ORAL ABSTRACT - SESSION A - ACUTE AND CHRONIC LEUKEMIA

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Clinical Outcomes and Characteristics of Patients (pts) with *FLT3*–Internal Tandem Duplication (*FLT3*-ITD)–Mutated Relapsed/Refractory (R/R) Acute Myeloid Leukemia (AML) Undergoing Hematopoietic Stem Cell Transplant (HSCT) after Quizartinib (Q) or Salvage Chemotherapy (SC) in the Quantum-R Trial

Siddhartha Ganguly MD, FACP[1], *Jorge E. Cortes MD*[2], *Alwin Krämer MD*[3], *Mark J. Levis MD, PhD*[4], *Giovanni Martinelli MD*[5], *Alexander E. Perl MD*[6], *Nigel H. Russell MD, PhD*[7], *Meena Arunachalam PharmD*[8], *Guy Gammon MBBS, MRCP*[8], *Arnaud Lesegretain*[8], *Derek E. Mires PharmD*[8], *Samer K. Khaled MD*[9].
[1] *The University of Kansas Health System, Kansas City, KS;* [2] *Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX;* [3] *Universität Heidelberg and German Cancer Research Center, Heidelberg, Germany;* [4] *Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD;* [5] *Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola (FC), Italy;* [6] *Abramson Cancer Center of the University of Pennsylvania, Philadelphia, PA;* [7] *Nottingham University Hospital, Nottingham, United Kingdom;* [8] *Daiichi Sankyo, Inc., Basking Ridge, NJ;* [9] *City of Hope National Medical Center, Duarte, CA*

Introduction: In QuANTUM-R, the once-daily, oral, highly potent and selective FLT3 inhibitor Q improved clinical benefit vs SC (median overall survival [mOS], 6.2 vs 4.7 mo [HR, 0.76 (95% CI, 0.58-0.98); $P = .02$]) in R/R *FLT3*-ITD AML (NCT02039726). Before randomization, 25% (Q) and 23% (SC) of pts had 1 prior HSCT.
Objective: To describe post hoc analyses in pts who underwent subsequent HSCT during QuANTUM-R.
Methods: Pts with *FLT3*-ITD R/R AML received Q (60 mg [30-mg lead-in]) or SC. Pts in the Q arm could resume Q 30-100 d after HSCT. Decisions to proceed to HSCT and resume Q after HSCT were made per investigator discretion/institutional policy.
Results: Of 367 randomized pts, 85 in the Q arm underwent any subsequent HSCT (allogeneic HSCT [allo-HSCT], 84 [6 with and 78 w/o additional AML therapy]; autologous HSCT, 1), and 19 in the SC arm underwent any HSCT (5 with and 14 w/o additional AML therapy]).
Q + SC pooled data showed a longer mOS (95% CI) in 104 pts with any HSCT vs 263 w/o (12.2 [10.0-24.1] vs 4.4 [4.1-4.9] mo; $P < .0001$; Fig 1); 1-year OS rates were 50% vs 13%. Among pts preselected for low-intensity therapy, 13/57 in the Q arm and 0/29 in the SC arm underwent any HSCT. Q + SC pooled data also showed a longer mOS (95% CI) in pts with a composite complete remission (CRc) as last recorded response before allo-HSCT vs pts w/o CRc (20.1 [11.7-NA] vs 8.8 [7.0-11.4] mo). Regardless of treatment, mOS was longer with any HSCT vs w/o (Q, 11.9 [10.2-25.1] vs 4.5 [4.1-5.4] mo; SC, 12.7 [6.1-NA] vs 4.0 [2.7-5.0] mo); respective 1-year OS rates were 50% vs 13% and 51% vs 12%.
In the Q arm, mOS (95% CI) was longer in pts with a best response of CRc who resumed Q after allo-HSCT (27.1 [18.2-NA] mo) vs pts not resuming Q (5.4 [4.7-11.4] mo; Fig 2). In 48 pts (62%) in the Q arm resuming Q after allo-HSCT, median time from allo-HSCT to Q resumption was 65 d (range, 30-106 d). Four pts (5%) in the Q arm died < 30 d after allo-HSCT. As of 2/22/2018, 46/78 pts in the Q arm (59%) and 9/14 pts in the SC arm (64%) with allo-HSCT w/o additional AML therapy died, mostly due to AML progression (Q, 31 [40%]; SC, 7 [50%]). The frequency of treatment-emergent adverse events (TEAEs) and TEAEs of interest was similar in pts resuming Q after allo-HSCT and in the overall Q population.
Conclusion: Independent of HSCT, Q improved survival vs SC in pts with *FLT3*-ITD R/R AML in QuANTUM-R. Q + SC pooled analyses showed longer survival in pts with HSCT vs pts w/o and in pts with CRc before allo-HSCT. Survival in transplanted pts was similar in both arms, indicating that HSCT-eligible pts received transplants appropriately, and the higher HSCT rate in the Q arm was beneficial. In pts preselected for low-intensity SC at study entry, 13 were able to undergo HSCT after Q treatment. Q resumption after HSCT was associated with better survival outcomes and was tolerable. These data illustrate the value of using Q to target the *FLT3*-ITD mutation as a part of the overall treatment sequence in pts with *FLT3*-ITD R/R AML.

