THE COST-EFFECTIVENESS OF THERAPEUTIC DRUG MONITORING OF GENERIC IMATINIB FOR THE TREATMENT OF CHRONIC MYELOGENOUS LEUKEMIA

Salvatore Salamone, Ph.D.1, Russell Becker, MA2, William Padula, Ph.D.3, and Rena M Conti, Ph.D.4

1Saladax Biomedical, Inc., Bethlehem, NJ; 2Russell Becker Consulting, Chicago, IL; 3Department of Health Policy & Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; 4Departments of Pediatrics & Public Health Sciences, The University of Chicago, Illinois

INTRODUCTION

Many studies have demonstrated a correlation with imatinib mesylate (IM) blood levels > 1,500 ng/mL and response in chronic myelogenous leukemia (CML).1-8 A blood level of 1,000 ng/mL has been recommended as the therapeutic target.9 A recent clinical study in CML used therapeutic drug monitoring (TDM) of IM to adjust doses so that blood levels in the personalized dosing arm reached the therapeutic range.10 The study found that the major molecular response (MR) rate at 12 months was significantly improved with IM TDM compared to standard therapy without dose adjustment.11 Given that second generation tyrosine kinase inhibitors (TKI) had previously lost of patent exclusivity in the US, no studies have considered the cost-effectiveness of using TDM provides new clinical information when selecting a CML treatment.

A recent cost-effectiveness analysis of TKI for CML found that, when considering the pending loss of patent exclusivity of IM, using IM as a first-line treatment is the most cost-effective treatment option where as physicians’ choice of dasatinib or nilotinib was not cost-effective.12 However, since the loss of imatinib patent exclusivity in the US, no studies have considered the cost-effectiveness of IM with the loss of patent exclusivity, nor has the cost-effectiveness of IM TDM been evaluated.

OBJECTIVE

The objective of the study was to determine the cost-effectiveness of using generic IM TDM for the first-line treatment of CML.

METHODS

A peer-reviewed and published TKI cost-effectiveness model in CML13 was modified to include IM TDM as a treatment option. Efficacy inputs for major molecular response (MMR) rates were taken from published clinical studies: IM alone 37%, IM TDM 65%, dasatinib 52%, nilotinib 53%.13-18 Using the Federal Supply Schedule (FSS) and average and lowest acquisition cost (WAC) as price bases, alternative estimates were used for drug prices including generic IM19. The cost of TDM for IM was added to the IM TDM comparator arm at $228 annually (6 tests at $38 each) over 5 years. Other input data from the Padula, et al. model were updated to 2016 U.S. Dollars using the Medical Service index of the Consumer Price Index.

The model compared two scenarios: (1) first-line IM TDM versus first-line IM alone, and (2) first-line IM TDM to first-line dasatinib or nilotinib. For the base case, it was assumed that half of the patients in the dasatinib/nilotinib arm received dasatinib and half received nilotinib as first-line treatment. As with the original model, for second-line TKI patients were assumed to switch once to a second-generation TKI in equal proportion in all comparator arms of the model. The two scenarios outcomes were compared in terms of costs, quality-adjusted life-years (QALYs), and cost-effectiveness. A U.S. payer perspective was used with a 5-year time horizon and a 3.0% discount rate. Univariate (one-way) and multivariate sensitivity analyses were performed on all key clinical and economic parameters.

RESULTS

The model with the inclusion of IM TDM gave the following base case results for first-line treatment of CML:

• IM TDM is more cost effective than IM alone [Table 2].
• IM TDM is a dominant treatment strategy (greater effectiveness and lower costs) versus IM alone.
• Total savings with IM TDM ranged from $15,452 with Average WAC pricing to $36,940 with FSS pricing.
• 0.25 QALYs were gained with IM TDM.
• IM TDM is more cost-effective than dasatinib/nilotinib [Table 3].
• IM TDM is a dominant treatment strategy over dasatinib/nilotinib.
• Total cost savings with IM TDM ranged from $117,006 with Low WAC pricing to $172,420 with FSS pricing.
• 0.08 QALYs were gained with IM TDM.

