Minimum Follow-up of 4 Years for Ongoing Patients with Chronic-Phase Chronic Myeloid Leukemia (CP-CML) in a Phase 1 Trial of Ponatinib
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INTRODUCTION
- Ponatinib is an oral tyrosine kinase inhibitor (TKI) with potent activity against native BCR-ABL and resistant mutants, including T315I.
- Ponatinib is approved in the United States and European Union for adult patients with refractory chronic myeloid leukemia (CML) or Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) and those with the T315I mutation.7

METHODS
- Inclusion/exclusion criteria and study design have been previously reported.6
- Adult patients (age ≥18 years) with resistant/refractory hematologic malignancies were enrolled in this open-label, dose-escalation (3 × 3 design), phase 1 trial.
- Patients who had CP-CML are the focus of this analysis; data as of February 2, 2015, are reported.
- Median follow-up for all CP-CML patients was 53.1 (1.7–69.9) months; follow-up for ongoing CP-CML patients was at least 4 years (52.7–69.9 months).

RESULTS
- With a median follow-up of 53.1 months, 22 of 43 (51%) CP-CML patients remain on study and continue to receive ponatinib.
- The most common reasons for discontinuation in CP-CML patients were AEs (n=1 for 27.4% [10.6–29.6]) and disease progression (n=4 [9.5%]).
- No AEs have led to discontinuation since the last presentation of those of the overall study population.
- Median daily dose between first dose date and last dose date was 40.3 (14.3–59.5) mg.
- Most patients were estimated to maintain responses for at least 4 years.
- At the time of analysis, 20/21 patients with MCyR at any time (18/20 in continuous MCyR), 20/28 patients with CCyR at any time (12/20 in continuous CCyR), and 19/24 patients with MMR at any time (13/19 with continuous MMR) remained on study; 10/11 patients with the T315I mutation who had MCyR at any time (8/10 in continuous MCyR) remained on study.
- These data, representing the longest follow-up with ponatinib in ongoing CP-CML patients (52.7–69.9 months), demonstrate that ponatinib continues to provide benefit to patients with prior TKI failure and limited treatment options.
- CP-CML patients achieved deep and durable responses with ponatinib:
  - MCyR rates were 72% (15/21) and 63% (13/21) in patients with continuous and intermittent doses, respectively.
  - The majority (64%) of ongoing patients are on a dose of 15 mg/d or less (mean current dose, 22.5 mg).
- Most AEs were Grades 1–2 and, as reported previously, most occurred in the first year of treatment.

Table 1. Baseline Characteristics
- CP on Patients

Table 2. Patient Disposition and Exposure
- 81 patients were enrolled, of whom 43 had CP-CML.
- Baseline characteristics for CP-CML patients were broadly similar to those of the overall study population.
- 42/43 (98%) CP-CML patients had received at least 2 prior TKIs.

Figure 1A. Response to Ponatinib in CP-CML (n=43)

Figure 1B. Response to Ponatinib: Current Response in CP-CML Patients Remaining on Study (n=22)

Figure 2. Duration of Response in CP-CML Patients

Figure 3. Treatment-Emergent AEs (TEAEs) in ≥25% of CP-CML Patients (n=43)

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REFERENCES
- Cortes JE, Kantarjian HM, Talpaz M, et al. A phase 1 dose-escalation study evaluated the safety, tolerability, and pharmacokinetics of ponatinib in patients with relapsed/refractory hematologic malignancies (N=81), and evaluated antileukemic activity in patients with Ph+ leukemias (n=65). The primary publication of this phase 1 study reported robust clinical activity of ponatinib in heavily pretreated Ph+ patients— including patients with chronic-phase (CP)-CML, accelerated-phase (AP)-CML, blast-phase (BP)-CML, and Ph+ ALL— with a median follow-up of 56 (2–140) weeks. This report focuses on CP-CML patients only, with a minimum follow-up of 4 years (52.7–69.9 months) for ongoing patients—the longest follow-up of ponatinib-treated patients to date.

Table 2. Patient Disposition and Exposure

Table 3. Response to Ponatinib in CP-CML Patients by Starting Dose Lower Than 45 mg

Table 4. Treatment-Emergent AEs (TEAEs) in ≥25% of CP-CML Patients (n=43)

Table 5. Arterial Occlusive Events (AOEs) and Venous Thromboembolic Events (VTEs) in CP-CML Patients

Figure 1A. Response to Ponatinib in CP-CML (n=43)

Figure 1B. Response to Ponatinib: Current Response in CP-CML Patients Remaining on Study (n=22)

Figure 2. Duration of Response in CP-CML Patients

Figure 3. Treatment-Emergent AEs (TEAEs) in ≥25% of CP-CML Patients (n=43)

Figure 4. Duration of Response in CP-CML Patients

Figure 5. Treatment-Emergent AEs (TEAEs) in ≥25% of CP-CML Patients (n=43)

Figure 6. Duration of Response in CP-CML Patients

Figure 7. Treatment-Emergent AEs (TEAEs) in ≥25% of CP-CML Patients (n=43)