Efficacy and safety of telitacicept in participants with Sjögren's disease: Results from a multicenter, randomized, double-blind, placebo-controlled, phase 3 clinical study

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Background

- SjD is a chronic systemic autoimmune disease. B-cells play an important role in the pathogenesis
- Telitacicept, a novel fusion protein, dually inhibits BAFF and APRIL, leading to upstream modulation of B-cell survival, downstream reduction of pathogenic antibodies, and re-balancing of dysregulated B-cell immunity (Figure 1). Telitacicept has previously demonstrated efficacy and safety in a phase 2 study in SjD

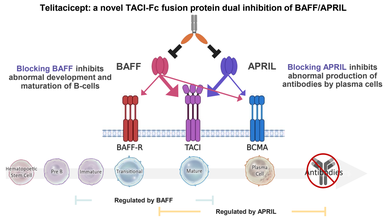

Figure 1: Mechanism of action for telitacicept.

Objective

- To assess the efficacy and safety of telitacicept in adult participants with SjD in a phase 3 study

Methods

- This randomized, double-blind, placebo-controlled, phase 3 study (NCT05673993), conducted in 79 research centers in China, enrolled participants aged 18–70 years who met the 2016 ACR/EULAR criteria for SjD and who were anti-SSA antibody positive with ESSDAI ≥5. The study design is shown in Figure 2

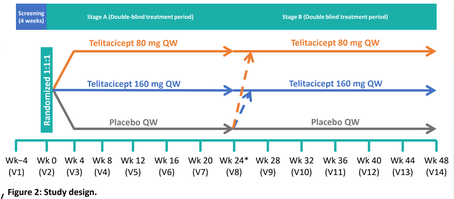

Figure 2: Study design.
*During the period from Week 24–48, participants with inadequate response to treatment in the placebo group could switch to telitacicept 160 mg or telitacicept 80 mg at a ratio of 1:1 under blind conditions.

- The primary efficacy endpoint was changed from baseline in ESSDAI score at Week 24
- The secondary endpoints included change from baseline in ESSDAI score at Week 48; proportion of participants with: ≥3-point reduction from baseline in ESSDAI score; ESSDAI score <5; ≥1-point or ≥15% reduction from baseline in ESSPRI; and change from baseline in ESSPRI total score (all at Week 24 and Week 48). The proportion of STAR responders was also assessed, along with AEs and immunological parameters

Results

- Baseline characteristics are shown in Table 1 and participant flow through the study is detailed in Figure 3
- Primary and secondary endpoint data are presented in Figure 4 and Table 2
- Safety data are presented in Tables 3 and 4

Characteristic, mean (SD)	Telitacicept 160 mg (N=127)	Telitacicept 80 mg (N=127)	Placebo* (N=127)	Total (N=381)
Age, years	45.9 (12.3)	44.6 (12.1)	47.3 (12.8)	46.0 (12.4)
Body mass index, kg/m^2	22.0 (3.2)	22.3 (3.2)	22.2 (3.6)	22.2 (3.3)
Sex, n(%), Male Female	3 (2.4) 124 (97.6)	3 (2.4) 124 (97.6)	4 (3.1) 123 (96.9)	10 (2.6) 371 (97.4)
ESSDAI score	10.0 (3.8)	9.8 (3.5)	10.2 (4.2)	10.0 (3.8)
ESSPRI score	5.1 (1.6)	4.9 (1.7)	5.1 (1.8)	5.0 (1.7)
Disease duration, months	21.39 (36.32)	25.83 (46.90)	19.93 (39.57)	22.38 (41.14)

Table 1: Participant baseline and disease characteristics. *Participants randomized to the placebo group.

