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SAT0171

REVERSIBLE DECREASES IN ABSOLUTE NEUTROPHIL COUNT (ANC) IN RHEUMATOID ARTHRITIS (RA) PATIENTS (PTS) ON SARILUMAB: COMPARISON OF DOSE DELAY AND DOSE DECREASE VS CONTINUED TREATMENT

J. R. Curtis¹, G. St John², M. Panucci², J. A. Maldonado-Cocco³, ¹Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, United States, ²Regeneron Pharmaceuticals, Inc, Tarrytown, United States, ³Universidad de Buenos Aires, Buenos Aires, Argentina

Background: In randomized studies (RCTs: MOBILITY, TARGET and MONARCH), and open-label [OLE] EXTEND, for those patients who experienced decreases in ANC this typically occurred early after initiating sarilumab. For sarilumab patients with decreased ANC in the RCTs and the OLE, we assessed the outcomes associated with either continuing treatment, decreasing the sarilumab dose or delaying the dose.

Objectives: The effects of a dose decrease (200 to 150 mg), dose delay (>17 days), vs no change in treatment were evaluated in RA patients who experienced decreased ANC while on sarilumab 150 or 200 mg q2w. Outcomes data from patients in MONARCH, MOBILITY and TARGET, and MOBILITY and TARGET patients entering EXTEND were analyzed to compare the three strategies. In MONARCH, patients received sarilumab 200 mg q2w. In MOBILITY and TARGET, patients received sarilumab 150 or 200 mg q2w. In EXTEND, patients were switched to, or initiated on, 200 mg q2w.

Table 1 Outcomes following dose delay, dose decrease, or continued treatment with sarilumab among pts who experienced ANC <1000/mm³ at any time

	RCTs		OLE	
Total treated (N)	1346		1353	
ANC <1000/mm ³ at any time (n, %)	105 (8)		147 (11)	
Pts who did not continue* (n, %)	24 (23)		15 (10)	
Pts that continued, delayed, or decreased sarilumab dose (n, %)	81 (77)		132 (90)	
	Continued without change (n=38)	Dose delay (n=43)	Continued without change (n=31)	Dose delay (n=82)
Normalized on treatment after ≥1 episodes of ANC <1000/mm ³ (n, %)	25 (66)	27 (63)	29 (94)	66 (80)
Median time to normalization for patients with 1 episode (days)	9	15	27	17
Pts with ≥1 episode of ANC <1000/mm ³ who normalized on treatment** (n)	6	6	3	33
Normalized after treatment discontinuation (n, %)	2 (5)	9 (21)	1 (3)	7 (9)
Did not normalize after ≥1 episode of ANC <1000/mm ³ (n, %)	11* (29)	7* (16)	1 (3)	9 (11)
Discontinued treatment due to abnormal ANC after last episode (n)	1	1	1	9
ANC @ last episode (<2000/<1500/<1000/mm ³)	0/1/0	0/0/1	1/0/0	2/6/1
ANC @ last episode (<2000/<1500/<1000/mm ³)	1/4/1			

*10 and % pts enrolled into EXTEND

**ANC<500/mm³ confirmed or had evidence of an infection or had ANC 500 to 1000/mm³ and were discontinued at the investigators discretion.

**pts: ≥1 episode of ANC <1000/mm³ was defined as pts who, at least once, experienced ANC <1000/mm³, then displayed normalized ANC levels and were able to resume treatment, but later experienced ANC <1000/mm³ again.

