Abstract

Objectives: To estimate cost-effectiveness of dasatinib vs. imatinib in chronic-phase CML, after failure of first-line imatinib from the perspective of the Austrian Social Healthcare Insurance System.

Methods: Long-term cost-effectiveness of dasatinib (140 mg/day) vs. imatinib (400 mg/day) was evaluated within a Markov model using initial best response from a randomized clinical trial in chronic-phase CML patients, randomized to 400 or 600 mg imatinib. Model simulation runs were monthly cycles until all patients have died. Disease progression is dependent on initial best response and current health status, and was simulated according to literature-based monthly transition probabilities. Incidence of serious adverse events (SAEs) was drawn from trial observations. Utilities were obtained from a CML utility study using EQ-5D. Life expectancy from national statistics. Healthcare utilization and costs were derived from panels of clinical and financial experts, databases of 24 hospitals across Austria and Austrian drug price lists. Both costs and effects were discounted annually at 5%. Sensitivity analyses on effectivity, costs and utilities were performed.

Results: Treating patients with dasatinib is a dominant treatment strategy compared to treatment with high doses of imatinib over lifetime. Over lifetime, dasatinib is associated with a gain of 0.57 QALY and savings of €152,133 (95% CI: €150,000 to €154,226).

Conclusions: Dasatinib is associated with increased effectiveness and cost savings to the Austrian healthcare system, and can be considered an improvement in treatment of chronic-phase CML patients, after failure of first-line imatinib.

Background

Tyrosine Kinase inhibitors (TKi) have dramatically improved survival and quality of life in patients with chronic myeloid leukemia (CML).

Objective: To estimate the cost-effectiveness of dasatinib vs. imatinib in chronic-phase CML, patients after failure of first-line imatinib, from the perspective of the Austrian Social Healthcare Insurance System.

Methods

Model Overview

An existing Markov model, simulating disease progression over chronic-, accelerated- and blast-phase CML, was adapted to the Austrian clinical setting (Figure 1).

Utilities and Cost Inputs

• Patients disease progression (flow through the model) depends on initial best response to treatment at 3 months and current health status. For each clinical practice, initial best response categories can be used: No Response (NR), Complete Hematological Response (CHR), Partial and Complete Cytogenetic Response (PR, and CCyR), respectively.
• Transition probabilities for the AP and BP compartments were based on the model, which was based on progression-free survival observed in two single-arm phase II studies of INF-α resistant CML patients treated with imatinib 600-800 mg (CP: median follow-up approximately 20 months).13
• Transition probabilities for the AP and BP were based on data from a Simon comparison on imatinib-resistant and -refractory CML patients enrolled in CML-1000700 (AP: n=124, BP: n=11, median follow-up 25 months) and on the Kaplan-Meier estimates of 3 large phase III trials of imatinib in IFN-resistant CML patients (CP: n=572, AP: n=214, BP: n=260).14

Utilities and Cost Inputs

• Utility values for the different CML health states were obtained from a CML utility study in laypeople in the United Kingdom (p<0.05) (Table 3). The study used time-trade-off methodology to determine health-related quality of life associated with CML health states.

Table 3: Utility values

<table>
<thead>
<tr>
<th>CML Phase</th>
<th>AP</th>
<th>BP</th>
<th>NR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Remaining</td>
<td>0.91</td>
<td>0.91</td>
<td>0.91</td>
</tr>
</tbody>
</table>

• Healthcare utilization was estimated for each health state by 3 international clinical experts and validated by an Austrian expert in hematologic-oncology.

• Costs inputs were obtained from the databases of 24 hospitals (GP and 4 private) across 9 Austrian provinces, and the panel of 3 private general practitioners (GP) and 3 hematologic-oncologists (GP and specialist practices). Drug prices reimbursed by Austrian Social Funds (Kassenärztliche Vereinigungen) were used (Table 2).

Results

• Both costs and effects were discounted at 5%, in accordance with the recommended Austrian pharmacy and economic guidelines.10

Sensitivity Analyses

• Probabilistic sensitivity analyses (PSA) were performed to investigate the robustness of the results.

• The following input parameters were varied within their uncertainty distributions: basic survival probability, transition probabilities, utilities and cost estimates (except for drug cost of dasatinib and imatinib).

Conclusions

• Dasatinib or high-dose imatinib for chronic-phase CML after failure of first-line imatinib: a cost-utility analysis of Sprycel® in Austria

References

3. O'Brien S, Talpaz M,/imgae.png