although neutropenia was more frequent with sarilumab. Safety of sarilumab was generally comparable in monotherapy and combination studies; monotherapy was associated with fewer ALT elevations >3 × ULN compared with combination therapy: MONARCH, 3%; MOBILITY, 8%; TARGET, 4%.
Conclusions: Sarilumab 200 mg q2w + csDMARDs significantly reduced disease activity and improved physical function to a similar extent regardless of population (MTX-IR or TNF-IR) and as monotherapy. Safety profile of sarilumab was generally comparable across all 3 trials, with monotherapy resulting in fewer ALT elevations.
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SAT0181 LOW DOSE INTERLEUKIN-2 COMBINED WITH TOCILIZUMAB SELECTIVELY INCREASES REGULATORY T CELLS HELPING REFRACTORY RHEUMATOID ARTHRITIS PATIENTS ACHIEVE REMISSION MORE RAPIDLY

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Background: Rheumatoid arthritis (RA) is a prevalent chronic autoimmune inflammatory disease. Its pathogenesis is closely associated with a failure of endogenous immune tolerance that caused by the imbalance of pro-inflammatory T helper 17 (Th17) cells and anti-inflammatory regulatory T (Treg) cells. Low-dose Interleukin-2 (IL-2) has been showed to induce both Th17 and Treg cells' expansion and activation while IL-6 antagonist Tocilizumab suppresses the differentiation of Th17, which is expected to control the development of RA.
Objectives: To study the influence of the combination of IL-2 and Tocilizumab on T cells subgroups and its clinical efficacy and safety on refractory RA.
Methods: Total 50 RA patients with low Treg cells, who had been treated with glucocorticoids and DMARDs for over 6 months, were divided into three groups randomly. Patients in non-IL-2 group (n=15) were still given conventional glucocorticoids and DMARDs. Patients in IL-2 group (n=26) were not only given those treatments, but injected subcutaneously human IL-2 (aldesleukin) at 50 WIU per day for a 5 day course. Patients in IL-2 and Tocilizumab group (n=9) were not only received the treatment like IL-2 group, but also treated with Tocilizumab at the dosage of 160mg during the day 1 and day 3. The demographic features, clinical manifestations and laboratory indicators were compared before and after the treatment.
Results: There was no difference among all groups in gender, age and course of the disease (p >0.05). The ratios of Th1/Th2 and Th17/Treg were significant correlated with ESR, the number of tender or swollen joints and DAS28-ESR (p<0.05) in all three groups of patients. After treatment, the number of Th17 cells and Treg cells was significantly increased in IL-2 group (p<0.01). In IL-2/Tocilizumab group after the treatment, the number of Treg cells were also significantly increased (p<0.05), but not the Th17 cells (p>0.05), leading to a quickly decrease in their ratio (p<0.05). Before the treatment, there was no difference in clinical manifestations among all three groups (p>0.05), but compared with non-IL-2 group, there was a significantly decrease in the number of tender joints (p<0.01) or swollen joints (p<0.05) and DAS28-ESR (p<0.01) in IL-2 group and IL-2/Tocilizumab group after the treatment. Patients in IL-2/Tocilizumab group had better clinical manifestations' remission although no significant difference compared with IL-2 group (p>0.05). There was no difference in blood routine, liver and renal functions both before and after the treatment among all groups (p>0.05).
Conclusions: IL-2 can effectively increase the level of Treg cells as well as that of Th17 to some degree; while IL-2 combined with Tocilizumab only effectively expand Treg cell number without Th17 increasing, thereby quickly recovers the balance of Th17 and Treg cells. This combination selectively stimulate Treg Cells leading to induce autoimmune tolerance, and seems to help RA patients achieve remission in a rapid way without over-treatment and evaluated side effect, though the long term benefits of this therapy are required to further study in more patients.
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SAT0182 SIRUKUMAB LEADS TO SIGNIFICANT AND CLINICALLY MEANINGFUL IMPROVEMENTS IN HEALTH-RELATED QUALITY OF LIFE THAT MEET OR EXCEED NORMATIVE VALUES IN PATIENTS WITH RHEUMATOID ARTHRITIS REFRACTORY TO TNF INHIBITORS IN POST HOC ANALYSES OF A PHASE 3 TRIAL

