Final Analysis of the Efficacy and Safety of Omacetaxine Mepesuccinate in Patients With Chronic- or Accelerated-Phase Chronic Myeloid Leukemia: Results With 24 Months of Follow-Up

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Final Analysis of Efficacy and Safety of Omacetaxine Mepesuccinate in Patients With Chronic Phase (CP) or Accelerated Phase (AP) Chronic Myeloid Leukemia (CML): 24-Month Minimum Follow-Up Results

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Abstract

Background—Omacetaxine, a protein synthesis inhibitor, is indicated in the US for the treatment of patients with chronic (CP) or accelerated phase (AP) chronic myeloid leukemia (CML) with resistance and/or intolerance to two or more tyrosine kinase inhibitors.

Methods—This final analysis, with 24-month follow-up, includes additional efficacy and safety analyses to assess the benefit of long-term omacetaxine administration (1.25 mg/m² bid for 14 days q 28 days followed by 7 days q 28 days) in CP- and AP-CML patients receiving ≥3 cycles.

Results—Eighteen percent of CP-CML patients achieved major cytogenetic response (MCyR) with a median duration 12.5 months (95% confidence interval [CI], 3.5-not reached [NR]).

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responses were maintained for ≥12 months in 3 of 14 responders and median overall survival (OS) was 40.3 months (95% CI, 23.8–not reached). In patients with AP-CML, 14% achieved or maintained major hematologic response for a median of 4.7 months (95% CI, 3.6–NR); MCyR was not achieved and median OS was 14.3 months (95% CI, 6.7–18.7). In patients with CP- or AP-CML who received >3 cycles of treatment (n=50 and 14, respectively), median OS was 49.3 months (95% CI, 23.8–NR) and 24.6 months (95% CI, 12–37.2), respectively. Grade ≥3 hematologic toxicity was the major side effect (79%/73% in CP-CML/AP-CML), with discontinuation due to toxicity in 10% of CP and 5% of AP patients.

Conclusions—These results suggest that long-term administration of omacetaxine is feasible with dose adjustments to manage toxicities, and that omacetaxine provides durable benefit in some patients.

Keywords
TKI; intolerance; resistance; T315I; protein synthesis inhibitor

Introduction
Chronic myeloid leukemia (CML) is characterized by the expression of the BCR-ABL1 oncprotein, and overall survival (OS) in patients with CML has greatly improved since the introduction of tyrosine kinase inhibitors (TKIs) that target BCR-ABL1. Most patients are responsive to TKI therapy; however, over time, patients may develop resistance to TKI therapy, often due to mutations in BCR-ABL1 or increases in BCR-ABL1 expression. Furthermore, TKI intolerance may occur, occasionally with cross-intolerance between multiple TKIs. Thus, a non-TKI approach is warranted in patients who are resistant or intolerant to multiple TKIs.

Omacetaxine mepesuccinate (“omacetaxine”), a protein synthesis inhibitor, binds directly to the ribosome and blocks the initial step of protein translation. Omacetaxine induces apoptosis by reducing levels of multiple short-lived oncoproteins, including Bcr-Abl1, Mcl-1, cMyc, and cyclin D1. Because direct Bcr-Abl1 binding is not required for omacetaxine activity, it is unaffected by mutations in BCR-ABL1 that confer resistance to TKIs, including the “gatekeeper” mutation T315I.

Omacetaxine was approved in the US for the treatment of patients with chronic (CP) or accelerated phase (AP) CML with resistance and/or intolerance to 2 or more TKIs based on an analysis (CML-300) of data pooled from two phase 2, open-label, international, multicenter studies (CML-202 and CML-203). Initial results from CML-300 showed that 20% of patients with CP-CML achieved durable major cytogenetic response (MCyR) with a median response duration of 17.7 months, and 27% of patients with AP-CML achieved major hematologic response (MHR) that was maintained for a median of 9 months.

Here, we report the final efficacy and safety data for omacetaxine in the CML-300 cohort, after a minimum of 24 months of follow-up. We also evaluate the benefit and safety of long-
term omacetaxine administration by examining the outcome of those who received >3 cycles of treatment.

