Tocilizumab efficacy and safety in rheumatoid arthritis patients after inadequate response to disease-modifying anti-rheumatic drugs or anti-tumor necrosis factor

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BACKGROUND: Tocilizumab (TCZ) is a humanized anti-human IL-6R antibody, a novel therapy for rheumatoid arthritis (RA) patients who fail treatment with disease modifying anti-rheumatic drugs (DMARDs) or anti-tumor necrosis factor (anti-TNFs).

OBJECTIVE: To assess the safety and efficacy of TCZ monotherapy or in combination with non-biologic DMARDs or anti-TNFs in moderate to severe active RA.

DESIGN: Prospective, phase III, multi-center, open-label, single arm, 24-week trial.

SETTING: Three centers in Saudi Arabia.

PATIENTS AND METHODS: The study included consecutive RA patients infused with TCZ (8 mg/kg) over 60 minutes every 4 weeks (up to 6 times), either alone or with non-biologic DMARDs. Patients were followed for 24 weeks. Patients with good/moderate European League Against Rheumatism responses, continued on TCZ as long as commerically available or for 1 year.

MAIN OUTCOME MEASURE(S): Disease activity measured by DAS28 score.

RESULTS: Of 28 patients enrolled from 2 November 2011 to 12 May 2013 (18 months), 21 completed (77.8%) and 7 (25%) discontinued TCZ therapy. One patient was excluded from the intent-to-treat analysis. Efficacy analysis showed a significant difference (P<.0001) in the Disease Activity Score based on 28 joints and on swollen and tender joint counts. Three (10.7%) patients experienced at least one AE that was considered related to study drug (one probably and two possibly). Only one (3.6%) patient reported a severe adverse event (neutropenia and thrombocytopenia). No adverse events led to dose modification or death.

CONCLUSION: TCZ monotherapy or in combination with non-biologic DMARDs resulted in a significant effect on the endpoints in moderate to severe RA in Saudi Arabia, which is consistent with other published reports.

LIMITATIONS: No information on tapering of steroid therapy, lack of follow-up data of all 28 patients, lack of data on long-term effects of TCZ on lipid levels and the need for statins. (ClinicalTrials.gov identifier: NCT01326962).
PATIENTS AND METHODS

Males or non-pregnant, non-nursing females, aged ≥18 years, diagnosed with moderate to severe RA (Disease Activity Score Based on 28 Joints [DAS28] >3.2 at screening) for 6 months, who received one nonbiologic DMARD and/or anti-TNF therapy, at a stable dose for 8 weeks with inadequate clinical response or received oral corticosteroid at a stable dose of ≥25 days prior to treatment were included in the study.

Exclusion criteria included:
- Major surgery more than 8 weeks prior to screening or planned major surgery within 6 months following enrollment.
- Rheumatoid autoimmune disease or inflammatory joint disease excluding RA, interstitial pulmonary fibrosis (class IV as defined by the American College of Rheumatology [ACR]);
- Current or prior treatment with anakinra, calcineurin inhibitors, mycophenolate mofetil, mycophenolic acid sodium within 4 weeks or 5 half-lives of an investigational agent before screening; cell-depleting therapies, abatacept, TCZ alkylation agents, leflunomide + MTX (coadministration increased risk of hepatotoxicity), intravenous gamma globulin, plasmapheresis, Prosorba column within 6 months before baseline and intra-articular or parenteral corticosteroids within 6 weeks prior to baseline, immunization with a live attenuated vaccine within 4 weeks prior to baseline or a history of severe allergic or anaphylactic reactions to humanized or murine monoclonal antibodies;
- Clinically significant abnormality on chest x-ray, serum creatinine: >142 µmol/L (females), >168 µmol/L (males), active renal disease; alanine transaminase (ALT) or aspartate transaminase (AST) >1.5 upper limit of normal (ULN), platelet count <100×10⁹/L, hemoglobin <85 g/L, white blood cell count <1.0×10⁹/L, absolute neutrophil count <1×10⁹/L, absolute lymphocyte count <0.5×10⁹/L, positive hepatitis B surface antigen (HBsAg) or hepatitis C antibody, total bilirubin >ULN and triglycerides >10 mmol/L at screening;
- History of or active serious uncontrolled disease or body weight >150 kg;
- History of or active primary or secondary immunodeficiency, malignant disease diagnosed within the previous 5 years, latent or active tuberculosis requiring treatment within the previous 3 years;
- Alcohol, drug or chemical abuse within 6 months prior to screening, neuropathies or other painful conditions that might interfere with pain evaluation, or lack of peripheral venous access.

