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Stem Cell Transplant for Multiple Sclerosis: Clinical Effectiveness, Cost-Effectiveness, and Guidelines

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Research Questions

1. What is the clinical effectiveness of stem cell transplant for individuals with multiple sclerosis?
2. What is the cost-effectiveness of stem cell transplant for individuals with multiple sclerosis?
3. What are the evidence-based guidelines regarding stem cell transplant for individuals with multiple sclerosis?

Key Findings

Two randomized controlled trials and one non-randomized study were identified regarding the clinical effectiveness of stem cell transplant for individuals with multiple sclerosis. One systematic review was identified regarding the cost-effectiveness of stem cell transplant for individuals with multiple sclerosis. Four evidence-based guidelines were identified regarding stem cell transplant for individuals with multiple sclerosis.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including Medline and EMBASE via OVID, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were stem cell transplant and multiple sclerosis. Filters were applied to limit the retrieval to health technology assessments, systematic reviews, and meta analyses, randomized controlled trials, and non-randomized studies, economic studies, and guidelines. The search was also limited to English language documents published between January 1, 2015 and November 9, 2020. Internet links are provided where available.

Selection Criteria

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. Open access full-text versions of evidence-based guidelines were reviewed when abstracts were not available.

Table 1: Selection Criteria

Population	Individuals with multiple sclerosis
Intervention	Autologous hematopoietic stem cell transplant (HSCT)
Comparator	Q1-Q2: Standard of care (i.e., disease modifying therapy) Q3: Not applicable
Outcomes	Q1: Clinical effectiveness (e.g., disability, progression free survival, quality of life, pain, treatment-related mortality) Q2: Cost-effectiveness (e.g., cost per quality-adjusted life-year gained) Q3: Recommendations regarding best practices
Study Designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, economic evaluations, evidence-based guidelines

Results

Two randomized controlled trials[2,3] and one non-randomized study[4] were identified regarding the clinical effectiveness of stem cell transplant for individuals with multiple sclerosis. One systematic review was identified regarding the cost-effectiveness of stem cell transplant for individuals with multiple sclerosis.[1] Four evidence-based guidelines[5-8] were identified regarding stem cell transplant for individuals with multiple sclerosis. No health technology assessments or economic evaluations were identified.

Additional references of potential interest that did not meet the inclusion criteria are provided in the appendix.

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

1. Nagpal A, Milte R, Kim SW, et al. Economic evaluation of stem cell therapies in neurological diseases: a systematic review. *Value Health*. 2019 Feb;22(2):254-262. PubMed: PM30711072

Randomized Controlled Trials

2. Burt RK, Balabanov R, Burman J, et al. Effect of nonmyeloablative hematopoietic stem cell transplantation vs continued disease-modifying therapy on disease progression in patients with relapsing-remitting multiple sclerosis: a randomized clinical trial. *JAMA*. 2019 Feb;321(2):165-174. PubMed: PM30644983

3. Mancardi GL, Sormani MP, Gualandi F, et al. Autologous hematopoietic stem cell transplantation in multiple sclerosis: a phase II trial. *Neurology*. 2015 Mar 10;84(10):981-988. PubMed: PM25672923

Non-Randomized Studies

4. Mariottini A, Innocenti C, Forci B, et al. Safety and efficacy of autologous hematopoietic stem-cell transplantation following natalizumab discontinuation in aggressive multiple sclerosis. *Eur J Neurol*. 2019 Apr;26(4):624-630. PubMed: PM30414315

Economic Evaluations

No literature identified.

Guidelines and Recommendations

5. Miller AE, Chitnis T, Cohen BA, et al. Autologous hematopoietic stem cell transplant in multiple sclerosis: recommendations of the National Multiple Sclerosis Society. *JAMA Neurology*. 2020 Oct 26. PubMed: PM33104165

6. Sharrack B, Saccardi R, Alexander T, et al. Autologous haematopoietic stem cell transplantation and other cellular therapy in multiple sclerosis and immune-mediated neurological diseases: updated guidelines and recommendations from the EBMT Autoimmune Diseases Working Party (ADWP) and the Joint Accreditation Committee of EBMT and ISCT (JACIE). *Bone Marrow Transplant*. 2020 Feb;55(2):283-306. PubMed: PM31558790

7. Cohen JA, Baldassari LE, Atkins HL, et al. Autologous hematopoietic cell transplantation for treatment-refractory relapsing multiple sclerosis: position statement from the American Society for Blood and Marrow Transplantation. *Biol Blood Marrow Transplant*. 2019 May;25(5):845-854. PubMed: PM30794930

8. Healthcare Improvement Scotland. Autologous haematopoietic stem cell transplant for patients with highly active relapsing remitting multiple sclerosis not responding to high efficacy disease modifying therapies [*SHGT advice statement 07-19*]. Edinburgh, Scotland: Healthcare Improvement Scotland; 2019 Oct: http://www.healthcareimprovementscotland.org/our_work/technologies_and_medicines/topics_assessed/shtg_07-19.aspx Accessed 2020 Nov 11.
See: Advice for NHSScotland (p1); Clinical Effectiveness – Guidelines (p9-10).