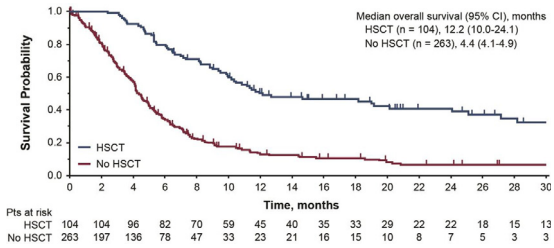

Figure 1. Kaplan-Meier Plot of OS in Pts with or without Any HSCT Regardless of Treatment Arm.

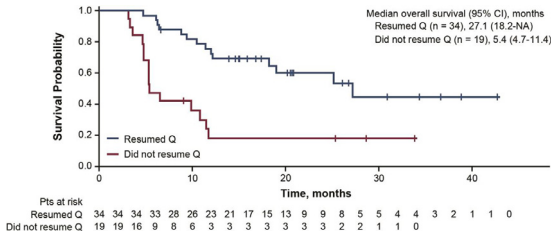

Figure 2. Kaplan-Meier Plot of OS in Pts Who Achieved a Best Overall Response of CRc with Q Who Underwent Allo-HSCT with or without Q Resumption.

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Allogeneic Stem Cell Transplantation for AML Patients with RUNX1 Mutation in First Complete Remission: A Study on Behalf of the ALWP of the EBMT

Johanna Waidhauser MD[1], *Myriam Labopin MD*[2,3,4], *Jordi Esteve MD*[5], *Nicolaus Kröger MD*[6], *Jan Cornelissen MD, PhD*[7], *Tobias Gedde-Dahl MD*[8], *Gwendolyn Van Gorkom MD*[9], *Jürgen Finke MD*[10], *Montserrat Rovira MD, PhD*[11], *Nicolaas Schaap MD*[12], *Eefke Petersen MD, PhD*[13], *Dietrich Wilhelm Beelen MD, PhD*[14], *Donald W. Bunjes MD*[15], *Christoph Schmid MD*[16], *Arnon Nagler MD, MSc*[17], *Mohamad Mohty MD*[3,18]. [1] *Department of Hematology and Clinical Oncology, University Medical Center Augsburg, Augsburg, Germany;* [2] *EBMT Paris study office, Paris, France;* [3] *INSERM UMR 938, Paris, France;* [4] *Department of Hematology, Hopital Saint-Antoine, Paris, France;* [5] *Hematology department, IDIBAPS, Hospital Clínic, Barcelona, Spain;* [6] *Department of Stem Cell Transplantation, University Medical Center Hamburg-Eppendorf, Hamburg, Germany;* [7] *Hematology, Erasmus MC Cancer Institute, University Medical Center Rotterdam, Rotterdam, Netherlands;* [8] *Department of Hematology, Section for Stem Cell*