Study design

This phase III, multi-center, open-label, single arm trial was conducted at three centers in Saudi Arabia. The protocol was approved by the institutional review boards, ethics committees and Saudi regulatory authorities of King Fahd Medical City, Riyadh, King Fahd Specialist Hospital, Damman and King Abdulaziz University Hospital, Jeddah. Written informed consent from each patient was obtained as per the Declaration of Helsinki. All patients received TCZ (8 mg/kg) IV infusion over 60 minutes, once every 4 weeks up to 6 times (Weeks 1, 4, 8, 12, 16, 20), monotherapy or in combination with nonbiologic DMARDs or anti-TNF therapy. Patients had a follow-up visit every 4 weeks with a final follow-up visit at Week 24. Patients who achieved good/moderate EULAR responses continued to take TCZ until no longer available commercially or 1 year treatment, whichever came first.

The concomitant non-biologic DMARD therapy dose was stabilized for 8 weeks or later and the oral corticosteroid dose was stabilized for 25 or more of 28 days, prior to TCZ initiation. To minimize potential MTX toxicity, all patients received either folic acid or leucovorin. Medications that were individually dose-adjusted and metabolized via CYP450, 3A4, 1A2, or 2C9 were monitored to maintain therapeutic effect. Lipid parameters were assessed 4 to 8 weeks following initiation of TCZ.

Study endpoints

The primary endpoint was disease activity as measured by DAS28 score, number (%) of patients achieving remission (DAS28 <2.6) at every visit and time to DAS28 remission. EULAR moderate represents a DAS28-joint assessment for swelling and tenderness of >5.1 and an improvement from 0.6 to 1.2; good represents a DAS28 score of <3.2 and an improvement of >1.2; low disease activity represents a DAS28 score of <3.2; remission represents a DAS28 score of <2.6.

Secondary endpoints include:
- ACR responses i.e., number (%) of patients that achieved improvement in RA represented by: ACR20, ACR70, ACR50 which indicated by a 20%, 70% and 50% improvement in tender joint (TJ) and swollen joint counts of >50% for 28 joints.

Safer and Efficacy of TCZ
joint (SJ) counts respectively, plus improvement in 3 of the 5 following measurements: patient pain assessment, patient global assessment, physician global assessment, patient self-assessed disability and acute-phase reactant (ESR) at every visit.

- The proportion of patients that achieved improvements in physical function response as measured by Health Assessment Questionnaire by at least by 0.22 units from baseline in the Health Assessment Questionnaire Disability Index (HAQ DI), improvement in medical Short Form Health Survey (SF-36) score, changes in patient fatigue assessed using the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score and reduction in fatigue as measured using the Fatigue Visual Analog Scale (VAS) at every visit
- Adverse events (AEs), serious adverse events (SAEs) and laboratory data (C-reactive protein [CRP] and erythrocyte sedimentation rate [ESR]) at every visit including follow-up.

### Statistical analysis

A moderate effect size of $w=0.53$ was considered for a matched paired $t$ test with a significance level of 5% and a power of 80% to calculate a sample size of 30 patients for detecting a drop in DAS28 scores. Taking a 10% drop-out rate for any reason into consideration, the enrolment figure could have been rounded up to 35 eligible patients. The primary efficacy analysis was based on the intent-to-treat (ITT) population (all patients who received at least one dose of TCZ) and repeated in the per-protocol (PP) population (patients with protocol violations excluded) to confirm the overall study results. All safety analyses were based on the safety population (all patients who received at least one dose of TCZ).

Change in DAS28 was assessed using the Friedmann test (non-parametric repeated measures ANOVA) model with baseline DAS28. EULAR response (DAS28 and ACR20, 50, 70, 90 improvement rates were calculated using a Cochran-Mantel-Haenszel test at every visit. $P$ values apply to comparisons of visits up to Visit 12. Quality of life, according to the HAQ DI, SF-36 and FACIT fatigue score were summarized by descriptive statistics. No changes from the planned analysis occurred.

