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■ Summary

Autologous Hematopoietic Stem Cell Transplantation for the Treatment of Multiple Sclerosis — Guidance Statement

Key Messages

The CADTH Health Technology Expert Review Panel (HTERP) offers the following guidance to help health systems prepare for potential uptake of autologous hematopoietic stem cell transplantation (AHSCT) for the treatment of multiple sclerosis (MS) should emerging evidence continue to signal clinical benefit and an appropriate safety profile:

Develop and implement systematic strategies for offering monitoring and follow-up care closer to home for individuals currently offered AHSCT for the treatment of MS and those who may be offered AHSCT for the treatment of MS in the future.

Build interprovincial and territorial agreements and other mechanisms that include consideration of financial and logistical support when travel and short-term relocation are required to access AHSCT for MS.

Develop clear and transparent guidelines and protocols, including related training, that are acceptable for potential AHSCT candidates, their caregivers, and their clinicians.

Ensure transplant centre capacity, budget, and other required resources.

Support novel relationships and collaboration among MS and AHSCT health care professionals who would be involved in delivering care.

Ensure equity in access and equitable approaches to care delivery are guiding principles in providing AHSCT for treating MS.

Context

Multiple sclerosis (MS) is a chronic inflammatory autoimmune disorder that affects the central nervous system. Early symptoms may include fatigue, visual blurring, and difficulties in walking. In advanced stages, people with MS may develop paralysis, pain, tremor, and loss of mobility, which can severely affect their day-to-day life. There are different clinical courses of MS, which are characterized by disease activity and disability progression. The most common course, relapse-remitting MS (RRMS), affects approximately 85% of people with MS and is marked by periods of distinct symptom flare-up followed by periods of remission when symptoms may completely

recover, although some symptoms may persist permanently. The standard treatment for MS is disease-modifying therapies (DMTs). DMTs, primarily in people with RRMS, have been shown to be clinically effective. However, the effectiveness typically lasts for 3 years or less, and the treatment is provided on an ongoing basis.

Technology

Autologous hematopoietic stem cell transplantation (AHSCT), a well-established therapy for many blood cancers, is an emerging treatment for MS and other autoimmune disorders. Existing evidence suggests that AHSCT might be a therapeutic option for select people with aggressive or highly active RRMS for whom DMTs provide limited disease control. During AHSCT, patients are treated with an immune-system conditioning regimen to partially or completely destroy the cells that may be damaging their central nervous system. Then, their immune system is reconstituted using stem cells that had previously been harvested from them and could provide an immune-system reset. In contrast with DMTs, AHSCT may provide effective disease control as a one-time procedure. Therefore, AHSCT could potentially alleviate the need for ongoing administration of DMTs that may have adverse events and be associated with recurring costs. AHSCT is offered as an option to treat MS for eligible recipients at 2 transplant centres in Canada, with some interprovincial agreements in place.

Issue

Published research suggests that AHSCT might be a clinically effective and safe alternative to DMTs for select people with aggressive or highly active RRMS. Although this research has methodological limitations that contribute to clinical equipoise (i.e., uncertainty on how one treatment compares with the other), emerging data from ongoing phase III randomized controlled trials (RCTs) could resolve some aspects of clinical equipoise. Given the need for additional treatment options for MS, if research on AHSCT for MS continues to signal that is has a clinical benefit and an appropriate safety profile, health systems will need to be prepared to offer the treatment to eligible people. Therefore, CADTH convened the Health Technology Expert Review Panel (HTERP) to develop guidance on what Canadian health systems would need to do to ensure it is ready to offer AHSCT to eligible people, if ongoing research continues to signal benefit.

Methods

The HTERP guidance is based a CADTH Horizon Scan; an accompanying Rapid Response review; insights provided by clinical experts and a patient expert; and published international guidelines, recommendations, and position statements. Based on the evidence, information, and perspectives presented through these sources, HTERP members developed the guidance through discussion, deliberation, and consensus. A draft version of the guidance was peer reviewed by 2 clinical experts, and the final guidance reflects input received through a stakeholder feedback process.

Findings

Based on the evidence, information, and perspectives presented, HTERP members discussed a number of factors that jurisdictions and centres planning on or thinking of offering AHSCT for MS in the coming years could consider.

Anticipated Number of People in Canada Who Might Be Eligible for AHSCT

A conservative estimate is that, at any given time, 200 people living in Canada have RRMS and may be potentially eligible for AHSCT. However, the number who would be eligible following clinical assessment would be lower. Demand for the procedure would not be expected to overwhelm jurisdictions or centres with unmanageable volume in the current context and while clinical equipoise remains.

Data on AHSCT are available in registries, including 1 maintained by Cell Therapy Transplant Canada, which prospectively collects the number of patients who receive AHSCT for a variety of indications, and another maintained by the European Bone Marrow Transplant Autoimmune Diseases Working Party, which is an international registry. These registries could be monitored to help anticipate interest and demand.

Current and Future State of the Evidence

Evidence from 2 RCTs and 4 retrospective cohort studies suggests that treatment with AHSCT is associated with significant improvement in clinical outcomes, including disease progression, clinical relapse, MRI outcomes, the composite outcome "no evidence of disease activity," and quality of life compared with historical DMTs. AHSCT was also shown to be associated with expected short-term adverse events, including febrile neutropenia, organ infections, sepsis, and viral reactivations; long-term adverse events, including the development of new autoimmune diseases, mainly thyroid disease; and rare treatment-related mortality or life-threatening complications.

At least 3 phase III RCTs are under way to investigate the safety and efficacy of AHSCT compared with more recently developed DMTs. Data from these trials are expected to become available between 2024 and 2026, which may help clarify some aspects of clinical equipoise and provide an opportunity to align practice and guidelines. A health technology assessment that uses this data to perform economic analyses may help assess the overall cost-effectiveness of offering AHSCT for treating MS, given that there is potential for longer-term cost savings if DMTs are no longer required.

Models of Care and Funding

Decisions about models of care may need to be revisited once the results of ongoing phase III RCTs are published. For example, transplants could be centralized at designated specialist centres where specific experience and expertise could be further developed. Then, strategies could be implemented to facilitate access to those centres, which could include the development of interprovincial and territorial agreements. Alternately, the transplant capacity that already exists could be relied on more fully. These decisions must consider the importance of maintaining equitable access and approaches to care delivery.

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People undergoing the AHSCT procedure and their caregivers must travel away from their homes and stay at, or close to, the transplant centre for at least several months if they do not already live near a transplant centre. This leaves them responsible for many of the related costs, which introduces potential inequities in access due to geography and social and/or financial position. Therefore, opportunities to prepare them for, or to reduce, out-of-pocket expenses (including systems to support time away from work) should be considered. Public funding or the support of not-for-profit organizations could potentially be used to help provide financial and logistical support for travel and short-term relocation.

Existing Interest and Networks Across Canada

Offering AHSCT for the treatment of MS will require interest, motivation, and knowledge among MS health care professionals, including transplant physicians, neurologists, and MS specialists. In Canada, there is inconsistent interest in and knowledge of the procedure. To support health system planning, it would be helpful to understand the reasons for the inconsistent interest and work with MS health care professionals to identify barriers and opportunities for addressing them.

The Foundation for the Accreditation of Cellular Therapy (FACT) accredits centres for both autologous and allogenic transplants. Most transplant centres where AHSCT for MS could be provided are accredited by FACT and, therefore, those centres could serve as a network for sharing resources and protocols. Similarly, Cell Therapy Transplant Canada has members from all Canadian provinces and could provide a platform for AHSCT research, guidelines, and education to support decision-makers.