SAT0106

LONG-TERM SAFETY AND EFFICACY OF SARILUMAB OVER 5 YEARS IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH 1 OR >1 PRIOR TUMOR NECROSIS FACTOR INHIBITOR FAILURES

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Background: A proportion of adult patients with rheumatoid arthritis (RA) are refractory to tumor necrosis factor inhibitors (TNFi), and treatment with subsequent biologics is commonly associated with reduced response. Sarilumab is a human IL-6 receptor inhibitor approved for the treatment of adults with moderate to severely active RA. In the Phase 3 TARGET study (NCT01709578), significant improvements in the signs and symptoms of RA and physical function were shown with sarilumab plus conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) versus placebo in patients refractory to TNFi.

Objectives: To investigate long-term safety and efficacy of subcutaneous sarilumab over 5 years in patients with 1 or >1 TNFi treatment failure prior to their enrollment in TARGET, who continued onto the open-label extension (OLE) study, EXTEND (NCT01146652).

Methods: In the 24-week randomized controlled trial (RCT), patients received placebo, sarilumab 150 mg, or sarilumab 200 mg every 2 weeks (q2w), and were eligible to receive open-label sarilumab 200 mg q2w in the OLE. Dose reduction to 150 mg q2w was permitted per investigator's discretion, or to manage laboratory abnormalities. Safety outcomes are presented for the entire follow-up period from RCT baseline through the OLE. Efficacy was assessed using Clinical Disease Activity Index (CDAI) score.

Results: Of the 546 patients randomized in the RCT, 454 (83%) entered the OLE, of whom 339 had 1 TNFi failure and 115 had >1 TNFi failure. Patients with >1 TNFi failure were older and had a longer duration of RA than patients with 1 TNFi failure (mean age [SD] 55.3 [12.6] and 52.5 [11.9] years, mean RA duration [SD] 13.9 [9.1] and 11.1 [8.8] years, respectively). Kaplan–Meier estimates of the probability of continuation at 5 years were similar between groups: 48% and 54% for patients with >1 and 1 TNFi failure, respectively. At the time of data cut-off (January 15, 2019) 199/546 patients (36%) had discontinued through the RCT and OLE. The rates per 100 patient-years of treatment-emergent adverse events (AEs) and AEs leading to discontinuation for patients with >1 and 1 TNFi failure were 290.6 and 197.9, and 6.5 and 8.1, respectively. Clinical efficacy of sarilumab was sustained in the OLE through 5 years in both groups, regardless of initial treatment in the RCT (Table).

Table Mean CDAI and proportion of CDAI responders

Treatment allocation in 24-week RCT	Placebo +DMARD		Sarilumab 150 mg +DMARD		Sarilumab 200 mg +DMARD	
	(n=156)		(n=145)		(n=153)	
TNFi failures	1	>1	1	>1	1	>1
CDAI, mean (SD)						
RCT baseline	43.7 (12.7)	42.5 (10.3)	42.0 (13.0)	44.3 (13.5)	42.1 (13.5)	48.5 (13.0)
Change after 216 weeks' follow-up	-30.9 (17.5)	-32.6 (15.2)	-33.3 (15.8)	-33.1 (12.7)	-30.3 (13.6)	-36.0 (18.1)
CDAI ≤10, n (%)						
OLE baseline	48 (42)	14 (33)	59 (53)	16 (47)	56 (49)	20 (51)
After 216 weeks' follow-up	24 (21)	10 (24)	29 (26)	7 (21)	29 (25)	8 (21)

*Nonresponder imputation

Conclusion: The long-term safety and efficacy of sarilumab were similar in patients with 1 or >1 prior TNFi failure over 5 years' follow-up. Clinical efficacy could be sustained through 5 years of treatment.

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SAT0107

BIOLOGIC THERAPY WITH RITUXIMAB DECREASES PREVALENCE OF ANXIETY AND DEPRESSION IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Evidence suggests rheumatoid arthritis (RA) confers an increased risk of psychological morbidity, particularly anxiety and depression, which may affect the subsequent management and treatment adherence.^{1,2} Few studies have studied psychological factors over time in RA patients.³

Objectives: To evaluate the prevalence of anxiety and depression in RA patients following rituximab treatment.

Methods: 92 biologics-naïve RA patients [mean (SD) age 49.5 (9.9) years, 78 women; median (IQR) DAS28 5.67 (3.94–8.45); median (IQR) HAQ 1.87 (1.2–3.5)] were followed up for 27 months after commencing and continuing rituximab therapy (1, 2, 3 standard courses). Anxiety and depression, and health-related quality of life (HRQoL) were assessed at baseline, 3, 15 and 27 months using the Hospital Anxiety and Depression Scale (HADS) and the Short Form (SF-36 v.1) Health Survey questionnaire, respectively.

Results: Median anxiety and depression scores decreased significantly between baseline and 3 months and continued to decrease over the 27-month period – Table. The prevalence of depression cases decreased twice from baseline to 27 months (p<0.01), as did the prevalence of anxiety (p<0.01). Patients reported poor baseline HRQoL. SF-36 domain scores substantially rose after 15 and 27 months.

Anxiety, depression, and quality of life

	Baseline	3 months	15 months	27 months
	(n=92)	(n=92)	(n=53)	(n=14)
Anxiety cases (HADS-A score ≥8), n (%)	72 (78.3)	48 (52.2)	24 (45.3)*	5 (35.7)**
Median (IQR) Anxiety score	12.6 (10–15)	8.2 (5–12)*	6.4 (3–10)**	5.5 (3–8)***
Depression cases (HADS-D score ≥8), n (%)	62 (67.4)	50 (54.3)	19 (35.8)*	4 (28.6)**
Median (IQR) Depression score	9.2 (7.8–9.6)	5.6 (3–8)**	4.5 (2–7)**	3.6 (2–6)***
Mean (SD) Mental Health score	42.8 (15.2)	51.2 (18.3)	68.7 (11.2)*	72.9 (10.5)**
Mean (SD) Physical Function score	24.4 (8.3)	32.5 (9.8)	53.8 (10.5)*	54.5 (9.3)*
Mean (SD) Social Function score	48.2 (15.4)	56.8 (25.5)	59.8 (18.7)	65.9 (9.2)*
Mean (SD) General Health score	35.8 (11.2)	48.7 (10.8)	67.8 (8.6)**	75.9 (12.6)**

* p<0.05, ** p<0.01, *** p<0.001 differences between baseline and follow-up

Conclusion: Anxiety and depression levels decrease significantly in RA patients following commencement and continuity of rituximab. B cell-directed therapy for patients with RA helps achieve remission of both anxiety and depression, and improves HRQoL.

References:

- [1] McWilliams LA, Goodvin RD, Cox BJ. Depression and anxiety associated with three pain conditions: results from a nationally representative sample. *Pain* 2004;111:77–83.
- [2] Garcia-Cebrian A, Gandhi P, Demyttenaere K et al. The association of depression and painful physical symptoms: a review of the European literature. *Eur Psychiatry* 2006;21:379–88.
- [3] Overman CL, Bossema ER, van Middendorp H et al. The prospective association between psychological distress and disease activity in rheumatoid arthritis: a multilevel regression analysis. *Ann Rheum Dis* 2012;71:192–7.

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