EUROPEAN HEMATOLOGY ASSOCIATION

EHA2021 VIRTUAL

S138

EFFECT OF OLUTASIDENIB (FT-2102) ON COMPLETE REMISSIONS IN PATIENTS WITH RELAPSED/REFRACTORY MUTANT IDH1 ACUTE MYELOID LEUKEMIA. RESULTS FROM A PLANNED INTERIM ANALYSIS OF A PHASE 2 CLINICAL TRIAL

Topic: 04. Acute myeloid leukemia - Clinical

Keywords: Clinical trial | Complete remission | Refractory | Relapsed acute myeloid leukemia

Stéphane de Botton[1], Karen Yee[2], Recher Christian[3], Andrew Wei[4], Pau Montesinos[5], David Taussig[6], Arnaud Pigneux[7], Thorsten Braun[8], Antonio Curti[9], Jordi Esteve[10], Carolyn Grove[11], Brian A. Jonas[12], Asim Khwaja[13], Ollivier Legrand[14], Pierre Peterlin[15], Montserrat Arnan Sangerman[16], William G. Blum[17], Daniela Cilloni[18], Devendra K. Hiwase[19], Joseph G. Jurcic[20], Jürgen Krauter[21], Xavier Thomas[22], Justin M. Watts[23], Jay Yang[24], Olga Polyanskaya[25], Julie Brevard[25], Jennifer Sweeney[25], Patrick Henrick[25], Hesham Mohamed[25], Jorge Cortes[26], Pierre Fenaux[27]

[1] Institute Gustave Roussy, Villejuif, France
[2] Princess Margaret Cancer Center, Toronto, Canada
[3] IUCT-Oncopole, CHU de Toulouse, Toulouse, France
[4] The Alfred Hospital, Melbourne, Australia
[5] Hospital Universitari i Politècnic La Fe, Valencia, Spain
[6] Royal Marsden Hospital, London, United Kingdom
[7] Centre Hospitalier Universitaire (CHU) de Bordeaux, Université de Bordeaux, Bordeaux, France
[8] Avicenne Hospital Paris XIII University, Bobigny, France
[9] Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy
[10] Hospital Clínic de Barcelona, Barcelona, Spain
[11] PathWest & Sir Charles Gairdner Hospital, Nedlands, Australia
[12] University of California Davis School of Medicine, Sacramento, United States
[13] University College London, London, United Kingdom
[14] Hôpital Saint-Antoine, Université Pierre et Marie Curie, Paris, France
[15] CHU de Nantes, Service d'hématologie Clinique, Nantes, France
[16] Institut Catala d'Oncologia, Hospital Duran i Reynals, IDIBELL, L'Hospitalet de Llobregat Barcelona, Barcelona, Spain
[17] Winship Cancer Institute of Emory University, Atlanta, United States
[18] University of Turin, Turin, Italy
[19] Royal Adelaide Hospital and SA Pathology, Adelaide, Australia
[20] Columbia University Medical Center, New York, United States
[21] Braunschweig Municipal Hospital, Braunschweig, Germany
[22] Hospices Civils de Lyon, Lyon-Sud Hospital, Lyon, France
[23] University of Miami Sylvester Comprehensive Cancer Center, Miami, United States
[24] Karmanos Cancer Institute, Detroit, United States
[25] Forma Therapeutics, Inc., Watertown, United States
[26] Georgia Cancer Center, Augusta University, Augusta, United States
[27] Service d'Hématologie Séniors, Hôpital Saint-Antoine, Université Paris 7, Paris, France

Background: Olutasidenib, a potent, selective, oral, small molecule inhibitor of mutant IDH1 (m*IDH1*), has exhibited favorable tolerability and clinical activity in high-risk acute myeloid leukemia (AML) patients (pts) in a phase 1 trial (Watts, *Blood* 2019).

