POS0608

SWITCHING OF TREATMENT FROM REFERENCE ETANERCEPT TO SANDOZ ETANERCEPT BIOSIMILAR IN PATIENTS WITH RHEUMATIC DISEASES: AN INTERIM ANALYSIS OF REAL-WORLD DATA FROM THE COMPACT STUDY

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Background: Sandoz etanercept (SDZ ETN) is a biosimilar of etanercept (ETN). COMPACT is an ongoing, non-interventional study, evaluating the effectiveness, safety, and quality of life with SDZ ETN treatment in patients (pts) with rheumatoid arthritis (RA), axial-spondyloarthritis (axSpA) or psoriatic arthritis (PsA) in real-world conditions.

Objectives: We have reported an interim analysis, with the effectiveness and safety data focusing on pts who were in clinical remission or low disease activity under treatment with reference ETN or biosimilar ETN other than SDZ ETN (initial ETN; iETN) and switched to SDZ ETN.

Methods: Pts aged ≥18 years for whom treatment with SDZ ETN were initiated are being enrolled. Pts were categorized under four treatment groups based on prior treatment status: Group A, pts on clinical remission or low disease activity under treatment with iETN and switched to SDZ ETN; Group B, pts who received targeted therapies and switched to SDZ ETN; Group C, biologic naïve considered uncontrolled with conventional therapy; Group D, DMARD naïve with recent diagnosis of RA considered suitable for treatment initiation with a biologic and started on treatment with SDZ ETN. Effectiveness assessments included Disease Activity Score 28-joint count Erythrocyte Sedimentation Rate (DAS28-ESR) or Ankylosing Spondylitis Disease Activity Score (ASDAS) until Week 24 after enrollment (baseline; BL) in the study. Functional disability was measured by the Health Assessment Questionnaire Disability Index (HAQ-DI). The effectiveness and safety results are reported for the pts who switched from iETN (Group A).

Results: Of the 1437 pts recruited (analysis cut-off date: 16 Oct, 2020), 567 pts were switched from iETN, 163 were switched from other targeted therapies, 697 were biologic-naïve, and 10 were RA DMARD-naïve. Among pts who switched from iETN, 51.5% had RA, followed by axSpA (28.0%) and PsA (20.5%). Comorbidities were more frequent in pts with RA (70.2%) followed by PsA (58.6%) and axSpA (49.7%); musculoskeletal and connective tissue disorders were reported in 31.8% and 15.7% of pts with RA and axSpA, respectively. At BL, whilst receiving iETN, the mean (SD) DAS28-ESR scores were 2.5 (1.1) and 2.1 (1.1) in pts with RA and PsA, respectively (figure 1). The mean change from BL in DAS28-ESR score at Week 24 after switch to SDZ ETN was -0.1 (1.1) and 0 (1.0) in pts with RA and PsA, respectively. In pts with axSpA, the mean (SD) ASDAS score was 1.5 (0.7) at BL; mean change from BL in ASDAS score at Week 24 was 0.1 (0.5). At BL, the mean (SD) HAQ-DI scores were 0.8 (0.7), 0.5 (0.7) and 0.5 (0.6) in pts with RA, PsA and axSpA, respectively. Overall, the proportion of patients with at least one adverse event (AE) was 37.3%, 33.6% and 25.8% in pts with

RA, PsA and axSpA, respectively. Serious AEs were reported in 6.5%, 1.7% and 3.1% of pts with RA, PsA, and axSpA, respectively. Injections site reactions were reported in 2.7%, 0.9% and 1.3% of pts with RA, PsA and axSpA, respectively.

Figure 1. Disease activity in patients who switched from iETN to SDZ ETN

Conclusion: The interim analysis results shows that switch from iETN to SDZ ETN does not impact the effectiveness of ETN in pts with RA, axSpA or PsA, without any new safety signals.

