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Recommendation Report SCT-7

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Plerixafor for Autologous Hematopoietic Stem Cell Mobilization and Transplantation for Patients in Ontario

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An assessment conducted in February 2024 deferred review of Recommendation Report SCT-7. This means that the document remains current until it is assessed again next year. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol)

Recommendation Report SCT-7 is comprised of 3 sections. You can access the summary and full report here:

https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/226

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Recommendation Report SCT-7: Section 1

Plerixafor for Autologous Hematopoietic Stem Cell Mobilization and Transplantation for Patients in Ontario: Recommendations

RESEARCH QUESTIONS

1. Does the administration of plerixafor in combination with granulocyte-colony stimulating factor (G-CSF) for stem cell mobilization before autologous transplantation improve the outcome of patients who have not been mobilized before, when compared with G-CSF for stem cell mobilization alone or in combination with chemotherapy?

2. Does the administration of plerixafor in combination with G-CSF for stem cell mobilization before autologous transplantation improve the outcome of patients failing mobilization when compared with G-CSF for stem cell mobilization alone or in combination with chemotherapy?

3. Does the administration of plerixafor in combination with G-CSF for stem cell mobilization before autologous transplantation improve the outcome of patients who have failed a prior mobilization regimen when compared with G-CSF for stem cell mobilization alone or in combination with chemotherapy?

TARGET POPULATION

All adult patients considered for autologous stem cell transplantation (SCT) and meeting one of the following criteria:

- Have not been mobilized before (i.e., the case of up front mobilization in naïve patients who may or may not be at risk of being poor mobilizers)
- Are failing initial mobilization (based on peripheral blood $CD34^+$ cells count before first day of apheresis, or the total number of $CD34^+$ cells collected on the first day of apheresis)
- Have failed a prior mobilization attempt (i.e., are poor mobilizers)

Of particular interest are outcomes focused on the ability to mobilize and collect an adequate graft to get patients to autologous SCT, such as total number of $CD34^+$ cells collected during apheresis (the minimal required cell number for a graft is 2.0×10^6 $CD34^+$ cells/kg), number of apheresis procedures, proportion of patients who proceed to autologous SCT and survival rate post-SCT).

INTENDED PURPOSE

The purpose of this recommendation report is to summarize the available data regarding the efficacy of plerixafor in enhancing hamatopoietic stem cell mobilization and collection before autologous stem cell transplantation and to provide recommendations on its use. Evidence on the cost-effectiveness of plerixafor was not considered in this report.

INTENDED USERS

This recommendation report is intended for all healthcare physicians performing SCT in Ontario, as well as for policy makers, program planners and institutions involved in any STC program or team.

RECOMMENDATIONS, KEY EVIDENCE, AND JUSTIFICATION

RECOMMENDATION 1

Adding plerixafor to G-CSF is an option for initial mobilization for patients with non-Hodgkin lymphoma or multiple myeloma who are eligible for autologous SCT when chemotherapy cannot be used and only G-CSF mobilization is available.

Key Evidence for Recommendation 1

The studies described in the evidence involve patients with non-Hodgkin lymphoma, relapsed or refractory Hodgkin lymphoma, and multiple myeloma. All the patients received G-CSF either alone or as part of the initial mobilization therapy.

- Two randomized controlled trials detected that in patients with non-Hodgkin lymphoma or multiple myeloma, the addition of plerixafor to G-CSF resulted in a greater yield of stem cells and fewer days of apheresis, and allowed more patients to proceed to autologous SCT (auto-SCT) (1, 2).
- Likewise, three nonrandomized trials with historical controls (3-5) reported significantly higher response rates in favour of adding plerixafor.

Qualifying Statements for Recommendation 1

- The available evidence used patients receiving G-CSF alone as the control group. Therefore, the option of plerixafor as an up front therapy is specific to patients undergoing initial mobilization with G-CSF without chemotherapy.
- There is insufficient evidence to support the addition of plerixafor to G-CSF after chemotherapy as initial mobilization in patients eligible for autologous SCT.
- Adding plerixafor to G-CSF for initial mobilization therapy when chemotherapy cannot be used and only G-CSF mobilization is available is an option irrespective of the underlying malignancy (i.e., plasma cell dyscrasias [myeloma, amyloidosis], non-Hodgkin and Hodgkin lymphoma, germ cell tumours).
- Using plerixafor up front with G-CSF may not be cost-effective, as this strategy was not examined in this review, particularly if compared with the plerixafor "on demand" strategy as per the second recommendation. Therefore the members of the Working Group have determined that up front use may be an option rather than making a strict recommendation for its routine use when compared with G-CSF alone.

