



cGvHD, GvHD Prophylaxis

A meta-analysis of mesenchymal stromal cells for the prophylaxis of chronic graft-versus-host disease

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Previous studies have shown that mesenchymal stromal cells (MSCs) may be a possible novel prophylactic strategy to prevent graft-versus-host disease (GvHD). MSCs modulate immune responses by secreting soluble factors that can modify the stimulation, proliferation and maturation of T- and B lymphocytes, natural killer cells, and dendritic cells. Furthermore, MSCs also induce the differentiation of regulatory T cells and regulate the Th1/Th2 ratio. At present, there are several ongoing randomized trials investigating the impact of MSCs on GvHD prevention or treatment.¹

Li Wang from the Department of Hematology, Laoshan Branch of No. 401 Hospital of Chinese People's Liberation Army (PLA), Qingdao, China, and colleagues investigated randomized controlled trials on the efficacy and safety of MSCs for the prophylaxis of chronic GvHD in patients with hematological malignancies undergoing allogeneic hematopoietic stem cell transplantation (allo-HSCT). The meta-analysis was published in an issue of *Annals of Hematology*.²

Study selection and characteristics:

- Six studies were included in the analysis comprising 365 patients undergoing allo-HSCT with or without the prophylactic use of MSCs
- Sample sizes of the selected trials: range, 20–124 patients
- MSCs were collected from hematopoietic stem cell donors in two studies, from third party donors in three studies, and from either HSC or third party donors in one study
- MSCs were derived from the bone marrow (BM) in three studies or the umbilical cord in three studies

Key data:

- The incidence of chronic GvHD was significantly lower in patients receiving MSCs than patients in the control group: RR = 0.63 (95% CI, 0.46–0.86), $P = 0.004$
- The 2-year overall survival was not significantly different between patients receiving MSCs and control groups. However, overall survival was increased in patients receiving MSCs in comparison with the control group: RR = 1.13 (95% CI, 0.98–1.29), $P = 0.084$
- Favorable prophylactic effects of MSCs on cGVHD were observed with umbilical cord-derived, high-dose, and late-infusion MSCs, while bone marrow-derived, low-dose, and coinfused MSCs did not confer beneficial prophylactic effects
- Subgroup meta-analysis showed that pediatric patients experienced a decreased incidence of chronic GvHD, while adult patients did not: RR = 0.21 (95% CI, 0.05–0.86), $P = 0.030$ vs RR = 0.72 (95% CI, 0.30–1.74), $P = 0.466$; respectively

- The incidence of chronic GvHD was significantly lower in patients receiving UC-derived, high-dose, or late-infusion MSCs in comparison with the control groups: RR = 0.49 (95% CI 0.28–0.85), $P = 0.011$ vs RR = 0.55 (95% CI 0.37–0.83), $P = 0.005$ vs RR = 0.60 (95% CI 0.39–0.93), $P = 0.022$; respectively
- The risk of primary disease relapse and infection showed no significant difference between patients receiving MSC infusion and control patients: RR = 1.02 (95% CI, 0.70–1.50), $P = 0.913$; RR = 0.89 (95% CI, 0.44–1.81), $P = 0.752$; respectively

The results of the meta-analysis show that MSC prophylaxis is safe and effective in the prevention of chronic GvHD in patients with haematological malignancies who are undergoing allo-HSCT, moreover, MSC infusion could reduce the incidence of chronic GvHD without increasing the risk of disease relapse and infections. Further clinical trials are required to validate these observations.

References

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2. Wang L. et al. Efficacy and safety of mesenchymal stromal cells for the prophylaxis of chronic graft-versus-host disease after allogeneic hematopoietic stem cell transplantation: a meta-analysis of randomized controlled trials. Ann Hematol. 2018 Oct;97(10):1941-1950. DOI: [1007/s00277-018-3384-8](https://doi.org/10.1007/s00277-018-3384-8). 2018 Jun 8. [Epub ahead of print].

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