

Serum ferritin predicts response to tocilizumab in glucocorticoid-resistant adult-onset Still's disease: a prospective real-world cohort study

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Abstract

Objective

To evaluate the real-world effectiveness and safety of tocilizumab (TCZ) in glucocorticoid (GC)-resistant adult-onset Still's disease (AOSD) and explore predictors of clinical response.

Methods

This prospective, single-centre cohort study enrolled consecutive eligible patients with GC-resistant AOSD who initiated intravenous TCZ (4–8 mg/kg every four weeks) between June 2021 and June 2024. The primary outcome was clinical remission at 12 months per 2024 EULAR/PReS criteria (clinically inactive disease [CID] lasting ≥ 6 months). Secondary outcomes included CID rate at 6 months, laboratory and clinical activity scores, GC dose reduction, TCZ retention, and safety.

Results

Forty patients (median age 35.5 years; 80% female) were included. Clinical remission at 12 months was 55.0% (22/40); CID at 6 months was 62.5% (25/40). Significant improvements were observed in C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), serum ferritin (SF), and Pouchot scores (all $p < 0.001$). Median daily prednisone dose decreased by 91%, from 50.0 mg to 4.4 mg ($p < 0.001$). Baseline SF levels ≥ 2500 $\mu\text{g/L}$ were independently associated with lower remission rates (adjusted odds ratio 0.19, 95% CI 0.04–0.94; $p = 0.042$) and higher GC requirements at 12 months ($\beta = 5.55$, 95% CI 1.16–9.94; $p = 0.015$). The 12-month TCZ retention rate was 65.0%. Serious adverse events included macrophage activation syndrome (MAS, 7.5%) and lymphoma (2.5%).

Conclusion

TCZ is effective and steroid-sparing in GC-resistant AOSD. Baseline hyperferritinaemia (SF ≥ 2500 $\mu\text{g/L}$) is a potential biomarker for poorer outcomes, suggesting a need for tailored management.

Key words

adult-onset Still's disease, tocilizumab, serum ferritin, biomarker, glucocorticoid-resistant

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Introduction

Adult-onset Still's disease (AOSD) is a rare, multisystemic autoinflammatory disorder characterised by the classical triad of spiking fever, evanescent rash and arthritis (1). A life-threatening complication, macrophage activation syndrome (MAS) causes severe morbidity and mortality (2). Glucocorticoids (GCs) remain first-line therapy, but resistance or dependence is common, necessitating targeted alternatives (3).

Interleukin-6 (IL-6) plays a central role in AOSD pathogenesis (4, 5), providing a compelling rationale for its therapeutic targeting (6, 7). Tocilizumab (TCZ), an IL-6 receptor inhibitor, is conditionally recommended for refractory or GC-resistant AOSD in the 2024 EULAR/PRReS guidelines (8). While efficacy has been demonstrated in a phase III clinical trial (9) and supported by real-world retrospective studies (10), gaps remain regarding long-term outcomes, safety, and predictors of response.

This prospective cohort study was to evaluate the 12-month effectiveness and safety of TCZ in patients with GC-resistant AOSD and to assess whether baseline characteristics, particularly serum ferritin (SF), predicted treatment response.

Patients and methods

Study design and participants

We conducted a single-centre, prospective, observational cohort study at Peking University People's Hospital, China, enrolling all consecutive eligible patients with GC-resistant AOSD who initiated intravenous TCZ (4-8mg/kg every four weeks) between June 2021 and June 2024. The purpose of this real-world study was to evaluate the effectiveness and safety of TCZ in routine practice.

All patients met the Yamaguchi criteria for AOSD (11). GC-resistance was defined as: 1) failure to response to ≥ 0.5 mg/kg/day prednisone equivalent for at least 4 weeks (9); or 2) inability to taper prednisone below 0.1 mg/kg/day within 3 months without disease flare (8). Both incident and prevalent cases were included. Patients with previous exposure to conventional synthetic disease-modifying anti-rheumatic drugs (cs-

DMARDs), other biologic DMARDs or Janus kinase inhibitors (JAKi) were not excluded, ensuring the cohort reflected the spectrum of refractory disease encountered in clinical practice.

Data collection and outcomes

Data were collected prospectively at each visit (baseline, 3, 6, and 12 months) including inflammatory markers (C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), SF), disease activity (Pouchot score, patient's and medical doctor's global assessments (PGA, MDGA)), treatment response (achievement of clinically inactive disease (CID) and clinical remission) and safety outcomes (adverse events (AE), and reasons for TCZ discontinuation). CID required the absence of AOSD-related systemic and articular symptoms alongside normalised CRP and ESR (8). The primary outcome was clinical remission at 12 months, defined per the 2024 EULAR/PRReS guidelines as a CID duration for at least 6 months. Although these guidelines were published after the study initiation, they were applied prospectively to the available clinical and laboratory data for endpoints assessment. Secondary outcomes included CID rate at 6 months, GC dose reduction, changes in laboratory and clinical activity scores, TCZ drug retention rate, and adverse event occurrence.

