LITERATURE REVIEW ON THE CLINICAL AND ECONOMIC OUTCOMES ATTRIBUTABLE TO FIRST-LINE TREATMENT FOR CHRONIC MYELOID LEUKEMIA WITH IMATINIB MESYLATE AND BONE MARROW TRANSPLANTATION

INTRODUCTION

Chronic myeloid leukemia (CML) is diagnosed by the presence of a characteristic chromosome and a blood and marrow cell pattern, using cytogenetic and immunophenotypic techniques.

It is a rare disease with an estimated incidence ranging from 7 per million to as much as 61 per million in the 20-44 years age group and >65 years age group, respectively [1]. The median age at diagnosis is 53 years [2].

The natural course of the disease involves three sequential phases (chronic, accelerated, and blast crisis), each becoming progressively more resistant to treatment [3].

There is a high incidence of molecular resistance and the emergence of drug-resistant variants with chronic phase CML. When administered at the standard dose 400 mg is generally well tolerated with major toxicities manageable by reducing the dose. CML is associated with greater toxicities, a risk of graft failure and transplant-related mortality. Therefore, the recent emergence of reduced intensity conditioning regimens in CML have become progressively more resistant to the occurrence of hematological complications, lower transplant-related mortality, lower toxicity and improved remission and survival compared to standard BMT.

This review found that BMT-treated patients are more likely to achieve cytogenetic and hematological remission, whereas patients who survive a BMT are more likely to achieve molecular remission.

The existing studies estimated that the incremental cost-effectiveness of BMT relative to allogeneic BMT with matched unrelated donors was $5,000 per QALY. This cost-effectiveness may be as high as 82% of those who receive BMT [8].

The authors have no other conflicts of interest that are directly relevant to the content of this manuscript.

METHODS

A systematic literature search was performed using available computerized databases for papers on CML. Search terms were CML and one of the following: first-line treatment, remission, molecular, imatinib mesylate, bone marrow transplantation, stem cell transplantation, utilization, quality of life, effectiveness, costs, cost-effectiveness, condition-specific, treatment outcomes, economic cost. The search strategy was limited to studies available in English language in the reviewed academic journals.

A manual literature search was also undertaken, based on citations in the published papers.

In addition to prospective and retrospective studies, randomized and non-randomized controlled trials were included, as well as papers from clinical reviews evaluating clinical and economic outcomes associated with IM and BMT.

A meta-analysis was performed to estimate weighted (where possible) mean values from 20 publications that provided data on at least 4,071 IM-treated patients (2,189 patients who received BMT). Sample size was limited in some instances.

RESULTS

Event-free Survival

Ninety-six percent of IM-treated patients are expected to be event-free at year 1 compared to 64% of those who receive BMT. Moreover, event-free survival (defined by the study as time to relapse, death, or last follow-up) was measured over a period of 75 months or a higher among IM-treated patients in year 10 and 40%, indicating a better overall event-free survival among IM-treated patients (Figure 1, Page 4) [9,10,12].

Freedom from Progression

Freedom from progression to advanced stages was estimated to be 100% among patients who survive a BMT compared to 84% of IM-treated patients for the first year. However, by year 10 this advantage was reversed, with 46% of patients surviving a BMT and 36% of patients surviving IM (Figure 2, Page 4) [14,15,16,21].

Remission

The majority of patients receiving IM-first line treatment achieve remission, of which 90% achieve complete hematological remission, and 40% achieve molecular remission by year 1. Additionally, 50% achieve a major cytogenetic response and 85% a complete cytogenetic response by year 5 [9,14].

Overall Survival

One hundred percent of patients who receive IM as a first-line treatment are expected to survive the first 10 years compared to 72% of those who receive a BMT. The survival advantage continues up to year 9, however by year 10 this advantage was reversed, with 28% of patients surviving a BMT and 40% of patients surviving IM (Figure 3, Page 4) [9,10,12].

Relapse

Twenty percent of patients who have a BMT were found to relapse after a median 34 months (95% CI 33.1, 35.1). Of the patients who relapse 25% and 55% experienced a hematological and molecular relapse, respectively. [9,10,11].

Adverse Effects

The incidence of adverse events especially hematological complications appears to be lower among IM-treated patients than BMT patients.

Economic Outcomes

A cost-effectiveness analysis considering only direct medical costs from the perspective of a third-party payer in the US estimated the incremental cost of using IM-first line treatment over BMT to be €1.6 million. The direct cost of IM treatment would be as high as 82% of those who receive BMT [8].

Economic Outcomes

Economic outcomes evaluating the incremental cost of using IM-first line treatment over BMT to be €1.6 million. The direct cost of IM treatment would be as high as 82% of those who receive BMT [8].

CONCLUSION

Published evidence supports the use of IM in patients who are eligible for first-line treatment as an alternative to BMT to be a cost-effective treatment compared to BMT in the management of CML in the short-term, but longer-term published data are lacking.

REFERENCES


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Figure 1: Event-free survival

Percent of patients who survive event-free

Bone marrow transplantation

Imatinib

Time following treatment initiation (years)

0% 20% 40% 60% 80% 100%

Figure 2: Overall survival

Percent of patients who experience progression

Bone marrow transplantation

Imatinib

Time following treatment initiation (years)

0% 20% 40% 60% 80% 100%

Figure 3: Transition from progression

Percent of patients under BMT who experience treatment-related mortality

Bone marrow transplantation

Imatinib

Time following bone marrow transplant (years)

0% 10% 20% 30% 40%