Efficacy and safety of telitacicept in patients with systemic lupus erythematosus: a multicentre, retrospective, real-world study

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ABSTRACT

Objective To examine the efficacy and safety of telitacicept in the treatment of patients with SLE in everyday clinical practice.

Methods Seventy-two patients with active SLE who received telitacicept for more than 24 weeks at multiple centres in China between 2019 and 2022 were retrospectively identified. Twenty-one of these patients received 52 continuous weeks of treatment with telitacicept. Treatment outcomes were analysed separately according to whether patients had renal or haematological abnormalities. Trajectory analysis was performed to identify patients with a limited response. Factors contributing to a limited response were explored by multivariable logistic regression analysis.

Results After treatment with telitacicept for 4, 12, 24 and 52 weeks, 22.22%, 54.17%, 72.22% and 80.95% of patients, respectively, achieved an SLE Responder Index 4; 8.33%, 26.39%, 34.72% and 47.62% achieved a Lupus Low Disease Activity State; and 0%, 4.17%, 8.33% and 23.81% achieved remission. Significant decreases in serum IgA, IgG and IgM levels were observed at 4 weeks and showed a downward trend at 12, 24 and 52 weeks. The median 24-hour urinary protein declined from 1323.5 mg to 224.0 mg in patients with lupus nephritis after treatment with telitacicept for 52 weeks. Furthermore, a large proportion of patients (10 of 13) with haematological abnormalities recovered after 52 weeks of treatment with telitacicept. No severe adverse events were reported during the observation period. Age appeared to have a negative impact on treatment efficacy.

Conclusions Telitacicept demonstrated favourable efficacy and safety in patients with active SLE and improved the renal and haematological manifestations of the disease.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Randomised controlled trials have indicated that telitacicept, a dual B cell-activating factor/a proliferation-inducing ligand inhibitor, is an effective treatment for patients with SLE and active disease activity.

WHAT THIS STUDY ADDS

⇒ The findings of this multicentre real-world study confirm that telitacicept is effective in patients with active SLE and could be an option for patients with SLE with nephritis or haematological abnormalities.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings could serve as a reference for selection of biologics to treat patients with renal or haematological manifestations of SLE. Further investigations in larger cohorts are needed to confirm our findings.

INTRODUCTION

SLE is a chronic autoimmune disease characterised by a breach of immune tolerance and aberrant formation of autoantibodies, leading to multisystem injury.[1] Current treatment strategies for SLE rely heavily on glucocorticoids and immunosuppressive drugs.[2,3] However, considering the limited efficacy and adverse events associated with these treatments, there is an urgent need to develop novel targeted therapies.[4] The past decade has witnessed the advent of several innovative treatments for SLE, which have mainly been biologics or small-molecule agents that target B cells, including the BAFF (B cell-activating factor)/APRIL (a proliferation-inducing ligand) inhibitors.[5–7] Belimumab inhibits activation of B lymphocytes by binding to soluble BAFF[5,8] and in 2011 became the first biologic approved for treatment of active SLE by the US Food and Drug Administration. Thereafter, atacicept, another biologic that binds both BAFF and APRIL, was developed. A 24-week, randomised, double-blind, placebo-controlled phase IIb study found that the SLE Responder Index 4 (SRI-4) rate was significantly improved in patients with high disease activity and serologically active SLE who received atacicept.[9] However, a further two phase II/III randomised, double-blind,

placebo-controlled trials of atacicept in patients with moderate-to-severe SLE and lupus nephritis were prematurely terminated because of unacceptable number of severe infections.[10 11] Telitacicept is a novel human recombinant fusion protein that was conditionally approved in China for the treatment of patients with active SLE in March 2021.[12] This agent neutralises the activity of two cell-signalling molecules (ie, BAFF and APRIL) by competitively binding with the transmembrane activator and CAML interactor (TACI) site, thereby suppressing development and survival of plasma cells and mature B cells.

