THE EFFECT OF CERTOLIZUMAB DRUG CONCENTRATION AND ANTI-DRUG ANTIBODIES ON TNF NEUTRALISATION

L.C. Berkhoz1, E.H. Vogelzang2, M.H. Hart1, N.J. Derksen1, R. Wieringa2, W. van Leeuwen3, C.L. Krieckaert2, A. de Vries3, M.T. Nurmohamed4,5, G. Wolbing1,5,6, T. Rispen3,6,1, Department of Immunopathology, Sanquin Research; 2Amsterdam Rheumatology and Immunology Center, Reade; 3Biologics Lab, Sanquin Diagnostic Services; 4Amsterdam Rheumatology and Immunology Center, VU University Medical Center, Amsterdam, Netherlands

Background: Although tumour necrosis factor (TNF) inhibitors have proven to be a successful treatment option for patients with rheumatoid arthritis (RA), TNF inhibitors, including certolizumab, elicit an immunogenic response leading to the formation of anti-drug antibodies (ADAs) (reported range ~5%–39% of the patients). Objectives: We sought to investigate the relationship between certolizumab concentrations, ADAs, and the effective TNF neutralising capacity in sera of RA patients. TNF neutralising capacity of certolizumab was compared to the neutralising capacity of adalimumab.

Methods: Blood was collected of 35 consecutive certolizumab-treated RA patients at baseline and 4, 16, 28 and 52 weeks after treatment initiation. Certolizumab and ADA levels were quantified using a certolizumab bridging enzyme-linked immunosorbent assay (ELISA) and a drug-tolerant radioimmunoassay (RIA), respectively. TNF neutralisation of certolizumab and adalimumab in patient sera, in presence or absence of ADAs, was analysed using the TNF-sensitive serum concentration, while there was no association with ADAs (Pearson’s r = 0.087, p < 0.001 (n=12) and Pearson’s r = 0.212, p = 0.120 (n=12); figure 1B and C, respectively). Grey lines indicate log-log linear fit, weight by 1/Y^2). Similar results were obtained for adalimumab, although TNF neutralisation by adalimumab was less potent; the relative in vitro neutralising potency was 43 times higher for certolizumab compared to the neutralising potency of adalimumab.

Conclusions: Our study shows that certolizumab is highly immunogenic. In most cases where ADAs are detected, certolizumab is also present in high amounts, and can still potently neutralise TNF. Furthermore, TNF neutralisation is highly correlated with certolizumab concentrations. Therefore, measurement of certolizumab concentrations is the relevant parameter to assess clinically relevant immunogenicity.

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ADD-ON SHORT-COURSE TOCILIZUMAB ACCELERATES DOSE TAPERING OF GLUCOCORTICOIDS IN RHEUMATOID ARTHRITIS: RESULTS FROM A CHINESE PROSPECTIVE COHORT STUDY

J.-W. Wang1, Y.-Q. Mo1, X.-Y. Wang2, L.-F. Chen1, J.-D. Ma3, J.-Z. Lin1, D.-H. Zheng1, L. Dai1, Department of Rheumatology and Immunology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou; 2Department of Rheumatology and Immunology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China

Background: In real-world clinical practice, self-paid and expensive price limit the application of bDMARDs and only a few patients especially in developing countries could afford long-term use. Only 9.1%–11% of Chinese rheumatoid arthritis (RA) patients were treated with bDMARDs with mean course no more than 6 months. Such short course of bDMARDs had always been raised doubt about their efficacy and benefit for rare reported evidence.

Objectives: To explore the efficacy of additional short-course of Tocilizumab (TCZ) combined with csDMARDs in real-world RA management.

Methods: Consecutive patients with active RA (DAS28-ESR>2.6) who had completed 6 month follow-up were retrospectively recruited from a prospective RA cohort (n=582). All patients were treated according to the treat-to-target strategy and patient’s willingness especially biologics use. RA patients who finished at least 3 intusions of TCZ (8 mg/Kg/4 weeks) were included as add-on TCZ group, and matched RA patients without any bDMARDs by age, sex and disease activity at baseline with the ratio of 1:1 were included as csDMARDs group. Clinical data were collected according to the 2017 EULAR recommendation at baseline and regular visits at week 4, 12 and 24.

Results: (1) The baseline characteristics of 101 paired RA patients showed no significant difference except for lower csDMARDs-naive percentage between two groups (table 1). (2) During 24 week follow up, there were significantly higher percentage of patients in add-on TCZ group achieving therapeutic target (DAS28-ESR<3.2, at Week 4: 59% vs. 39%, P=0.005; at Week 12: 71% vs. 52%, P=0.006, figure 1) or remission (DAS28-ESR<2.6, at Week 4: 46% vs. 16%, P=0.001; at Week 12: 53% vs. 28%, P=0.001) than those in csDMARDs group. Furthermore, there were significantly higher percentage of patients in add-on TCZ group achieving deep remission (DAS28-ESR<1.6, at Week 4: 16% vs. 5%, P=0.015; at Week 12: 28% vs. 9%, P=0.001; at Week 24: 22% vs. 9%, P=0.046). (3) The patients were 76% RA patients in add-on TCZ group with glucocorticoids (GC) therapy, which is significantly lower than that in csDMARDs group (92%, P=0.002). Among patients with GC therapy, the GC dosage per day was tapered more rapidly at each visit and the cumulative dose at week 24 was significantly lower in add-on TCZ group than that in csDMARDs group (82±616 vs. 1128±519 mg, P=0.001).

Table 1. Baseline characteristics of RA patients in add-on TCZ group or csDMARDs group

Conclusions: Add-on short-course TCZ may be an alternative induction strategy for RA patients in developing countries which can quickly achieve target and accelerate dose tapering of GC.


Abstract THU0205 – Figure 1. Dynamic changes of therapy indexes between add-on TCZ group and csDMARDs group. (A-H) Comparison of disease activity indexes at baseline and week 4, 12 and 24. (I-K) Comparison of therapeutic effect. (L) Comparison of glucocorticoid dosage per day. Therapeutic target, remission and deep remission were defined as DAS28-ESR<3.2, <2.6 and <1.68, respectively. *P<0.05, **P<0.01, ***P<0.001.

Figure 1