The study protocol was approved by the Ethics Committee of Peking University People's Hospital (approval no.: 2021PHB370).

Statistical analysis

Given the rarity of GC-resistant AOSD, no formal sample size calculation was performed. All eligible patients during the study period were enrolled to maximise real-world evidence. IBM SPSS Statistics 26.0 was used for all statistical tests. Categorical variables were summarised as frequencies and percentages (n, %). Continuous variables with normal distribution were expressed as mean $\pm$ standard deviation (SD), non-normally distributed variables as median and interquartile range (Q1-Q3). Patients were stratified by baseline SF using a threshold of 2500 μ g/L, chosen based on prior literature linking this

level to severe disease manifestations in AOSD (12). A sensitivity analysis was performed using alternative cutoffs (1000 µg/L–3000 µg/L), as shown in Supplementary Table S2. In addition, patients were stratified by disease pattern into systemic and chronic articular subtypes. For paired comparisons (within-group changes over time), the paired t-test or Wilcoxon signed-rank test was used as appropriate. For between-group comparisons, including comparisons between SF-based groups (Group A vs. Group B), between clinical phenotype subgroups (systemic vs. chronic articular), and between remission and non-remission groups at 12 months (responders vs. non-responders), the chi-square test was used for categorical variables, the independent t-test for normally distributed continuous variables, and the Mann-Whitney -U test for non-normally distributed continuous variables.

Multivariable logistic regression (for remission) and linear regression (for 12-month GC dose) were performed, adjusting for a priori selected clinically relevant variables: disease duration before TCZ, baseline Pouchot score, baseline GC dose, and SF category (≥ 2500 vs. < 2500 µg/L). Covariates were selected based on clinical relevance and potential confounding, as informed by the literature. Model performance was assessed using C-statistic (logistic) and adjusted R^2 (linear). Results are presented with 95% confidence intervals (CIs). The Kaplan-Meier method was used to analyse time-to-event outcomes (TCZ drug retention). A two-tailed $p < 0.05$ was considered statistically significant.

Results

Patient characteristics

A total of 40 consecutive patients with GC-resistant AOSD were enrolled, including 8 men (20%) and 32 women (80%). Figure 1 shows the flow of participants through the study. The median age at TCZ initiation was 35.5 years (23.3–53.3), with a median disease duration of 6.0 (1.0–12.8) months before TCZ (Table I). Prior to TCZ initiation, 52.5% of patients had been treated with csDMARDs, with metho-