Although both telitacicept and atacicept are TACI-Ig Fc fusion proteins that bind to BAFF and APRIL, telitacicept does not contain the proprotein convertase restriction sites that render TACI susceptible to degradation while retaining the N-terminal region that maintains the bioactivity of TACI.[13] Furthermore, telitacicept maximally conserves the stalk region (cysteine-rich domain 2), which has strong affinity for BAFF/APRIL, thereby enhancing its bioactivity.[14] Telitacicept was confirmed to have efficacy superior to that of placebo as well as a favourable safety profile in a phase IIb clinical trial and by the preliminary data from a phase III study in China, but there are still limited real-world data to support its use in patients with SLE.[15 16] Therefore, in this study, we retrospectively reviewed patients with active SLE who received at least 24 weeks of treatment with telitacicept at any of three centres. Furthermore, we investigated the outcomes in patients with renal or haematological abnormalities, which have not been systematically reported, and sought factors associated with a limited response to treatment with this dual BAFF/APRIL inhibitor.

METHODS
Patients and study design
The study had a retrospective, multicentre, observational design and involved three hospital centres (figure 1). All the patients enrolled in the study met the 1997 American College of Rheumatology classification criteria[17] and the 2019 European Alliance of Associations for Rheumatology/American College of Rheumatology classification criteria[18] for SLE and had active disease with an SLEDAI-2K (SLE Disease Activity Index 2000) score of ≥4. None of the patients had severe hepatic or renal insufficiency. Patients who received less than 24 weeks of treatment with telitacicept and those who had received other B cell-specific biologics within 3 months were excluded. The primary end-up observation point was 24 weeks. Patients who received telitacicept for 52 weeks (n=21) were also observed for long-term efficacy, and their clinical and serological data at baseline and after 4, 12, 24 and 52 weeks of treatment were collected.

Study outcome
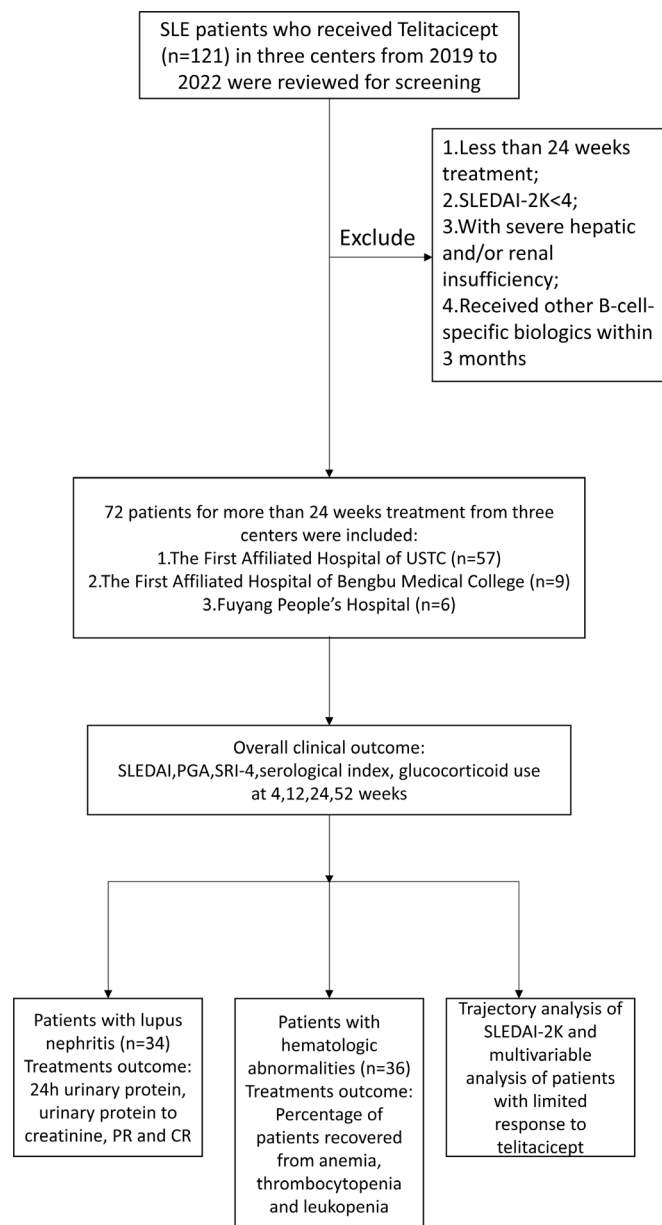The primary clinical outcomes for all patients were the SLEDAI-2K score, Physician Global Assessment (PGA)