Methods

Study Design
This report is the final analysis, with a minimum 24-month follow-up, of efficacy and safety data in patients with CP-CML or AP-CML with resistance or intolerance to ≥2 TKIs enrolled in two phase 2 clinical trials of omacetaxine. Patient enrollment criteria and omacetaxine administration have been described in detail previously.\textsuperscript{23, 24} History of T315I was required for patients in study CML-202 only.\textsuperscript{13} Additional post hoc efficacy and safety analyses were performed in the subset of patients who received >3 cycles of omacetaxine.

Patients
Patients aged ≥18 years with Philadelphia chromosome (Ph)-positive CML in either CP or AP were enrolled. Patients were required to have Eastern Cooperative Oncology Group (ECOG) performance status 0–2. Eligible patients were previously treated with imatinib and had documentation of resistance or intolerance to dasatinib and/or nilotinib.

Treatment
Omacetaxine 1.25 mg/m\textsuperscript{2} was administered subcutaneously twice daily for up to 14 consecutive days every 28 days for induction until hematologic response, followed by maintenance dosing (1.25 mg/m\textsuperscript{2} for up to 7 days per 28-day cycle) for up to 24 months or until progression or unacceptable toxicity. Patients without evidence of clinical response after 6 cycles of induction were removed from the study. In case of hematologic toxicity, the number of dosing days was decreased in 2-day increments to maintain absolute neutrophil count >0.5 × 10\textsuperscript{9}/L and platelet count > 50 × 10\textsuperscript{9}/L; no adjustments were made in patients with white blood cell (WBC) count >10 × 10\textsuperscript{9}/L, or absolute blast count >5 × 10\textsuperscript{9}/L. For nonhematologic toxicity, treatment delay was permitted for grade ≥2 events that were unresponsive to supportive care; after resolution, treatment could resume with a reduction in the consecutive treatment days.

Assessments
Laboratory analyses, including complete blood counts, were performed every 7 days during induction cycle(s) and every 14 days during maintenance or as clinically indicated. Bone marrow aspiration and cytogenetic analysis were performed every 3 months on study; hematologic and cytogenetic responses (as defined in Supplemental Information) were assessed by an independent review committee. Assessment of Bcr-Abl1 transcripts is described in Supplemental Information. Toxicities were assessed according to National Cancer Institute criteria (CTCAE version 3.0). Serious adverse events (AEs) include death or life-threatening events, or events that require hospitalization or intervention to prevent disability, permanent damage, or death.
**Statistical Analyses**

Safety was evaluated in the CML-300 population comprising CP-CML and AP-CML patients with resistance and/or intolerance to imatinib and at least 1 other TKI using data pooled from two phase 2 studies. A total of 11 patients from the CML-300 population were excluded from efficacy analyses were due to presence of response at baseline (CP-CML n=2; AP-CML n=6) or study site compliance issues (CP-CML n=3).

The primary endpoint was MCyR (complete cytogenetic response [CCyR] or partial cytogenetic response [PCyR]) in patients with CP-CML, and achievement of MHR (including complete hematologic response [CHR] maintained for ≥4 weeks or no evidence of leukemia [NEL]) and/or MCyR in patients with AP-CML. The Clopper-Pearson method was used to calculate 1-sided lower 95% confidence intervals (CIs) for primary efficacy measures. Time to progression and OS were analyzed by Kaplan-Meier methods (defined in Supplemental Information).

**Results**

**Patient Disposition and Exposure**

Eighty-one patients with CP-CML and 41 patients with AP-CML had resistance and/or intolerance to imatinib and at least 1 other TKI and were included in the safety analyses; for efficacy analyses, 76 patients with CP-CML and 35 patients with AP-CML were considered evaluable (Supplemental Figure 1). At the close of the study, 6 patients with CP-CML and 1 patient with AP-CML were continuing treatment (patients outside of the United States [US] were transferred to compassionate use and those within the US were able to receive commercially available drug). Overall, 65% of CP patients and 41% of AP-CML patients received >3 cycles of treatment (Table 1). In CP-CML patients, discontinuation due to AEs was more frequent in early cycles (Table 1). The most common cause of discontinuation across all cycles was progressive disease. Median duration of study participation for patients with CP-CML and AP-CML was 8.8 months (95% CI, 7.1–11.2) and 3.4 months (95% CI, 1.9–6.4), respectively. At the time of analysis, 74% of patients had updated (within 6 months) survival follow-up information.