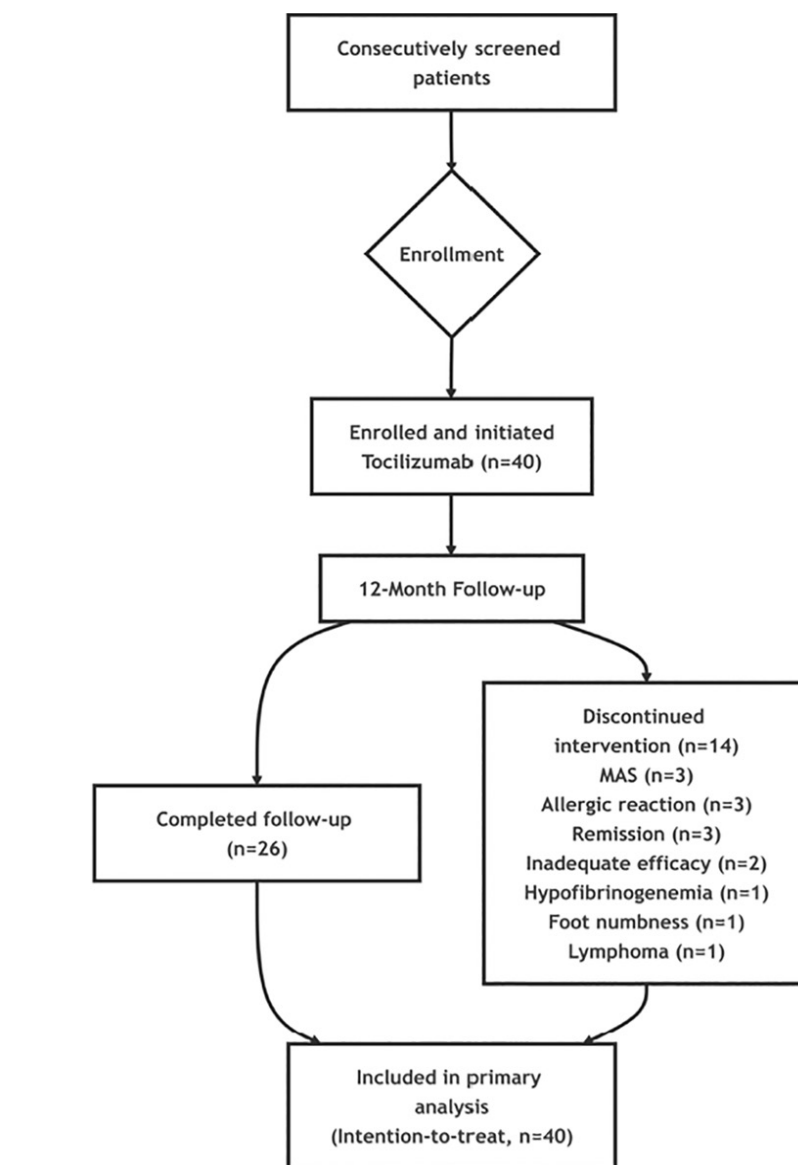


Fig. 1. Flow of participants through the study.

trexate being the most frequently used agent (42.5%). Additionally, 22.5% of patients had received JAK inhibitors (Table I), confirming the refractory nature of the cohort.

Treatment response and steroid-sparing effect

TCZ treatment resulted in significant and sustained improvements. Clinical remission was achieved at 12 months in 55.0% (22/40) patients, and CID at 6 months in 62.5% (25/40). A comparison of baseline characteristics between the remission and non-remission groups is provided in Supplementary Table S1. Following treatment, significant reductions were observed in CRP, ESR, SF,

Pouchot score, PGA and MDGA (all $p < 0.001$). The steroid-sparing effect over 12 months is illustrated in Figure 2. The median daily prednisone dose decreased from 50.0 (30.0–3.8) mg at baseline to 4.4 (2.5–10.0) mg at 12 months ($p < 0.001$) with 10.0% ($n = 4$) achieving complete GC discontinuation.

Stratification by baseline serum ferritin and clinical presentation

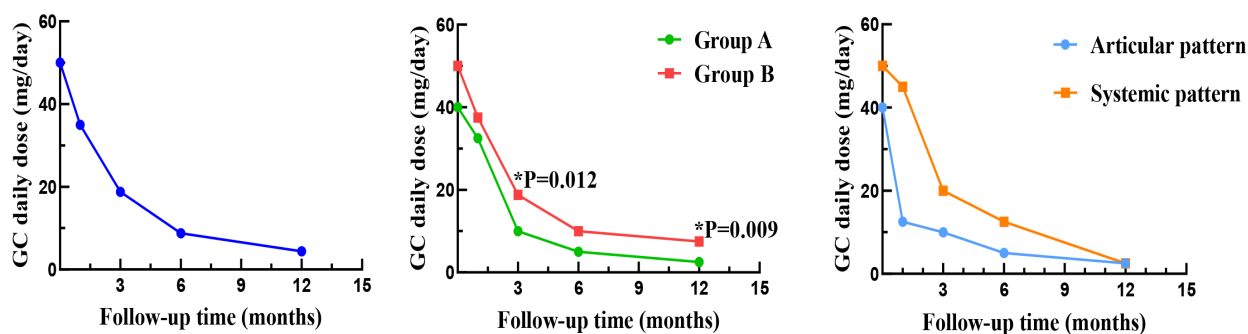
The cohort was stratified by baseline SF into Group A (SF < 2500 µg/L, $n = 21$, 52.5%) and Group B (SF ≥ 2500 µg/L, $n = 19$, 47.5%). Baseline characteristics: patients in Group B had significantly higher ALT, AST, LDH and baseline disease activity (Pouchot

Table I. Baseline demographic, clinical and pre-TCZ therapeutic characteristics of patients with glucocorticoid-resistant AOSD.