In a subgroup cost analysis of patients responding to IM TDM versus patients receiving first-line dasatinib/nilotinib, cost savings with IM TDM ranged from $114,577 (WAC average pricing) to $207,564 (FSS Average pricing) [Table 4].

All results were confirmed as robust by univariate and multivariate sensitivity analyses.

CONCLUSIONS

• Under a wide range of price scenarios as a first-line treatment for CML
  • IM TDM dominates IM alone.
  • IM TDM dominates dasatinib and nilotinib.
• A payor perspective analysis over 5 years demonstrated the potential of IM TDM to save hundreds of thousands of dollars.
• The analysis suggests that IM TDM is both a clinically and economically viable first-line treatment option for CML.

**TABLE 1: DRUG PRICE PER MG ($/MG) AND REGIMEN ANNUAL COST SUMMARY** ($)

<table>
<thead>
<tr>
<th>Drug</th>
<th>FSS Average</th>
<th>WAC Average</th>
<th>Low</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imatinib</td>
<td>0.12</td>
<td>0.39</td>
<td>0.59</td>
<td>65,848</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>0.69</td>
<td>0.93</td>
<td>0.87</td>
<td>97,416</td>
</tr>
<tr>
<td>Nilotinib</td>
<td>2.47</td>
<td>2.88</td>
<td>4.20</td>
<td>116,868</td>
</tr>
<tr>
<td>Nilotinib</td>
<td>0.40</td>
<td>0.50</td>
<td>0.83</td>
<td>99,097</td>
</tr>
</tbody>
</table>

*Assuming 76.3% Adherence rate (source: Tsung, et al. 2006, aslo ASCO 2006, abstr 6119

**TABLE 2: BASE CASE IM TDM & IM ALONE TOTAL COST ($) AND QALY

<table>
<thead>
<tr>
<th>Treatment</th>
<th>FSS Average</th>
<th>WAC Average</th>
<th>Low</th>
<th>Average QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>IM Alone</td>
<td>370 905</td>
<td>366 966</td>
<td>461 657</td>
<td>3.97</td>
</tr>
<tr>
<td>IM TDM</td>
<td>233 965</td>
<td>350 090</td>
<td>446 205</td>
<td>3.62</td>
</tr>
<tr>
<td>Difference</td>
<td>36 940</td>
<td>16 876</td>
<td>15 452</td>
<td>-0.25</td>
</tr>
</tbody>
</table>

**TABLE 3: BASE CASE IM TDM VS. DASATINIB OR NILOTINIB TOTAL COST ($) & QALY

<table>
<thead>
<tr>
<th>Treatment</th>
<th>FSS Average</th>
<th>WAC Average</th>
<th>Low</th>
<th>Average QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dasatinib</td>
<td>406 385</td>
<td>467 106</td>
<td>575 606</td>
<td>3.74</td>
</tr>
<tr>
<td>Nilotinib</td>
<td>350 090</td>
<td>446 205</td>
<td>461 029</td>
<td>3.82</td>
</tr>
<tr>
<td>Difference</td>
<td>172 420</td>
<td>117 006</td>
<td>129 401</td>
<td>-0.08</td>
</tr>
</tbody>
</table>

**TABLE 4: BASE CASE IM TDM 5-YR. RESPONDERS VS. DASATINIB OR NILOTINIB TOTAL COST ($)**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>FSS Average</th>
<th>WAC Average</th>
<th>Low</th>
<th>Average QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dasatinib</td>
<td>196 621</td>
<td>207 564</td>
<td>351 605</td>
<td>461 029</td>
</tr>
<tr>
<td>Nilotinib</td>
<td>155 501</td>
<td>114 577</td>
<td>461 029</td>
<td>3.82</td>
</tr>
</tbody>
</table>

REFERENCES


*signifies non-member of ASH