



The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL**Orelabrutinib Monotherapy in Patients with Relapsed or Refractory Waldenström's Macroglobulinemia in a Single-Arm, Multicenter, Open-Label, Phase 2 Study: Long Term Follow-up Results**

Xinxin Cao¹, Jie Jin², Fu Cheng Cheng, MD PhD³, Shuhua Yi⁴, Weili Zhao⁵, Zimin Sun, MDPH⁶, Wei Yang⁷, Dengju Li⁸, Guohui CUI⁹, Jianda Hu¹⁰, Ting Liu, MD¹¹, Yongping Song¹², Bing Xu, MD PhD¹³, Zunmin Zhu, MDPH¹⁴, Wei Xu¹⁵, Mingzhi Zhang¹⁶, Sichen Li¹⁷, Weige Wang, MDPH¹⁸, Renbin Zhao, PhD¹⁷, Daobin Zhou, MD¹⁹

¹ Department of Hematology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

² The First Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China

³ The First Affiliated Hospital of Soochow University, Suzhou, China

⁴ State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China

⁵ State Key Laboratory of Medical Genomics, Shanghai Institute of Hematology, National Research Center for Translational Medicine, Shanghai Rui Jin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

⁶ Anhui Provincial Hospital, Hefei, China

⁷ Department of Hematology, Shengjing Hospital of China Medical University, Shenyang, China

⁸ Department of Hematology, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

⁹ Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, WUHAN, CHN

¹⁰ Department of Hematology, The Second Affiliated Hospital of Fujian Medical University, Fuzhou, China

¹¹ Department of Hematology and Institute of Hematology, West China Hospital, Sichuan University, Chengdu, China

¹² Department of Hematology, Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou, China, Zhengzhou, China

¹³ The First Affiliated Hospital of Xiamen University, Xiamen, China

¹⁴ Henan Provincial People's Hospital, Zhengzhou, China

¹⁵ Department of Hematology, The First Affiliated Hospital of Nanjing Medical University, Jiangsu Province Hospital, Nanjing, China

¹⁶ The First Affiliated Hospital of Zhengzhou University and Lymphoma Diagnosis and Treatment Center of Henan Province, Zhengzhou, China

¹⁷ InnoCare Pharma Limited, Beijing, China

¹⁸ InnoCare Pharma Limited, Shanghai, China

¹⁹ Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China

Background

Orelabrutinib is a novel, small molecule, selective irreversible Bruton tyrosine kinase inhibitor, approved in China for the treatment of patients with relapsed/refractory (R/R) chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), mantle cell lymphoma (MCL), and marginal zone lymphoma (MZL). The previous publication of this study reported that orelabrutinib is highly active in R/R Waldenström's macroglobulinemia (WM), with a well-tolerated safety profile (EclinicalMedicine. 2022;52:101682). We present here the long-term results of this study.

Methods

This is a prospective, multicenter study of orelabrutinib in patients with WM who had at least one prior line of treatment (ClinicalTrials NO. : NCT04440059). Orelabrutinib was administered orally at a daily dose of 150 mg until disease progression or unacceptable toxicity. Genotyping using MYD88^{L265P} and CRCR4^{S338X} mutation were performed with qPCR assay. The

primary endpoint was major response rate (MRR) assessed by the Independent Review Committee (IRC) according to IWWM-6 (Br J Haematol. 2013; 160: 171-176).

Results

Between August 2019 and December 2020, 66 R/R WM patients were assessed for eligibility. Forty-seven eligible patients were evaluated for efficacy at a median follow-up of 31.9 months (interquartile range: 28.0,36.5). As assessed by IRC, the MRR was 80.9%, and the overall response rate was 91.5%. The PFS rates was estimated as 72.1% at 36 months and the median PFS has not been reached. There is no significant difference in PFS across various MYD88^{L265P} and CXCR4^{S338X} genotype (P=0.69; Figure 1). The 30-months PFS rate in MYD88^{L265P}/CXCR4^{NEG}, MYD88^{L265P}/CXCR4^{S338X}, and MYD88^{NEG}/CXCR4^{NEG} were 86.2%, 75% and 75%, respectively. Most adverse events were Grades 1 or 2 (63.8%). The common grade 3 or higher adverse events occurred were neutropenia (10.6%), thrombocytopenia (8.5%), and pneumonia (6.4%). Treatment related serious adverse events were reported in 8.5% patients. Adverse events leading to discontinuation occurred in 4 patients (8.5%). One treatment-related death was reported (hepatitis B reactivation).

