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Recommendation Report SCT-3 IN REVIEW

Stem Cell Transplantation in Myelodysplastic Syndromes and Acute Myeloid Leukemia

C.T. Kouroukis, R.B. Rumble, I. Walker, C. Bredeson, and A. Schuh

Report Date: March 29, 2012

An assessment conducted in March 2018 placed Recommendation Report SCT-3 IN REVIEW. This means that it is undergoing a review for currency and relevance. It is still appropriate for this document to be available while this updating process unfolds. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol)

Recommendation Report SCT-3 is comprised of 2 sections. You can access the summary and full report here: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/976

Section 1: Recommendations
Section 2: Summary of Methods and Evidence

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Recommendation Report SCT-3: Section 1

Stem Cell Transplantation in Myelodysplastic Syndromes and Acute Myeloid Leukemia: Recommendations

C.T. Kouroukis, R.B. Rumble, I. Walker, C. Bredeson, and A. Schuh

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CLINICAL QUESTIONS

Myelodysplastic syndrome (MDS)

What is the role of stem cell transplantation (SCT) in the treatment of MDS?

Acute Myeloid Leukemia (AML)

What is the role of SCT in the treatment of AML?

TARGET POPULATION

All adult patients with MDS or AML being considered for treatment that includes either blood or bone marrow transplantation.

RECOMMENDATIONS AND SUPPORTING EVIDENCE

MYELODYSPLASTIC SYNDROME (MDS)
Allogeneic transplantation is an option for patients with MDS. This is the only potentially curative therapy for MDS.
Evidence • One systematic review comprising a total of 22 studies demonstrated a long-term curative outcome for related, unrelated, either or unspecified allogeneic SCT (alloSCT) (1).
Autologous stem cell transplantation is not recommended for patients with MDS.
Evidence • One systematic review comprising a total of 22 studies did not detect any benefit associated with autologous SCT (ASCT), and does not recommend it outside of a clinical trial (1).

ACUTE MYELOID LEUKEMIA (AML)
First complete remission
Allogeneic transplantation is a treatment option for patients with AML in first complete remission (CR1), with high-risk features including intermediate or high-risk cytogenetic or molecular phenotypes, high-risk clinical features at presentation, and secondary or treatment-related AML.

Evidence

- One systematic review (2), comprising 24 clinical studies involving 6,007 patients with AML in CR1 comparing alloSCT, ASCT, chemotherapy (CT), or any combination of the three, found a significant RFS and OS benefit associated with allogeneic SCT. That review performed subgroup analyses for both recurrence or relapse-free survival (RFS) and overall survival (OS) according to patient risk (good, intermediate, or poor risk). Significant benefits in favour of alloSCT for both intermediate and poor risk patients ($p<0.01$) were detected, but no difference was detected with good risk patients. The OS subgroup analysis also detected significant benefits in favour of alloSCT for intermediate and poor risk patients ($p<0.01$) but not for good risk patients.
- One meta-analysis (3), that pooled data from two trials (AML 96 and AML 02) that compared alloSCT with ASCT with CT, including a total of 708 patients, detected significant differences in favour of alloSCT for both OS and leukemia-free survival (LFS) at two years. In a multivariate analysis, factors associated with better OS and longer LFS were being younger ($p=0.008$) and receiving an allogeneic transplant.
- One prospective cohort study (4) found significant benefits in favour of alloSCT compared with ASCT in the relative risk for eight-year disease-free survival (DFS).

ASCT is not recommended for patients with AML in first complete remission.

Evidence

- While associated with more favourable treatment-related mortality (TRM) rates, if long-term survival is the primary outcome of interest, then there is no evidence to support the use of ASCT in first complete remission.

Beyond first complete remission

Allogeneic transplantation is the recommended option for patients with AML who achieve a second or subsequent remission.

Evidence

- Evidence from one clinical practice guideline (5) demonstrated that if CR only occurs after a second course of induction therapy, myeloablative alloSCT from a fully-matched sibling donor is recommended, regardless of the risk, if the patient is under 55 years of age and has no other co-morbidities

There is insufficient evidence to support the use of ASCT for patients with AML in second or subsequent remission.

Evidence

- If long-term survival is the primary outcome of interest, then there is no evidence to support the use of ASCT in second or subsequent remission.

Autologous transplantation is recommended for acute promyelocytic leukemia (APL) in a molecularly-negative second remission.

Evidence

- No evidence was obtained in this update of the 2009 report (6), and the Expert Panel continues to support this recommendation.

Select patients with AML not in remission may derive benefit from allogeneic transplant.

Evidence

- Evidence from one clinical practice guideline (7) demonstrated that, when a patient does not experience a CR, then that patient should be offered entry into a clinical trial, or reduced intensity alloSCT within a clinical trial setting, or best supportive care (BSC).

[1] Stem Cell Transplantation in Adults, *K. Imrie, R.B. Rumble, M. Crump, the Advisory Panel on Bone Marrow and Stem Cell Transplantation, and the Hematology Disease Site Group of Cancer Care Ontario's Program in Evidence-based Care* [Report Date: January 30, 2009] (6).

QUALIFYING STATEMENT

The patient selection process and the ultimate decision to perform an SCT should take into account not only disease-related characteristics, but also co-morbidities and patient preferences. Patients with MDS or AML should be referred to a transplant centre for transplant assessment.

FUTURE RESEARCH

Ongoing studies in MDS and AML testing newer agents may or may not impact on the number of patients potentially requiring SCT. Reduced intensity transplant and newer methods of preventing or treating graft versus host disease may expand the eligible transplant population. In addition, stem cell procurement from alternative donors such as cord blood and haploidentical donors may also allow SCT to be an option for a greater number of patients.

IMPLICATIONS FOR POLICY

Given the potential increase in the numbers of patients with MDS and AML over time, and the possibility of new transplant methodologies resulting in better outcomes and more donors available thru newer sources, the number of patients eligible for SCT will likely increase.

RELATED PROGRAM IN EVIDENCE-BASED CARE REPORTS

- Imrie K, Rumble RB, Crump M; Advisory Panel on Bone Marrow and Stem Cell Transplantation; Hematology Disease Site Group of Cancer Care Ontario's Program in Evidence-based Care. Stem Cell Transplantation in Adults, [Report Date: January 30, 2009]. Available from: http://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=35448

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