

QUIZARTINIB SIGNIFICANTLY PROLONGS OVERALL SURVIVAL IN PATIENTS WITH FLT3-INTERNAL TANDEM DUPLICATION–MUTATED (MUT) RELAPSED/REFRACTORY AML IN THE PHASE 3, RANDOMIZED, CONTROLLED QUANTUM-R TRIAL

Author(s): Jorge Cortes, et al.

Abstract: LB2600

Type: Oral Presentation

Presentation during EHA23: On Saturday, June 16, 2018 from 13:15 - 13:30

Location: Room A1

Background

FLT3-internal tandem duplication (*FLT3*-ITD) is a common driver mutation in acute myeloid leukemia (AML) that is associated with high leukemic burden and poor prognosis—high risk of relapse, decreased response to salvage therapy, and shorter overall survival (OS). Currently, there are no approved targeted therapies for patients (pts) with relapsed/refractory (R/R) *FLT3*-ITD–mut AML, which represents a high unmet medical need. Quizartinib (Q) is a once-daily, oral, highly potent and selective FLT3 inhibitor (FLT3i) shown in phase 2 trials to have promising single-agent antileukemic activity and a manageable safety profile.

Aims

QuANTUM-R is a global, phase 3, randomized, controlled trial (NCT02039726) evaluating the efficacy and safety of Q vs salvage chemotherapy (SC) in pts with R/R *FLT3*-ITD–mut AML. The primary objective was to determine whether single-agent Q prolongs OS compared with investigator's choice SC.

Methods

Pts aged ≥ 18 years with *FLT3*-ITD–mut AML who were refractory to or relapsed (with duration of first complete remission [CR1] of 6 months or less) after standard AML therapy, w/wo hematopoietic stem cell transplantation (HSCT) were randomized 2:1 to receive Q (60-mg, with a 30-mg lead-in) or investigator's choice SC, which was selected prior to randomization. Allowed SC regimens were low dose cytarabine (LoDAC); mitoxantrone, etoposide, and intermediate-dose cytarabine (MEC); or fludarabine, cytarabine, and granulocyte-colony stimulating factor (GCSF) with idarubicin (FLAG-IDA). Up to 2 cycles of MEC or FLAG-IDA were permitted; Q and LoDAC were given until lack of benefit, unacceptable toxicity, or HSCT. Prior therapy with FLT3i (except the multikinase inhibitor, midostaurin) was not allowed. Pts receiving HSCT in the Q arm were allowed to resume Q therapy following following transplant. The primary endpoint was OS.

Results

367 pts were randomized to Q (n=245) and SC (n=122 [LoDAC, n=29; MEC, n=40; FLAG-IDA, n=53]). Median follow-up was 102.4 weeks at study analysis cutoff. Treatment groups were well-balanced for baseline characteristics. 80 (32.7%) pts treated with Q were refractory to and 165 (67.3%) relapsed after a CR1 of < 6 mo (w/wo HSCT); similarly, 41 (33.6%) pts treated with SC were refractory to and 81 (66.4%) relapsed after a CR1 < 6 mo (w/wo HSCT). Median age was 55 years (range, 19-81) in the Q arm and 57.5 years (range, 18-78) in the SC arm. Median drug exposure was 4 cycles (range, 1-43) in the Q arm and 1 cycle (range, 1-2) in the SC arm. OS hazard ratio of Q relative to SC was 0.76 (95% CI 0.58-0.98; stratified log-rank test, 1-sided $P=0.0177$). Median OS was 27 wks (95% CI 23.1-31.3) and 20.4 wks (95% CI 17.3-23.7) for pts treated with Q and SC, respectively. Estimated survival probability at 52 wks was 27% for the Q arm and 20% for the SC arm. Rates of treatment-emergent adverse events were comparable between the 2 arms. Only 2 pts discontinued Q due to QTcF prolongation. No events of torsades de pointes were reported. The Q safety profile appears consistent with that observed at similar doses in the Q program.

Conclusion

This is the first report of the results of the QuANTUM-R trial, showing that single-agent Q significantly prolonged OS in pts with R/R *FLT3*-ITD–mut AML compared with SC. These pivotal data confirm the efficacy and safety of Q and the value of targeting the *FLT3*-ITD driver mutation with a highly potent and selective FLT3i. These results represent the first positive phase 3 trial to demonstrate improved OS with FLT3i in the R/R *FLT3*-ITD–mut AML setting.

Session topic: 4. Acute myeloid leukemia - Clinical

Keyword(s): Relapse, Acute Myeloid Leukemia, Flt3 inhibitor, Refractory