### RESULTS

#### Demographics and baseline characteristics

Of 28 patients enrolled from 2 November 2011 to 12 May 2013 (18 months), 21 completed (75.0%) and 7 discontinued TCZ therapy. The ITT and safety analysis included 28 patients. The major reason for discontinuation was loss to follow up in 3 patients (10.7%). One withdrew due to an adverse event and one withdrew consent. At Visit 14, the drop in patient numbers was due to the nonavailability of TCZ.

The majority of patients were females (n=25, 89.3%). The mean age (and standard deviation) of all participants was 46 (12.4) years, the height was 157 (8.5) cm, the mean weight 78.86 (14.3) kg and the mean body mass index (BMI) 31.9 (5.5). Most patients in this study were taking DMARDs, mainly methotrexate (12/28, 42.9%). The most concomitantly used non-RA medication was paracetamol (n=2, 7.1%) and the most common RA medication was prednisolone (n=7, 25%). The major abnormality at baseline in the TJ and SJ was the wrist: 28 (100%) and 26 patients (92.9%) reported abnormalities in SJ in the left and right side, respectively; and 23 (82.1%) and 22 (78.6%) reported abnormalities in SJ in the left and right side, respectively. Other abnormalities were related to knees, MCP2 and MCP3 (monocyte chemotactic protein). The most common concurrent disease was hypertension in 3 (10.7%) patients.

#### Efficacy

A comparison of the DAS scores between visits showed an effect on the DAS28 score, and SJ and TJ counts ($P<.0001$) (Table 1). The mean (SD) time to response for clinically meaningful improvement in DAS scores was 189 (7.05) days. Comparison of EULAR response between visits showed a significant association between visit and EULAR response ($P<.0001$) (Table 2). The majority of patients reported a clinically meaningful improvement in DAS28 score at Visit 6 (88%) and the least at Visit 14 (66.7%). The proportion of patients with disease remission was lowest at Visit 3 (11.1%) and highest at Visit 10 (81.8%). Low disease activity was reported by fewer patients at each post-baseline visit (Table 3).

The mean time to response for a clinically meaningful improvement in DAS28 (the number of days from the first date of treatment to the date of response or event), and was 155 days (standard deviation, 7.04). The ACR response between visits indicated a significant association between visits and ACR response ($P<.0001$) (Table 4). At Visit 3, a majority of patients achieved ACR50 (40.7%) while at Visits 4 and 5 the majority of patients achieved ACR70 (40.0% and 56.0%, respectively), and at other scheduled visits (up to visit 12) the majority of patients achieved ACR90. Achievement of clinically meaningful HAQ responses (decrease of at least 0.22 units from baseline in the HAQ response) ranged from 9.5% to 28% over the visits. FACIT and VAS scores decreased versus baseline at all visits. The number of pa-
### Table 1. Comparison of DAS28 scores and swollen and tender joints between visits in the intent-to-treat population.

