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

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**Summary:** Idiopathic multicentric Castleman disease (iMCD) is a rare and heterogeneous lymphoproliferative disorder that lacks standardised treatment options for patients with refractory or relapsed (r/r) disease. Blocking Bruton's tyrosine kinase (BTK) has emerged as a promising therapeutic approach for iMCD without depleting B cells. This single-centre, retrospective study enrolled 10 patients with r/r iMCD who were treated with orelabrutinib, a novel, next-generation BTK inhibitor. Histopathologically, 90% were plasmacytic and 10% were mixed subtypes. All patients were classified as iMCD-NOS and seven fulfilled the criteria for iMCD-IPL. The median age at orelabrutinib initiation was 48 (range: 31-58) years. The overall response rate was 70% (7/10 patients, 95% CI: 34.8-93.3), with 20% (n = 2) achieving complete response and 50% (n = 5) achieving partial response. The median time to response was 9.8 (range: 5.9-20.5) months. Patients in the non-responder group also demonstrated a continuous improvement in haemoglobin (91-105 g/L) and albumin (32-38 g/L) levels at month 12 of treatment despite not fulfilling response criteria. No grade 3 or higher adverse events occurred during the median time to the next treatment of 29.0 (range: 15.0-36.2) months. No patient mortality was recorded during the median follow-up duration of 32.8 (range: 15.0-36.9) months. In conclusion, orelabrutinib is a safe and effective regimen for r/r iMCD.