Transplantation, Oslo University Hospital, Rikshospitalet, Clinic for Cancer Medicine, Oslo, Norway; [9] Internal Medicine Hematology/ Oncology, University Hospital Maastricht, Maastricht, Netherlands; [10] Dept of Medicine, Haematology and Oncology, University Medical Center Freiburg, Freiburg, Germany; [11] Institute of Hematology and Oncology, Dept. of Hematology, Hospital Clinic, Barcelona, Spain; [12] Department of Hematology, University Hospital of Nijmegen, Nijmegen, The Netherlands; [13] Department of Hematology, University Medical Centre Utrecht, Utrecht, Netherlands; [14] Department of Bone Marrow Transplantation, West German Cancer Center, University Hospital of Essen, Essen, Germany; [15] Department of Internal Medicine III, University of Ulm, Ulm, Germany; [16] Department of Hematology and Clinical Oncology, Section for Stem Cell Transplantation and Cellular Therapy, Universitiy Medical Center Augsburg, Augsburg, Germany; [17] Division of Hematology and Bone Marrow Transplantation, The Chaim Sheba Medical Center, Tel-Hashomer, Tel-Aviv university, Ramat-Gan, Israel; [18] EBMT Paris study office and Department of Haematology, Saint Antoine Hospital, Paris, France

Introduction: Acute myeloid leukemia bearing a *RUNX1* gene mutation (*RUNX1+* AML) has been proposed as a provisional entity in the 2016 WHO classification. Clinically, it has been associated with inferior response rates and outcome after conventional chemotherapy. Accordingly, *RUNX1+* AML is allocated in the unfavorable prognostic category of the 2017 European Leukemia Net classification. Following allogeneic stem cell transplantation (alloSCT), *RUNX1* was an unfavorable factor in one study in MDS/secondary AML, while data in *de novo* AML are scarce.
Objectives: Here, we present a retrospective study by the EBMT Acute Leukemia Working Party, aiming to elucidate the prognostic value of *RUNX1* mutation in patients undergoing alloSCT for AML in first complete remission (CR1).
Methods: Adults undergoing alloSCT for AML in CR1 from matched related or unrelated donors between 2013 and 2018 with complete information on conventional cytogenetics and *RUNX1* mutational status were selected from the EBMT registry. Variables of interest were overall and leukemia-free survival (OS/LFS), GvHD/relapse free survival (GRFS), cumulative relapse incidence (RI), non-relapse mortality (NRM) and GvHD. Log rank test, Gray test and Cox regression models were used.
Results: 128 *RUNX+* and 388 *RUNX-* patients were identified, >80% of both subgroups presenting as *de novo* AML. As expected, *RUNX1+* patients rarely had co-mutations in *NPM1* (6% vs. 26%, p=10^{-3}), and showed a positive correlation with *ASXL1* mutations (50% vs. 16%, p=10^{-4}). Cytogenetic categories and other mutations (*FLT3*-ITD, *CEBPA)* were equally distributed between the two groups, as were age, donor and graft type, CMV, conditioning and T cell depletion (TCD).
Median follow-up was 16.4 (*RUNX+)* and 19.8 (*RUNX-)* months. 2y OS/LFS of the entire cohort were 64% [59-69]/57% [52-62], with no difference between *RUNX1+* and *RUNX1-* patients either in univariate or multivariate analysis (2y OS: 67.9% [57.3-78.5] vs. 63.1%v[57.4-68.7]p=0.15; 2y LFS: 57.6% [46.4-68.7] vs. 57% [51.4-62.6], p=0.38], figure 1). *RUNX1* mutation neither had any impact among patients with normal karyotype (figure 2). Similarly, no other outcome parameter was influenced by *RUNX1* mutational status. Instead, multivariate analysis revealed age and donor type as risk factors for OS, LFS and NRM. Poor cytogenetic was associated with higher RI and inferior LFS/GRFS, in vivo TCD with a lower rate of aGvHD II-IV, cGvHD, and better GRFS. Among patients with available information, *FLT3*-ITD was an independent risk factor for relapse, LFS and GRFS. *RUNX1* did not modify the role of *FLT3*-ITD.
Conclusion: Within the limits of a retrospective registry analysis, we could not find a negative influence of *RUNX1* mutation on outcome after allogeneic SCT in CR1. Hence, transplantation in CR1 might overcome the unfavorable prognostic value of *RUNX1* mutation and can be recommended as consolidation treatment in this entity.