Conclusions

Results with longer follow-up continue to show that orelabrutinib has high, deep and durable response in patients with R/R WM. Data support the safety of long-term orelabrutinib treatment in R/R WM, with no new safety signals identified.

Disclosures No relevant conflicts of interest to declare.

OffLabel Disclosure: Orelabrutinib is a newly developed BTK inhibitor with high selectivity. It is highly potent against BTK with notable less off-target inhibition of other tyrosine kinases. High kinase selectivity, persistent BTK target occupancy, potent anti-tumor activity, and the safety profile support orelabrutinib as an alternative treatment option for WM

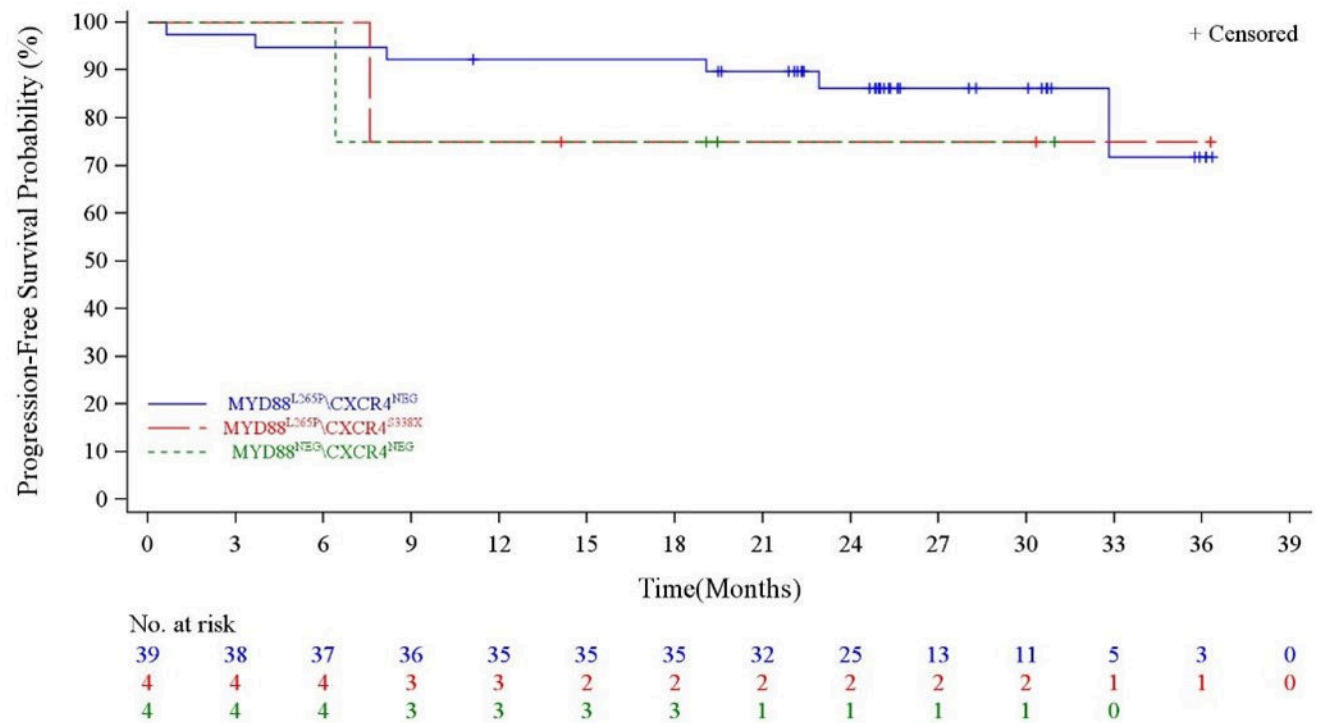


Figure 1

<https://doi.org/10.1182/blood-2023-181500>

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