**Baseline Characteristics**

Characteristics of the overall population and those who received >3 cycles are summarized in Supplemental Table 1. Baseline characteristics of patients who remained progression free and continued to received omacetaxine at study close (n=6) are presented in Supplemental Table 2; these patients were typically younger (<65 years) with good performance status. Four of the 6 ongoing CP patients had CHR at baseline.

**Exposure and Safety**

Omacetaxine exposure in the CML-300 population and in patients who received >3 cycles are summarized in Table 2. The safety profile of omacetaxine with extended follow-up did not differ substantially from that reported previously based on initial analyses23, 24 (Supplemental Table 3). Hematologic AEs were the most common grade 3/4 events; rates of grade 3/4 hematologic AEs were highest during the first 3 cycles and decreased after cycle 3.
with a corresponding decrease in median number of dosing days per cycle, particularly in patients with CP-CML (Figure 1). Incidence rates of grade 3/4 hematologic AEs during the first 3 cycles were similar in patients who received >3 cycles of omacetaxine compared with patients who received 1–3 cycles of omacetaxine (Figure 2). Treatment delays remained relatively common in both disease phases after cycle 3, with nearly all patients requiring a delay in at least 1 maintenance cycle. Neutropenia, thrombocytopenia, and patient scheduling or logistics were the most common causes of treatment delays in CP-CML and AP-CML patients after cycle 3.

The most common nonhematologic grade 3/4 AEs in patients receiving >3 cycles were infections, occurring in 13% of CP-CML and 41% of AP-CML patients (Supplemental Table 3). Grade 3/4 pneumonia was experienced by 4% of CP-CML patients and 18% of AP-CML patients. Most other nonhematologic AEs were grade 1/2; diarrhea, fatigue, and nausea were the most common. Incidence of grade 3/4 general symptoms (eg, fatigue, pyrexia), skin disorders, and administration site conditions were low.

Grade 3/4 events that first occurred during or after cycle 12 are summarized in Supplementary Table 4. Those considered related to treatment in CP-CML patients were anemia (n=3), thrombocytopenia (n=3), neutropenia (n=3), and insomnia, leukopenia, nausea, fatigue, lobar pneumonia, irregular heart rate, and lung infection (n=1 each); in CML-AP patients, they included anemia (n=2), neutropenia (n=2), leukopenia and thrombocytopenia (n=1 each).

Serious AEs occurred in 46 patients with CP-CML (57%) and 23 patients with AP-CML (56%). Incidence of serious AEs was generally similar between the overall population and patients with >3 cycles (Supplementary Table 5). The most common serious AEs were myelosuppression and related events, including gastrointestinal hemorrhage, pyrexia, and infections. One patient developed myelodysplastic syndrome (MDS) >30 days after the last dose of omacetaxine. This patient received 41 cycles of omacetaxine and had a history of several chemotherapy agents and 5 allogeneic transplants before omacetaxine treatment; the investigator considered the event to be possibly related to the study drug. Another patient who was excluded from the pivotal analysis (due to prior treatment with only 1 TKI) developed MDS after omacetaxine treatment. Patient history included prostate cancer, but treatment history was unavailable; the event was considered unrelated to treatment by the investigator.

Two CP-CML and 4 AP-CML patients died during treatment or within 30 days of last study dose (on-study deaths). No on-study deaths were considered related to study drug. Causes of on-study deaths in CP-CML patients included disease progression in 1 patient (during cycle 3) and multi-organ failure in 1 patient (during cycle 1). In AP-CML patients, causes of on-study deaths were disease progression (n=2, during cycle 2 and 5) and cerebral hemorrhage (n=2, both during cycle 2).

**Efficacy in CP-CML Patients**

At the time of final analysis, the MCyR rate was unchanged from the initial analysis. Among patients with resistance or intolerance to 2 or more TKIs, the MCyR rate was 20% (16/81;
In the evaluable population, MCyR rate was 18% (14/76; one-sided 95% LCL, 12%), including CCyR in 8% (6/76), with a median response duration of 12.5 months (95% CI, 3.5–not reached [NR]). Seventy percent (53/76) of evaluable patients achieved or maintained CHR, with median response duration of 11.1 months (95% CI, 8.4–23.3).