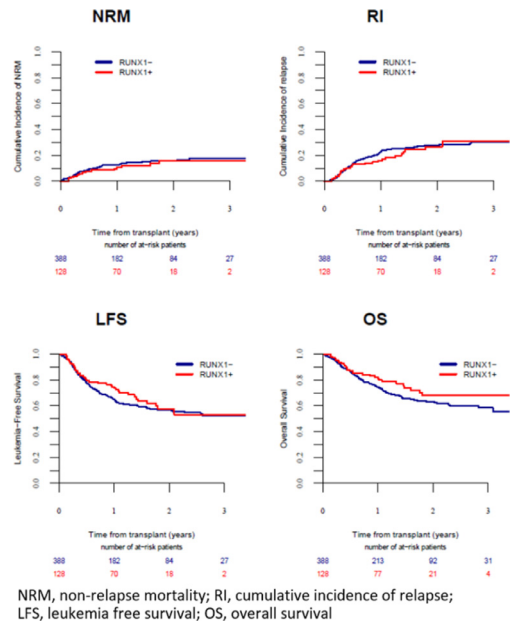

Figure 1. Outcome of patients with AML transplanted in first complete remission as of presence or absence of a RUNX1 mutation; Entke cohort (n=5151).

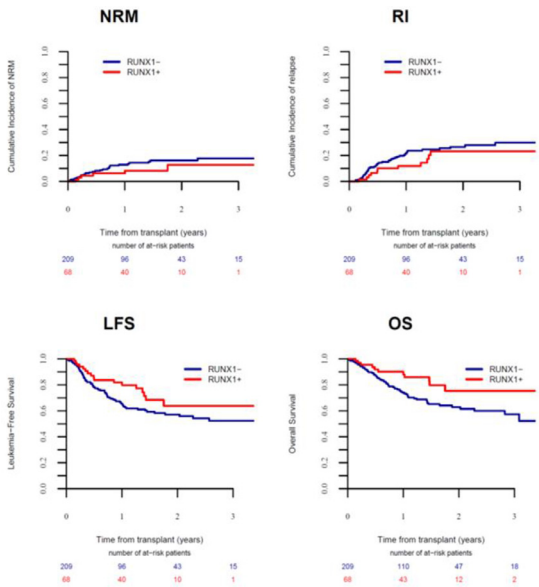

Figure 2. Outcome of patients with AML transplanted in first complete remission as of presence or absence of a RUNXI mutation; Patients with normal karyotype (n=277).

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Outcomes in Patients with Acute Myeloid Leukemia with Myelodysplasia-Related Changes (AML-MRC) Who Achieved Remission with CPX-351 Versus 7+3: Phase 3 Exploratory Analysis

***Daniel H. Ryan*[1]**, *Laura F. Newell MD*[2], *Ellen K. Ritchie*[3], *Stephen A. Strickland MD*[4], *Donna E. Hogge*[5], *Scott R. Solomon MD*[6], *Gary J. Schiller MD*[7],