Characteristic	Total (n=40)	Group A (SF <2500 µg/L) (n=21)	Group B (SF ≥2500 µg/L) (n=19)	p-value
Female, n (%)	32 (80.0)	18 (85.7)	14 (73.7)	0.342
Age, median (IQR), years	35.5 (23.3-53.3)	35.0 (25.0-51.5)	37.0 (22.0-54.0)	0.828
Disease duration, median (IQR), months	6.0 (1.0-12.8)	10.0 (1.5-41.0)	3.0 (1.0-9.0)	0.076
Follow-up duration, median (IQR), months	14.5 (11.3-19.0)	14.0 (10.5-21.5)	15.0 (12.0-19.0)	0.839
Pouchot score, median (IQR)	4.0 (3.0-6.8)	4.0 (2.0-5.0)	7.0 (4.5-8.0)	*0.003
PGA, median (IQR), 0-10	5.0 (5.0-6.0)	5.0 (4.0-6.0)	6.0 (5.0-7.0)	*0.020
MDGA, median (IQR), 0-10	5.0 (4.3-6.0)	5.0 (3.5-6.0)	6.0 (5.0-7.0)	*0.017
WBC, median (IQR), ×10 ⁹ /L	10.4 (7.8-15.5)	10.1 (7.8-12.7)	12.0 (8.2-17.4)	0.189
NE, median (IQR), ×10 ⁹ /L	8.3 (6.9-13.8)	8.1 (7.1-12.6)	10.6 (6.9-15.8)	0.379
LYM, median (IQR), ×10 ⁹ /L	1.1 (0.8-1.7)	1.1 (0.8-1.7)	1.0 (0.7-1.7)	0.919
Hb, median (IQR), g/L	110.0 (100.8-125.0)	110.0 (101.0-123.3)	107.0 (97.0-125.0)	0.424
PLT, mean ± SD, ×10 ⁹ /L	272.8 ± 128.9	285.4 ± 149.3	260.8 ± 118.5	0.655
ALT, median (IQR), IU/L	25.5 (13.8-69.0)	15.0 (10.8-25.0)	60.0 (30.0-182.0)	*<0.001
AST, median (IQR), IU/L	35.0 (20.8-63.3)	21.5 (15.5-38.7)	58.0 (34.0-104.0)	*0.005
LDH, median (IQR), IU/L	401.5 (272.0-576.5)	286.5 (212.3-401.3)	520.0 (303.0-785.0)	*0.004
CRP, median (IQR), mg/L	43.0 (17.0-81.7)	38.4 (15.6-59.8)	52.4 (8.0-101.3)	0.635
ESR, median (IQR), mm/H	37.5 (19.0-85.3)	31.0 (12.0-65.0)	51.0 (16.5-88.0)	0.196
SF, median (IQR), µg/L	2446.0 (619.8-5840.1)	334.0 (83.6-1642.0)	5448.0 (3578.0-14410.5)	*<0.001
Treatment				
Prednisone dose, median (IQR), mg/d	50.0 (30.0-73.8)	40.0 (22.5-70.0)	50.0 (45.0-80.0)	0.076
Prior csDMARDs/JAKi, n(%)				
Methotrexate	17 (42.5)	10 (47.6)	7 (36.8)	0.491
Hydroxychloroquine	6 (15.0)	3 (14.3)	3 (15.8)	0.894
Cyclosporin A	4 (10.0)	2 (9.5)	2 (10.5)	0.916
Leflunomide	3 (7.5)	3 (14.3)	0 (0.0)	0.087
Mycophenolate Mofetil	2 (5.0)	1 (4.8)	1 (5.3)	0.942
Tofacitinib	4 (10.0)	4 (19.0)	0 (0.0)	*0.045
Baricitinib	3 (7.5)	2 (9.5)	1 (5.3)	0.609
Ruxolitinib	2 (5.0)	1 (4.8)	1 (5.3)	0.924

Note: Data are presented as n (%), mean ± SD, or median (Q1, Q3). P-values are for comparisons between Group A and Group B ((Mann-Whitney U-test for continuous variables, chi-square test for categorical variables). * $p < 0.05$.

IQR: interquartile range; SD: standard deviation; PGA: patient's global assessments; MDGA: medical doctor's global assessments; WBC: white blood cell count; NE: neutrophils; LYM: lymphocyte; Hb: haemoglobin; PLT: platelet; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; SF: serum ferritin; DMARDs: disease-modifying anti-rheumatic drugs; JAKi: Janus kinase inhibitors.

**Fig. 2.** Steroid-sparing effect in glucocorticoid-resistant AOSD over 12 months stratified by phenotype.

A1: all patients. A2: the cohort is stratified by baseline serum ferritin: Group A (SF <2500 µg/L, n=21, green lines) and Group B (SF ≥2500 µg/L, n=19, red lines). A3: The cohort is stratified by disease pattern: systemic pattern (n=29, orange lines) and chronic articular pattern (n=11, blue lines). Data are presented as median. Statistical significance was determined by the Wilcoxon signed-rank test for within-group comparisons against baseline. * $p < 0.05$.

scores, PGA, MDGA, all $p < 0.05$) (Table I). Treatment outcomes: remission rates were significantly lower in Group B (SF ≥2500 µg/L, 31.6%) compared to Group A (SF <2500 µg/L, 76.2%; $p = 0.005$). Figure 3 illustrates the dynamic changes in inflammatory mark-

ers and clinical scores stratified by serum ferritin. Despite comparable improvements in disease activity scores between groups, significantly higher GC doses were required in Group B at 3 and 12 months ($p = 0.012$ and $p = 0.009$, respectively) (Fig. 2).