Appendix — Further Information

Systematic Reviews and Meta-analyses

Comparator – No Comparison Group Specified

9. Zhang P, Liu B. Effect of autologous hematopoietic stem cell transplantation on multiple sclerosis and neuromyelitis optica spectrum disorder: a PRISMA-compliant meta-analysis. *Bone Marrow Transplant*. 2020 Oct;55(10):1928-1934. PubMed: PM32020080

10. Ge F, Lin H, Li Z, Chang T. Efficacy and safety of autologous hematopoietic stem-cell transplantation in multiple sclerosis: a systematic review and meta-analysis. *Neurol Sci*. 2019 Mar;40(3):479-487. PubMed: PM30535563

11. Sormani MP, Muraro PA, Schiavetti I, et al. Autologous hematopoietic stem cell transplantation in multiple sclerosis: a meta-analysis. *Neurology*. 2017 May 30;88(22):2115-2122. PubMed: PM28455383

Guidelines – Methods Not Specified

12. Alberta Health Services. Alberta bone marrow and blood cell transplant program: standard practice manual. Edmonton (AB): Cancer Control Alberta, Alberta Health Services; 2020 Oct (*updated*): https://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-bmt-manual.pdf Accessed 2020 Nov 11.
See: Multiple Sclerosis - Selection Criteria for Autologous Hematopoietic Stem Cell Transplant in MS.

13. Welsh Health Specialised Services Committee. Haematopoietic Stem Cell Transplantation (HSCT) for adults [*Specialised services policy position PP142*]. Pontypridd, Wales: NHS Wales; 2020 Jan: http://www.whssc.wales.nhs.uk/sitesplus/documents/1119/PP142%20HSCT%20v1.01.pdf Accessed 2020 Nov 11.
See: 1.5 What NHS Wales has decided (p8).

14. Zephir H, Puyade M, Gueguen A, et al. [Indications and follow-up for autologous hematopoietic stem cell transplantation in multiple sclerosis: guidelines from the Francophone Society of Bone Marrow Transplantation and Cellular Therapy (SFGM-TC) in association with the Francophone Society of Multiple Sclerosis]. *Bull Cancer*. 2019 Jan;106(Suppl 1):S92-S101. PubMed: PM30527815

15. Coles A, Price S, Giavannoni G, et al. Treatment algorithm for multiple sclerosis disease-modifying therapies. London, England: NHS England; 2018 Sep: https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2019/03/Treatment-Algorithm-for-Multiple-Sclerosis-Disease-Modifying-Therapies-08-03-2019-1.pdf Accessed 2020 Nov 11.
See: Flowchart 12. Treatment algorithm for disease activity on second-line therapy, and note 14 (p10).

16. Laureys G, Willekens B, Vanopdenbosch L, et al. A Belgian consensus protocol for autologous hematopoietic stem cell transplantation in multiple sclerosis. *Acta Neurol Belg*. 2018 Jun;118(2):161-168.
PubMed: PM29536270

Review Articles

17. Bose G, Thebault SDX, Atkins HL, Freedman MS. Does resetting the immune system fix multiple sclerosis? *Can J Neurol Sci*. 2020 Jan;47(1):1-10.
PubMed: PM31511117

18. Lycke J, Lenhoff S. Intensive immunosuppression followed by autologous hematopoietic stem cell transplantation for the treatment of multiple sclerosis. *Ther Adv Neurol Disord*. 2020 Jun;13:1756286420929467.
PubMed: PM32636931

19. Mariottini A, De Matteis E, Muraro PA. Haematopoietic stem cell transplantation for multiple sclerosis: current status. *Biodrugs*. 2020 Jun;34(3):307-325.
PubMed: PM32166703

20. Dunn-Pirio AM, Heyman BM, Kaufman DS, Kinkel RP. Outcomes and cost-effectiveness of autologous hematopoietic cell transplant for multiple sclerosis. *Curr Treat Options Neurol*. 2019 Oct;21(10):53.
PubMed: PM31624926

21. Gavriilaki M, Sakellari I, Gavriilaki E, Kimiskidis VK, Anagnostopoulos A. Autologous hematopoietic cell transplantation in multiple sclerosis: changing paradigms in the era of novel agents. *Stem Cells Int*. 2019 Jun;2019:5840286.
PubMed: PM31341484

22. Ismail A, et al. Autologous haematopoietic stem cell therapy for multiple sclerosis: a review for supportive care clinicians on behalf of the Autoimmune Diseases Working Party of the European Society for Blood and Marrow Transplantation. *Curr Opin Supp Palliat Care*. 2019 Dec;13(4):394-401.
PubMed: PM31599815

23. Macaron G, Feng J, Moodley M, Rensel M. Newer treatment approaches in pediatric-onset multiple sclerosis. *Curr Treat Options Neurol*. 2019 Sep 27;21(10):50.
PubMed: PM31560095

24. Atkins HL, Freedman MS. Five questions answered: a review of autologous hematopoietic stem cell transplantation for the treatment of multiple sclerosis. *Neurotherapeutics*. 2017 Oct;14(4):888-893.
PubMed: PM28822119

25. Muraro PA, Martin R, Mancardi GL, Nicholas R, Sormani MP, Saccardi R. Autologous haematopoietic stem cell transplantation for treatment of multiple sclerosis. *Nat Rev Neurol*. 2017 Jul;13(7):391-405.
PubMed: PM28621766