Figure 1 Flow chart showing the design of the study. CR, complete renal response; PGA, Physician Global Assessment; PR, primary efficacy renal response; SLEDAI-2K, SLE Disease Activity Index 2000; SRI-4, SLE Responder Index 4; USTC, University of Science and Technology of China.

score and the SRI value. According to this index, a responder is a patient with at least a 4-point reduction in the Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score, no new British Isles Lupus Assessment Group (BILAG) A score, no more than one new BILAG B organ domain score and no worsening of the PGA score (<0.3 points) when compared with baseline.[19] The Lupus Low Disease Activity State (LLDAS)[20] and Definitions Of Remission in SLE (DORIS)[21] on therapy were used as additional indicators. Serological indices, including serum IgA, IgG and IgM concentrations and the proportions of patients with

normal C3 and C4 levels after treatment, were assessed for improvement at 4, 12, 24 and 52 weeks. The glucocorticoid dose was divided into three categories, namely high (≥30 mg), moderate (10–<30 mg) and low (≤10 mg).

Patients with lupus nephritis or haematological manifestations of SLE were specifically selected to assess whether telitacicept improved these abnormalities. Lupus nephritis was defined by the American College of Rheumatology criteria as (1) persistent daily proteinuria of >500 mg, (2) greater than 3+ by dipstick, and/or (3) cellular casts or biopsy evidence of immune complex-mediated glomerulonephritis compatible with lupus nephritis.[22] The primary renal outcomes were the primary efficacy renal response (PR) and complete renal response (CR) rates according to the Belimumab International Study in Lupus Nephritis (BLISS-LN).[23] The urinary protein-to-creatinine ratio and 24-hour urinary protein quantification were also recorded at 4, 12, 24 and 52 weeks. Improvements in haematological manifestations were reflected by the proportions of patients whose anaemia, leucopenia and thrombocytopenia recovered and whose corresponding routine blood indicators returned to the reference range during the observation period.

Safety
The incidence and severity of all adverse events were recorded. The National Institutes of Health Common Terminology Criteria for Adverse Events (V.5.0) were used to describe adverse events and laboratory abnormalities.

Trajectory analysis of changes in SLEDAI-2K score
Patients were grouped according to their disease activity at baseline and response to treatment with telitacicept. Patients who did not achieve a treatment response (ΔSLEDAI <4) after 24 weeks were identified as a limited response group.

Statistical analysis
Patient characteristics are expressed as the mean±SD, median (IQR) or number (percentage). Continuous variables that were normally distributed were compared using the Student's t-test, and those that were not normally distributed were compared using the Mann-Whitney U test. Pearson's X^2 test was used to compare categorical variables. All reported p values are two sided and were not adjusted for multiple testing. All statistical analyses were performed using SPSS software V.27.0 (IBM Corp). The level of statistical significance was set at $p<0.05$.

Patient and public involvement
No patients or members of the public were involved in the design, conduct, reporting or plans for dissemination of this research.

RESULTS
Patient characteristics
Seventy-two patients were enrolled in the study. As shown in table 1, the patients were primarily female (94.4%),

Table 1 Patient demographic and clinical characteristics

Parameters	Mean±SD/N (%)
Age (years)	32.72±10.93
Sex, n (%, female)	68 (94.4)
Duration (years)	6.48±5.68
SLEDAI-2K	9.88±4.50
PGA	1.40±0.70
System involvement	N (%)
Skin	24 (33.3)
Arthritis	24 (33.3)
Serositis	7 (9.7)
Central nervous system	3 (4.2)
Kidney	34 (47.2)
Blood system	36 (50.0)
Serological	Mean±SD/N (%)
IgA (g/L)	2.42±0.94
IgG (g/L)	13.17±6.49
IgM (g/L)	1.06±0.70
Low C3	58 (80.6)
Low C4	59 (81.9)
ANA positive	66 (91.7)
High anti-dsDNA	53 (73.6)
Glucocorticoid use	Mean±SD/N (%)
At baseline (mg)	19.15±14.52
GC ≤10 mg	33 (45.8)
10 mg<GC<30 mg	13 (18.1)
GC ≥30 mg	26 (36.1)
Stable GC dose for 3 months before biologics	44 (61.1)
Immunosuppressants	N (%)
HCQ	68 (94.4)
MMF	36 (50.0)
CYC	12 (16.7)
LEF	6 (8.3)
THAL	1 (1.4)

