ELSEVIER

Blood 142 (2023) 3039–3040

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 Cao[1], Jie Jin[2], Fu Cheng Cheng, MD PhD[3], Shuhua Yi[4], Weili Zhao[5], Zimin Sun, MDPhD[6], Wei Yang[7], Dengju Li[8], Guohui CUI[9], Jianda Hu[10], Ting Liu, MD[11], Yongping Song[12], Bing Xu, MD PhD[13], Zunmin Zhu, MDPhD[14], Wei Xu[15], Mingzhi Zhang[16], Sichen Li[17], Weige Wang, MDPhD[18], Renbin Zhao, PhD[17], Daobin Zhou, MD[19]

[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 CRCR4 ^{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

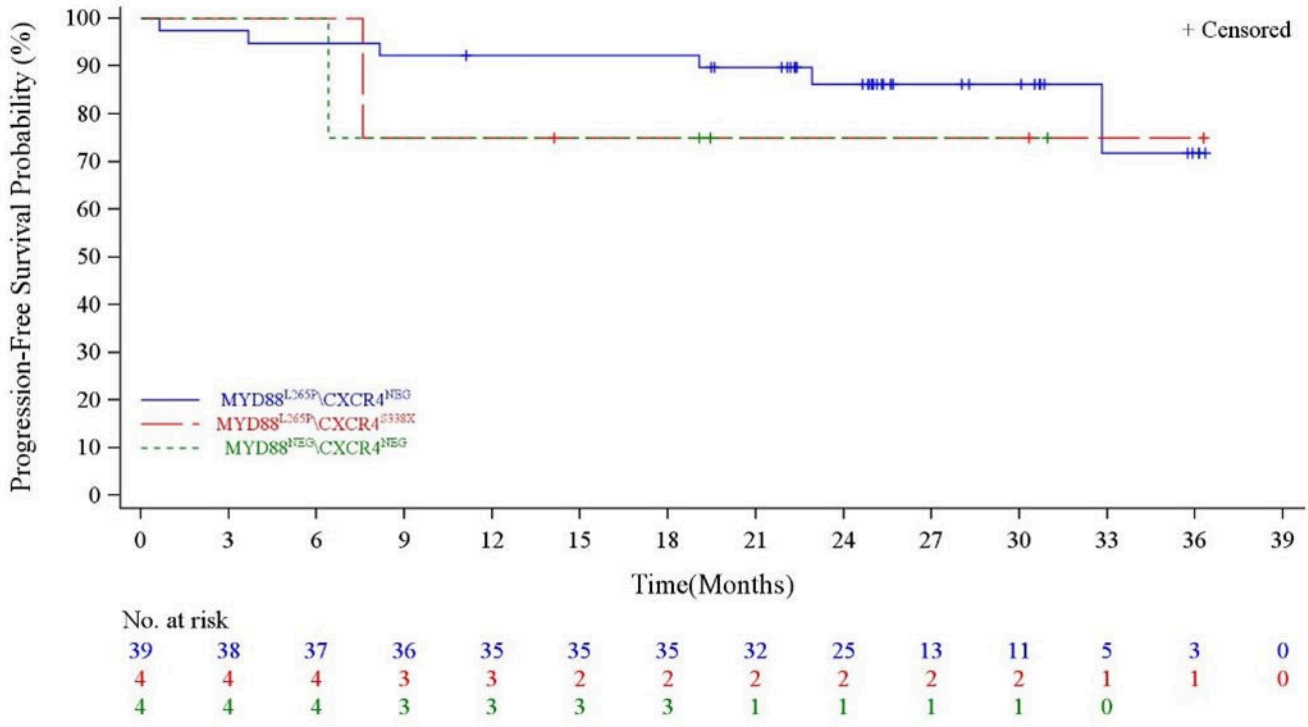

Figure 1

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