Abstract: P572

Title: QUANTUM-FIRST: PATIENT-REPORTED OUTCOMES (PROS) IN NEWLY DIAGNOSED (ND) FLT3-ITD+ ACUTE MYELOID LEUKEMIA (AML) PATIENTS (PTS) RECEIVING STANDARD CHEMOTHERAPY (CTX) PLUS QUIZARTINIB (Q) OR PLACEBO (P)

Abstract Type: Poster Presentation

Topic: Acute myeloid leukemia - Clinical

Background:

The phase 3 study QuANTUM-First (NCT02668653) evaluated the efficacy and safety of the oral, highly potent, selective, type 2 FLT3 inhibitor Q + standard induction and consolidation CTx, which could include allogeneic hematopoietic cell transplantation (allo-HCT), followed by Q or P continuation monotherapy for ≤36 cycles (C) in pts 18-75 years (y) old with *FLT3*-ITD+ AML. Q demonstrated a clinically meaningful and statistically significant improvement in overall survival (OS) vs P (PMID: 37116523). An exploratory endpoint was the impact of Q on health-related quality of life (HRQoL).

Aims:

To report the longitudinal results of the PRO measures (PROMs) from QuANTUM-First.

Methods:

Pts were randomized to receive CTx + Q or CTx + P. PROMs were the European Organization for Research and Treatment of Cancer QLQ-C30 (EORTC QLQ-C30). Measurements were collected on day (D) 8 of induction C1 (baseline) and repeated on D28 of induction C1-2, D6&28 of consolidation C1-4, and D1 of continuation C1-34 at 3-C intervals. The analysis included mean (95% CI) score for each subscale of the EORTC QLQ-C30, and mean change from baseline (CFB) score at each timepoint. A minimal clinically important difference (MCID) score ≥10 points for each subscale, was considered clinically meaningful. A mixed-effect model for repeated measures (MMRM) and time until definitive deterioration (TUDD) were used to assess the longitudinal impact of treatment on PROs. TUDD was defined as time from baseline 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. Additional analyses explored the potential impact of allo-HCT status and age (≤60 y and >60 y) on Global Health Status (GHS)/Quality of Life (QoL) scores. No adjustment for multiplicity was performed for these analyses.

Results:

Of 539 pts from the trial, 509 (254 Q; 255 P) had PRO data to be included in the analysis. Questionnaire completion rates at the beginning of each treatment phase were high and similar for both arms and most scales (GHS/QoL completion rate (%) on induction C1, consolidation C1, and continuation C1: 99.2, 95.3, 93.4, respectively). Baseline PRO scores were comparable between arms and worse than the general population norm EORTC QLQ-C30 scores for EU/US (**Table 1**). Per MMRM, there were clinically meaningful improvements from baseline in GHS/QoL (**Figure 1**) in both arms. There was no meaningful difference between arms in the CFB score; however, the P arm had numerically better CFB score during continuation (treatment difference in estimated MMRM mean scores for Q−P: −2.0 [95% CI: −4.8, 0.7] for GHS/QoL). Similar trends of clinically meaningful score improvement over time for both arms, albeit not different between arms, were found in most functional and symptom scale index scores. For fatigue, a prevalent AE in AML pts, the treatment difference in estimated MMRM mean scores for Q−P was 3.0 (95% CI: −0.1, 6.1). By TUDD analysis, Q arm showed longer time to deterioration in many scales (GHS/QoL, cognitive function, appetite loss, and constipation). When allo-HCT status was considered as a time-dependent covariate by MMRM, the changes in GHS/QoL scores over time suggested a potential favorable impact of allo-HCT. No meaningful difference was observed in GHS/QoL scores between arms in either ≤60 y pts or in >60 y pts.