| Statistics        | Baseline n=28 | Visit 3 n=27 | Visit 4 n=26 | Visit 5 n=25 | Visit 6 n=25 | Visit 7 n=25 | Visit 8 n=23 | Visit 9 n=21 | Visit 10 n=22 | Visit 11 n=21 | Visit 12 n=17 | Visit 13 n=13 | Visit 14 n=6 | P       |
|-------------------|---------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|------------|---------|
| **DAS28 Score**   |               |              |              |              |              |              |              |              |              |              |              |              |           |         |
| Median            | 5.4           | 3.5          | 2.8          | 2.2          | 1.9          | 1.7          | 1.7          | 2.0          | 2.3          | 2.1          | 1.5          | <.0001       |           |         |
| Min, Max          | 4.1, 7.9      | 1.9, 5.7     | 0.9, 5.5     | 1.3, 4.2     | 0.4, 4.6     | 0.5, 3.4     | 0.5, 3.7     | 0.0, 3.2     | 0.1, 5.0     | 1.0, 4.4     | 0.1, 3.6     | 0.1, 5.6     |           |         |
| **Swollen joint count** |               |              |              |              |              |              |              |              |              |              |              |              |           |         |
| Median            | 4.0           | 2.0          | 2.0          | 1.0          | 0.0          | 0.0          | 0.0          | 0.0          | 0.0          | 0.0          | 0.0          | 0.0          | 0.0        | <.0001  |
| Min, Max          | 0.0, 26.0     | 0.0, 8.0     | 0.0, 7.0     | 0.0, 10.0    | 0.0, 4.0     | 0.0, 2.0     | 0.0, 4.0     | 0.0, 1.0     | 0.0, 4.0     | 0.0, 1.0     | 0.0, 2.0     | 0.0, 2.0     |           |         |
| **Tender joint count** |               |              |              |              |              |              |              |              |              |              |              |              |           |         |
| Median            | 10.0          | 6.0          | 2.0          | 0.5          | 0.0          | 0.0          | 0.0          | 0.0          | 1.0          | 1.0          | 0.0          | 0.0          | 0.0        | <.0001  |
| Min, Max          | 2.0, 28.0     | 0.0, 26.0    | 0.0, 9.0     | 0.0, 11.0    | 0.0, 12.0    | 0.0, 4.0     | 0.0, 6.0     | 0.0, 12.0    | 0.0, 12.0    | 0.0, 8.0     | 2.0          | 2.0, 14.0    |           |         |

P value for comparison of visits up to Visit 12.

### Table 2. Comparison of EULAR response between visits in the intent-to-treat population.

| EULAR Response | Visit 3 n=27 | Visit 4 n=26 | Visit 5 n=25 | Visit 6 n=25 | Visit 7 n=25 | Visit 8 n=23 | Visit 9 n=21 | Visit 10 n=22 | Visit 11 n=21 | Visit 12 n=17 | Visit 13 n=13 | Visit 14 n=6 | P       |
|----------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|---------|
| Good response  | 10 (40.0)    | 15 (65.2)    | 18 (90.0)    | 21 (95.5)    | 21 (100.0)   | 19 (95.0)    | 19 (94.7)    | 19 (95.0)    | 14 (82.4)    | 11 (91.7)    | 9 (81.8)     | 4 (80.0)    | <.0001  |
| Moderate response | 13 (52.0)   | 7 (30.4)     | 2 (10.0)     | 1 (4.5)      | 0 (0.0)      | 1 (5.0)      | 1 (5.0)      | 3 (17.6)     | 1 (8.3)      | 2 (18.2)     | 0 (0.0)      | <.0001       |         |
| No response    | 2 (8.0)      | 1 (4.3)      | 0 (0.0)      | 0 (0.0)      | 0 (0.0)      | 0 (0.0)      | 0 (0.0)      | 0 (0.0)      | 0 (0.0)      | 0 (0.0)      | 1 (20.0)     |           |         |

Values are n (%). EULAR: European League Against Rheumatism.

### Table 3. Number and percentage of patients in DAS28 categories in intent-to-treat population.

| DAS28 categories         | Visit 3 n=27 | Visit 4 n=26 | Visit 5 n=25 | Visit 6 n=25 | Visit 7 n=25 | Visit 8 n=23 | Visit 9 n=21 | Visit 10 n=22 | Visit 11 n=21 | Visit 12 n=17 | Visit 13 n=13 | Visit 14 n=6 |
|--------------------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|------------|
| Low disease activity (>2.6 - <=3.2) | 7 (25.9) | 9 (34.6) | 7 (28.0) | 7 (28.0) | 4 (16.0) | 3 (13.0) | 3 (14.3) | 2 (9.1) | 2 (9.5) | 4 (23.5) | 1 (7.7) | 0 |
| Remission (<2.6)          | 3 (11.1) | 7 (26.9) | 12 (48.0) | 14 (56.0) | 17 (68.0) | 16 (69.6) | 15 (71.4) | 18 (81.8) | 13 (61.9) | 7 (41.2) | 8 (61.5) | 4 (66.7) |
| Clinically meaningful improvement* | 21 (77.8) | 20 (76.9) | 20 (80.0) | 22 (88.0) | 21 (84.0) | 20 (87.0) | 19 (90.5) | 20 (90.9) | 17 (81.0) | 12 (70.6) | 11 (84.6) | 4 (66.7) |

Values are n (%). *A clinically meaningful improvement in DAS28 was a reduction of at least 1.2 units from baseline.
patients with abnormal values for both CRP and ESR are presented in Table 5.

