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ORAL ABSTRACTS

906.OUTCOMES RESEARCH-MYELOID MALIGNANCIES

Patient-Reported Outcomes in Acute Myeloid Leukemia Patients with *FLT3*-ITD Mutation Receiving Quizartinib Vs. Standard Chemotherapy: Results from the Quantum-First Trial

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Introduction: QuANTUM-First (NCT02668653) is a multicenter, global, randomized, double-blind phase 3 clinical trial evaluating the efficacy and safety of the novel oral fms-like tyrosine kinase 3 inhibitor (FLT3i) quizartinib in combination with standard induction and consolidation chemotherapy, and as maintenance monotherapy for up to 36 cycles in patients 18-75 years old with *FLT3*-ITD positive acute myeloid leukemia (AML). Quizartinib demonstrated a clinically meaningful and statistically significant improvement in overall survival (OS) versus placebo. An exploratory endpoint of the trial was to assess the impact of quizartinib on patient-reported outcomes (PROs). This is the first report of the longitudinal results of the PRO measures (PROMs) collected in the QuANTUM-First trial.
Methods: Patients were randomized to receive chemotherapy + quizartinib or chemotherapy + placebo. PROMs were the European Organization for Research and Treatment of Cancer QLQ-C30 (EORTC QLQ-C30) and EuroQol EQ-5D-5L. Baseline measurement was collected on day 8 of the first induction cycle, and repeated measurements were collected on day 28 of induction cycles 1-2, day 6 and 28 of consolidation cycles 1-4, and day 1 of continuation cycles 1-34 at 3-cycle intervals. EORTC QLQ-C30 and EQ-5D-5L scores were calculated as per their respective scoring manuals and included mean (95% CI, p-value) score for each domain of the EORTC QLQ-C30 and EQ-5D-5L index score, as well as mean change from baseline score at each timepoint. A minimal clinically important difference (MCID) score $\geq$10 points for each domain of the EORTC QLQ-C30, was considered clinically meaningful. A mixed-effect model for repeated measures (MMRM) and time until definitive deterioration (TUDD) was used to assess the longitudinal impact of treatment on PROs. TUDD was defined as time from baseline PRO score to first deterioration of the score beyond the MCID as compared to the baseline without further improvement of more than one MCID as compared to the reference score or without any further available score.
Results: A total of 509 out of 539 patients from the trial (254 quizartinib; 255 placebo) were included for PRO analysis. Patient compliance to questionnaire completion at the beginning of each phase was high and similar for both arms and most scales (Global Health Status [GHS] completion rate (%) on induction cycle 1, consolidation cycle 1, and continuation cycle 1: 99.2, 95.3, 93.4, respectively) Baseline PRO scores were comparable between arms and were lower than the general population norm EORTC QLQ-C30 and EQ-5D-5L scores for EU and US (Table 1). Per MMRM, there were clinically meaningful improvements from baseline in GHS (Figure 1) and fatigue in both arms. However, there was no significant difference between arms for the change from baseline score although placebo arm had numerically better scores specifically during the maintenance phase (treatment difference for quizartinib - placebo was -2.0 [95% CI: -4.8, 0.7], p=0.1479 for GHS and 3.0 [95% CI: -0.1, 6.1], p=0.0600 for fatigue). Similar trends towards clinically meaningful improvement in score over time for both arms and no significant differences between arms were observed in most of the functional and symptom scales of EORTC QLQ-C30 and EQ-5D-5L index scores. By TUDD analysis, quizartinib arm showed slower deterioration in several scales (specifically GHS, cognitive function, appetite loss, and constipation) but the differences did not reach statistical significance.
Conclusions: QuANTUM-First is the first study to explore the impact of quizartinib on PROs. Quizartinib showed improvement in OS without any detrimental impact on quality of life and symptoms when added to standard chemotherapy followed by maintenance monotherapy in patients with newly diagnosed *FLT3*-ITD AML.

Disclosures Oliva: *Daiichi:* Consultancy, Honoraria; *Grande Ospedale Metropolitano BMM:* Current Employment; *Ryvu:* Consultancy, Honoraria; *Bristol Myers Squibb:* Consultancy, Honoraria, Speakers Bureau; *Janssen:* Consultancy, Honoraria; *Alexion:* Consultancy, Honoraria, Speakers Bureau; *Novartis:* Honoraria, Speakers Bureau; *Amgen:* Honoraria, Speakers Bureau; *Sobi:* Honoraria, Speakers Bureau; *Servier:* Patents & Royalties. **Unni:** *Daiichi Sankyo Inc.:* Current Employment, Current holder of *stock options* in a privately-held company. **Cottone:** *Daiichi Sankyo Inc.:* Current Employment. **Vashi:** *Daiichi Sankyo Inc.:* Current Employment. **Li:** *OPEN Health:* Current Employment; *Daiichi Sankyo:* Consultancy. **Cortes:** *Forma Therapuetic:* Consultancy; *Abbvie:* Consultancy, Research Funding; *Pfizer:* Consultancy, Research Funding; *Biopath Holdings:* Consultancy, Current holder of *stock options* in a privately-held company, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Gilead:* Consultancy; *Takeda:* Consultancy, Honoraria; *Novartis:* Consultancy, Research Funding. **Sekeres:** *Geron:* Membership on an entity's Board of Directors or advisory committees; *Novartis:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Kurome:* Consultancy, Current holder of *stock options* in a privately-held company; *BMS:* Consultancy, Membership on an entity's Board of Directors or advisory committees.

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