Summary/Conclusion:

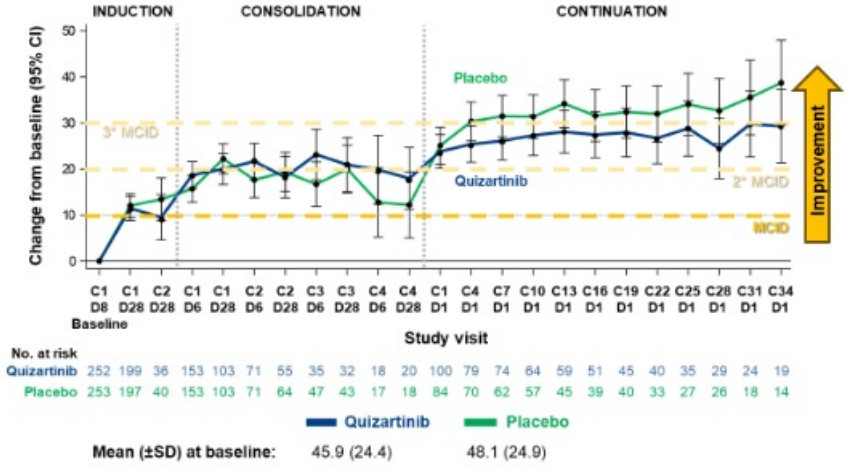
QuANTUM-First is the first study to explore the impact of Q on HRQoL. Results suggest that Q improved OS with no detrimental impact on QoL and symptoms in nd *FLT3*-ITD+ AML pts.

Table 1. EORTC QLQ-C30 Mean Scores (SD) at Baseline for Quizartinib vs Placebo vs General Population Norm Data for EU and US

	Quizartinib (n=254)	Placebo (n=255)	Ref, EU*	Ref, US*
Global QoL†				
GHS/QoL	45.9 (24.4)	48.1 (24.9)	66.1 (21.7)	63.9 (22.9)
Functional subscale†				
Physical	68.5 (28.2)	68.9 (26.8)	85.1 (18.9)	80.8 (25.2)
Role	52.2 (35.1)	49.9 (38.0)	84.3 (24.6)	81.7 (28.2)
Emotional	71.7 (24.3)	72.3 (24.3)	74.2 (24.7)	73.3 (28.0)
Cognitive	80.4 (22.8)	81.9 (22.6)	84.8 (21.3)	80.9 (25.6)
Social	53.5 (34.3)	53.4 (36.1)	86.2 (24.1)	81.6 (29.4)
Symptom Subscale§				
Fatigue	51.0 (29.2)	48.0 (29.0)	29.5 (25.5)	31.9 (27.8)
Nausea/vomiting	19.0 (23.7)	19.7 (24.7)	5.9 (16.0)	10.9 (22.6)
Pain	28.6 (29.1)	28.3 (29.8)	23.5 (27.1)	27.5 (30.2)
Dyspnea	23.4 (29.2)	23.8 (29.8)	15.9 (24.6)	19.9 (28.5)
Insomnia	34.8 (31.2)	33.3 (33.3)	26.6 (30.3)	30.8 (33.2)
Appetite loss	45.0 (34.4)	46.5 (35.7)	10.0 (21.6)	14.1 (25.3)
Constipation	18.7 (28.4)	15.8 (25.3)	12.5 (23.3)	18.6 (28.6)
Diarrhea	30.7 (35.2)	25.3 (30.5)	9.5 (20.9)	13.7 (27.1)
Financial difficulties	27.2 (33.0)	25.0 (32.8)	10.6 (23.6)	17.5 (30.8)

*Nolte S. et al. *Eur J Cancer.* 2019;107:153-163 (values were adjusted by age and sex). †Higher scores are better. §Lower scores are better. EU: Austria, Denmark, France, Germany, Hungary, Italy, The Netherlands, Poland, Spain, Sweden, and United Kingdom. EU, European Union; GHS, global health status; QoL, quality of life; SD, standard deviation; US, United States.

Figure 1. EORTC QLQ-C30 Global Health Status/QoL Scale Mixed Model with Repeated Measures for Change in Score from Baseline for Quizartinib vs Placebo



C, cycle; CI, confidence interval; D, day; MCID, minimal clinically important difference; SD, standard deviation.

Keywords: AML, PRO, Flt3-ITD