Interpretation of Evidence for Recommendation 1

The primary outcomes considered to inform the recommendation include the proportion of patients demonstrating successful apheresis harvest (primary end point $\geq 5x10^6$ $CD34^+$ cells/kg), the median collection of $CD34^+$ cells/kg, and the proportion of patients able to proceed to autologous SCT. The certainty of the evidence on the efficacy of G-CSF plus

plerixafor compared with G-CSF alone as up front mobilization therapy in patients with non-Hodgkin lymphoma or myeloma is good. This recommendation is generalizable to all patients with non-Hodgkin lymphoma or myeloma who have not been mobilized before and are eligible for autologous SCT.

The certainty of the evidence for patients with Hodgkin lymphoma is low and therefore this recommendation cannot be easily generalized to patients with hodkin lymphoma. Only two nonrandomized studies with historical controls reported a significantly greater yield of stem cells with plerixafor, but the proportion of patients that were able to proceed to autologous SCT for each individual group was not reported (3, 5).

RECOMMENDATION 2

For patients with low peripheral blood $CD34^+$ cells counts (e.g., <10/uL) at the time of anticipated stem cell harvesting, or with an inadequate first-day apheresis collection, it is recommended that plerixafor be added to the mobilization regimen to maximize stem cell collection and to prevent the need for remobilization.

Key Evidence for Recommendation 2

- Seven nonrandomized studies reported a variety of outcomes including numbers of stem cells collected and number of days of apheresis (5-11). These studies in general detect that better mobilization response is achieved in patients failing their first mobilization attempt when plerixafor is added to their current mobilization regimens.
- Additionally, three studies demonstrated that a significant proportion of patients were able to proceed to auto-SCT with plerixafor (7, 10, 11).

Qualifying Statements for Recommendation 2

- Poor mobilization has been variably defined in these studies, but <10 $CD34^+$ cells per µL is a commonly used criterion. Historical data and consensus opinion have identified that the likelihood of successful stem cell harvest is low among patients with <10 $CD34^+$ cells/µL. In these patients, who appear to be at high risk of failing initial mobilization, a strategy of on demand use of plerixafor may prevent the need for remobilization and therefore minimize further delays in proceeding to auto-SCT.
- Plerixafor is recommended irrespective of the underlying malignancy (i.e., plasma cell dyscrasias [myeloma, amyloidosis], non-Hodgkin and Hodgkin lymphoma, germ cell tumours).

Interpretation of Evidence for Recommendation 2

The primary outcomes considered to inform the recommendation include the proportion of patients demonstrating successful apheresis harvest and the median number of apheresis procedures in patients failing their first mobilization attempt.

The certainty of the evidence on the efficacy of adding plerixafor to current mobilization regimens to maximize stem cell collection is moderate. This recommendation is generalizable to patients eligible for autologous SCT and failing their first mobilization attempt irrespective of the underlying malignancy.

RECOMMENDATION 3
For patients who have failed a previous mobilization attempt, it is recommended that they undergo remobilization with G-CSF and plerixafor, with or without chemotherapy.

Key Evidence for Recommendation 3

Several single-arm studies detected that a significant proportion of patients can still collect enough $CD34^+$ cells to proceed to auto-SCT with plerixafor and G-CSF with or without chemotherapy (1, 2, 7, 12-20).

Qualifying Statements for Recommendation 3

- The definition of failed mobilization in this group of studies is variable and includes patients who have not attained at least the minimum number of $CD34^+$ cells or patients who had low numbers of circulating $CD34^+$ cells prior to apheresis. It is recognized that every attempt should be made to collect enough $CD34^+$ cells in such patients to allow them to proceed to definitive therapy with auto-SCT.
- Plerixafor is recommended irrespective of the underlying malignancy (i.e., plasma cell dyscrasias [myeloma, amyloidosis], non-Hodgkin and Hodgkin lymphoma, germ cell tumours).

Interpretation of Evidence for Recommendation 3

The primary outcomes considered to inform the recommendation include successful apheresis harvest, the median number of apheresis procedures, and the proportion of patients that are able to proceed to autologous SCT after remobilization with G-CSF and plerixafor with or without chemotherapy.

The certainty of the evidence on the efficacy of G-CSF plus plerixafor, with or without chemotherapy, to remobilize patients who have failed previous mobilization attempts is moderate. This recommendation is generalizable to patients eligible for autologous SCT that have failed previous mobilization attempts, irrespective of the underlying malignancy.

RELATED GUIDELINES

- Imrie K, Rumble RB, Crump M. Stem cell transplantation in adults. Toronto (ON): Cancer Care Ontario; 2009 January 30. Program in Evidence-Based Care: Recommendation Report. Available at: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/951
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