

(PF463) CD71-TARGETED AND ROS-RESPONSIVE MICELLES FOR HOMOHARRINGTONINE DELIVERY TO ENHANCE THERAPEUTIC EFFICIENCY AGAINST FLT3-ITD ACUTE MYELOID LEUKEMIA

Topic: 03. Acute myeloid leukemia - Biology & translational research

Yuqian Tang*¹, Yuping Gong¹

¹West China Hospital, Sichuan University, Department of Hematology, Chengdu, China;

Background

The FLT3-ITD (FMS-like tyrosine kinase 3- internal tandem duplication) subtype of acute myeloid leukemia (AML) is associated with poor clinical outcomes. Homoharringtonine (HHT), a natural protein inhibitor, has shown strong activity against FLT3-ITD AML. However, its clinical use is limited by rapid clearance and systemic toxicity.

Aims

To address these limitations, a CD71-targeted, ROS-responsive micelle (TDTP/HHT) was developed for precise and efficient HHT delivery.

Methods

CD71 expression was assessed in AML patient samples and cell lines. TDTP/HHT was prepared by self-assembly using a D-peptide ligand (^DT7) for CD71 targeting and a ROS-cleavable linker for stimuli-responsive drug release. Cellular uptake, cytotoxicity and signaling pathway inhibition were evaluated *in vitro* across AML cell lines with distinct FLT3 statuses. The therapeutic efficacy of TDTP/HHT was further validated in a disseminated AML xenograft mouse model.

Results

Cytotoxicity analysis revealed that FLT3-ITD AML is intrinsically sensitive to HHT. Analysis of patient samples and cell lines revealed high CD71 expression and elevated ROS levels in AML, most predominantly in the FLT3-ITD subtype. The designed TDTP/HHT showed prolonged circulation time, ROS-responsive drug release, and stable targeting capacity. It did not compete with endogenous transferrin for binding sites but instead demonstrated transferrin-promoted cellular uptake. Both *in vitro* and *in vivo* studies confirmed that TDTP/HHT significantly inhibited the growth of FLT3-ITD AML cells. Mechanistically, TDTP/HHT suppressed multiple key downstream signaling proteins of FLT3-ITD.

Summary/Conclusion

This study presents a novel targeted nanodrug that exploits the intrinsic HHT sensitivity of FLT3-ITD AML cells and their characteristic high CD71 expression and elevated ROS levels. By enabling specific intracellular accumulation of HHT and multitarget inhibition of FLT3-ITD signaling pathways, this system achieves superior anti-AML efficacy both *in vitro* and *in vivo*, offering strong potential for future clinical translation.

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.