DSEN ABSTRACT

Is there an impact of sex (biologically male/female) differences between donors and recipients on safety and efficacy of cell therapies for immune system and autoimmune conditions?

Summary

- Hematopoietic stem cell transplantation (HSCT) is a promising option for persons with refractory autoimmune disease but is linked to toxicity.
- Data from Canada, the USA and Europe provide relevant real-world evidence of HSCT's safety/effectiveness.
- Overall, we observed high survival and low relapse in AD patients after HSCT.
- In allogenic HSCT (for AA and other AD), overall mortality was linked with age, CMV in donor/recipient, peripheral blood and cord blood cell source, HLA mismatch, and patient comorbidities.
- In those surviving to 2 years, lower late mortality was seen in male-to-female stem cell donation (vs female-to-male or male-to-male).
- In Canadian data autologous HSCT (mostly for multiple sclerosis and scleroderma) overall survival was 93.6% at 2 years and 88.9% at 5 years. Opportunistic infection and organ failure were among the main causes of death. Similar results were found for male vs female patients.

Authors: S. Bernatsky, MG. Birck

For more information, please contact:
Sasha.bernatsky@mcgill.ca

This initiative was funded by CIHR – Drug Safety and Effectiveness Network.

What is the current situation?

Allogeneic and autologous hematopoietic stem cell transplantation (HSCT) has been increasingly used as a potentially life-saving treatment for severe autoimmune disease (AD). Limited evidence has suggested an effect of donor-recipient sex differences after HSCT on overall and progression-free survival and risk factors for graft-versus-host-disease (GVHD). Health Canada requested real-world analyses of the safety and effectiveness of HSCT in AD, particularly regarding whether the sex of the donor and recipient contribute to poor outcomes.

What were the aims of the study?

1. To describe characteristics of AD patients undergoing autologous/allogeneic HSCT;
2. To assess the clinical effectiveness and safety of autologous/allogeneic HSCT in AD;
3. To evaluate the impact of patients (and donor, in allogeneic) characteristics on the clinical effectiveness and safety of autologous/allogeneic HSCT to treat AD.

How was the study conducted?

This retrospective observational study evaluated persons with AD undergoing HSCT. We used open-access data from the North American Center for International Blood and Marrow Transplant Research (**CIBMTR**) registry, the European Society for Bone and Marrow Transplantation (**EBMT**) Registry, and chart review at two **Canadian HSCT programs**.

What did the study find?

Overall, a high survival rate was observed for allogeneic and autologous HSCT, supporting previously published findings by other authors. No clear difference was found related to biological sex of the recipient, but donor-recipient mismatches were an important factor associated with poor prognosis after allogeneic HSCT. We observed a relatively low relapse rate in AD patients undergoing autologous HSCT.

CIBTMR (651 severe aplastic anemia (SAA), 1,091 AA and 12 other AD – allogeneic HSCT):

- For overall mortality, factors associated with higher risk: increasing age, CMV presence in donor and recipient (vs no presence), HLA donor-recipient mismatch (vs identical HLA-match), peripheral blood & cord blood cell source (vs bone marrow), recipient comorbidities. Anti-thymocyte globulin (ATG) use (vs no ATG/ alemtuzumab) was associated with lower risk. Sex of donor/recipient was not a clear risk factor for overall mortality.
- Factors associated with late mortality (death after 2 years) were peripheral blood cell source (vs bone marrow), increasing age, total body irradiation and chemotherapy-based myeloablative conditioning therapy (vs non-myeloablative or reduced-intensity), poor function (Karnofsky Performance Scale <90), and chronic GVHD. Lower late mortality was seen in male-to-female stem cell donation (vs female-to-male and male-to-male).

EBMT (1,389 AD patients, 68% multiple sclerosis (MS) and 21% scleroderma (Scl)autologous):

- At 2 years of HSCT, overall survival was 95.5% (95% CI 94.2-96.5%), progression-free survival was 82% (95% CI 79.6-84.2%), AD relapse incidence was 14.8% (95% CI 12.7-17.0%), and non-relapse mortality was 3.2% (95% CI 2.3-4.3%).
- Results were similar when stratified by biologic sex.

Canadian HSCT programs (228 AD patients, 42% MS and 26% Scl – autologous HSCT):

- After HSCT, 28 patients (12.3%) died, about half within 3 years
- Just over a third (35%) died from transplant-related causes, and 27% died from disease progression/relapse.
- Opportunistic infection and organ failure were among the main causes of death.
- Overall survival was 93.6% (95% CI 90.4-96.9%) at 2 years and 88.9% (95% CI 84.3-93.9%) at 5 years.
- Similar results were found for male and female patients.