Based on clinical presentation, 29 patients (72.5%) had a systemic pattern, and 11 patients (27.5%) had a chronic articular pattern. In contrast to the SF-based stratification, no significant differences in any baseline parameters (Suppl. Table S2) and treatment out-

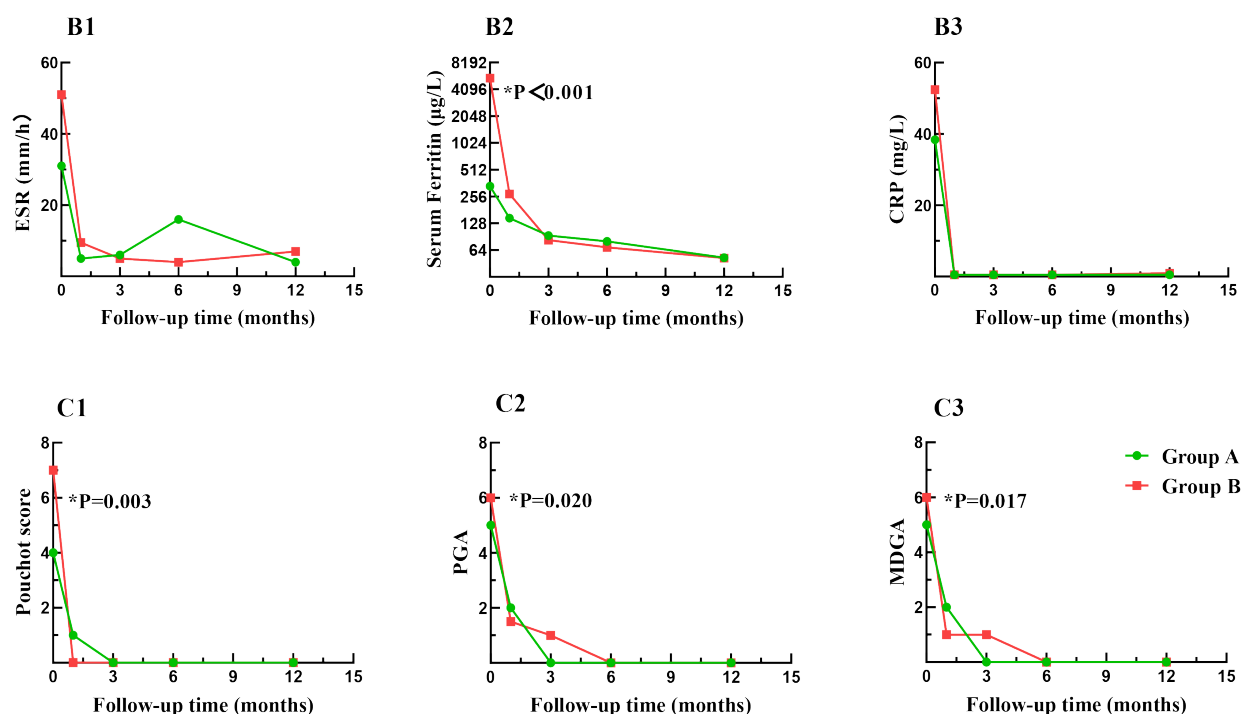


Fig. 3. Tocilizumab response in glucocorticoid-resistant AOSD over 12 months stratified by serum ferritin.

Panel B: Dynamic changes in systemic inflammatory markers B1: erythrocyte sedimentation rate (ESR). B2: serum ferritin levels. B3: serum C-reactive protein (CRP) levels. **Panel C:** Dynamic changes in clinical disease activity scores. C1: Pouchot score. C2: patient global assessment (PGA, 0-10 cm visual analogue scale). C3: medical doctor's global assessments (MDGA, 0-10 cm visual analogue scale).

Data are presented as median (Q1, Q3). The cohort is stratified by serum ferritin: Group A (SF < 2500 µg/L, n=21, green lines) and Group B (SF ≥ 2500 µg/L, n=19, red lines). Data are presented as median. Statistical significance was determined by the Wilcoxon signed-rank test for within-group comparisons against baseline. *p < 0.05.

