AB0390 EFFICACY AND SAFETY OF YISAIPU, A RECOMBINANT HUMAN TUMOR NECROSIS FACTOR-α RECEPTOR II IGG FC FUSION PROTEIN IN CHINESE PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is characterized by chronic autoimmune diseases of progressive synovitis and joint destruction, which can eventually lead to joint deformation and disability. A number of clinical studies showed the effectiveness of tumor necrosis factor antagonist combined with methotrexate in the treatment of RA. Yisaipu used in this study is produced by CPGC Company (Shanghai, China), which was approved to treat RA by Chinese Food and Drug Administration, in 2005, which is biosimilar of etanercept (a soluble recombinant human receptor antibody fusion protein, an immunoglobulin molecule which connects two TNF receptors (p75) to the human IgG1 FC division). Etanercept had been confirmed the effectiveness in rheumatoid arthritis already in many clinical trial.[5–8] However, there is rare randomized control study published regarding Yisaipu in international journals. We conducted an open-label, randomized controlled study for 24 weeks to evaluate the efficacy and safety of Yisaipu in combination with DMARDs in comparison with low or medium dose of glucocorticoid in patients with moderate to severe RA.

Objectives: to evaluate the efficacy and safety of Yisaipu in combination with DMARDs in comparison with low or medium dose of glucocorticoid in patients with moderate to severe RA.

Methods: Eighty four patients with moderate to severe rheumatoid arthritis were randomly assigned into 4 groups: group 1: methotrexate plus Yisaipu; group 2: methotrexate plus medium-dose prednisone (30mg/d, reduced to 15 mg/d after 2 weeks); group 3: methotrexate plus low-dose prednisone (prednisone 7.5mg/d); group 4: methotrexate alone. Each group was treated with MTX (12.5mg once weekly, the next day with folic acid 10mg) and hydroxychloroquine sulfate (200 mg twice a day) concomitantly. The primary endpoint was ACR20 response rate at week 24. Secondary efficacy endpoints were ACR20, ACR50, ACR70, DAS-28, Health Assessment Questionnaire (HAQ) and EULAR remission rate at week 4, 12 and 24.

Results: At week 24, a higher proportion of patients in the group 1and group 2 than the other two groups met the ACR20 response criteria (85.7% in group 1 and 71.4% in group 2 vs. group 3 and group 4, $P<0.05$). The reductions of HAQ at week 24 showed significant improvement in group 1 and group 2 compared to group 3 and 4 (-2.96 and -2.69 respectively, $P<0.05$). Reduction of DAS-28 in group 1 and group 2 were significantly higher than the other two groups ($P<0.05$). The percentage of EULAR remission rate of group 1 and group 2 is significantly higher than group 3 and group 4 at week 24 (47.6% in group 1, 33.3% in group 2, 23.8% in group 3 and 14.3% in group 4, $P<0.05$). There were no significant differences of adverse event among four groups.

Conclusions: Yisaipu plus MTX or GCs plus MTX in Chinese patients with moderate to severe RA is safe and effective in our study. More studies are needed to compare the long-term safety and cost-effectiveness between Yisaipu and GCs in treatment with RA.

Disclosure of Interest: None declared

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AB0391 SIMILAR PHARMACOKINETICS, SAFETY AND TOLERABILITY OF THE ADALIMUMAB BIOSIMILAR CANDIDATE BI 695501 ADMINISTERED SUBCUTANEOUSLY VIA PREFILLED SYRINGE (PFS) OR AUTOINJECTOR (AI) (VOLTAIRE®-AI)

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Background: PK bioequivalence of BI 695501, an adalimumab biosimilar candidate, and the adalimumab originator was demonstrated previously (VOLTAIRE®-PK: Wynne et al., Expert Opin Investig Drugs 2016;25:1361–70). Administration in chronic inflammatory diseases benefits from patient-friendly PFSs or AIs, the development of which requires assessment of PK, safety, immunogenicity, and local tolerability.

Objectives: To compare PK, safety, immunogenicity, and tolerability of BI 695501 after subcutaneous (SC) injection using either a PFS or an AI.

