Abstract: S142

Title: QUANTUM-FIRST: EFFICACY IN NEWLY DIAGNOSED PATIENTS WITH FMS-LIKE TYROSINE KINASE 3-INTERNAL TANDEM DUPLICATION–POSITIVE (FLT3-ITD+) ACUTE MYELOID LEUKEMIA (AML) WHO RECEIVED CONTINUATION THERAPY

Abstract Type: Oral Presentation

Session Title: Acute myeloid leukemia - Clinical 3

Background:

The phase 3 QuANTUM-First study (NCT02668653) demonstrated that in newly diagnosed patients (pts) with *FLT3*-ITD+ AML, adding the oral, highly potent, selective, type 2 FLT3 inhibitor quizartinib (Q) to standard chemotherapy (CTx) ± allogeneic hematopoietic cell transplantation (allo-HCT), followed by Q or placebo (P) continuation (CONT) monotherapy for up to 36 cycles (3 years [y]), decreased the relative risk of death by 22% vs P (PMID: 37116523).

Aims:

To evaluate impact of CONT therapy on Q efficacy in newly diagnosed*FLT3*-ITD+ AML pts, by analyzing rates of overall survival (OS), relapse-free survival (RFS), and cumulative incidence of relapse (CIR).

Methods:

Adult pts (aged 18-75 y) with *FLT3*-ITD+ AML were randomized 1:1 to Q (40 mg/d) or P, each with standard induction 7+3 CTx, and stratified by region, age, and white blood cell (WBC) count at diagnosis. Pts in complete remission (CR) or CR with incomplete neutrophil or platelet recovery (CRi) received up to 4 cycles of high-dose standard consolidation CTx combined with Q (40 mg/d) or P and/or allo-HCT (Q/P were stopped ≥ 7 days before the conditioning regimen and not given with allo-HCT), followed by CONT of single-agent Q (30-60 mg/d) or P for up to 36 4-week cycles. OS was calculated from randomization in the intent-to-treat population who received CONT; CIR and RFS were calculated on pts who achieved CR at end of induction and received CONT. RFS was a prespecified exploratory analysis, while OS and CIR were post hoc analyses. Propensity score (PS)–based analyses for OS and RFS were conducted based on baseline covariates (age, sex, WBC count, *NPM1* mutational status, percent of bone marrow blasts), and also allo-HCT before CONT and type of anthracycline.

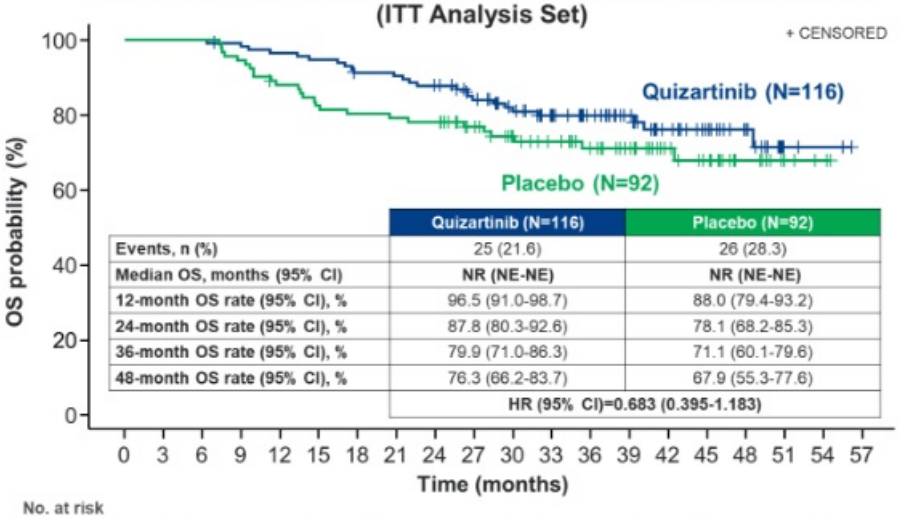
Results:

