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SUMMARY WITH CRITICAL APPRAISAL

Eltrombopag for the treatment of Aplastic Anemia: A Review of Clinical and Cost-Effectiveness

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Authors: Chuong Ho, Sarah Visintini

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Context and Policy Issues

Aplastic anemia (AA) is a rare, life-threatening disorder due to either inherited or acquired bone marrow failure to produce blood cells, leading to progressive pancytopenia.[1] AA affects patients of all ages, with an incidence ranging from 0.6 to 6.1 cases per million population in North America.[2,3] Treatment for AA is determined by a number of factors including AA severity, age of the patient, stem cell donor availability, and access to optimal therapies. For newly diagnosed severe AA, bone marrow transplant is usually pursued in all pediatric and younger adult patients when a matched donor is available.[4,5] In older adult patients and in all patients lacking a matched donor, immunosuppressive therapy (IST) with antithymocyte globulin and cyclosporine A has been the front line therapy.[4,5]

Eltrombopag, a thrombopoietin (TPO) agonist, has been found effective for the treatment of immune thrombocytopenia and has been emerging as a treatment option for severe AA that is not responding to immunosuppression with antithymocyte globulin and cyclosporine.[6-12]

This Rapid Response report aims to review the comparative clinical and cost-effectiveness of eltrombopag versus other options for the treatment AA.

Research Question

1. What is the clinical effectiveness of eltrombopag in the treatment of aplastic anemia?

2. What is the cost-effectiveness of eltrombopag in the treatment of aplastic anemia?

Key Findings

There were no studies that met the pre-specified criteria regarding the comparative clinical effectiveness and cost-effectiveness of eltrombopag for the treatment of aplastic anemia.

Methods

A limited literature search was conducted on key resources including Medline in Ovid, Embase in Ovid, PubMed, the Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2008 and June 14, 2018.

Rapid Response reports are organized so that the evidence for each research question is presented separately.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Patients of any age with aplastic anemia
Intervention	Eltrombopag
Comparator	Q1. Pharmacological treatments (e.g,, cyclophosphamide, cyclosporine, antithymocyte globulin), stem cell transplant Q2. No Comparator
Outcomes	Q1. Clinical effectiveness (e.g., hematological response, increase in blood count, quality of life, need for rescue treatments, adverse events) Q2. Cost-effectiveness
Study Designs	Heath technology assessments (HTAs), systematic reviews (SRs) and meta-analyses (MAs), randomized controlled trials (RCTs), non-RCTs

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2008. Studies that examined the clinical effectiveness of eltrombopag without a comparator were excluded.

Critical Appraisal of Individual Studies

Critical appraisal was not performed as no eligible studies were identified.

Summary of Evidence

Quantity of Research Available

A total of 96 citations were identified in the literature search. Following screening of titles and abstracts, 86citations were excluded and 10 potentially relevant reports from the electronic search were retrieved for full-text review. No potentially relevant publication was retrieved from the grey literature search. Of these potentially relevant articles, 10 publications were excluded for various reasons, and no publications met the inclusion criteria and were included in this report. Appendix 1 presents the PRISMA flowchart of the study selection.

Summary of Findings

No relevant HTAs, SRs, MAs, RCTs, or non-RCTs on the clinical effectiveness or cost-effectiveness of eltrombopag compared to other pharmacological treatments were identified.

Conclusions and Implications for Decision or Policy Making

There were no studies that met the pre-specified criteria on the comparative clinical effectiveness or the cost-effectiveness of eltrombopag in the treatment of aplastic anemia.

In patients with refractory and severe AA, many uncontrolled observational studies consistently found that eltrombopag, alone or in combination with immunosuppressive therapies, was effective to improve hematologic response, including persistent increase of plasma TPO, with few side effects, and reduced transfusion independence.[13-18] Despite being generally well-tolerated, eltrombopag may be associated with dose-dependent cutaneous toxicity[19] and the presence of high eltrombopag concentrations in blood samples may cause interference in routine chemistry testing such as total cholesterol levels.[20] This should be interpreted with caution, as the results are from non-comparative studies that were not eligible for inclusion in this review.

Randomized controlled trials comparing eltrombopag with other immunosuppressive therapies and stem cell transplantation are needed to reduce uncertainty regarding its clinical effectiveness. Cost-effectiveness evaluations on eltrombopag in a Canadian context in patients with severe AA are also needed.

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Appendix 1: Selection of Included Studies