Methods: In this 16-week randomised, single-dose, open-label, parallel-group study (NCT02606903), 40mg BI 695501 was administered either via PFS or AI in healthy, Caucasian, male, non-athletic volunteers aged 18–65 years with body mass index (BMI) of ≥18 to ≤30 kg/m^2. The study end points included AUC_{0-1032}, C_{max}, and $AUC_{0-\infty}$, analysed using an ANOVA model with fixed effects for treatment and BMI group. Safety assessment included the proportion of subjects with drug-related adverse events (AEs). Immunogenicity parameters were: proportion of subjects with binding/neutralising anti-drug antibodies (ADAs), and ADA titers.

Results: Seventy-one volunteers were randomised: PFS, n=36; AI, n=35. Key demographic and baseline characteristics were well balanced between the treatment groups. PK end point results are shown in Table 1. Estimates for AI/PFS geometric mean (gMean) ratios were within the standard bioequivalence acceptance range (80–125%). Mean plasma concentration-time profiles and total exposure for BI 695501 administered via PFS or AI were similar over the observation period; treatment-emergent AEs (TEAEs) and administration site conditions (ASC) are shown in Table 2.

Table 1. PK Parameters over All Subjects for BI 695501 via PFS or AI

Parameter	PFS		AI		Adjusted gMean ratio (AI/PFS)*	2-sided 90% CI*
	n	Adjusted gMean*	n	Adjusted gMean*		
$AUC_{0-\infty}$† [μg·h/mL]	35‡	2270	35	2280	100.22	82.13, 122.29
AUC_{0-1032} [μg·h/mL]	35‡	1960	35	1960	100.14	85.15, 117.76
C_{max} [μg/mL]	36	3.76	35	4.14	110.19	96.80, 125.44

*Adjusted for treatment and BMI group as fixed effects; †Based on observed last concentration values; ‡AUC values could not be calculated for one subject (Subject 1001-0110), due to the lack of appropriate terminal phase (only one non-BLQ [below the limit of quantification] value in the elimination phase).

Table 2. TEAEs and ASC

n (%)	PFS (n=36)	AI (n=35)
≥1 TEAE	29 (80.6)	29 (82.9)
≥1 TEAE related to trial drug	16 (44.4)	20 (57.1)
≥1 non-serious TEAE	29 (80.6)	29 (82.9)
≥1 serious TEAE	0	0
ASC*	14 (38.9)	20 (57.1)
Injection site erythema	13 (36.1)	18 (51.4)
Injection site swelling	3 (8.3)	7 (20.0)
Injection site induration	1 (2.8)	4 (11.4)

*Injection-site reactions are those events recorded within the electronic case report form "Administration site reactions" (narrow) list.

Similar frequencies of patients tested positive for ADAs (57.6% in the PFS group and 51.5% in the AI group), and for neutralising antibodies (33.3%% in the PFS group and 30.3% in the AI group) at the end of the study.

Conclusions: PK, safety, tolerability, and immunogenicity of BI 695501 after SC injection with a PFS or an AI were comparable.

Disclosure of Interest: S. Ramael: None declared, V. Moschetti Employee of: Boehringer Ingelheim, N. Peter Employee of: Boehringer Ingelheim, I. Sonderegger Employee of: Boehringer Ingelheim, S. Wiebe Employee of: Boehringer Ingelheim, B. Liedert Employee of: Boehringer Ingelheim

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AB0392 SAFETY AND EFFECTIVENESS OF CT-P13 IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM 24 MONTHS NATIONWIDE REGISTRY IN KOREA

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Background: CT-P13 is approved in both European Union and United States, and licensed for use in 79 countries around the world as a biosimilar to innovator infliximab (INX). The independent registries of CT-P13 have been conducted in a number of European countries and Korea [1].

Objectives: To evaluate safety and effectiveness of CT-P13 when administered in a real-life setting in active RA patients.

Methods: This study collected data of patients who were treated with CT-P13 from 2013 December to 2016 June. Efficacy was assessed at baseline and every 6 months thereafter using DAS28 (ESR) and/or DAS28 (CRP) and collection of adverse events (AEs) was performed. Immunogenicity was assessed at baseline, Week 30 and every year during CT-P13 treatment period.

Results: Total 125 patients were enrolled; 104 patients started treatment with CT-P13 (Naïve group) and 21 patients (8 from INX, 13 from other anti-TNFs) switched treatment to CT-P13 (Switching group). The mean (SD) duration since RA diagnosis was 6.5 (±6.85) years for all patients.

