QUANTUM-FIRST TRIAL: FMS-LIKE TYROSINE KINASE 3-INTERNAL TANDEM DUPLICATION–SPECIFIC MEASURABLE RESIDUAL DISEASE CLEARANCE ASSESSED THROUGH INDUCTION AND CONSOLIDATION IS ASSOCIATED WITH IMPROVED OVERALL SURVIVAL IN NEWLY DIAGNOSED *FLT3*-ITD+ AML PATIENTS

Alexander E. Perl[1], Harry P. Erba[2], Pau Montesinos[3], Radovan Vrhovac[4], Elżbieta Patkowska[5], Hee-Je Kim[6], Pavel Zak[7], Po-Nan Wang[8], Sebastian Heck[9]*, Jaime E. Connolly Rohrbach[10], Ken C.N. Chang[10], Li Liu[10], Yasser Mostafa Kamel[10], Karima Imadalou[10], Arnaud Lesegretain[10], Jorge Cortes[11], Mikkael A. Sekeres[12], Hervé Dombret[13], Sergio Amadori[14], Jianxiang Wang[15], Richard F. Schlenk[16], Mark J. Levis[17]

[1]University of Pennsylvania, Philadelphia, PA, USA; [2]Duke Cancer Institute, Durham, NC, USA; [3]La Fe University and Polytechnic Hospital, Valencia, Spain; [4]University Hospital Centre Zagreb, Zagreb, Croatia; [5] Hematology, IHIT Institute of Hematology and Blood Transfusion, Warsaw, Poland;[6]Catholic Hematology Hospital, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea; [7]University Hospital Hradec Kralove, Hradec Kralove, Czechia; [8]Chang Gung Medical Foundation, Linkou, Taiwan; [9]Daiichi Sankyo Germany, Munich Germany; [10]Daiichi Sankyo, Inc, Basking Ridge, NJ, USA; [11]Georgia Cancer Center at Augusta University, Augusta, GA, USA; [12]Sylvester Cancer Center, University of Miami Health System, Miami, FL, USA; [13]Saint Louis Hospital, University of Paris, Paris, France; [14]Tor Vergata Polyclinic Hospital Rome, Rome, Italy; [15]Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Tianjin, China; [16]Heidelberg University Hospital and German Cancer Research Center, Heidelberg, Germany; [17]Johns Hopkins University, Baltimore, MD, USA

*Presenting on behalf of the original authors'

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Background

In the phase 3 QuANTUM-First trial, quizartinib significantly improved OS vs placebo when added to intensive chemotherapy and as maintenance monotherapy in patients with *FLT3*-ITD+ ND-AML. We analyzed the impact of *FLT3*-ITD-specific MRD in QuANTUM-First.

Methods

Genomic DNA was collected from patients with remission after induction and after consolidation (pre-transplant for HCT patients), analyzed by *FLT3*-ITD PCR-NGS. ITD mutations post-induction were cross-validated against enrollment; ITD VAFs were calculated (~10^{-5} sensitivity) and MRD was classified as undetectable (0 cutoff) or as MRD^{-} using a predefined 10^{-} cutoff. CRc (CR+CRi) rates by MRD status were compared between arms by stratified CMH test and ITD VAFs were compared by Wilcoxon rank-sum test.

Results

539 patients were randomized (quizartinib/placebo, 268/271); 368 (68.3%) achieved CRc and MRD was assessed in 321 (87.2%) of these patients (quizartinib/placebo, 162/159) during induction response assessments. MRD was also assessed in 337 patients (quizartinib/placebo, 172/165) at end of consolidation prior to continuation; 166 (quizartinib/placebo, 87/79) received HCT. The CRc rate at end of induction with ITD MRD <10^{-4} was similar between arms (quizartinib/placebo, 25.4%/21.8%; *P*=0.3430), but more patients had CRc with undetectable MRD with quizartinib (12.3% vs 7.0%, respectively; *P*=0.0403). For CRc patients, median best ITD VAF by end of consolidation was lower with quizartinib vs placebo (0% vs 0.0017%; *P*=0.0006). Using the undetectable ITD (0 VAF) cutoff at end of induction, OS was longer with quizartinib vs placebo regardless of MRD status (HR: 0.79 in MRD−, 0.75 in MRD+). In MRD+ patients, median OS was not reached with quizartinib and 35.4 months with placebo. Results

were similar using the 10^{-4} MRD^{-} cutoff.

Conclusions

These findings demonstrate the prognostic utility of ITD-specific MRD measurements for patients with *FLT3*-ITD+ AML, and suggest that long-term OS benefits with quizartinib derive in part from a deep and sustained reduction of *FLT3*-ITD.