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**Stem Cell Transplantation for Refractory Crohn’s: Outcomes and Immune Mechanisms**

**Guisado D, Talware S, Wang X, et al. Reparative immunological consequences of stem cell transplantation as a cellular therapy for refractory Crohn’s disease. Gut 2025; 74: 894-905. doi: 10.1136/gutjnl-2024-333558**

In a phase II trial, 19 adults with severe Crohn’s disease (CD) unresponsive to all standard therapies were treated with autologous haematopoietic stem cell transplantation (HSCT). Patients received high-dose melphalan plus anti-thymocyte globulin, followed by reinfusion of mobilised autologous stem cells. Among the 14 patients who reached 6 months post-transplant, 10 achieved endoscopic remission, 13 had a major endoscopic response (>50% endoscopic improvement), and 8 showed histological healing of the intestinal lining. These outcomes illustrate that HSCT can induce substantial clinical and mucosal improvement in refractory CD.

Immune profiling of blood and gut samples revealed that HSCT primarily alters the intestinal myeloid cell compartment. After transplant, pro-inflammatory immune cells in the intestine were greatly reduced and replaced by macrophages that promote tissue repair and mucosal healing. This shift indicates that HSCT helps restore a healing-oriented immune environment in the gut.

The findings underscore the crucial role of macrophages: Guisado et al. propose that refractory CD may result not just from ongoing inflammation, but from a failure of the immune system to support mucosal healing. This mechanism may be critical to how stem cells reinforce disease pathophysiology, especially in the myeloid lineage. By rebuilding the immune system from stem cells, HSCT may correct this imbalance. The study also noted variability in patients’ stem cell grafts, where some had impaired ability to reconstitute the immune system, potentially affecting individual outcomes. Overall, the results support the rationale of HSCT as a cellular therapy that “resets” the immune system, restoring immune balance and enabling mucosal healing in CD.