An Open-labeled Phase II Trial of VDJ-001, a High-Affinity IL-6R Antagonist Antibody, for the Treatment of Patients with Idiopathic Multicentric Castleman Disease

Lu Zhang[1], Yujun Dong[2], Rui Chen[3], Qin Wang[4], Xiaorui Zhang[5], Jun Zhang[5], Jian Li[1]

1. Department of Hematology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College; 2. Department of Hematology, Peking University First Hospital; 3. Clinical Pharmacology Research Center, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College; 4. Department of Radiology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College; 5. Beijing VDJBio Co., Ltd.

Introduction

- **Interleukin-6 (IL-6)** targeted therapy has been recommended as the most important treatment option for idiopathic Multicentric Castleman Disease (iMCD). However, the effective rate of siltuximab, the single FDA approved IL-6 blocking antibody, was not highly satisfactory (34% in clinical trial) for iMCD.
- **VDJ-001** is a novel IL-6R monoclonal antibody (mAb) with high-affinity and potent activities for antagonizing the IL-6 mediated signaling pathway. The present study is to assess the safety and efficacy of VDJ-001 in iMCD following its pre-clinical and early clinical evaluation.

Methods

- A total of 9 iMCD patients with active disease were enrolled in this single-arm, open-label, multi-center, dose-escalation study from April 2022 to September 2022.
- All patients received VDJ-001 infusion in three dose groups (4mg/kg, n=3; 6mg/kg, n=3; 8mg/kg, n=3) every 2 weeks (each infusion was considered as a cycle) for 22 cycles. Based on its early therapeutic index, 4mg/kg dose were subsequently given to all patients since C23D1.
- **The safety profile** was recorded by Common Toxicity Criteria for Adverse Events version 5.0.
- **The treatment responses** were evaluated according to the Castleman Disease Collaborative Network (CDCN) criteria. As a 2-year analysis, this report collected data up to May 31, 2024.

Results

The median age at the time of enrollment was 42 (29-52) years old. The male to female ratio was 2:1. By May 31, 2024, a median of 46 cycles (38-52 cycles) of treatment were given to patients.

Safety

- All three doses of VDJ-001 were safe and well-tolerated, even during the Covid-19 pandemic.
- Most of them revealed low grade 1-2 of adverse reaction
- 3 patients experienced Grade 3 level of adverse events without obvious dose-dependency:
  - 1 patient (6mg/kg group) experienced Grade 3 of neutropenia/lymphopenia
  - 1 patient (6mg/kg group) had Grade 3 of hypertriglyceridemia who were changed the dose to 4mg/kg of VDJ001 since C6D1
  - 1 patient (8mg/kg group) had Grade 3 of eosinophilia.
- None of these AEs lead to discontinuation of the study drug.

Efficacy

- There was a time-dependent overall response to VDJ-001 administration including a 22 cycles of 3-seperate doses and a dose-consolidation to 4mg/kg from C23D1.
  - By Week 8, the overall response rate (ORR) was 55.56%; by week 20, the ORR was 77.78%;
  - By week 32, the ORR was 88.89%
  - By week 80, the ORR was 100%.
- A significant improvement was observed in key biochemical parameters such as hemoglobin, albumin and C-reactive protein which was consistent with the high biochemical response rates achieved with this investigative drug (Figure 1).

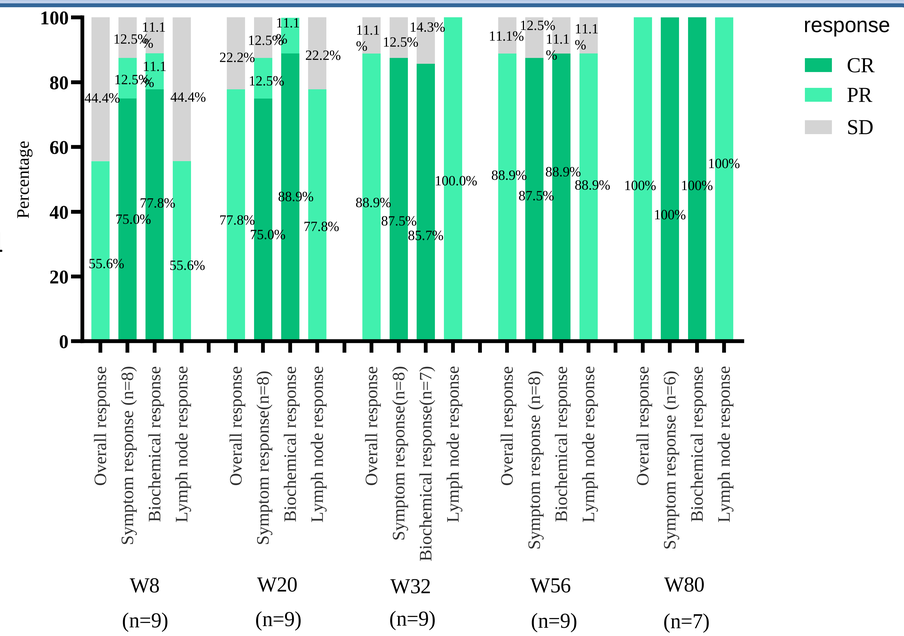

Figure 1. Evaluation of treatment responses according to CDCN criteria.

Conclusion

VDJ-001, a novel high-affinity anti-IL-6R mAb, exhibited excellent safety and efficacy profiles in iMCD patients.