Real-world data of siltuximab for Chinese patients with iMCD: combination with BCD regimen benefits severe cases

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Introduction

Idiopathic multicentric Castleman disease (iMCD) accounts for a significant portion of Castleman disease (CD) cases. It is predominantly driven by a cytokine storm, with interleukin-6 (IL-6) being the key mediator. Siltuximab, which targets IL-6, is recommended by the Castleman Disease Collaborative Network (CDCN) as a first-line treatment for iMCD, showing high response rates in non-severe iMCD patients. Severe iMCD patients encounter aggressive cytokine storms, requiring more intensive interventions. However, substantial real-world data on the use of siltuximab in China were lacking, and treatment for patients with severe iMCD remains challenging. Following the approval of siltuximab and its subsequent commercial availability in China in July 2022, we initiated **the first real-world retrospective study** to focus on the effectiveness and safety of siltuximab in Chinese patients with iMCD, offering crucial real-world insights.

Methods

- This single-center, retrospective study was conducted at the Peking Union Medical College Hospital, involving iMCD patients treated with siltuximab from July 2022 to March 2024.
- The diagnostic criteria for iMCD were based on the criteria proposed by Fajgenbaum et al. in 2017[1].Patients were classified into iMCD-TAFRO and iMCD-NOS based on specific diagnostic criteria. Treatment response was evaluated as per the CDCN consensus guidelines and the overall response was defined as the symptomatic and biochemical response, except for the lymph node response in imaging.

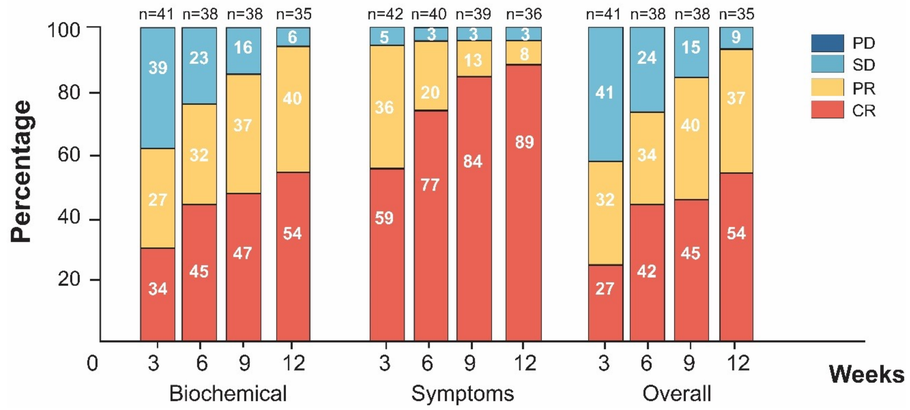

Fig 1. Efficacy evaluation within 12 weeks of siltuximab treatment.
CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease.

Results

- This study included 43 iMCD patients in China, with a median follow-up time of 4.6 months (range: 1.5-9.5 months). Severe iMCD was observed in 20 patients (46.5%).
- The overall response rate was 59% at week 3 and increased to 91% at week 12, with complete and partial response rates of 54% and 37%, respectively (Figure 1).
- Patients who received siltuximab as a first-line treatment showed better treatment response (OR = 0.040, 95% CI, 0.004-0.390, p=0.006). Inflammatory markers (IL-6 and hsCRP) and pathologic types showed no predictive role in the treatment responses.
- 18 patients, who were classified as severe iMCD, received combined therapy with BCD, the overall response rate was 50% at week 3, which increased to 100% at week 12 (Table 1).
- During the follow-up, adverse reactions included mild skin-related reactions (grade 1 or 2) in three patients, and severe pneumonia (grade 3) in one patient.

Table 1. Comparison of efficacy between patients treated with siltuximab + BCD and siltuximab±steroids.

Characteristic	Siltuximab + BCD (n=18)	Siltuximab ± steroids (n=25)	p value
iMCD-TAFRO, n (%)	12 (66.7%)	0 (0%)	< 0.001
Severe iMCD, n (%)	18 (100%)	2 (8%)	< 0.001
Overall response rate, n/N (%)			
3-week	9/18 (50%)	15/23 (65.2%)	0.326
6-week	12/16 (75%)	17/22 (77.3%)	0.871
9-week	15/16 (93.8%)	17/22 (77.3%)	0.355
12-week	14/14 (100%)	18/21 (85.7%)	0.259

Conclusion

The study reinforced the existing evidence regarding the efficacy and safety of siltuximab in treating iMCD and underscored the remarkable effectiveness of the combination therapy of siltuximab with the BCD regimen, especially for patients with severe iMCD.

Reference: [1] Fajgenbaum DC, Uldrick TS, Bagg A, et al. International, evidence-based consensus diagnostic criteria for HHV-8-negative/idiopathic multicentric Castleman disease.Blood.2017;129(12):1646-1657.