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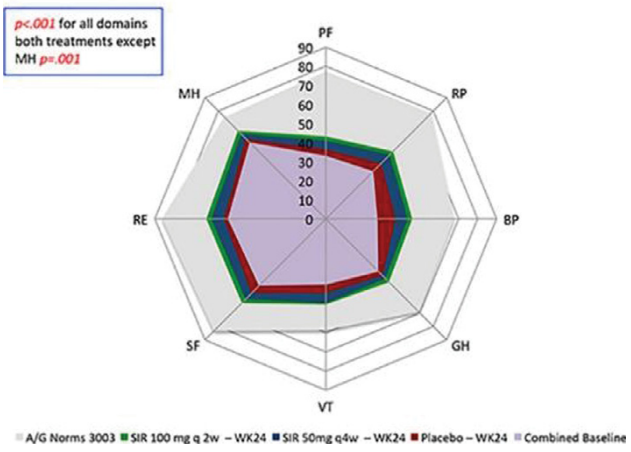
Background: Patients (pts) with rheumatoid arthritis (RA) experience reduced health-related quality of life (HRQoL). Sirukumab (SIR) is an anti–interleukin-6 (IL-6) monoclonal antibody.
Objectives: These post hoc analyses evaluated improvements over time in HRQoL relative to an age/gender-matched normative population in RA pts with inadequate responses to tumor necrosis factor inhibitors (TNF-IR) from the phase 3 SIRROUND-T trial.
Methods: 878 pts received SIR 50mg every 4 weeks (q4w), SIR 100mg every 2 weeks (q2w), or placebo (pbo) q2w. Health-related physical/emotional well-being were measured at baseline (BL) and Wk 24 by the 36-item Short Form Questionnaire (SF-36), fatigue by Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue (FACIT-F), and physical function by Health Assessment Questionnaire-Disability Index (HAQ-DI).
Results: SF-36 physical and mental component summary (PCS and MCS) mean scores at BL for pbo, SIR 50mg q4w, and 100mg q2w indicated substantial impairment (PCS: 33.2, 31.8, and 32.4; MCS: 41.9, 41.2, and 42.1). Significantly greater improvements from BL were reported at Wk 24 with SIR 50mg q4w and 100mg q2w vs pbo in PCS (4.8 and 5.1 vs 1.7) and MCS (3.9 and 4.0 vs 1.1) mean scores (all P<0.001), exceeding the minimum clinically important difference (MCID) of 2.5. Significantly greater least squares mean changes in the 8 SF-36 domain raw scores were reported with both doses of SIR vs pbo at Wk 24; all were >MCID of 5.0 (Table; Figure). More pts receiving SIR 50mg q4w or 100mg q2w reported SF-36 domain scores ≥normative values (ranges: 11–34% and 13–42%) vs pbo (range: 6–29%). For pbo, SIR 50mg q4w, and SIR 100mg q2w, BL FACIT-F scores were 26.0, 24.2, and 25.2; clinically meaningful improvements ≥MCID (4 points) were reported by 54.3 and 51.4% of pts receiving SIR 50mg q4w and 100mg q2w vs 33.7% with pbo (P<0.001). Numerically greater percentages of pts reported scores ≥normative values with both doses of SIR vs pbo (27 and 28% vs 16%). BL HAQ-DI scores were 1.57, 1.65, and 1.61 with pbo, SIR 50mg q4w, and 100mg q2w. Clinically meaningful improvements (change of ≤-0.22) were reported by significantly higher proportions of pts receiving SIR 50mg q4w (52.2%) or 100mg q2w (54.8%) vs pbo (37.4%; P<0.001). Numerically more pts reported HAQ-DI scores ≥normative values with SIR 50mg q4w and 100mg q2w vs pbo (13 and 16% vs 9%).

Table 1. Improvements in SF-36 Domain Scores at Wk 24 (all P<0.001)

Domain	LSM change SIR 50mg q4w	LSM change SIR 100mg q2w	LSM change pbo
Physical function	9.38	10.75	0.47
Role-physical	12.85	13.52	5.03
Bodily pain	17.66	17.51	7.46
General health	6.81	7.76	1.57
Vitality	10.10	9.68	4.14
Social function	12.40	11.75	3.68
Role-emotional	9.29	9.86	0.42
Mental health	6.73	7.96	2.10

LSM, least squares mean.

Figure. SF-36 domains at Wk 24 for SIR 50mg q4w and SIR 100mg q2w



Conclusions: In TNF-IR RA pts, SIR treatment resulted in greater and clinically meaningful improvements in HRQoL vs pbo that met or exceeded population normative values, with similar results for SIR 50mg q4w and 100mg q2w.
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