CYC, ciclosporin; dsDNA, double-stranded DNA; GC, glucocorticoid; HCQ, hydroxychloroquine; LEF, leflunomide; MMF, mycophenolate mofetil; PGA, Physician Global Assessment; SLEDAI-2K, SLE Disease Activity Index 2000; THAL, thalidomide.

with a mean age of 32.72 years and mean disease duration of 6.48 years.

The mean SLEDAI-2K score was 9.88 and the mean PGA score was 1.40, indicating moderate-to-severe disease in most cases at baseline. Systems involvement before starting on telitacicept was variable, with the most frequently reported manifestations of SLE involving the renal system (47.2%) or haematological system (50.0%). Other specific manifestations of SLE, including rash (33.3%), arthritis (33.3%), serositis (9.7%) and
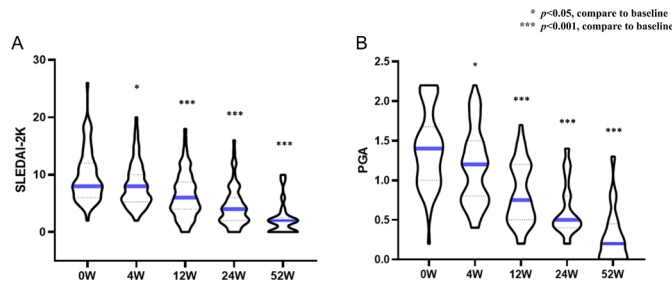
Figure 2 Changes in the SLEDAI-2K (A) and PGA (B) scores after 4, 12, 24 and 52 weeks of treatment with telitacicept. PGA, Physician Global Assessment; SLEDAI-2K, SLE Disease Activity Index 2000.

encephalopathy syndrome (4.2%), were also reported. In terms of the serological index, a majority of patients had a low C3 (80.6%) or C4 (81.9%) level and a high anti-double-stranded DNA level (73.6%), indicating active disease before starting treatment with telitacicept in most cases.

In the 3 months before telitacicept therapy was added, 61.1% of patients had maintained a stable oral glucocorticoid dose. The average glucocorticoid dose at baseline was 19.15 mg/day; the dose was low in 45.8% of patients, intermediate in 18.1% and high in 36.1%. In total, 94.4% of patients were also treated with anti-malarial agents. Other concomitant immunosuppressants at baseline were mycophenolate (50.0%), ciclosporin (16.7%), leflunomide (8.3%) and thalidomide (1.4%).

Overall clinical outcomes

After 24 weeks of treatment with telitacicept, the mean SLEDAI-2K score had declined from 9.88 to 4.43 and the mean PGA score from 1.4 to 0.6. For patients who received 52 weeks of treatment, the SLEDAI-2K score decreased to 2.29 and the PGA score to 0.3 (figure 2A,B). The respective percentages of responders with an SRI-4 at 4, 12, 24 and 52 weeks were 22.22%, 54.17%, 72.22% and 80.95%. In terms of other indicators of disease activity, 8.33%, 26.39%, 34.72% and 47.62% of patients had low disease activity (LLDAS) and 0%, 4.17%, 8.33% and 23.81% were in remission (DORIS definition) at 4, 12, 24 and 52 weeks (table 2). There was also a large improvement in the serological index, with significant decreases in IgA, IgG and IgM; nearly half of the patients returned to having normal serum C3 (48.61%) and C4 (58.33%) levels after 24 weeks of treatment with telitacicept. At 52 weeks, 76.19% of patients had a normal C3 level and 100.00% had a normal C4 level.

The mean glucocorticoid dosage decreased from 19.15 mg/day before treatment with telitacicept to 8.99 mg/day after 24 weeks of treatment. The proportion of patients on a low glucocorticoid dose (≤10 mg) increased from 45.8% at baseline to 88.9% at 24 weeks. All 21 patients who completed 52 weeks of treatment with telitacicept were on a low glucocorticoid dose by that time.

