Efficacy and safety of orelabrutinib in relapsed/refractory idiopathic multicentric Castleman disease: a single-centre, retrospective study

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Introduction

Despite advances in therapy, idiopathic multicentric Castleman disease (iMCD) remains incurable, with fluctuating disease activity, leading to an urgent need for additional therapeutic options, particularly for refractory or relapsed (r/r) patients. Currently, no standardized treatment regimen for r/r iMCD exists, and approaches often rely on intensive chemotherapy strategies, such as pulse administration with or without rituximab, which might bring safety concerns and are inadequate for sustained long-term drug administration, leading to challenges in maintaining long-term disease control. Bruton's tyrosine kinase (BTK) stands as a critical component of multiple signalings that regulate B cell proliferation, survival, and functionality. Blocking BTK emerges as a promising therapeutic approach for iMCD without depleting B cells. Oral orelabrutinib is a novel, next-generation BTK inhibitor (BTKi) with a well-demonstrated efficacy and safety profiles in patients with various indolent B-cell malignancies, autoimmune diseases. This retrospective study aimed to investigate the efficacy and safety of orelabrutinib in patients with r/r iMCD.

Methods

This single-center study enrolled patients with r/r iMCD who received orelabrutinib treatment for more than 3 months between 2021-2022. The diagnostic criteria for iMCD were based on the Castleman Disease Collaborative Network (CDCN) consensus. For all enrolled patients, oral orelabrutinib was initiated at a daily dose of 150 mg. Dose adjustments were made based on the patient's tolerance or concurrent use of any inhibitor of cytochrome P450 3A4. All patients received a minimum daily dose of 50 mg. The primary endpoint of the study was the overall response (symptomatic response and biochemical response) during the study. Responder was defined as achieving at least partial remission according to the CDCN criteria. Secondary endpoints included trends in biochemical parameters at month 12.

Results

- Ten patients with r/r iMCD were included in the study, with a male-to-female ratio of 1:1. The median age at orelabrutinib initiation was 48 (31–58) years. All patients were classified as iMCD-NOS and seven fulfilled the criteria for iMCD-IPL.
- The ORR was 70% (7/10 patients, 95% CI: 34.8-93.3%); 20% (n = 2) achieved complete remission and 50% (n = 5) achieved partial remission. The median TTR was 9.8 months (range: 5.9–20.5 months).
- In the responder group, significant improvements were observed by month 12: haemoglobin levels had increased from 104 to 123 g/L (p=0.039); CRP had decreased from 67.33 to 14.54 mg/L (P=0.009); and IL-6 had decreased from 11.80 to 5.31 pg/mL (P=0.008). Additionally, albumin levels had normalised, increasing from a minimum value of 26 to 37 g/L (Figure 1).
- Patients in the non-responder group also demonstrated a continuous improvement in haemoglobin (91 to 105 g/L) and albumin (32 to 38 g/L) levels at month 12 of treatment despite not fulfilling response criteria.
- No grade 3 or higher adverse events occurred and no patient mortality was recorded. The median follow-up duration was 32.8 (range: 15.0–36.9) months.

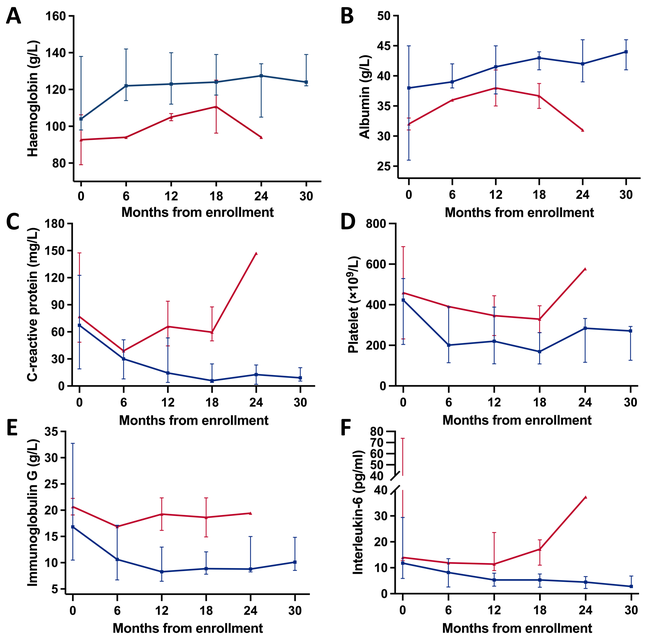

Fig1. Changes biochemical indexes for responders (blue line) and non-responders (red line).

Conclusion

Orelabrutinib can serve as a safe and effective regimen for r/r iMCD.