**Safety**

Four (14.3%) patients experienced at least one AE considered by the investigator as related to study medication (two with probable relation, two with possible relation). Three patients reported mild AEs followed by moderate and severe AEs (1 each). Only one patient (3.6%) reported an SAE, namely neutropenia and thrombocytopenia. No AE led to dose modification or death (Table 6). Analysis of laboratory data and vital signs showed no significant results. The majority of the patients reported abnormalities in blood urea nitrogen (BUN) followed by lactate dehydrogenase (LDH). The proportion of patients who reported abnormal ALT and AST was very low at all visits. The highest proportion of patients that reported abnormal ALT levels was in the range of 22% to 27% for Weeks 4 to 16.

**DISCUSSION**

This is the first study in Saudi Arabia demonstrating the efficacy and safety of TCZ in patients with an inadequate response to TNF antagonist treatment. Treatment with TCZ, especially at the 8 mg/kg dose, and non-biologic DMARD or anti-TNF, provided a rapid and sustained improvement in RA symptoms and was well tolerated. TCZ is registered and available in Saudi Arabia.

In this study, most patients reported a clinically meaningful improvement in DAS28 scores at Visit 6 (88.0%)

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### Table 4. Number and percentage of patients in ACR categories in the intent-to-treat population.

| ACR categories | Visit 3 n=27 | Visit 4 n=26 | Visit 5 n=25 | Visit 6 n=25 | Visit 7 n=25 | Visit 8 n=23 | Visit 9 n=21 | Visit 10 n=22 | Visit 11 n=21 | Visit 12 n=17 | Visit 13 n=13 | Visit 14 n=6 |
|----------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
| Patients having no improvement | 3 (1.1) | 1 (4.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (16.7) |
| Patients achieved ACR20 | 3 (11.1) | 4 (16.0) | 1 (4.0) | 1 (4.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (9.5) | 1 (5.9) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Patients achieved ACR50 | 11 (40.7) | 7 (28.0) | 1 (4.0) | 1 (4.0) | 2 (8.3) | 1 (4.3) | 1 (4.5) | 0 (0.0) | 0 (0.0) | 1 (8.3) | 1 (16.7) | 0 (0.0) |
| Patients achieved ACR70 | 7 (25.9) | 10 (40.0) | 14 (56.0) | 8 (32.0) | 3 (12.5) | 6 (26.1) | 5 (22.7) | 6 (27.3) | 6 (28.6) | 5 (29.4) | 5 (41.7) | 0 (0.0) |
| Patients achieved ACR90 | 2 (7.4) | 3 (12.0) | 8 (32.0) | 13 (52.0) | 18 (75.0) | 15 (65.2) | 14 (63.6) | 14 (63.6) | 12 (57.1) | 10 (58.8) | 5 (41.7) | 3 (50.0) |
| Patients not assessed | 1 (3.7) | 1 (4.0) | 1 (4.0) | 1 (4.0) | 2 (8.3) | 1 (4.3) | 1 (4.5) | 1 (4.8) | 1 (5.9) | 2 (16.7) | 2 (33.3) | 0 (0.0) |

Values are n (%).

### Table 5. Number and percentage of patients outside normal ranges for erythrocyte sedimentation rate and C-reactive protein in intent-to-treat population.

| Parameter (unit) | Baseline n=28 | Visit 3 n=27 | Visit 4 n=26 | Visit 5 n=25 | Visit 6 n=25 | Visit 7 n=25 | Visit 8 n=23 | Visit 9 n=21 | Visit 10 n=22 | Visit 11 n=21 | Visit 12 n=17 | Visit 13 n=13 | Visit 14 n=6 |
|------------------|---------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
| CRP (mg/L)       | 16 (59.3)     | 8 (29.6)     | 7 (25.9)     | 2 (7.4)      | 5 (18.5)     | 6 (22.2)     | 7 (25.9)     | 7 (25.9)     | 9 (33.3)     | 9 (33.3)     | 8 (29.6)     | 7 (25.9)     | 2 (7.4)     |
| ESR (mm/hr)      | 13 (48.1)     | 5 (18.5)     | 3 (11.1)     | 1 (3.7)      | 0 (0.0)      | 1 (3.7)      | 2 (7.4)      | 3 (11.1)     | 0 (0.0)      | 0 (0.0)      | 0 (0.0)      | 2 (7.4)      | 1 (3.7)     |