No patient was receiving a high glucocorticoid dose (≥30 mg) after 24 weeks of treatment with telitacicept, which indicates that telitacicept add-on therapy can reduce the glucocorticoid dose.

Table 2 Changes in the disease activity evaluation index, serological index and glucocorticoid dose after 4, 12, 24 and 52 weeks of treatment with telitacicept

	Baseline (n=72)	4 weeks (n=72)	12 weeks (n=72)	24 weeks (n=72)	52 weeks (n=21)
Disease activity					
SRI-4, n (%)	–	16 (22.22)	39 (54.17)	52 (72.22)	17 (80.95)
LLDAS, n (%)	–	6 (8.33)	19 (26.39)	25 (34.72)	10 (47.62)
Remission, n (%)	–	0 (0)	3 (4.17)	6 (8.33)	5 (23.81)
Serological index					
IgA, g/L (mean±SD)	2.42±0.94	2.01±0.88	1.90±0.89	1.82±0.75	1.85±0.71
IgG, g/L (mean±SD)	13.17±6.49	10.84±5.32	10.68±5.77	10.94±6.22	9.99±5.13
IgM, g/L (mean±SD)	1.06±0.70	0.80±0.49	0.72±0.56	0.64±0.36	0.60±0.36
Normal C3, n (%)	14 (19.44)	26 (36.11)	31 (43.05)	35 (48.61)	16 (76.19)
Normal C4, n (%)	13 (18.05)	26 (36.11)	38 (52.78)	42 (58.33)	21 (100.00)
Glucocorticoid (GC) dosage					
GC ≤10 mg, n (%)	33 (45.8)	39 (54.2)	50 (69.4)	64 (88.9)	21 (100.0)
10 mg<GC<30 mg, n (%)	13 (18.1)	17 (23.6)	21 (29.2)	8 (11.1)	0 (0.00)
GC ≥30 mg, n (%)	26 (36.1)	16 (22.2)	1 (1.4)	0 (0.0)	0 (0.00)
Mean±SD, mg	19.15±14.52	16.32±10.64	11.25±5.19	8.99±3.24	8.21±2.11

LLDAS, Lupus Low Disease Activity State; SRI-4, SLE Responder Index 4.

Table 3 Renal index in patients with lupus nephritis treated with telitacicept for 12, 24 and 52 weeks

	Baseline (n=34)	12 weeks (n=34)	24 weeks (n=34)	52 weeks (n=9)
24-hour protein quantification (mg) Median (Q1–Q3)	1323.5 (728.0–2293.7)	582 (385.0–1051.0)	305.0 (213.25–738.5)	224 (87.5–492.5)
Urinary protein/creatinine Median (Q1–Q3)	1.20 (0.70–2.76)	0.5 (0.28–1.02)	0.30 (0.13–0.77)	0.28 (0.10–0.47)
Primary renal response n (%)	–	22 (64.70)	26 (76.47)	7 (77.78)
Complete renal response n (%)	–	16 (47.05)	24 (70.58)	6 (66.67)

Treatment outcome in patients with renal or haematological abnormalities

Thirty-four of the patients were diagnosed with lupus nephritis. Kidney biopsy was performed in 12 of these patients and the distribution according to pathological classification was III (n=1), IV (n=1), III+V (n=3) and IV+V (n=7) (online supplemental table 1). The median 24-hour urinary protein quantification for the patients with nephritis decreased markedly from 1323.5 mg at baseline to 582.0 mg at 12 weeks and to 305.0 mg at 24 weeks (table 3). Consistent with the 24-hour urinary protein outcome, the urinary protein-to-creatinine ratio decreased sharply at 12 and 24 weeks. Nine of the 34 patients with nephritis received more than 52 weeks of treatment with telitacicept. The median 24-hour urinary protein quantification and urinary protein-to-creatinine ratio in these patients decreased to 224 mg and 0.28, respectively. To explore the effectiveness of telitacicept in lupus nephritis further, we evaluated the PR and CR rates according to the BLISS-LN criteria. At 12 weeks, 22 patients (64.7%) achieved a PR and 16 (47.5%) achieved a CR. By 24 weeks, the proportions of patients who attained a PR and a CR increased to 76.47% and 70.58%, respectively. Seven of the nine patients with nephritis who received 52 weeks of therapy achieved a PR and six achieved a CR. Overall, telitacicept demonstrated effectiveness in lupus nephritis.