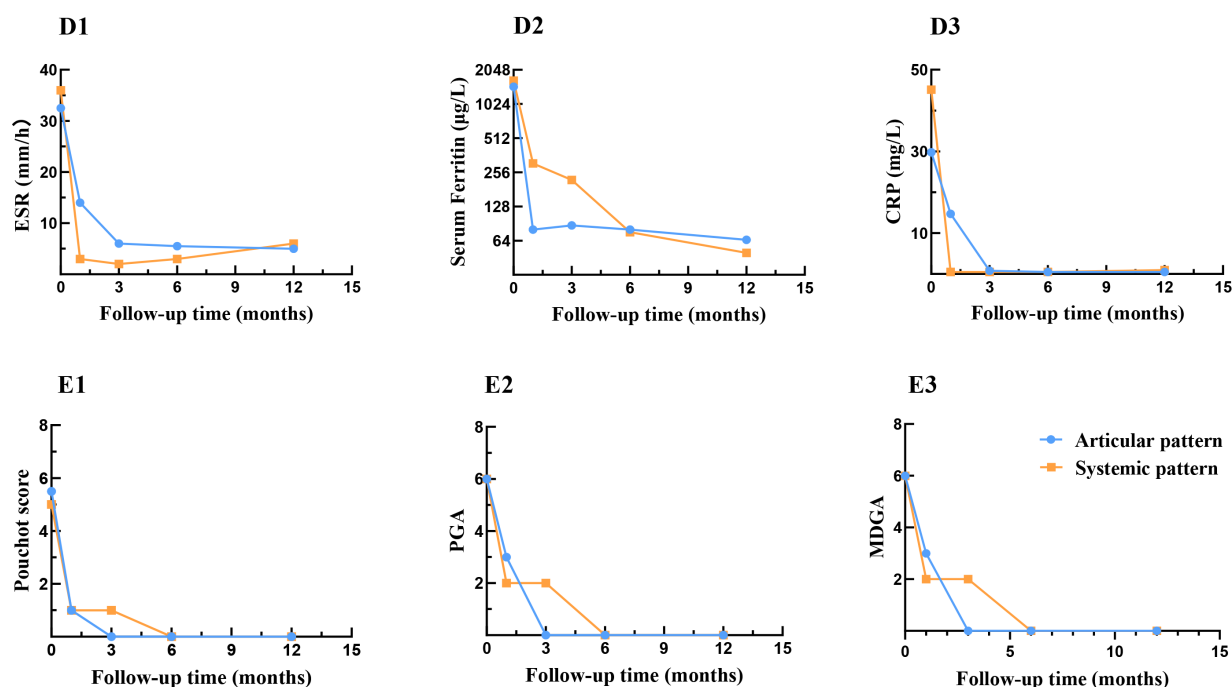


Fig. 4. Tocilizumab response in glucocorticoid-resistant AOSD over 12 months stratified by clinical phenotype.

Panel D: Dynamic changes in systemic inflammatory markers D1: erythrocyte sedimentation rate (ESR). D2: serum ferritin levels. D3: serum C-reactive protein (CRP) levels. **Panel E:** Dynamic changes in clinical disease activity scores. E1: Pouchot score. E2: patient global assessment (PGA, 0-10 cm visual analogue scale). E3: medical doctor's global assessments (MDGA, 0-10 cm visual analogue scale).

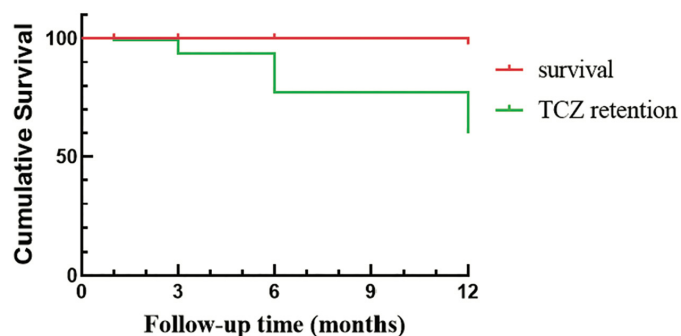
Data are presented as median (Q1, Q3). The cohort is stratified by disease pattern: systemic pattern (n=29, orange lines) and chronic articular pattern (n=11, blue lines). Statistical significance was determined by the Wilcoxon signed-rank test for within-group comparisons against baseline. *p < 0.05.

Table II. Multivariate analysis for predictors of clinical remission at 12 months.

Variable	Adjusted OR (95% CI)	p-value
Baseline SF ≥ 2500 $\mu\text{g/L}$ (vs. <2500)	0.19 (0.04 - 0.94)	*0.042
Baseline Pouchot score	1.32 (0.92 - 1.89)	0.138
Disease duration prior to TCZ	1.00 (0.98 - 1.02)	0.980
Baseline GC dose (mg/day, prednisone equivalent)	1.00 (0.99 - 1.00)	0.321

The multivariable logistic models were adjusted for all factors listed above. * $p < 0.05$.