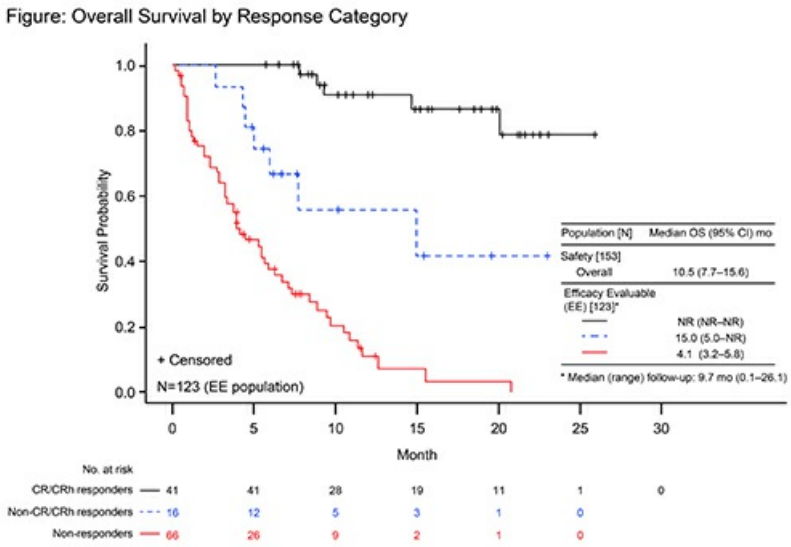
Aims: Here, we present interim analysis results of a phase 2 trial (NCT02719574) in relapsed/refractory (R/R) m*IDH1* AML pts receiving olutasidenib monotherapy 150 mg twice daily.

Methods: The efficacy evaluable (EE) set comprised m*IDH1*^{R132X} pts whose first dose was ≥180 days before the data cut-off (18-JUN-20). The primary endpoint was CR + CRh (complete remission [CR] or CR with partial hematologic recovery [CRh] according to modified IWG 2003 criteria) rate. CRh was defined as bone marrow blasts <5%, absolute neutrophil count >0.5×10^9/L, *and* platelet count >50×10^9/L. Overall response rate (ORR) comprised CR + CRh + CR with incomplete recovery (CRi) + morphologic leukemia-free state (MLFS) + partial response (PR). Duration of treatment (DOT), duration of response (DOR), and overall survival (OS) were estimated using Kaplan-Meier methodology.

Results: This clinical trial met its pre-specified early enrollment-stopping criteria for efficacy. A total of 153 pts with R/R AML received olutasidenib; median DOT, 5.5 months (95% CI: 4.4–8.7). 43 pts (28%) remain on treatment and 110 pts (72%) discontinued, most commonly due to: disease progression (31%), AEs (14%), death (10%), and transplant (8%). For the EE set (123 pts), the median age was 71 y (range: 32–87) with a median number of prior therapies of 2 (1–7). The ORR was 46% with a median duration of ORR of 11.7 months. Notably, the CR + CRh rate was 33% including 30% of pts in CR. The median duration of CR + CRh was not reached (NR) but found to be 13.8 months based on a sensitivity analysis when HSCT or relapse was deemed end of response. Of responders who were transfusion-dependent at baseline, 56-day platelet transfusion independence (TI) and RBC TI were gained by 100% and 83%, respectively, of pts who achieved CR + CRh, and by 56% and 50% who did not. The median OS was 10.5 months. For patients with CR + CRh, the median OS was NR and the estimated 18-month OS was 87%; the median OS for non-CR/CRh responders was 15.0 months (Figure). TEAEs in ≥25% of pts were: nausea (38%), constipation (25%), and leukocytosis (25%). Grade 3/4 all-causality AEs in >10% of pts were: febrile neutropenia (20%), anemia (19%), thrombocytopenia (16%), and neutropenia (13%). TEAEs of QTc prolongation (all grades) were reported in 13 pts (8.5%) with one grade 3 event in 1 pt (<1%). No events led to dose reduction or discontinuation. Hepatobiliary TEAEs associated with liver enzyme abnormalities (all grades) were reported in 32 pts (21%) with grade 3/4 events in 16 pts (10%)/3 pts (2%). Most pts (n=25) had no dose modification or continued after a rechallenge; 7 pts with grade 3/4 events discontinued treatment (4 pts after positive rechallenge). There were no Hy's law cases. Investigator-assessed IDH1 differentiation syndrome (any grade) was observed in 21 pts (14%); most cases resolved with treatment interruption, dexamethasone, and/or supportive treatment; one case was fatal; 19 pts had concomitant leukocytosis.

Image:

Figure: Overall Survival by Response Category



Summary/Conclusion: Olutasidenib induced durable CRs in a subset of high-risk R/R m*IDH1* AML pts. TI was achieved in all response groups, particularly in those achieving CR. Clinical benefit, as evidenced by DOR and OS, extended to pts who responded but didn't achieve CR/CRh. A favorable tolerability profile was observed; additional analyses of safety and efficacy will be presented.

Abstract Book Citations: Authors, Title, HemaSphere, 2021;5:(S2):pages. Abstract Book, DOI:
http://dx.doi.org/10.1097/HS9.0000000000000566

EHA2021 Virtual

JUNE 9-17 2021

POWERED BY M-ANAGE.COM