1475 Efficacy and Safety of Bosutinib in Previously Treated Patients with Chronic Myeloid Leukemia: Final Results from the Byond Trial.

Program: Oral and Poster Abstracts

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Introduction: Bosutinib is approved for patients with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) resistant/intolerant to prior therapy and patients with newly diagnosed Ph+ chronic phase (CP) CML. The phase 4 BYOND trial (NCT02228382) further evaluated the efficacy and safety of bosutinib in patients with previously treated CML. We report the final results from BYOND.

Methods: Patients with CML resistant/intolerant to previous tyrosine kinase inhibitor therapy received bosutinib 500 mg once daily. This final analysis was based on a November 23, 2020 database lock, after 3 years of follow-up.

Results: Of 163 patients who received bosutinib, 156 had Ph+ CP CML; 4 patients with accelerated phase CML and 3 with Ph−/*BCR-ABL1*+ CML were analyzed separately. At study completion (median follow-up, 47.8 months), 48.1% of patient with Ph+ CP CML were still receiving treatment, and 68.6% completed the study. Most common primary reason for treatment discontinuation was adverse events (AEs) (26.9% [n=42/156]). Median treatment duration was 40.9 months (range, 0.2−50.1) and median dose intensity 306.4 mg/day (range, 79.7−560.6). Dose interruptions due to AEs occurred in 76.3% of patients and dose reductions in 79.5% of patients. Dose reduction (without further reduction) to 400, 300, or 200 mg/day occurred in 35 (22.4%), 46 (29.5%), and 38 (24.4%) patients, respectively.

In evaluable patients with Ph+ CP CML, 81.1% (95% CI: 73.7–87.2), 71.8% (95% CI: 63.9–78.9), 59.7% (95% CI: 51.4–67.7) and 48.3% (95% CI: 40.1−56.6) attained or maintained complete cytogenetic response, major molecular response (MMR), MR^4, and $MR^{4.5}$ respectively, at any time on treatment. The majority of patients achieved a deeper molecular response relative to baseline while on bosutinib (Table 1). Among responders, the Kaplan-Meier probabilities (95% CI) of maintaining MMR and MR^4 at 36 months were 87.2% (78.0−92.7) and 80.7% (69.4−88.1), respectively. No patients with Ph+ CP CML progressed to accelerated/blast phase on-treatment. At 48 months, the cumulative incidence of progression free-survival events was 5.1% (95% CI: 2.4–9.4) and the Kaplan-Meier overall survival rate 88.3% (95% CI: 81.8–92.6). There were 17 deaths; 2 were considered CML-related (off-treatment progression to AP/BP, n=1; cardiogenic shock, n=1) and none were considered to be treatment-related by the investigator.

In the overall patient population (N=163), any grade treatment-emergent AEs (TEAEs) were reported by 99.4% of patients and grade 3/4 TEAEs were reported by 79.1% of patients (Table 2). Most common (≥10%) TEAEs leading to dose reduction were diarrhea (27.0%) and increased ALT (12.3%) and most common TEAEs leading to temporary dose interruption were diarrhea (30.7%), increased ALT (14.7%), vomiting (13.5%), increased AST (11.0%), and nausea (10.4%). AEs leading to treatment discontinuation in ≥2% of patients were increased ALT (4.9%) and AST (2.5%).

Conclusions: After 3 years, bosutinib continued to show efficacy in previously treated patients with Ph+ CP CML. Long-term AEs were generally manageable and consistent with previous reports of bosutinib. These results confirm the use of bosutinib as a standard of care in previously treated patients with CML.

Table 1. Shift from Baseline by *BCR-ABL1* Transcript Levels in Patients with CP CML*

	Best response on treatment, *BCR-ABL1* IS, n (%)						
	Baseline Total (N)	>10%	>1 to 10%	>0.1 to 1%	>0.01 to 0.1%	≤0.01%	Not Evaluable
Baseline *BCR-ABL1* IS							
>10%	27	14 (51.9)	1 (3.7)	0	3 (11.1)	5 (18.5)	4 (14.8)
>1 to 10%	24	2 (8.3)	2 (8.3)	2 (8.3)	4 (16.7)	13 (54.2)	1 (4.2)
>0.1 to 1%	28	0	1 (3.6)	5 (17.9)	7 (25.0)	15 (53.6)	0
>0.01 to 0.1%	33	0	1 (3.0)	1 (3.0)	4 (12.1)	26 (78.8)	1 (3.0)
≤ 0.01%	37	0	0	1 (2.7)	2 (5.4)	32 (86.5)	2 (5.4)

*Includes patients with a valid baseline assessment.

IS=international scale.

Table 2. Summary of TEAEs

	Total (N=163)	
n (%)*	**Any Grade**	**Grade 3/4**
Any TEAE	162 (99.4)	129 (79.1)
Diarrhea	145 (89.0)	27 (16.6)
Nausea	70 (42.9)	4 (2.5)
Vomiting	55 (33.7)	7 (4.3)
Abdominal pain	49 (30.1)	8 (4.9)
Headache	47 (28.8)	1 (0.6)
Fatigue	46 (28.2)	3 (1.8)
Increased ALT	44 (27.0)	24 (14.7)
Dyspnea	39 (23.9)	6 (3.7)
Upper abdominal pain	37 (22.7)	2 (1.2)
Arthralgia	37 (22.7)	1 (0.6)
Asthenia	36 (22.1)	4 (2.5)
Increased AST	33 (20.2)	7 (4.3)

*Any grade TEAEs occurring in ≥20% of patients and/or Grade 3/4 TEAEs occurring in ≥10% of patients.

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