Thirty-six patients developed haematological abnormalities, which consisted of anaemia, leucopenia and thrombocytopenia (online supplemental table 2). Among the patients with anaemia, 24.14% (7 of 29) presented with haemolytic anaemia. There was an upward trend in the proportion of patients in whom anaemia recovered after treatment with telitacicept for 12 and 24 weeks (table 4), irrespective of whether the anaemia was haemolytic or non-haemolytic. By 24 weeks, 57.14% (4 of 7) of the patients with haemolytic anaemia had recovered and 68.18% (15 of 22) of those with non-haemolytic anaemia had recovered. Improvements were also observed in patients with thrombocytopenia and leucopenia. The proportions of patients who recovered from thrombocytopenia and leucopenia reached 80.00% (12 of 15) and 88.89% (8 of 9), respectively, after 24 weeks of telitacicept. Thirteen patients with haematological abnormalities completed 52 weeks of treatment; 10 of these patients recovered, including 7 of 8 (87.5%) who had non-haemolytic anaemia, 1 of 2 (50.0%) who had haemolytic anaemia and 2 of 3 (66.67%) who had thrombocytopenia.

Adverse events

Table 5 shows the adverse events that were documented during the observation period. Overall, 26.39% of patients experienced adverse events after starting telitacicept. The proportion of patients who developed infection in the telitacicept group was 23.6%. Among the different categories of infection, the incidence of urinary tract infection was highest (occurring in seven patients). No serious adverse events were recorded during treatment with telitacicept. Similarly, there were no reports of allergy to telitacicept or neoplasia during this time.

Table 4 Proportions of patients with various haematological abnormalities that recovered after 4, 12, 24 and 52 weeks of treatment with telitacicept

	4 weeks	12 weeks	24 weeks	52 weeks
Patients without haemolysis	n=22	n=22	n=22	n=8
Recovered after treatment, n (%)	8 (36.36)	10 (45.45)	15 (68.18)	7 (87.5)
Patients with haemolysis	n=7	n=7	n=7	n=2
Recovered after treatment, n (%)	2 (28.57)	4 (57.14)	4 (57.14)	1 (50.00)
Patients with thrombocytopenia	n=15	n=15	n=15	n=3
Recovered after treatment, n (%)	6 (40.00)	8 (53.33)	12 (80.00)	2 (66.67)
Patients with leucopenia	n=9	n=9	n=9	n=0
Recovered after treatment, n (%)	8 (88.89)	8 (88.89)	8 (88.89)	–

Table 5 Adverse events after introduction of telitacicept therapy

Adverse events	N (%)
Any adverse event after start of therapy, n (%)	19 (26.39)
Serious adverse events, n (%)	0 (0.0)
Infection, n (%)	17 (23.6)
Upper respiratory tract infection, n (%)	5 (6.9)
Urinary tract infection, n (%)	7 (9.7)
Herpes zoster, n (%)	1 (1.4)
Herpes simplex, n (%)	2 (2.7)
Cytomegalovirus, n (%)	2 (2.7)
Gastrointestinal disorders, n (%)	2 (2.7)
Diarrhoea, n (%)	1 (1.4)
Leucopenia, n (%)	0 (0)

Trajectory analysis of the SLEDAI-2K score and factors associated with a limited response