In patients receiving >3 cycles in the evaluable population (n=50), MCyR rate was 22%; 3 patients (6%) maintained response for ≥12 months (Table 3). Further analyses in this subgroup showed that among patients with the T315I mutation (n=16), 3 achieved MCyR (19%; 1-sided 95% LCL, 5%) (Table 3). One achieved confirmed CCyR at cycle 2 and received a total of 41 cycles of omacetaxine; the estimated proportion of T315I transcripts decreased from 100% at baseline to 0% by cycle 11 and remained low until discontinuation. The second patient, who achieved unconfirmed CCyR at cycle 6, continued receiving omacetaxine treatment and maintained CHR for 22 cycles. In this patient, the estimated proportion of T315I transcripts was reduced from 100% at baseline to 0% by cycle 11 and remained low until discontinuation. The third patient achieved a confirmed PCyR; the proportion of T315I transcripts decreased from 50% at baseline to 40% at cycle 1. No other assessments of mutant transcript level were documented for this patient. Among CP-CML patients who received >12 cycles of omacetaxine (n=21), the MCyR rate was 29% (n=6); half of the responders (n=3) maintained response for ≥12 months (Table 3).

Median progression-free survival (PFS) for the evaluable population was 9.6 months (95% CI, 6.8–11.3 months) and median OS was 40.3 months (95% CI, 23.8–NR). Among those who received >3 cycles of omacetaxine, median PFS and OS were 9.9 months (95% CI, 7–12 months) and 49.3 months (95% CI, 23.8–NR), respectively.

**Efficacy in AP-CML Patients**

At the time of this final analysis, MHR rate was 14% (5/35), including CHR in 4 patients and NEL in 1 patient; median duration of MHR was 4.7 months (95% CI, 3.6–NR). None of the patients with AP-CML achieved MCyR. The median PFS and OS in all AP-CML patients were 3.6 months (95% CI, 1.9–6.5 months) and 14.3 months (95% CI, 6.7–18.7 months), respectively.

Fourteen patients with AP-CML received >3 cycles of omacetaxine treatment; 29% achieved MHR. Three patients with AP-CML received ≥2 cycles. One patient with response received a total of 22 cycles and maintained MHR for 11.4 months; duration of MHR in the other 3 responders was between 3 and 5 months. Two AP patients who received ≥3 cycles had confirmed T315I at baseline: one patient achieved NEL and one had no hematologic response; in both patients T315I transcript levels remained high throughout study treatment. In CML-AP patients with >3 cycles, median PFS was 7 months (95% CI, 4.8–12 months) and median OS was 24.6 months (95% CI, 12–37.2 months).

**Discussion**

The efficacy and safety profile of omacetaxine observed with 24 months minimum follow-up is consistent with that observed in earlier analyses. Median OS was 40.3 months in
CP patients (33.9 months in the initial report), while median PFS remained unchanged.\textsuperscript{23} In AP patients, median values for both PFS and OS are similar to those reported in earlier analyses.\textsuperscript{24} Patients with more than 3 cycles of omacetaxine treatment displayed a trend toward longer PFS and OS than the overall population. Furthermore, extended exposure to omacetaxine in these heavily pretreated patients was feasible and safe, and a small number of CP patients demonstrated durable responses (>12 months), suggesting that omacetaxine may be considered as part of a long-term strategy or as bridge therapy to transplantation in patients who are eligible for the procedure.

CP-CML and AP-CML patients received up to 58 and 29 treatment cycles, respectively; a small subset of patients (5 with CP-CML and 1 with AP-CML) continued to receive omacetaxine treatment for more than 3.5 years. While hematologic and cytogenetic responses in CP-CML and AP-CML patients were often achieved within the first 3 cycles, a number of patients achieved MCyR after cycle 3, and onset of CCyR occurred as late as 8.5 months, suggesting some patients without response after initial cycles may achieve late responses.