OR: odds ratio; CI: confidence interval; SF: serum ferritin; TCZ: tocilizumab; GC: glucocorticoid.

**Fig. 5.** Drug retention rate and patient survival analysed using the Kaplan-Meier method.

comes were observed between these two subtypes (Fig. 4).

Baseline hyperferritinaemia is an independent predictor of poorer outcomes

Multivariable analysis confirmed the independent predictive value of baseline hyperferritinaemia. After adjusting for baseline Pouchot score, disease duration prior to TCZ and baseline GC dose, an SF level ≥ 2500 $\mu\text{g/L}$ remained independently associated with a lower likelihood of achieving clinical remission at 12 months (adjusted odds ratio 0.19, 95% CI 0.04–0.94; $p=0.042$) (Ta-

ble II). In a linear regression model, baseline hyperferritinaemia also predicted higher GC dose at 12 months (β coefficient 5.55, 95% CI 1.16 - 9.94; $p=0.015$). Sensitivity analyses confirmed the robustness of the 2500 $\mu\text{g/L}$ threshold (Suppl. Table S2).

Drug retention and safety

The 12-month TCZ retention rate was 65.0% (Fig. 5). Discontinuation occurred in 14 patients (35.0%), due to adverse events ($n=9$, 22.5%) (Table III), sustained remission ($n=3$, 7.5%) and inadequate efficacy ($n=2$, 5.0%). The safety profile was consistent with

previous reports. Common AEs included herpes zoster infection ($n=1$, 2.5%), peripheral neuropathy ($n=1$, 2.5%), infusion-related reactions ($n=3$, 7.5%) and hypofibrinogenaemia ($n=5$, 12.5%). The herpes zoster infection resolved with antiviral therapy after TCZ was temporarily interrupted. One patient developed reversible peripheral neuropathy (numbness over the dorsum of the foot) without exposure to other neuropathic agents, which resolved completely after switching from TCZ to baricitinib. Infusion-related reactions (nausea/vomiting, palpitations/dyspnoea, chills/fever) all improved after TCZ discontinuation. Hypofibrinogenaemia resolved with dose reduction ($n=4$) or drug withdrawal ($n=1$, from a nadir of 108 mg/dL), and no patients experienced a serious bleeding event. Serious AEs occurred in 4 patients (10.0%): three MAS events (7.5%), and one case of lymphoma (2.5%). The three MAS events comprised: one developed MAS after the first TCZ infusion and was treated with cyclosporine following initial response to high-dose glucocorticoid; one occurred after the second TCZ infusion, with improvement after ruxolitinib treatment and subsequent switch to tofacitinib; one fatal event occurred during CID with concurrent cytomegalovirus (CMV) infection after 11 months of TCZ therapy. The single case of diffuse large B-cell lymphoma was diagnosed after 8 months of TCZ treatment, with GC being the only prior

Table III. Summary of adverse events.

Adverse event	n (%)	Severity	Management	Discontinuation, n (%)
Herpes zoster	1 (2.5)	Mild	Antiviral therapy	0 (0.0)
Peripheral neuropathy	1 (2.5)	moderate	TCZ discontinuation, JAK inhibitor therapy	1 (2.5)
Infusion-related reactions	3 (7.5)	moderate	TCZ discontinuation	3 (7.5)
Hypofibrinogenaemia	5 (12.5)	Mild to moderate	Observation, TCZ dose adjustment	1 (2.5)
Lymphoma	1 (2.5)	Severe	TCZ discontinuation, oncology referral	1 (2.5)
MAS, early-onset (within 8 weeks of TCZ treatment)	2 (5.0)	Severe	TCZ discontinuation, high-dose GC, Ruxolitinib, supportive care	2 (5.0)
MAS, late-onset (associated with CMV infection)	1 (2.5)	Severe (fatal)	TCZ discontinuation, antiviral therapy, high-dose GC, etoposide, anakinra, supportive care	1 (2.5)

Adverse events led to discontinuation in 9 patients (22.5%). An additional 5 patients discontinued due to sustained remission ($n=3$) and inadequate efficacy ($n=2$).

TCZ: tocilizumab; GC: glucocorticoid; CMV: cytomegalovirus.

therapy. A detailed summary of all adverse events is provided in Table III.

Discussion

This prospective cohort study demonstrates that TCZ is a viable and relatively safe option for patients with GC-resistant AOSD, allowing significant steroid reduction and sustained disease control over 12 months. Our findings fill knowledge gaps regarding the long-term clinical effectiveness and safety of TCZ in real world practice and identify baseline hyperferritinaemia as a potential biomarker for treatment stratification.