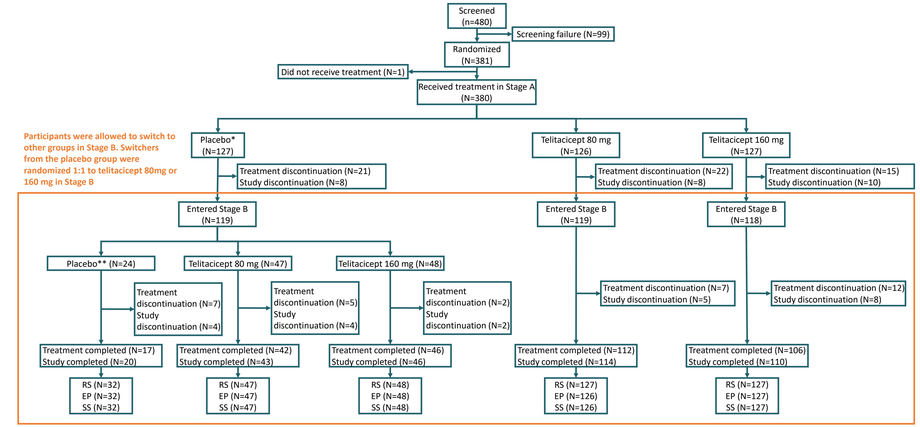

Figure 3: Participant disposition. * Participants randomized to the placebo group; ** Participants who did not switch treatment throughout the trial.

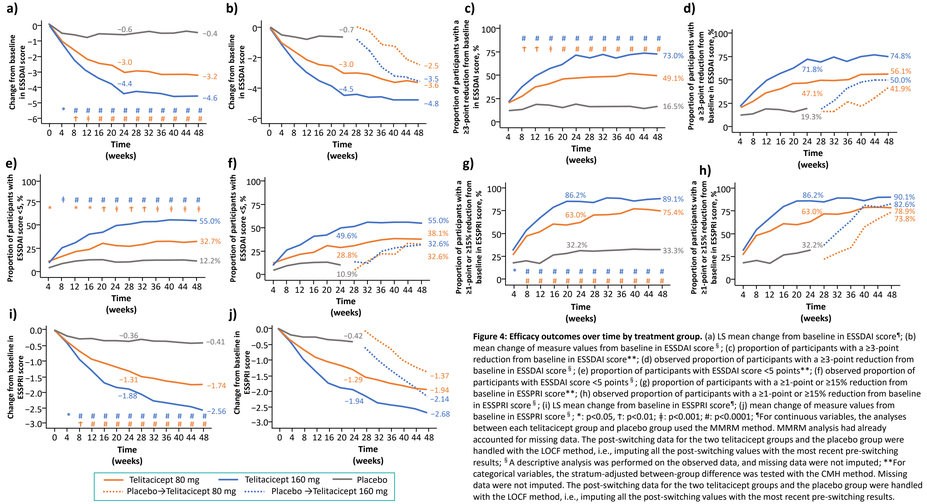

Figure 4: Efficacy outcomes over time by treatment group. (a) LS mean change from baseline in ESSDAI score¶; (b) mean change of measure values from baseline in ESSDAI score §; (c) proportion of participants with a ≥3-point reduction from baseline in ESSDAI score**†; (d) observed proportion of participants with a ≥3-point reduction from baseline in ESSDAI score §; (e) proportion of participants with ESSDAI score <5 points**†; (f) observed proportion of participants with ESSDAI score <5 points §; (g) proportion of participants with a ≥1-point or ≥15% reduction from baseline in ESSPRI score**†; (h) observed proportion of participants with a ≥1-point or ≥15% reduction from baseline in ESSPRI score §; (i) LS mean change from baseline in ESSPRI score¶; (j) mean change of measure values from baseline in ESSPRI score §; *: p<0.05, †: p<0.01; ‡: p<0.001; #: p<0.0001; ¶For continuous variables, the analyses between each telitacicept group and placebo group used the MMRM method. MMRM analysis had already accounted for missing data. The post-switching data for the two telitacicept groups and the placebo group were handled with the LOCF method, i.e., imputing all the post-switching values with the most recent pre-switching results; § A descriptive analysis was performed on the observed data, and missing data were not imputed; **For categorical variables, the stratum-adjusted between-group difference was tested with the CMH method. Missing data were not imputed. The post-switching data for the two telitacicept groups and the placebo group were handled with the LOCF method, i.e., imputing all the post-switching values with the most recent pre-switching results.