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A TOCILIZUMAB DOSING STRATEGY IN RHEUMATOID ARTHRITIS PATIENTS WITH STABLE DISEASE AIMING TO PREVENT OVERTREATMENT AND UNNECESSARY COSTS

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Background: Tocilizumab (TCZ) is a humanized interleukin 6 (IL-6) antibody that competitively inhibits IL-6 signalling by binding both membrane-bound and soluble IL-6 receptors. The EULAR recommends the use of TCZ, as a biological disease-modifying antirheumatic drug (DMARD), as second line therapy in rheumatoid arthritis (RA) when

conventional DMARDs have failed achieving treatment target. The labelled dosing regimen for TCZ in RA is 8mg/kg (maximum 800mg) every 4 weeks. A TCZ predose serum concentration (TCZpsc) >1mg/L normalizes C-reactive protein, while clinical trials found mean TCZpsc of 19.9 ± 17.0 mg/L in patients receiving the standard regimen. On the basis of these data, it can be hypothesized that cost-effectiveness of therapy can be improved.

Objectives: In this study we evaluated TCZpsc in stable RA-patients to determine whether the TCZ 8mg/kg dose could be lowered while meeting the minimal required concentration for effective blockage of the IL-6 inflammatory cascade.

Methods: Adult RA patients with stable disease (i.e. at least 3 months without treatment change) treated with intravenous TCZ were investigated in a prospective cohort study. TCZpsc before two different TCZ infusions over time was assessed. A validated ELISA was used to measure TCZpsc, immunogenicity was measured by quantifying human antibodies using antigen-binding tests (radioimmunoassay).

A population pharmacokinetic (PK) model was constructed using maximum a posteriori Bayesian estimation applied on the available PK data in the literature combined with the collected data on dosing and predose concentrations in the study patients. Body surface area, creatinine clearance and gender were included as covariates in the model. A patient individual dose tapering strategy was predicted based on the derived model.

The target TCZpsc was set on 8-10mg/L taking the measurement error of 15%, the use of the entire content of the vials and intra-individual variation into consideration.

Results: A total of 44 patients were included [median (IQR) age: 63 (58-72), 75% female, mean (SD) DAS28-ESR: 1.5 (0.8)]. Half of the patients received TCZ in combination with a conventional DMARD, 32% used methotrexate (MTX). Patients received 7.7 ± 0.8 mg/kg (range 5.7-9.7) TCZ. Mean TCZpsc was 27.6 ± 12.6 mg/L. The intra-individual variance of TCZpsc was low; mean difference in individual TCZpsc was 0.56 (5.2) mg/L. Higher dosages (in mg/kg) were significantly associated with higher TCZpsc (regression coefficient 7.32 95%CI 2.73;11.9), suggesting overtreatment. No drug-neutralizing auto-antibodies were measured. Co-treatment with MTX did not influence the median TCZpsc (21.0mg/L versus 26.5mg/L without MTX, $p=0.84$).

According to the measured TCZpsc, TCZ dosage could be lowered in 36 patients (92%). In a 28-days regimen, target-TCZpsc would be reached with a 0.4-4.6mg/kg dose-reduction (Figure 1). Extending the interval between two administrations would lead to low TCZpsc (<1mg/L).

Figure 1. Intended dose reduction related to the measured tocilizumab predose serum concentration

Considering the aimed average dose-reduction of 2.1 mg/kg per administration, efficacy would be expected to maintain (TCZpsc >1 mg/L) while reducing yearly costs with $\pm\text{€}3.900,-$ per patient. On average patients were started on TCZ treatment 63 months (SD26) earlier. As maximum efficacy of TCZ treatment can be achieved after 3 months, TCZpsc-guided dose reduction 3 months after start could have resulted in a total drug cost reduction of $\pm\text{€}750.000,-$ in our study population ($\pm\text{€}19.500,-$ per patient).

Conclusion: Measured TCZpsc under standard TCZ therapy was much higher than the minimal required concentration. These results suggest that the labelled TCZ dose leads to overtreatment and unnecessary costs in patients with stable RA. The TCZpsc seems supportive as an instrument for dose reduction strategies. Future prospective studies should assess its use in TCZ dose adjustment and confirm whether treatment efficacy is maintained.

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