Our data supported the central role of IL-6 in AOSD pathogenesis. We found rapid and significant decreases in IL-6-driven biomarkers (CRP, ESR, and importantly SF) returning to normal in most patients. Clinical improvements paralleled this biochemical response, with resolution of systemic symptoms and sharp reductions in Pouchot scores, PGA, and MDGA. These findings are consistent with mechanistic explanations of IL-6 blockade (4, 14) and the phase III trial of TCZ in AOSD (9). Additionally, the median daily prednisone dose was reduced by over 90% by 12 months, and 10% of patients discontinued GC completely, consistent with the conditional endorsement of TCZ as a steroid-sparing therapy in current EULAR/PReS guideline (8).

Our observed 12-month remission rate (55%) is numerically lower than that reported in the phase III trial by Kaneko et al. (approximately 70%) (9) and the AIDA registry by Sota et al. (approximately 68%) (13). This difference likely reflects our prospective design and inclusion of exclusively GC-resistant, highly refractory patients. While direct head-to-head comparisons between IL-1 and IL-6 inhibition remain limited, published meta-analyses suggest comparable efficacy but different safety profiles (14, 15). Rather than claiming superiority over IL-1 blockade, our study proposes that baseline ferritin could serve as a potential stratification biomarker to help guide biologic selection in future studies.

This study identifies baseline SF ≥ 2500 $\mu\text{g/L}$ as an independent predictor of

lower clinical remission rates and higher GC dependency. This association may indicate not only a higher burden of IL-6-mediated inflammation but also activation of additional cytokines (e.g. IL-1 β , IL-18, interferon- γ) that are typically active in hyperferritinaemic conditions and may not be sufficiently counteracted by IL-6 blockade alone (16, 17). Although Kaneko and Takeuchi proposed that IL-6 inhibition may be more effective for chronic articular disease (4), we did not observe significant differences in treatment outcomes between patients with chronic articular and systemic phenotypes. This suggests that the prognostic value of hyperferritinaemia transcends the traditional phenotypic dichotomy and may reflect underlying cytokine profiles that are not fully captured by clinical presentation alone. Our results provide a biomarker-based perspective that supplements the 2024 EULAR/PReS guidelines, which has not yet identified specific biomarkers to stratify biologic therapy (8). Patients with baseline hyperferritinaemia may represent a unique clinical subgroup that could benefit from earlier or more aggressive treatment modalities.

The safety profile of TCZ was generally manageable and consistent with the literature (6, 8, 18). The 7.5% incidence of MAS in our cohort, including early and late presentation, highlights the difficulty of managing AOSD. Distinguishing between MAS as natural disease progression *versus* TCZ related is a clinical challenge (19–22). Early-onset MAS may reflect uncontrolled underlying disease activity, whereas late-onset fatal MAS linked to CMV infection illustrates the risk of MAS even during CID. Of note, TCZ itself has been used effectively to treat MAS in some settings (19), indicating the dual impact of IL-6 pathway suppression on macrophage activation. Our data emphasise the need for heightened vigilance for MAS, especially when TCZ is introduced in patients with extreme hyperinflammation or intercurrent infections. The single case of lymphoma, although infrequent, underscores the known immunosurveillance risks of biologic therapies.

Several limitations should be acknowledged. First, this was a single centre study with a small sample size ($n=40$), inherent to rare disease research. Second, the lack of control group limits causal inferences. Third, the primary outcome was defined using the 2024 EULAR/PReS criteria, which were published after the study started; however, prospective application of these criteria strengthens the rigor of our remission assessment. Fourth, despite multivariable adjustment for clinically relevant confounders, residual confounding due to the observational, single-centre design cannot be fully excluded. Finally, long-term follow-up is needed to comprehensively evaluate safety outcomes, including malignancy and opportunistic infection risks.

In conclusion, this prospective, real-world cohort study provides evidence that TCZ is an effective and well-tolerated option for GC-resistant AOSD. It induces and maintains clinical remission, has a strong steroid-sparing effect, and has a manageable safety profile. Baseline hyperferritinaemia (SF ≥ 2500 $\mu\text{g/L}$) is a potential biomarker for poorer response and higher steroid dependence, suggesting that such patients may require more aggressive or alternative treatment approaches. IL-6 inhibition should be integrated into the treatment algorithm for refractory AOSD as supported by recent guidelines. Future multi-centre studies with larger cohorts and long-term follow-up are needed to validate these findings, define predictors of response, and further refine the long-term risk-benefit profile of TCZ in AOSD.

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Take home messages

- Tocilizumab facilitates disease control and glucocorticoid tapering in adult-onset Still's disease.
- Baseline hyperferritinaemia independently predicts poorer treatment response and higher steroid dependence.

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