Of all patients treated with CT-P13, only 4.8% (6/125) of patients changed to other anti-TNFs. Two of six patients changed treatment within 8 month after starting CT-P13.

The proportion of patients achieving clinical remission by DAS28 (ESR/CRP) increased gradually (Figure 1). DAS28 (ESR/CRP) value decreased from baseline at 6 months and it maintained thereafter (Table 1). Switching group also showed similar results that remission rate by DAS28 (CRP) was 42.9% (3/7) and mean actual value was 2.85 at 12 months.

For Naïve group, 50% (52/104) of patients had at least one positive anti-drug antibody result and it is consistent to other published study [2].
Overall safety summarized as the percentage of patients with at least one treatment emergent AE (TEAE) was similar or lower after switching to CT-P13 (Table 2). No cases of active tuberculosis were reported.

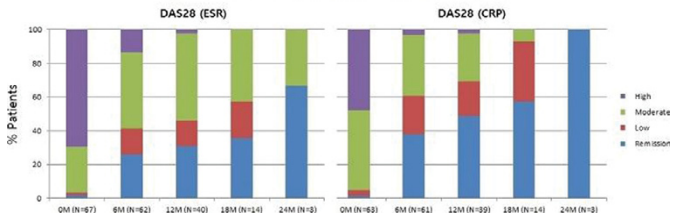
Table 1. DAS28 in CT-P13 Naïve group over 24 months

		Baseline	6 months	12 months	18 months	24 months
DAS28 (ESR)	n	67	62	40	14	3
	Mean	5.78	3.61	3.30	3.01	2.42
	SD	1.14	1.40	1.22	1.03	0.74
DAS28 (CRP)	n	63	61	39	14	3
	Mean	5.06	2.97	2.59	2.35	1.81
	SD	1.19	1.21	1.06	0.69	0.63

Table 2. Safety results in CT-P13 Naïve and Switching group

	Naïve group	Switching group
TEAEs	80.8% (84/104)	66.7% (14/21)
Related TEAEs	31.7% (33/104)	28.6% (6/21)
Infection and Infestation	42.3% (44/104)	33.3% (7/21)

Figure 1. Disease Activity by DAS28 in CT-P13 Naïve group



Conclusions: The overall safety profile revealed that CT-P13 is well-tolerated in patients with RA and remission rate for 24 months also showed that CT-P13 is efficacious under real world practice.
References:
[1] Glintborg et al. ACR 2016.
[2] Krintel et al. Rheumatology 2013.
Disclosure of Interest: None declared
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AB0393 ADVERSE SKIN REACTIONS IN RHEUMATOID ARTHRITIS PATIENTS RECIEVING TUMOR NECROSIS FACTOR ALPHA INHIBITOR – AN ANALYSIS OF DATA FROM THE SLOVENIAN BIOLOGICAL REGISTRY

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Background: Paradoxical skin reactions (PSR) are defined as a new onset or worsening of skin conditions during treatment with tumour necrosis factor alpha (TNF-α) inhibitors that generally improve or respond to this therapy. The list of PSR is growing. The most commonly reported are psoriasiform skin eruptions.
Objectives: To evaluate the frequency of PSR in the group of rheumatoid arthritis (RA) patients treated with TNF-α inhibitor at the time of development of skin eruption.
Methods: We conducted the analysis of the data from the mandatory Slovenian national registry of patients treated with bDMARDs (BioRx.si) which includes spontaneous adverse reaction reports between 01.01.2008–31.05.2016. The analyses were limited to patients with RA.
Results: During the observation period, 1,046 RA (82% female; median (IQR) age at initiation of TNF-α inhibitors 56 (49–63) years) patients treated with TNF-α inhibitors for 3,140 person years. We identified 14 cases with PSR (71% female, median age (IQR) 45 (53–62)). There were 6 PSR cases on adalimumab, 4 on etanercept, 3 on certolizumab – pegol, and 1 on infliximab. 10 patients developed psoriatic/psoriasiform eruptions, 2 patient leucocytoclastic vasculitis, one had lichen planus, and one undifferentiated skin changes. The incidence rate of new onset of psoriasis in RA patients treated with TNF-α inhibitors was estimated at 3.2 cases/1000 patient-years (95% CI 2.58 to 3.82). The incidence rate of leucocytolastic vasculitis was 0.64/1000 person-years (95% CI 0.36 to 0.92), and of lichen planus 0.32/1000 person-years (95% CI 0.12 to 0.52).
Conclusions: The most commonly reported PSR in RA patients treated with TNF-α inhibitor was psoriasiorm PSR, which is in line with published data.
Disclosure of Interest: None declared
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AB0394 TAPERING TNF INHIBITORS IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE STUDY

