.

4. Contemporary cardiovascular and vascular guidelines should control statements concerning reperfusion, guideline-directed medical therapy, revascularization, secondary prevention, and limb-threatening ischemia management.

5. Product identity, disease phenotype, route, dose, comparator, endpoint, background therapy, and follow-up must be matched before cardiovascular evidence is generalized.