We divided the trajectory of the SLEDAI-2K score based on the patient's baseline disease activity level and response to treatment at 24 weeks. The patients were classified into three groups: group 1, which included patients who had high disease activity at baseline (SLEDAI-2K score >10) and achieved a treatment response after 24 weeks (ΔSLEDAI-2K score $\geq$4); group 2, which comprised patients who had moderate disease activity at baseline (SLEDAI-2K score of >4–10) and achieved a treatment response after 24 weeks; and group 3, which included patients in whom telitacicept had limited efficacy, with no response achieved by 24 weeks (figure 3). The proportions of patients in groups 1, 2 and 3 were 33.33%, 38.89% and 27.78%, respectively. Group 3, which included 20 patients, was defined as the limited response group. A multivariable analysis was performed to identify factors associated with a limited treatment response (table 6). The variables used in this analysis were age, sex, duration of SLE, glucocorticoid dose, ANA titre, complement
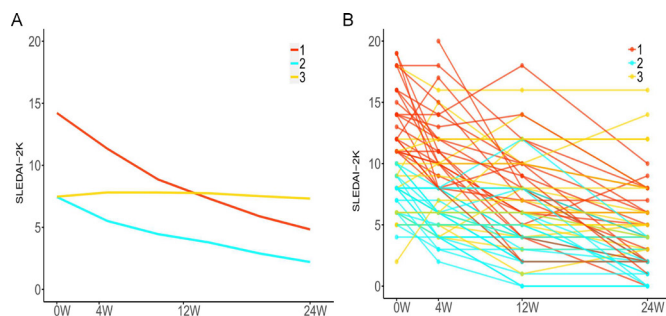

Figure 3 Patient SLEDAI-2K changes classified by disease activity and treatment response. (A) Lines are locally estimated scatterplot smoothing trajectories for the three trajectory groups. (B) Changes in the SLEDAI-2K score in each trajectory subgroup. The red line indicates group 1, the blue line indicates group 2 and the yellow line indicates group 3. SLEDAI-2K, SLE Disease Activity Index 2000.

level, SLEDAI-2K score and number of disease-modifying antirheumatic drugs used before treatment with telitacicept. The results showed that older patients were more likely to have a limited response to telitacicept (p=0.048) and that patients with higher disease activity were more likely to respond to this treatment.

DISCUSSION

This multicentre, non-interventional, retrospective, observational study describes the real-world clinical experience of telitacicept in the treatment of patients with SLE. Consistent with previously published data, we observed that the SLEDAI-2K and PGA scores declined after telitacicept add-on therapy in all patients with SLE.[24] In the phase IIb clinical trial, telitacicept-treated patients had a significantly higher SRI-4 response rate than the placebo group at week 48 (71.0% in the 80 mg group). The proportion of SRI-4 responders in our study was 72.22% at 24 weeks, suggesting marked effectiveness of telitacicept in clinical practice. We also collected data from the 21 patients who received telitacicept for 52 weeks so that we could assess long-term efficacy. The SRI-4 reached 80.95% (17 of 21) at 52 weeks. Serological indices, including IgA, IgM and IgG, were significantly decreased at 4 weeks and declined slightly at 12, 24 and 52 weeks, indicating that telitacicept may play an immunosuppressive role at an early stage of treatment.

We found that a considerable proportion of patients in this study had renal (47.2%) or haematological (50.0%) abnormalities. However, data on the results of treatment with telitacicept in patients with SLE with lupus nephritis or haematological abnormalities are limited.[25] A domestic phase II trial found that telitacicept reduced proteinuria in patients with high-risk IgA nephropathy, but its effectiveness in other autoimmune nephropathies, especially lupus nephritis, is still unknown.[26 27] We identified 34 patients with a diagnosis of lupus nephritis and observed improvement in renal function after treatment with telitacicept. Both 24-hour urinary protein quantification and the urinary protein-to-creatinine ratio showed a significant decrease. For other indicators of renal function, we referred to the BLISS-LN and found that the PR and CR rates were both beyond 70% at 24 weeks.[23] The PR and CR rates in patients with nephritis who received 52 continuous weeks of telitacicept were 77.78% (seven of nine) and 66.67% (six of nine), respectively. In real-world practice, the number of patients with SLE and manifest haematological abnormalities is not negligible. Noteworthy is that telitacicept was also effective in patients with anaemia, thrombocytopenia and leucopenia.