A reduction in T315I transcripts was observed in some patients with the T315I mutation, including one CP-CML patient with confirmed CCyR who had an estimated 100% T315I transcripts at baseline and reduced to below detection limit by cycle 11. Previous studies in a preclinical mouse model\textsuperscript{15} and in patients with T315I with prior TKI treatments\textsuperscript{13, 26, 27} showed that omacetaxine treatment reduced the proportion of T315I-positive cells, which may enable rechallenge with second-generation TKIs. Furthermore, one patient with CP-CML who demonstrated pan-TKI resistance achieved stable, long-lasting (>5 years) major molecular response with omacetaxine treatment.\textsuperscript{13, 26–28} Whether this is a direct effect of omacetaxine on the mutated clone or a result of withdrawal of the TKI, as has been previously suggested,\textsuperscript{27} cannot be determined in this analysis. In future studies, it will be interesting to explore whether there is indeed a correlation between omacetaxine exposure and mutant transcript level, and confirm whether reduction in mutant transcripts is associated with objective response in patients.

Nonhematologic toxicities observed were generally mild, with the exception of infection. Incidence of grade 3/4 hematologic events was generally highest during the first 3 cycles and correlated with increased exposure to omacetaxine during induction, suggesting that toxicities are reversible and manageable with dose adjustments. Dose delays and reduction of the number of dosing days are encouraged as needed to manage myelosuppression and limit treatment discontinuation during the first 3 cycles. Continued management of symptoms during maintenance may also be necessary to prolong disease control.

In summary, the results of extended follow-up analyses are consistent with earlier results and suggest that long-term administration of omacetaxine is feasible and safe with dose adjustments to manage toxicities. Durable hematologic and cytogenetic responses may be achieved and sustained in a minority of patients.
Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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25. Synribo® (omacetaxine mepesuccinate) [prescribing information]. North Wales, PA: Teva Pharmaceutical, USA, Inc; 2014.


Figure 1.
The proportion of patients who experienced grade 3/4 thrombocytopenia, anemia, or neutropenia and median exposure to omacetaxine by cycle in chronic phase (A) and accelerated phase (B) patients who received omacetaxine (CML-300 population). (Note: only patients with laboratory test results are included.)
Any Grade 3 or 4 Hematologic Event in CP-CML

<table>
<thead>
<tr>
<th>Cycle number</th>
<th>≤ 3 cycles</th>
<th>&gt; 3 cycles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with ≤ 3 cycles, n</td>
<td>27</td>
<td>12</td>
</tr>
<tr>
<td>Patients with &gt; 3 cycles, n</td>
<td>53</td>
<td>53</td>
</tr>
</tbody>
</table>
Figure 2.
The proportion of chronic phase (A) and accelerated phase (B) patients with grade 3/4 thrombocytopenia, anemia, or neutropenia during the first 3 cycles of omacetaxine treatment in patients with ≤3 versus those who received > 3 cycles of treatment (CML-300 population). (Note: only patients with laboratory test results are included.)
## Table 1

Disposition of patients treated with omacetaxine (CML-300 population)

<table>
<thead>
<tr>
<th>Cycles</th>
<th>CP Patients</th>
<th>AP Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All 1–3 4–6 7–12 &gt;12</td>
<td>All 1–3 4–6 7–12 &gt;12</td>
</tr>
<tr>
<td>Patients who received any treatment, n</td>
<td>81 81 53 38 21 41 41 17 10 5</td>
<td>81 81 53 38 21 41 41 17 10 5</td>
</tr>
</tbody>
</table>

| Patients who discontinued study, n (%) | 75 (93) 28 (35) 15 (28) 17 (45) 15 (71) 40 (98) 24 (59) 7 (41) 5 (50) 4 (80) |

<table>
<thead>
<tr>
<th>Reason for discontinuation, n</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Progressive disease</td>
<td>26</td>
<td>8</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>21</td>
<td>12</td>
<td>2</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Lack of efficacy</td>
<td>12</td>
<td>-</td>
<td>4</td>
<td>6</td>
<td>2</td>
<td>7</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Patient request</td>
<td>12</td>
<td>6</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Adverse event</td>
<td>8</td>
<td>6</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Other (ie, sent to transplant)</td>
<td>9</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>-</td>
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<td>-</td>
<td>-</td>
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<tr>
<td>Death</td>
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<td>2</td>
<td>5</td>
<td>3</td>
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<td>Noncompliance</td>
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<tr>
<td>Lost to follow-up</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

AP, accelerated phase; CML, chronic myeloid leukemia; CP, chronic phase.

