P717 BOSUTINIB IN NEWLY DIAGNOSED CHRONIC MYELOID LEUKEMIA: GASTROINTESTINAL, LIVER, EFFUSION AND RENAL SAFETY CHARACTERIZATION IN THE BFORE TRIAL. Topic: 08. Chronic myeloid leukemia – Clinical**.** Jorge E Cortes1, Dragana Milojkovic2, Carlo Gambacorti-Passerini3, ***Valentín García-Gutiérrez4***, Michael J Mauro5, Eric Leip6, Simon Purcell7, Andrea Viqueira8, Tim H Brümmendorf9 1 *Georgia Cancer Center, Augusta, United States;*2 *Hammersmith Hospital, London, United Kingdom;*3 *University of Milano-Bicocca, Monza, Italy;****4 Universitario Ramón y Cajal, Ramón y Cajal Health Research Institute, Madrid, Spain****;*5 *Memorial Sloan Kettering Cancer Center, New York, United States;*6 *Pfizer Inc, Cambridge, United States;*7 *Pfizer Ltd, London, United Kingdom;*8 *Pfizer SLU, Madrid, Spain;*9 *Universitätsklinikum RWTH Aachen, Aachen, Germany*

Background: Bosutinib is approved for the treatment of Philadelphia chromosome‑positive (Ph+) chronic myeloid leukemia (CML) resistant/intolerant to prior therapy and newly diagnosed Ph+ chronic phase (CP) CML. Efficacy and safety of bosutinib vs imatinib in patients with newly diagnosed CP CML was assessed in the phase 3 BFORE trial (NCT02130557).

Aims: The safety profile of bosutinib after 5 years follow-up, with a focus on gastrointestinal, liver, effusion and renal treatment-emergent adverse events (TEAEs), was characterized.

Methods: Patients who received ≥1 dose of bosutinib (n=268) or imatinib (n=265) 400 mg/day in BFORE were included. Adverse events (AEs) of special interest were analyzed by selecting prespecified MedDRA terms to generate TEAE clusters. This analysis is based on the final database lock: June 12, 2020.

Results: Median duration of treatment was 55 months for patients receiving bosutinib or imatinib; respective median (range) dose intensity was 393.6 (39‑583) vs 400.0 (189‑765) mg/d. Any grade TEAEs occurred in 98.9% and 98.9% of bosutinib- vs imatinib-treated patients. The most common newly occurring TEAEs (any grade) after 12 months were increased lipase (9.0%) with bosutinib, and diarrhea (8.3%) with imatinib. In bosutinib- vs imatinib-treated patients, 25.4% vs 14.3% had AEs leading to permanent treatment discontinuation; the majority discontinued in year 1 (14.2% vs 10.6%). The most frequent AEs leading to discontinuation were increased ALT (overall, 4.9%; year 1, 4.5%) with bosutinib vs thrombocytopenia (overall, 1.5%; year 1, 1.5%) with imatinib. Gastrointestinal, liver, effusion and renal TEAEs, respectively, occurred in 79.9%, 44.0%, 6.0% and 10.4% (maximum grade 3/4 [G3/4]: 9.0%, 26.9%, 1.1% and 2.2%) of bosutinib- vs 61.5%, 15.5%, 2.3% and 9.8% (G3/4: 1.1%, 4.2%, 0.4% and 0.8%) imatinib-treated patients. One grade 5 renal TEAE occurred in the bosutinib arm and was not considered related to treatment. Cumulative rates per treatment year are shown in the Table. The most common gastrointestinal TEAEs were diarrhea (bosutinib vs imatinib: 75.0% vs 40.4% [G3/4: 9.0% vs 1.1%]) with bosutinib, and nausea (37.3% vs 42.3% [G3/4: 0% vs 0%]) with imatinib. In both arms, the most common liver, effusion and renal TEAEs, respectively, were increased ALT and/or AST (34.0% vs 8.3% [G3/4: 22.0% vs 2.3%]), pleural effusion (5.2% vs 1.9% [G3/4: 0.7% vs 0.4%]) and increased blood creatinine (6.7% vs 8.3% [G3/4: 0.4% vs 0.4%]). Gastrointestinal, liver, effusion and renal TEAEs infrequently led to treatment discontinuation (1.9%, 7.8%, 0.7% and 0.7% vs 1.1%, 0.8%, 0% and 0.4%).

Image:

Table. Cumulative rate of patients with gastrointestinal, liver, effusion and renal TEAEs by year

%	Bosutinib (n=268)					Imatinib (n=265)				
	Year 1	Year 2	Year 3	Year 4	Year 5+	Year 1	Year 2	Year 3	Year 4	Year 5+
Gastrointestinal	76.5	78.0	79.5	79.5	79.9	52.8	56.6	58.5	61.1	61.5
Liver	39.2	41.4	42.2	42.9	44.0	11.7	13.6	14.0	14.3	15.5
Effusion	2.2	3.0	4.5	6.0	6.0	1.5	1.5	1.5	1.5	2.3
Renal	6.0	7.8	8.2	9.7	10.4	6.0	8.3	8.7	8.7	9.8

Summary/Conclusion: The safety profiles of bosutinib and imatinib in BFORE were distinct, with no new safety signals identified after 5 years of follow-up. The onset of TEAEs occurred primarily during year 1 (e.g., gastrointestinal and liver), with an increased incidence of some TEAEs (e.g., effusion and renal) in later years. Discontinuations due to AEs generally occurred early into treatment, with low rates of discontinuation due to gastrointestinal, liver, effusion and renal AEs. These long-term safety results further support the use of first-line bosutinib as a standard of care in patients with CP CML.