Endpoint	Telitacicept 160 mg (N=127)	Telitacicept 80 mg (N=126)	Placebo (N=127)
Primary endpoint			
Change from baseline in ESSDAI score at Week 24, LS mean (95% CI)*	-4.4 (-5.0, -3.8)	-3.0 (-3.6, -2.4)	-0.6 (-1.2, -0.0)
LS mean difference (95% CI); p value	-3.8 (-4.6, -3.0); <0.0001	-2.4 (-3.2, -1.6); <0.0001	
Secondary and other endpoints			
Change from baseline in ESSDAI score at Week 48, LS mean (95% CI)*	-4.6 (-5.3, -4.0)	-3.2 (-3.9, -2.6)	-0.4 (-1.1, 0.2)
LS mean difference (95% CI); p value	-4.2 (-5.1, -3.3); <0.0001	-2.8 (-3.7, -1.9); <0.0001	
Proportion of participants with a ≥3-point reduction in ESSDAI score†			
Week 24, n (%)	84 (71.8%)	56 (47.1%)	23 (19.3%)
Difference in proportion (95% CI); p value	52.3% (41.53%, 63.09%); <0.0001	27.9% (16.77%, 39.06%); <0.0001	
Week 48, n (%)	81 (73.0%)	56 (49.1%)	19 (16.5%)
Difference in proportion (95% CI); p value	56.4% (45.72%, 67.09%); <0.0001	32.7% (21.51%, 43.88%); <0.0001	
Proportion of participants with an ESSDAI score <5 points†			
Week 24, n (%)	58 (49.6%)	34 (28.8%)	13 (10.9%)
Difference in proportion (95% CI); p value	39.2% (29.13%, 49.23%); <0.0001	17.8% (8.20%, 27.41%); 0.0004	
Week 48, n (%)	61 (55.0%)	37 (32.7%)	14 (12.2%)
Difference in proportion (95% CI); p value	43.0% (32.38%, 53.57%); <0.0001	20.6% (10.41%, 30.71%); 0.0001	
Proportion of participants with a ≥1 point or ≥15% reduction in ESSPRI score†			
Week 24, n (%)	100 (86.2%)	75 (63.0%)	38 (32.2%)
Difference in proportion (95% CI); p value	54.0% (43.45%, 64.64%); <0.0001	30.8% (18.69%, 42.96%); <0.0001	
Week 48, n (%)	98 (89.1%)	86 (75.4%)	38 (33.3%)
Difference in proportion (95% CI); p value	55.7% (45.31%, 66.18%); <0.0001	42.1% (30.39%, 53.82%); <0.0001	
Proportion of participants who achieved STAR response			
Week 24, n (%)	96 (82.1%)	68 (57.1%)	29 (24.4%)
Difference in proportion (95% CI); p value	57.7% (47.33%, 68.12%); <0.0001	32.9% (21.13%, 44.59%); <0.0001	
Week 48, n (%); p value	91 (82.7%)	73 (64.6%)	27 (25.0%)
Difference in proportion (95% CI)	57.7% (46.90%, 68.51%); <0.0001	39.5% (27.52%, 51.85%); <0.0001	
Change from baseline in ESSPRI score*			
Week 24, LS mean (95% CI)	-1.88 (-2.13, -1.63)	-1.31 (-1.56, -1.06)	-0.36 (-0.60, -0.11)
LS mean difference (95% CI); p value	-1.52 (-1.87, -1.17); <0.0001	-0.95 (-1.30, -0.60); <0.0001	
Week 48, LS mean (95% CI)	-2.56 (-2.84, -2.27)	-1.74 (-2.03, -1.46)	-0.41 (-0.69, -0.13)
LS mean difference (95% CI); p value	-2.15 (-2.55, -1.75); <0.0001	-1.34 (-1.74, -0.94); <0.0001	

