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Evidence-based Series 6-19 IN REVIEW

Iodine-131 Tositumomab in Lymphoma

The Hematology Disease Site Group

A Quality Initiative of the
Program in Evidence-based Care (PEBC), Cancer Care Ontario (CCO)
Developed by the Hematology Disease Site Group.

Report Date: January 18, 2007

An assessment conducted in November 2012 placed Evidence-based Series (EBS) 6-19 IN REVIEW, which means that it is undergoing assessment for currency and relevance. The Hematology Disease Site Group (DSG) has determined that it is still appropriate for this document to continue to be available while this updating process unfolds.

The full EBS6-19 is comprised of 3 sections and is available on the CCO website (http://www.cancercare.on.ca)
PEBC Hematology DSG page at:
http://www.cancercare.on.ca/toolbox/qualityguidelines/diseasesite/hema-ebs/

Section 1: Clinical Practice Guideline
Section 2: Systematic Review
Section 3: Guideline Development and External Review

For information about the PEBC and the most current version of all reports, please visit the CCO website at http://www.cancercare.on.ca/ or contact the PEBC office at:
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Guideline Citation (Vancouver Style): The Hematology Disease Site Group. Iodine-131 Tositumomab in lymphoma. Toronto (ON): Cancer Care Ontario; 2007 Jan 18 [In review 2012 Nov]. Program in Evidence-based Care Evidence-based Series No.: 6-19 IN REVIEW.

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Evidence-based Series #6-19: Section 1

Iodine-131 Tositumomab in Lymphoma: A Clinical Practice Guideline

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Questions

In adult patients with lymphoma of any type, at any stage of disease, and for any level of performance status:

1. What are the benefits associated with treatment with Iodine-131 (^{131}I) tositumomab? Outcomes of interest include survival, quality of life, time-to-progression, response duration, and response rate.
2. What is the toxicity associated with the use of ^{131}I tositumomab?
3. Which patients are more or less likely to benefit from treatment with ^{131}I tositumomab?
4. Is performance of imaging or dosimetry required for treatment with ^{131}I tositumomab to be safe and effective?

Recommendations

There is a lack of high quality evidence to explicitly inform the guideline questions. Notwithstanding, the following recommendations, based on a consensus of expert clinical opinion of the Hematology Disease Site Group and the best available evidence, are offered:

- ^{131}I tositumomab is an active agent in relapsed and refractory CD20+ non-Hodgkin's lymphoma that should be made available to selected patients. Based on currently available data, patients who should be prioritized for therapy with ^{131}I tositumomab are those with follicular non-Hodgkin's lymphoma who are refractory to chemotherapy and rituximab and to patients with transformed non-Hodgkin's lymphoma that is refractory to at least one prior course of chemotherapy, with or without rituximab.

- It is the opinion of the Hematology Disease Site Group that the benefit of ^{131}I tositumomab may be generalizable to other relapsed or refractory CD20+ indolent non-Hodgkin's lymphomas, including mantle cell lymphoma, previously treated with rituximab. However, the benefit may not extend to patients with chronic lymphocytic

leukemia/small lymphocytic lymphoma, and ^{131}I tositumomab cannot be routinely recommended in this group of patients.

- There is insufficient evidence to support the use of ^{131}I tositumomab in patients with refractory or relapsed low-grade or follicular non-Hodgkin's lymphoma prior to the use of rituximab.

- Based on the available evidence, dosimetry (calculation of actual radiation absorbed to specific organs) is required to determine the dose to be administered.

Qualifying Statements

- ^{131}I tositumomab should be administered according to published dosing strategies and based on each patient's pharmacokinetics as described in the package insert. A detailed description of dosing can be found in Vose et al (1). Dose reductions should occur if platelets are 100-150x10^9/L. ^{131}I tositumomab should not be administered if platelets are less than 100x10^9/L, absolute neutrophil count is less than 1.5x10^9/L, or bone marrow involvement is greater than 25%.

Key Evidence

The primary evidence regarding ^{131}I tositumomab is described in nine trials:

- A randomized trial (2) compared ^{131}I tositumomab to unlabelled tositumomab in patients with relapsed or refractory CD20+ non-Hodgkin's lymphoma. No conclusion could be drawn from the comparison of the two arms. The objective response rate in the ^{131}I tositumomab arm was 55%, with a median time-to-progression of 6.3 months.
- Six single-arm trials (1,3-7) included patients who had non-Hodgkin's lymphoma that was relapsed or refractory to chemotherapy without rituximab. The objective response rates ranged from 57% to 100%, with a median time-to-progression ranging from 8.4 months to 12 months. The complete response rates ranged from 20% to 84%, with median durations of complete response ranging from 19.9 months to not-yet-reached.
- Two additional single arm trials (8,9) included patients who had non-Hodgkin's lymphoma that was relapsed or refractory to rituximab. The objective response rates were 65% and 72%, with one trial reporting median time-to-progression of 10.4 months. The complete response rates were 27% and 38%.

Related Guidelines

Program in Evidence-based Care Practice Guideline (PG) or Evidence-based Series (EBS):

- PG #6-2: *Treatment with Fludarabine for Patients with Follicular and other Low Grade Non-Hodgkin's Lymphoma and Waldenstrom's Macroglobulinemia.*
- EBS #6-8: *Rituximab in Lymphoma and Chronic Lymphocytic Leukemia.*
- EBS #6-17: *Ibritumomab Tiuxetan in Lymphoma*.

Funding

The PEBC is supported by Cancer Care Ontario (CCO) and the Ontario Ministry of Health and Long-Term Care. All work produced by the PEBC is editorially independent from its funding agencies.

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