Of 539 randomized pts, 208 (38.6%; 116 Q, 92 P) received CONT therapy (median of 16 cycles in the Q arm and 17 cycles in the P arm). Pt baseline characteristics (Q vs P) were median (range) age, 53.0 y (23-73) vs 56.5 y (20-74); females, 54.3% vs 58.7%; Eastern Cooperative Oncology Group performance status ≥1, 63.8% vs 62.0%; mutated *NPM1* / *CEBPA*, 59.5% vs 65.2% / 25.0% vs 27.2%;*FLT3*-ITD variant allele frequency >25%, 61.2% vs 54.3%; and WBC count at diagnosis ≥40×109/L, 50.9% vs 37.0%. Among 208 pts who received CONT, 201 had achieved CR/CRi in induction (114 Q; 87 P). After median follow-up of 39.2 mo, median OS was not reached in either treatment arm, with a hazard ratio (HR) of 0.683 (95% CI, 0.395-1.183), in favor of Q (**Fig. 1**), which compares favorably with the HR of the primary OS analysis (0.78; 95% CI, 0.62-0.98). The 3-y OS was 79.9% (Q) vs 71.1% (P). Among 89 pts who received CONT and had not undergone allo-HCT before CONT, a remarkable OS advantage was observed with Q (HR, 0.401; 95% CI, 0.192-0.838; **Fig. 2**). The HR for OS in 119 pts who had allo-HCT and received CONT was 1.622 (95% CI, 0.623-4.220). Among 166 pts who achieved CR at end of induction and received CONT (94 Q; 72 P), HR for RFS was in favor of Q (0.738; 95% CI, 0.442-1.230), with 3-y RFS rates higher in the Q arm (67.1%) than in the P arm (59.6%). In addition, among these 166 pts, CIR decreased at 12, 24, and 36 months in the Q arm vs the P arm, with CIR at 3 y of 25.9% on Q vs 34.4% on P. PS-based analyses of OS and RFS favored Q over P.

Summary/Conclusion:

This exploratory analysis revealed a clinical benefit for CONT therapy with Q over P in newly diagnosed*FLT3*-ITD+ AML pts, specifically for those not undergoing allo-HCT, suggesting that Q CONT therapy in these pts is associated with delayed relapse or death. Future measurable residual disease analysis in CONT may help define the benefit of Q CONT

Figure 1. OS in Patients Who Received Continuation Monotherapy (ITT Analysis Set)



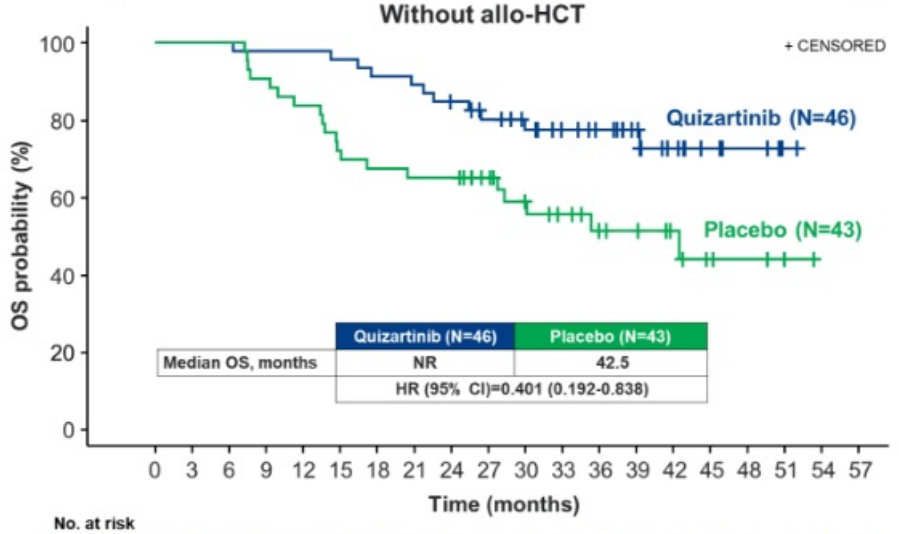
	Quizartinib (N=116)	Placebo (N=92)
Events, n (%)	25 (21.6)	26 (28.3)
Median OS, months (95% CI)	NR (NE-NE)	NR (NE-NE)
12-month OS rate (95% CI), %	96.5 (91.0-98.7)	88.0 (79.4-93.2)
24-month OS rate (95% CI), %	87.8 (80.3-92.6)	78.1 (68.2-85.3)
36-month OS rate (95% CI), %	79.9 (71.0-86.3)	71.1 (60.1-79.6)
48-month OS rate (95% CI), %	76.3 (66.2-83.7)	67.9 (55.3-77.6)
	HR (95% CI)=0.683 (0.395-1.183)	

No. at risk

Quizartinib	116	116	116	114	111	109	104	103	99	89	77	67	58	48	36	26	18	4	2	0
Placebo	92	92	92	87	80	75	73	72	71	61	52	47	40	33	23	18	10	4	2	0

CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; NE, not estimable; NR, not reached; OS, overall survival.

Figure 2. OS in Patients Who Received Continuation Monotherapy Without allo-HCT



	Quizartinib (N=46)	Placebo (N=43)
Median OS, months	NR	42.5
	HR (95% CI)=0.401 (0.192-0.838)	

No. at risk

Quizartinib	46	46	46	45	45	44	42	41	38	34	29	25	22	17	11	7	5	1	0	0
Placebo	43	43	43	39	36	31	29	28	28	23	18	15	12	10	7	4	3	1	0	0

allo-HCT, allogeneic hematopoietic cell transplantation; CI, confidence interval; HR, hazard ratio; NR, not reached; OS, overall survival.

Keywords: Flt3-ITD, Maintenance, AML