Table 2: Efficacy analysis. The efficacy analysis was based on the estimand population. *This analysis was performed using a MMRM, with group, visit, the group-by-visit interaction, and baseline score as variables in the model; the MMRM analysis model already includes handling of missing data. The post-switching data for the two telitacicept groups and the placebo group were handled with the LOCF method, i.e., imputing all the post-switching values with the most recent pre-switching results. †The stratum-adjusted between-group difference was tested with the CMH method. The post-switching data for the two telitacicept groups and the placebo group were handled with the LOCF method, i.e., imputing all the post-switching values with the most recent pre-switching results. Missing data were not imputed.

Safety

Event, n (%)	Telitacicept 160 mg (N=127)	Telitacicept 80 mg (N=126)	Placebo* (N=127)
TEAEs	122 (96.1)	119 (94.4)	112 (88.2)
TRAEs	107 (84.3)	106 (84.1)	74 (58.3)
TESAEs	11 (8.7)	14 (11.1)	10 (7.9)
TRSAEs	2 (1.6)	5 (4.0)	4 (3.1)
Severe TEAEs	3 (2.4)	5 (4.0)	3 (2.4)
Severe TRAEs	0	1 (0.8)	1 (0.8)
Death	0	0	0

Table 3: Overview of AEs. *AEs in the placebo group were only counted as those occurring during the period when participants were receiving placebo treatment (i.e., from randomization to before crossover).

Common TEAE (incidence ≥10% in any group), n (%)	Telitacicept 160 mg (N=127)	Telitacicept 80 mg (N=126)	Placebo* (N=127)
Upper respiratory tract infection	80 (63.0)	85 (67.5)	74 (58.3)
Urinary tract infection	8 (6.3)	15 (11.9)	7 (5.5)
Cough	11 (8.7)	14 (11.1)	8 (6.3)
Hepatic function abnormal	7 (5.5)	16 (12.7)	7 (5.5)
Injection site reaction	53 (41.7)	51 (40.5)	5 (3.9)
Pyrexia	4 (3.1)	14 (11.1)	4 (3.1)

Table 4: Common TEAEs. *AEs in the placebo group were only counted as those occurring during the period when participants were receiving placebo treatment (i.e., from randomization to before crossover).

Conclusions

- **The primary efficacy endpoint was reached in this study**
- **Compared with placebo, both telitacicept 160 mg and 80 mg demonstrated consistent clinical symptom improvement through 48 weeks and a favorable safety profile; greater improvements were observed in the telitacicept 160 mg group**

AE, adverse event; APRIL, a proliferation-inducing ligand; BAFF, B-cell activating factor; CI, confidence interval; CMH, Cochran–Mantel–Haenszel; EP, estimand population; ESSDAI, EULAR Sjögren's syndrome disease activity index; ESSPRI, EULAR Sjögren's syndrome participant reported index; LOCF, last observation carried forward; LS, least-squares; MMRM, mixed models for repeated measures; RS, randomized set; SjD, Sjögren's disease; SS, safety set; SSA, Sjögren's syndrome type A; STAR, Sjögren's Tool for Assessing Response; SD, standard deviation; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event; TRAE, treatment-related adverse event; TRSAE, treatment-related serious adverse event.

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Disclosures: **Dong Xu:** Nothing to declare; **Shangzhu Zhang:** Nothing to declare; **Lin Qiao:** Nothing to declare; **Li Zhang:** Nothing to declare; **Wenxiang Wang:** Employee of RemeGen Co.; **Lin Li:** Employee of RemeGen Co.; **Binghua Xiao:** Employee of RemeGen Co.; **Jing Zhang:** Employee of RemeGen Co.; **Qing Zuraw:** Employee of Vor Biopharma Inc.; **Jianmin Fang:** Employee of RemeGen Co., Ltd.; **Xiaofeng Zeng:** Nothing to declare.