EP750 BOSUTINIB IN PATIENTS WITH CHRONIC PHASE CHRONIC MYELOID LEUKEMIA INTOLERANT TO PRIOR TYROSINE KINASE INHIBITORS: ANALYSES FROM THE BYOND STUDY

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Background: Bosutinib is approved for patients with Philadelphia chromosome (Ph)+ chronic myeloid leukemia (CML) resistant/intolerant to prior therapy and in newly diagnosed patients in chronic phase (CP). Aims: To evaluate the efficacy and safety of bosutinib in patients with CML intolerant to all prior tyrosine kinase inhibitors (TKIs).

Methods: The ongoing phase 4 BYOND study (NCT02228382) is further evaluating efficacy and safety of bosutinib (starting dose 500 mg/d) for CML resistant/intolerant to prior TKIs. We report findings in patients intolerant to all prior TKIs. Data are reported ≥1 y after the last enrolled patient (~85% TKI-intolerant patients had ≥2 y follow-up). Results: Of 163 patients who received bosutinib, 156 had Ph+ CP CML. 73 patients entered the study due to intolerance; 29, 26 and 18 had 1 (CP2L), 2 (CP3L) and 3 (CP4L) prior TKIs, respectively. After a median follow-up of 30.4 months, median treatment duration across all 3 cohorts (CP2L, CP3L, CP4L, respectively) was 25.3 months (29.2, 24.6, 17.6) and median dose intensity was 292.0 mg/d (304.5, 284.8, 272.1). Across CP CML cohorts (CP2L, CP3L, CP4L, respectively), 84.9% of patients (82.8%, 88.5%, 83.3%) had ≥1 dose reduction and 83.6% (79.3%, 84.6%, 88.9%) had ≥1 dose interruption due to adverse events (AEs). At the data cutoff, 53.4% (CP2L 65.5%, CP3L 42.3%, CP4L 50.0%) were still receiving bosutinib. The most common reason for discontinuation was AEs (28.8%). The most common (> 40%) treatment-emergent AEs (TEAEs) were diarrhea (87.7%) and nausea (43.8%). Grade 3/4 TEAEs in > 10% of patients were diarrhea (16.4%), increased alanine aminotransferase (19.2%) and increased lipase (12.3%). Most patients with a valid baseline assessment achieved cytogenetic and molecular responses across therapy lines (Table). Deaths occurred in 4 patients (CP2L 1, CP3L 3, CP4L 0); none were related to bosutinib or CML. Overall survival rate (95% CI) at 2 y in TKI-intolerant patients was 97.2% (89.2–99.3); rates were 96.4% (77.2–99.5), 96.0% (74.8–99.4) and 100% (100–100) in CP2L, CP3L and CP4L patients, respectively.

Cumulative response	CP2L		CP3L		CP4L		Total	
	n/N	% (95% CI)	n/N	% (95% CI)	n/N	% (95% CI)	n/N	% (95% CI)
CCyR*	24/27	88.9 (70.8–97.6)	19/22	86.4 (65.1–97.1)	15/18	83.3 (58.6–96.4)	58/67	86.6 (76.0–93.7)
Excluding patients with baseline CCyR	5/6	83.3 (35.9–99.6)	4/6	66.7 (22.3–95.7)	4/6	66.7 (22.3–95.7)	13/18	72.2 (46.5–90.3)
MMR	26/29	89.7 (72.6–97.8)	22/26	84.6 (65.1–95.6)	12/18	66.7 (41.0–86.7)	60/73	82.2 (71.5–90.2)
Excluding patients with baseline MMR	10/11	90.9 (58.7–99.8)	9/11	81.8 (48.2–97.7)	6/9	66.7 (29.9–92.5)	25/31	80.6 (62.5–92.5)

*CCyR imputed from MMR if no valid cytogenetic assessment available on a specific date.
CCyR=complete cytogenetic response

Summary/Conclusion: A long duration of treatment and high response rate were observed in TKI-intolerant patients treated with bosutinib. Despite being intolerant to all prior therapies, ≥50% of patients in the overall intolerant cohort remained on bosutinib treatment at the data cutoff and > 80% achieved/maintained major molecular responses (MMR). These results further support bosutinib use in patients with Ph+ CP CML and intolerance to all prior TKIs.