Methods: In RCTs, patients were required to have baseline neutrophil levels ≥2000/mm³. In RCTs and EXTEND, patients who experienced ANC <500/mm³ (grade 4 [G4] neutropenia) or ≥500 to <1000/mm³ (grade 3 [G3] neutropenia) and signs of infection were required to permanently discontinue treatment. Patients with G3 neutropenia (no signs of infection) temporarily discontinued treatment (or permanently discontinued at the investigators discretion); patients were retested ≤48 hrs after identifying decreased ANC and before the next scheduled dose, and could resume if ANC ≥1000/mm³. In RCTs, patients restarted sarilumab at their randomized dose. In OLE, patients restarted sarilumab at 150 mg q2w, as per the protocol, or otherwise were able to restart at 200 mg q2w at the investigators discretion. In OLE, patients who required a dose decrease to 150 mg q2w sarilumab

received the reduced dose for the remainder of the treatment period. ANC normalization was defined as a return to the patient's baseline or within normal ranges.

Results: Of the 8–11% of patients who experienced ANC <1000/mm³ at any time, 81/105 (RCTs) and 132/147 (OLE) were able to continue or reinstate sarilumab; the majority of patients who experienced ANC <1000/mm³ one or more times displayed normalized ANC levels and continued treatment when ANC ≥1000/mm³ (25/38 in RCTs; 29/31 in OLE). The majority of patients who dose delayed (27/43 in RCTs; 66/82 in OLE) or dose decreased (51/62, OLE) before ANC normalized resumed treatment.

Conclusions: More than three-quarters of patients who discontinued treatment until ANC normalized were able to reinstate at their randomized dose (RCT), or at the open-label study dose (200 mg q2w; OLE) or were able to resume at the lower dose (150 mg q2w; OLE).

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SAT0172

LONG-TERM EFFICACY WITH 5-YEAR-RADIOGRAPHIC RESULTS AND SAFETY OF SARILUMAB IN COMBINATION WITH csDMARDs IN PATIENTS WITH RHEUMATOID ARTHRITIS

G. R. Burmester¹, Y. Lin², G. St John³, S. Wang², J. J. Gomez-Reino⁴, J. A. Maldonado-Cocco⁵, J. C. Salazar⁶, D. van der Heijde⁷, M. C. Genovese⁸.

¹Charité – University Medicine Berlin, Berlin, Germany, ²Sanofi Genzyme, Bridgewater, NJ, ³Regeneron Pharmaceuticals, Inc, Tarrytown, NY, United States, ⁴IDIS, Complejo Hospitalario Universitario de Santiago, Santiago, Spain, ⁵School of Medicine, Buenos Aires University, Buenos Aires, Argentina, ⁶Clinical Research at Riesgo de Fractura S.A, CAYRE, Bogotá, Colombia, ⁷Leiden University Medical Center, Leiden, Netherlands, ⁸Stanford University Medical Center, Palo Alto, CA, United States

Background: Long-term data are being collected on sarilumab in combination with csDMARDs in patients with RA originally enrolled in six trials (TARGET, NCT01709578; MOBILITY, NCT01061736; NCT01764997; NCT01768572; NCT02057250; NCT01217814) including those who continued into extension trials.

Objectives: To assess efficacy and safety of long-term treatment with sarilumab plus csDMARDs in patients with RA.

Methods: Long-term efficacy and safety data were available in patients enrolled in placebo-controlled trials of sarilumab 150 or 200 mg sc q2w who continued into the open-label EXTEND trial of sarilumab 200 or 150 mg sc q2w (NCT0146652). Safety data were evaluated in 2887 patients who received ≥1 dose of sarilumab sc in combination with csDMARDs.

Results: Clinical and radiographic efficacy of sarilumab plus csDMARDs was maintained over 5 years' follow-up (table 1; figure 1). Initial treatment with either dose of sarilumab was associated with significantly better radiographic outcome than placebo. Initial treatment with sarilumab 200 mg portended better radiographic outcome than sarilumab 150 mg or placebo. Mean duration of sarilumab treatment in the safety population was 2.6 years (max 6.8), representing 7412 cumulative patient-years of exposure. Incidence rate of adverse events of special interest (AESIs; table 2) was generally stable over >5 years' treatment, with no signal for increased rate of any AESI (including serious AEs and serious infection) over time. Incidences of injection site reaction, ANC <1 Giga/L, & elevated ALT declined over time.