SCE 0801 Public Evidence Appendix

Hematology

Literature review date: September 13, 2026

Controlling principle. Hematopoietic stem-cell transplantation and MSC/EV interventions are biologically and clinically distinct. Established hematopoietic therapies must not be conflated with investigational stromal-cell or extracellular-vesicle applications.

Evidence map

Domain	Evidence posture	Interpretive boundary
Hematopoietic transplantation	Established clinical platform for selected malignant and nonmalignant hematologic diseases; MSCs/EVs have been studied as adjunctive or supportive interventions.	Evidence for HSCT efficacy cannot be transferred to MSC or EV products simply because all are discussed under a broad 'stem-cell' label.
Marrow failure	Biological rationale exists because MSCs are components of the marrow microenvironment; clinical restoration of durable hematopoiesis by exogenous MSC/EV therapy remains product- and disease-specific.	Supportive marrow biology is not equivalent to proven correction of aplastic anemia or other marrow-failure syndromes.
Hemoglobinopathies	Curative-intent approaches may include HSCT or gene therapy for selected patients; MSC/EV roles remain investigational and generally adjunctive.	Evidence for sickle cell disease or beta-thalassemia must be separated from claims about unrelated cell products or indications.
Graft-versus-host disease	MSC-based products have been investigated for immune modulation, including difficult steroid-refractory settings; results vary by product, population, route, and endpoint.	A signal in GVHD does not establish class-wide effectiveness across MSC products or other immune diseases.
Immune reconstitution	Recovery of neutrophils, lymphocytes, NK cells, T cells, and B cells occurs on different timelines and may be influenced by disease, conditioning, graft source, infection, immunosuppression, and adjunctive therapy.	Improvement in one immune subset or biomarker does not prove restoration of functional immune competence.

Key evidence conclusions

Terminology is critical. Hematopoietic stem cells and mesenchymal stromal cells are different cell populations with different biological roles and clinical uses.

Established and investigational therapies must remain separate. The existence of established HSCT does not establish effectiveness of MSC or EV therapies in hematology.

Clinical context is highly specific. Disease, donor type, graft source, conditioning, HLA matching, infection risk, immunosuppression, relapse risk, and transplant-center practice all influence interpretation.

Regulatory conclusions are product- and jurisdiction-specific. Authorization of one defined product for one defined indication does not imply class-wide approval.

Principal references

1. Copelan EA. Hematopoietic stem-cell transplantation. N Engl J Med. 2006;354:1813-1826.

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

3. Zeiser R, Blazar BR. Acute graft-versus-host disease — biologic process, prevention, and therapy. N Engl J Med. 2017;377:2167-2179.

4. Relevant contemporary consensus and clinical literature concerning hematopoietic transplantation, marrow failure, hemoglobinopathies, GVHD, immune reconstitution, and MSC-based investigational therapies.

5. Regulatory status must be verified for the exact product, indication, jurisdiction, and date; authorization does not imply class-wide approval.