INTRODUCTION

Background

- Patients with chronic phase (CP) chronic myeloid leukemia (CML) generally achieve high response rates when treated with tyrosine kinase inhibitors (TKIs) in first-line therapy.1 In second-line, however, as many as one-third of patients will not achieve optimal response, and over time, up to one-half of responders will lose response.1,3
- Ponatinib and bosutinib are new therapeutic options with demonstrated efficacy for patients who require third-line (3L) treatment for CML.4,5
- As clinical evidence suggests that ponatinib and bosutinib have different benefit-risk profiles,6 some physicians may reserve ponatinib for patients who fail 3L bosutinib. However, it is unknown if reserving ponatinib for fourth-line (4L) after bosutinib is associated with decreased efficacy.

Objective

To estimate the efficacy difference associated with reserving ponatinib for 4L or later (4L+) vs using ponatinib as 3L therapy.

METHODS

We examined efficacy outcomes among CP-CML patients in the PACE trial who received 3L ponatinib vs those treated with ponatinib in 4L+ and 4L+ post-bosutinib.

The PACE trial design has been previously described.6
- Single-arm phase 2 efficacy and safety trial
- Patients with Philadelphia chromosome-positive leukemia resistant or intolerant to dasatinib or nilotinib, and those with the T315I mutation
- Ponatinib evaluated at a starting dose of 45 mg QD

Primary endpoint for CP-CML patients: major cytogenetic response (MCyR) by 12 months
- Secondary endpoints: complete hematologic response (CHR), major molecular response (MMR), time to and duration of responses, progression-free survival (PFS), overall survival (OS), safety
- Response assessments conducted every 3 months for CP-CML patients

Key outcomes examined in the current analysis were:
- Treatment response: MCyR, complete cytogenetic response [CCyR], MMR
- Durability of MCyR
- PFS

Data were evaluated at a median follow-up of approximately 4 years (48.2 months, range 0.1–58.5 months).

Durability of MCyR was estimated using Kaplan–Meier methods.

RESULTS

Baseline patient-level data from the PACE study were stratified by line of therapy (Table 1). Prior lines of therapy included any approved TKI.

Patients remained on ponatinib for a median (range) of 3.2 (0.01–4.8), 2.3 (0.01–4.8), and 2.2 (0.01–4.5) years in the 3L, 4L+, and 4L+ post-bosutinib groups, respectively.

Baseline treatment response was higher for ponatinib in 3L than in 4L+ or 4L+ post-bosutinib across all measures (Figure 2).

Among patients who achieved MCyR, 89% of those who received 3L ponatinib vs 81% who received ponatinib 4L+ were estimated to retain responses at 3 years (log-rank test comparing entire curve for each of the two groups: P=0.168, Figure 3).

- A significantly higher percentage of patients retained MCyR at 3 years with ponatinib in 3L than in 4L+ or 4L+ post-bosutinib (log-rank test comparing entire curve for each of the two groups: P=0.004).

CONCLUSIONS

This post-hoc analysis was not adjusted for patient demographic or clinical characteristics.

- A small number of patients in PACE received 4L+ ponatinib post-bosutinib.

- Protocol-driven patient selection and CML management in PACE may limit generalizability of findings.

- Safety data were not compared in this analysis. Appropriate consideration of risks is also important when making treatment decisions.

References


Figure 1. Study discontinuations (data cut-off: August 3, 2015)

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- Patients remained on ponatinib for a median (range) of 3.2 (0.01–4.8), 2.3 (0.01–4.8), and 2.2 (0.01–4.5) years in the 3L, 4L+, and 4L+ post-bosutinib groups, respectively.

Figure 2. Response rates among CP-CML patients in 3L, 4L+ and 4L+ post-bosutinib

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Figure 3. Response durability among CP-CML patients who achieved MCyR in 3L, 4L+ and 4L+ post-bosutinib

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- A significantly higher percentage of patients retained MCyR at 3 years with ponatinib in 3L than in 4L+ or 4L+ post-bosutinib (log-rank test comparing entire curve for each of the two groups: P=0.004).