

(PF499) POOR RESPONSE OF VENETOCLAX AND AZACITIDINE IN MONOCYTIC ACUTE MYELOID LEUKEMIA IS ASSOCIATED WITH GENETIC PATTERNS AND IS IMPROVED BY ADDITION OF HOMOHARRINGTONINE, A MULTI-CENTER COHORT STUDY

Topic: 04. Acute myeloid leukemia - Clinical

Guopan Yu^{*1, 1}, Rong Hu¹, Yishan Chen¹, Zhao Yin¹, Dandan Chen¹, Dan Xu¹, Qifa Liu¹, Hua Jin¹, Jiacheng Xu¹, Zhao Weihua², Nie Danian³, Guangyang Weng⁴, Ziwen Guo⁵, Dongjun Lin⁶, Li Xuan¹

¹Nanfang Hospital, Southern Medical University, Guangzhou, China; ²First Affiliated Hospital of Guangxi Medical University, Nanning, China; ³Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, China; ⁴Shenzhen Second People's Hospital, Shenzhen, China; ⁵Zhongshan City People's Hospital, Zhongshan, China; ⁶The Seventh Affiliated Hospital of Sun Yat-Sen University, Shenzhen, China;

Background

Monocytic acute myeloid leukemia (AML) responds poorly to venetoclax and azacitidine (VA) treatment, yet the mechanism remains not totally clear. Our previous studies revealed homoharringtonine (HHT) enhances the anti-leukemia effect of VA. Whether HHT could increase the response of VA in monocytic AML is unknown.

Aims

In this study we explored the factors impacting on the response of VA in monocytic AML and whether addition of HHT could enhance the response.

Methods

321 patients with relapsed/refractory (RR) AML from our previous study (NCT05456048), being treated with VA or VA combined with HHT (VAH), were analyzed. Patients with AML-M4/M5 were classified into monocytic group, while those with non-M4/M5 were defined as nonmonocytic group.

Results

There were 139 patients with monocytic AML and 182 in non-monocytic group, of whom 149 were treated with VA and 172 with VAH. In the cohort with VA treatment, the patients with monocytic AML had a significantly lower response than those with nonmonocytic AML, presenting as overall response rate (ORR) of 27/57(47.4%) vs. 60/92(65.2%) ($P=0.032$). Meanwhile, in the cohort with VAH treatment, monocytic AML patients had comparable response to those with nonmonocytic AML. In addition, in the patients with monocytic AML, VAH significantly improved the response compared to VA (ORR, 27/57(47.4%), $P=0.001$; CRc rate, 21/57(36.8%), $P=0.002$). Also, the patients with monocytic AML had better survival with VAH than those with VA treatment (median overall survival (mOS), no reach vs. 12.4 months, $P=0.087$; median event-free survival (mEFS), 14.0 vs. 2.0 months, $P<0.001$). The poor response of VA in monocytic AML was associated with the disparate impact of mutant FLT3, DNMT3A and MLL rearrangement in the monocytic versus nonmonocytic AML, which might be partly due to the different co-mutations. The poor influence of FLT3, RAS, DNMT3A and NPM1 mutations in monocytic AML was significantly overcome by VAH.

Summary/Conclusion

Poor response of VA in monocytic AML is associated with genotype-phenotype. Addition of HHT to VA significantly improves the response and mitigates the negative impact of the adverse genotype.

Copyright Information: (Online) ISSN: 2572-9241

©2026 The Author(s). HemaSphere is published by John Wiley & Sons Ltd on behalf of European Hematology Association. This is an open access Abstract Book distributed under the Attribution-NonCommercial-NoDerivs (CC BY-NC-ND), which allows third parties to download the articles and share them with others as long as they credit the author and the Abstract Book, but they cannot change the content in any way or use them commercially. **Abstract Book Citations:** Authors, Title, HemaSphere, 2026;10;(S1):pages. The abstract book DOIs can be found on the "Author Information" page.

Disclaimer: Articles published in the journal HemaSphere exclusively reflect the opinions of the authors. The authors are responsible for all content in their abstracts including accuracy of the facts, statements, citing resources, etc.