Values are n (%).
Table 6. Summary of adverse events.

| Incidence of adverse events | Tocilizumab (n=28) |
|----------------------------|--------------------|
| Patients with serious adverse events | 1 (3.6) |
| Deaths | 0 (0.0) |
| Patients with study drug-related adverse event | 3 (10.7) |
| Remote | 1 (3.6) |
| Possible | 2 (7.1) |
| Probable | 1 (3.6) |
| Patients with any adverse event | 3 (10.7) |
| Mild | 3 (10.7) |
| Moderate | 1 (3.6) |
| Severe | 1 (3.6) |

Values are n (%).

and the least improvement at Visit 14 (66.7%). The proportion of patients with disease remission was lowest at Visit 3 (11.1%) and highest at Visit 10 (81.8%). The mean time to response for clinically meaningful improvement in DAS scores was 189 days. Thus, patients responded regardless of a recently failed anti-TMF treatment or the number of failed treatments. This is consistent with the results of the RADIATE study wherein DAS28 remission rates at week 24 were dose related, being achieved by 30.1% of the TCZ 8 mg/kg group (P<.001 versus control). In addition, a significantly higher proportion of patients treated with TCZ 8 mg/kg plus MTX achieved a DAS28 remission by 52 weeks compared with the control (47.2% versus 7.9%, respectively, P<.0001).7

The number of patients with a clinically meaningful HAQ response ranged from 9.5% to 28% over the visits. Overall, there was a decrease in HAQ score versus baseline. The fatigue and VAS scores showed a decrease in the scores at all visits compared with baseline. The number of patients with abnormal CRP (n=16) and ESR (n=13) at baseline was reduced drastically (CRP [n=2], ESR [n=1]). This outcome was similar to the results from other TCZ trials wherein CRP concentrations and ESR normalized by week 2 of treatment with TCZ 8 mg/kg and remained within the normal range until the end of the study (P<.0001 versus baseline).4,6

At visit 3, a majority of patients achieved ACR50, while at Visits 4 and 5, the majority achieved ACR70, and at other scheduled visits (up to visit 12) a majority of patients achieved ACR 90. In the OPTION study, ACR50 and ACR70 responses were also significantly higher in TCZ 8 mg/kg group compared to the placebo group (ACR50 44%, and 11%, respectively, P<.001; ACR70 22%, and 2%, respectively, P<.001). Collectively, the efficacy data support the use of 8 mg/kg TCZ plus non-biologic DMARDs or anti-TNF agents in this patient population, via improvements in HAQ and improvement in RA signs and symptoms in inadequate responders to anti-TNF therapy.

AEs occurred in 3 (10.7%), SAEs (neutropenia and thrombocytopenia) occurred in 1 (3.6%), drug-related AEs in 3 (10.7%) patients. Most AEs were mild or moderate in intensity. No AEs leading to dose modification or deaths were reported. Consistent with previous reports, TCZ treatment was associated with episodic increases in hepatic aminotransferases with the proportion of patients reporting abnormal ALT and AST values being low at all visits. The highest proportion of patients with abnormal ALT values was 42.9% at Week 12 and abnormal AST was 35.7% at Week 4. Numerous laboratory abnormalities were reported in the key TCZ trials including deranged liver function tests, lipid abnormalities, and neutropenia.4,6,7

Overall, all TCZ studies have consistently found that combination therapy with TCZ plus a DMARD is more effective than placebo at improving the ACR50 and ACR70 (OR 3.79 ACR50, OR 5.94 ACR70 versus DMARD). A TCZ dose of 8 mg/kg was more likely to lead to DAS28 remission (OR 10.6 versus DMARD) and a greater improvement in HAQ-DI scores, with no significant increase in SAEs.8

The limitations of his study are that information on the tapering of steroid therapy was not collected, follow-up data on all 28 patients is not presented, and the long-term effects of TCZ on lipid levels and the requirement for the use of statins needs to be studied.

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