EUROPEAN HEMATOLOGY ASSOCIATION

EHA2021 VIRTUAL

S137

MEASURABLE RESIDUAL DISEASE RESPONSE IN ACUTE MYELOID LEUKEMIA TREATED WITH VENETOCLAX AND AZACITIDINE

Topic: 04. Acute myeloid leukemia - Clinical

Keywords: Acute myeloid leukemia | Clinical trial | MRD

Keith W. Pratz[1], Brian A. Jonas[2], Vinod Pullarkat[3], Christian Recher[4], Andre C. Schuh[5], Michael J. Thirman[6], Jacqueline S. Garcia[7], Courtney DiNardo[8], Vladimir Vorobyev[9], Nicola Fracchiolla[10], Su-Peng Yeh[11], Jun Ho Jang[12], Muhit Ozcan[13], Kazuhito Yamamoto[14], Arpad Illes[15], Ying Zhou[16], Monique Dail[17], Brenda Chyla[16], Jalaja Potluri[16], Hartmut Döhner[18]

[1] Abramson Cancer Center, University of Pennsylvania, Philadelphia, United States
[2] Department of Internal Medicine, Division of Hematology and Oncology, University of California Davis School of Medicine, Sacramento, United States
[3] Department of Hematology and Hematopoietic Cell Transplantation and Gehr Family Center for Leukemia Research, City of Hope Comprehensive Cancer Center, Duarte, United States
[4] Centre Hospitalier Universitaire de Toulouse, Toulouse, France
[5] Department of Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, Canada
[6] Section of Hematology/Oncology, Department of Medicine, The University of Chicago Medicine, Chicago, United States
[7] Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, United States
[8] Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, United States
[9] Department of Hematology, S. P. Botkin City Clinical Hospital, Moscow, Russian Federation
[10] UOC Ematologia, Fondazione IRCCS Ca' Granda-Ospedale Maggiore Policlinico, Milan, Italy
[11] Department of Internal Medicine, China Medical University Hospital, Taichung, Taiwan, Province of China
[12] Department of Hematology-Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic Of
[13] Department of Hematology, Ankara University School of Medicine, Ankara, Turkey
[14] Department of Hematology and Cell Therapy, Aichi Cancer Center Hospital, Nagoya, Japan
[15] University of Debrecen, Faculty of Medicine, Department of Hematology, Debrecen, Hungary
[16] AbbVie Inc., North Chicago, United States
[17] Genentech Inc., South San Francisco, United States
[18] Department of Internal Medicine III, University Hospital, Ulm, Germany

Background: In the phase 3 VIALE-A trial, rates of composite complete remission (CRc; complete remission [CR] + CR with incomplete hematologic recovery [CRi]) and measurable residual disease response (MRD<10^{-3}) were higher in patients (pts) treated with venetoclax (Ven) + azacitidine (Aza) compared to Aza alone (23.4%/7.6%, p<0.001). There is limited evidence of the clinical significance of MRD monitoring in pts receiving low-intensity chemotherapy.

Aims: We explored the outcomes of pts treated with Ven+Aza who achieved both CRc and MRD<10^{-3} in the VIALE-A trial (NCT02993523).

Methods: Enrolled pts were ≥18 years and unfit for intensive chemotherapy. Pts received Ven 400 mg orally; days 1–28 and Aza 75 mg/m^2; days 1-7/28-day cycle. Bone marrow aspirate samples for multiparametric flow cytometry assessments by integrated leukemia-associated immunophenotypes and different than normal procedures were collected for central analysis (Covance Central Laboratory Services) at baseline, end of cycle 1, and every 3 cycles thereafter. Assessments were performed independent of disease responses. MRD response was defined as <1 residual blast /1000 leukocytes (<10^{-3}). CRc, DoR, OS, and EFS were assessed. Disease assessments were per modified International Working Group response criteria for AML.

Results: 211/286 (74%) pts treated with Ven+Aza with at least one valid post-baseline MRD assessment were considered MRD evaluable; 78/211 (37%) achieved MRD<10^{-3} and 133/211 (63%) had MRD≥10^{-3}. Median age (MRD<10^{-3}/ MRD≥10^{-3}) was 76 (range: 49-89)/77 (58-91) years.

Pts (MRD<10^{-3}/ MRD≥10^{-3}) received median of 14.5 (range: 1-28) /7.0 (1-30) cycles of Ven+Aza. At a median follow-up of 22.0 (range: 20.1-23.0)/20.8 (19.8-22.3) months (mos), CRc + MRD<10^{-3}/ MRD≥10^{-3} was achieved by 67 (86%)/ 97 (73%); 20/67 (30%) achieved CRc + MRD<10^{-3} by end of cycle 1.

Median DoR, OS, and EFS were not reached in pts with CRc + MRD<10^{-3} response (Table). The 12-mo estimates for DoR, OS, and EFS for pts with CRc + MRD<10^{-3}response were 81.2%, 94.0%, and 83.2%, respectively. Adverse events ≥grade 3 (MRD<10^{-3}/ MRD≥10^{-3}) were febrile neutropenia (50%/43%), neutropenia (50%/35%), and thrombocytopenia (44%/44%), similar to the overall population.

Image:

Table: DoR, OS, and EFS in patients with composite complete response treated with venetoclax and azacitidine

	12-mos estimate % (95% CI)		Median months (95% CI)	
	MRD<10^{-3} n=67	MRD≥10^{-3} n=97	MRD<10^{-3} n=67	MRD≥10^{-3} n=97
Duration of response	81.2(69.3, 88.9)	46.6(35.6, 56.8)	NR(19.3, NR)	9.7(8.0. 15.8)
Overall survival	94.0(84.7, 97.7)	67.9(57.6, 76.2)	NR(24.4, NR)	18.7(12.9, NR)
Event-free survival	83.2(71.6, 90.3)	45.4(35.2, 55.0)	NR(19.7, NR)	10.6(9.0, 13.9)

CI: Confidence interval; MRD: measurable residual disease; NR: not reached

Summary/Conclusion: Pts with best response of CRc who achieved MRD<10^{-3}response with Ven+Aza treatment had longer DoR, OS, and EFS than pts who were CRc and MRD positive.

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