\(^a\)Information regarding transplantation was not specifically collected.

\(^b\)Deaths occurring up to 30 days after the last dose of study medication were considered under discontinuation.
### Table 2
Omacetaxine exposure in the CML-300 population and in patients who received > 3 cycles

<table>
<thead>
<tr>
<th>Total Cycles</th>
<th>Patients With &gt;3 Cycles</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CP (N=81)</td>
</tr>
<tr>
<td>Median (range) number of cycles</td>
<td>6 (1–58)</td>
</tr>
<tr>
<td>Median (range) duration of exposure, months</td>
<td>8 (0–65)</td>
</tr>
<tr>
<td>Median (range) total dose delivered, mg</td>
<td>204 (3–2007)</td>
</tr>
<tr>
<td>Median (range) treatment days per cycle</td>
<td>9 (1–15)</td>
</tr>
<tr>
<td>Median (range) number of cycle delays per patient</td>
<td>4 (0–39)</td>
</tr>
<tr>
<td>Patients with any delay, n (%)</td>
<td>56 (86)</td>
</tr>
</tbody>
</table>

AP, accelerated phase; CML, chronic myeloid leukemia; CP, chronic phase.

*Induction cycles are defined as cycles with ≥8 dosing days in cycles 1 through 6.

*Maintenance cycles are defined as any cycles with ≤7 dosing days in cycle 2–6 and any cycles >6 (regardless of number of dosing days).
Table 3
Response to omacetaxine in patients with CML-CP who received >3 or ≥12 treatment cycles

<table>
<thead>
<tr>
<th></th>
<th>CHR</th>
<th>MCyR</th>
<th>CCyR(^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall (n=76)</td>
<td>Patients with &gt;3 cycles (n=50)</td>
<td>Patients with ≥12 cycles (n=21)</td>
</tr>
<tr>
<td><strong>Response rate</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>53 (70)</td>
<td>47 (94)</td>
<td>20 (95)</td>
</tr>
<tr>
<td>With T315I at baseline</td>
<td>18/22 (82)</td>
<td>15/16 (94)</td>
<td>7/7 (100)</td>
</tr>
<tr>
<td>With 2 prior TKIs</td>
<td>31/40 (78)</td>
<td>27/28 (96)</td>
<td>12/12 (100)</td>
</tr>
<tr>
<td>With 3 prior TKIs</td>
<td>22/36 (61)</td>
<td>20/22 (91)</td>
<td>8/9 (89)</td>
</tr>
<tr>
<td><strong>Time to onset of response</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHR at baseline</td>
<td>16 (21)</td>
<td>13 (26)</td>
<td>4 (19)</td>
</tr>
<tr>
<td>&gt;0 to &lt;3 months</td>
<td>34 (45)</td>
<td>31 (62)</td>
<td>14 (67)</td>
</tr>
<tr>
<td>3 to &lt;6 months</td>
<td>3 (4)</td>
<td>3 (6)</td>
<td>2 (10)</td>
</tr>
<tr>
<td><strong>Response duration</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;12 months</td>
<td>39 (51)</td>
<td>34 (68)</td>
<td>7 (33)</td>
</tr>
<tr>
<td>≥12 to &lt;18 months</td>
<td>5 (7)</td>
<td>4 (8)</td>
<td>4 (19)</td>
</tr>
<tr>
<td>≥18 months</td>
<td>9 (12)</td>
<td>9 (18)</td>
<td>9 (43)</td>
</tr>
</tbody>
</table>

CCyR, complete cytogenetic response; CHR, complete hematologic response; CP, chronic phase; MCyR, major cytogenetic response; TKI, tyrosine kinase inhibitor.

\(^d\)Includes confirmed and unconfirmed responses. Confirmed responses were based on two bone marrow cytogenetic evaluations performed at least one month apart. Unconfirmed responses were based on a single cytogenetic evaluation.