SLE has a complex aetiology and various manifestations. Apart from conventional glucocorticoids and immunosuppressants, few biological agents are available. Rituximab, which directly depletes CD20^{+} B cells, did not achieve the primary endpoint in the EXPLORE trial.[28] Subsequent development and application of belimumab gradually led to a focus on

Table 6 Factors associated with a limited response to telitacicept identified by univariable and multivariable logistic regression analyses

	Univariable analysis		Multivariable analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Age	1.06 (1.01 to 1.12)	0.021*	1.07 (1.00 to 1.14)	0.048*
Sex	3.00 (0.34 to 26.61)	0.290	3.14 (0.25 to 45.54)	0.366
Duration	1.07 (0.98 to 1.18)	0.132	1.01 (0.89 to 1.15)	0.825
GC dose	0.98 (0.94 to 1.01)	0.227	1.00 (0.94 to 1.05)	0.887
Number of immunosuppressants used	1.09 (0.50 to 2.44)	0.830	0.80 (0.29 to 2.24)	0.670
ANA titres	0.69 (0.12 to 5.32)	0.688	0.86 (0.11 to 9.37)	0.894
SLEDAI-2K	0.79 (0.64 to 0.93)	0.011*	0.75 (1.07 to 1.74)	0.020*
C3	3.68 (0.65 to 23.03)	0.145	1.04 (0.04 to 22.64)	0.981
C4	67.88 (0.10 to 53 896.68)	0.200	0.06 (0.00 to 2976.78)	0.606

*$p<0.05$
GC, glucocorticoid; SLEDAI-2K, SLE Disease Activity Index 2000.

targeted therapy for B cell-related cytokines.[8 29] BAFF and APRIL, both of which are members of the tumour necrosis factor family, play important roles in the activation and survival of B cells and show increased expression in various B cell-mediated autoimmune diseases, including SLE.[6 30 31] BAFF and APRIL share two receptors, TACI and B cell maturation antigen (BCMA), which contribute to transformation of mature B cells into plasma cells and formation of antibodies. APRIL binds strongly to BCMA and moderately to TACI, whereas BAFF binds weakly to BCMA and strongly to TACI.[32] Therefore, binding of belimumab to soluble BAFF can inhibit the proliferation and maturation of B cells but may have no effect on long-lived plasma cells. Ataicept and telitacicept bind both BAFF and APRIL and can inhibit the transformation of mature B cells into plasma cells and promote apoptosis of long-lived plasma cells.[33] Whether there are differences in effectiveness between these two BAFF/APRIL inhibitors is unclear. Moreover, although both are TACI-Ig Fc fusion proteins, telitacicept possesses a more stable structure, and the stalk region of TACI, which has strong affinity for BAFF/APRIL, is more highly conserved in telitacicept than in ataicept.[34] In this study, no serious adverse events or fatal infections were observed.

By analysing the trajectory of changes in the SLEDAI-2K score, we classified our patients into three groups according to their disease activity at baseline and treatment response after 24 weeks. Multivariable analysis was performed to identify factors associated with group 3 (limited response to telitacicept). The results indicated that age had a negative impact on the response to treatment with telitacicept, and consistent with our clinical experience, patients with higher disease activity were more sensitive to biological treatment.

The study had some limitations. First, because of the short approval time for clinical application, only a small group of Chinese patients with SLE could be enrolled. Therefore, the findings of our study may not be applicable to all patients with active SLE. Encouragingly, a global multicentre phase III clinical trial was approved by the European Union and the National Medicines Administration in September 2022. Second, the 24-week follow-up period was relatively short and might have underestimated the effect of telitacicept. Moreover, only a small number of patients (n=21) received 52 weeks of treatment with telitacicept. A longer observation period in a larger cohort is needed to confirm our findings. Third, the proportions of patients presenting with nephritis and haematological abnormalities were relatively high. This could reflect selection bias or be otherwise relevant to the choice of medication by physicians in clinical practice. Generally, patients with lupus and nephritis or haematological abnormalities, especially severe anaemia and thrombocytopenia, show rapid disease progression, and a biologic is likely to be chosen as an additional treatment to control disease activity at this time.

The findings of this observational retrospective study are in line with the results of previous clinical trials of telitacicept in patients with active SLE in a real-world setting. Key findings included the high rate of SRI-4 responders and effectiveness in patients with renal and haematological manifestations of SLE. Further investigations in larger cohorts are needed to confirm our present findings.

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