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Evidence-based Series 6-9 IN REVIEW

The Management of Malignant Thrombocytosis in Philadelphia Chromosome-Negative Myeloproliferative Disease

J. H. Matthews, C.A. Smith, J. Herst, D. Lee, K. Imrie, and 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 (DSG)

Report Date: January 15, 2008

An assessment conducted in November 2012 placed Evidence-based Series (EBS) 6-9 IN REVIEW. This means that it is undergoing a review 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.

Evidence-based Series (EBS) 6-9, consists of three sections:

Section 1: Guideline Recommendations
Section 2: Evidentiary Base
Section 3: EBS Development Methods and External Review Process

and is available on the CCO Web site (http://www.cancercare.on.ca)
PEBC Hematology DSG page at:
https://www.cancercare.on.ca/toolbox/qualityguidelines/diseasesite/hema-ebs/

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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Evidence-based Series #6-9: Section 1

The Management of Malignant Thrombocytosis in Philadelphia Chromosome-Negative Myeloproliferative Disease: Guideline Recommendations

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QUESTIONS

This evidence summary was developed to provide information to aid clinicians in the management of patients with essential thrombocythemia (ET) and polycythemia vera (PV). The following questions were addressed:

1. Is there a definable subgroup of patients who are at a high risk of either thrombosis or bleeding?
2. Does controlling the platelet count with cytoreductive agents improve clinical outcomes such as overall survival, major and minor thrombosis, hemorrhage, and the development of myelofibrosis?
3. Does cytoreductive therapy produce additional transformation to acute leukemia (AL)?
4. What effect does aspirin therapy have on the occurrence of thrombosis or hemorrhage?

TARGET POPULATION

Patients with Philadelphia chromosome-negative myeloproliferative diseases, specifically ET or PV.

RECOMMENDATIONS

- All ET and PV patients with thrombocytosis should be managed with low-dose aspirin. Special precautions should be taken in the case of patients with greater bleeding risk or allergies (see “Qualifying Statements” for additional information).
- Management without cytoreductive therapy is a reasonable option for asymptomatic patients.
- Cytoreductive therapy should be considered as an option for patients with thrombocytosis who have thrombosis. Hydroxyurea is the preferred agent and should be administered to

maintain a platelet count of less than 600 x 10^9/L (see "Qualifying Statements" for additional information).
- If treatment with hydroxyurea is not appropriate, then either interferon or anagrelide are options. Physicians who choose anagrelide to reduce the risk of arterial thrombosis should be aware that there are data suggesting that it is inferior to hydroxyurea, and its efficacy in comparison to no cytoreductive therapy has not been established. Other than reducing the platelet count, interferon is of unknown efficacy.

QUALIFYING STATEMENTS

- Hydroxyurea should be regarded as a possible leukemogen in patients with myeloproliferative disease.
- The European Collaboration on Low-dose Aspirin in Polycythemia Vera (ECLAP) 2003 study used a 100 mg dose of aspirin. However, only an 81 mg pill is available in Canada for use in adults, and the Hematology DSG regards this as a reasonable dosage.
- In the randomized studies, target platelet counts of both <600 and <400 x 10^9/L were shown to be safe and effective.

KEY EVIDENCE

- Evidence from one randomized controlled trial (RCT) showed low-dose aspirin (100 mg/day) reduces the risk of thrombosis (relative risk [RR]=0.4, $p < 0.05$) in patients with PV treated with cytoreductive therapy. A non-randomized cohort study found a similar, though not statistically significant, effect (RR=0.6). Direct evidence for ET is limited.
- Data from a number of retrospective studies show that initial symptoms may be an important predictor of subsequent thrombosis. They do not show that age, platelet count, or vascular risk factors can define a group of high-risk patients needing cytoreductive therapy.
- There is strong evidence showing hydroxyurea reduces the incidence of total arterial thrombosis in ET when compared with anagrelide (4.2% versus [vs.] 9.1%, $p < 0.05$) or with no initial treatment (9% vs. 45%, $p < 0.05$). However, no effect of hydroxyurea has been shown for stroke, myocardial infarction, or overall survival.
- Anagrelide is inferior to hydroxyurea in controlling arterial thrombosis, and its efficacy in comparison to no cytoreductive therapy has not yet been established.

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