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Background: Increasing evidence suggests the feasibility of biologic DMARD tapering in RA patients after achieving and maintaining good control of disease activity. Current guidelines on RA treatment also recommend tapering of biologic and non-biologic DMARDs for patients in remission. Data on biologic DMARD tapering reflecting real life settings are limited.
Objectives: To collect information on biologic DMARD tapering and its outcome in RA patients who are followed-up in a rheumatology outpatient clinic.
Methods: In this retrospective study we used the hospital administrative database to identify patients with a diagnosis of RA and a first time prescription of a biologic DMARD that was specifically limited to one of the 3 TNF inhibitors (etanercept, adalimumab, infliximab) between January 2012 and the end of December 2013. Demographics and information regarding treatment and outcome were taken from the medical charts.
Results: Of the 125 patients identified at the database search, 104 were belonging to our clinic and had available follow-up data until June 2016. Seventy-nine of them were women and 25 were men. Their mean age was 47.7±13 SD years and their mean disease duration was 7.4±6.9 SD years. 60% were prescribed etanercept, 23% adalimumab and 17% infliximab. After a mean duration of 14.0±7.6 SD months a dose reduction of TNF inhibitors was made in 44 patients (42%). This was in the form of spacing in 39 patients (Etanercept =16, Infliximab =14, Adalimumab =9) and dose tapering in 5 (all Etanercept). All of these were due to good clinical response except for 1 patient's own request for fear from adverse effects. Following dose reduction increased disease activity was seen in 16 patients (36%) mandating restoration to original dose within a mean of 8.8±9.7 SD months with good response. Twenty-eight patients (64%) preserved their good clinical response during a mean follow-up of 46.1±6.3 SD months which enabled further dose reductions in 20 patients. There was also reductions in the mean number of synthetic DMARD's (1.4±0.8 SD at the initiation of TNF inhibitors and 0.7±0.8 SD at the end of follow-up) and in the percentage of patients using steroids (78% to 33%). At the end of the follow-up, among the whole group of 104 patients, only 73 (70%) were using biologics (TNF inhibitors =49, non-TNF biologics =24). The reasons for stopping biologics in the remaining 31 patients were ongoing remission (16 patients), pregnancy (1 patient), non-compliance (4 patients), injection site reactions (3 patients), fear from adverse events (1 patient), deciding to try complementary medicine (1 patient) and other issues such as losing insurance and family issues (5 patients).
Conclusions: Tapering of TNF inhibitors was possible in 40% of RA patients during their routine follow-up. Half of the patients maintained good clinical response after tapering allowing further dose reductions in one third.
Disclosure of Interest: None declared
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Rheumatoid arthritis - other biologic treatment

AB0395 SUBCUTANEOUS TOCILIZUMAB AS MONOTHERAPY OR IN COMBINATION WITH A CSDMARD IN PATIENTS WITH RHEUMATOID ARTHRITIS: 24 WEEKS RESULTS OF THE FRENCH PHASE IIIB STUDY, "TOSCA"

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Background: After the two global pivotal studies, which evaluated the safety and efficacy of subcutaneous tocilizumab (TCZ-SC) in combination (combo) with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), it was important to understand the efficacy and safety profile of TCZ-SC both as monotherapy (mono) and in combo with csDMARDs in patients (pts) managed in conditions less strict than those of pivotal clinical trials.
Objectives: To evaluate the efficacy and safety of TCZ-SC 162 mg once weekly (qw) as mono and in combo with csDMARDs over 24 weeks in adult pts with moderate to severe RA. The primary efficacy criterion was the change in DAS28-ESR from baseline to week 24 (W24).
Methods: TOSCA is a national, multicenter, open-label phase IIIb study, part of the international umbrella study (TOZURA). It aimed to enroll TCZ-naïve pts who were csdMARDs inadequate responders (IR) and/or biological DMARD-IR. Pts received TCZ-SC 162 mg qw for 24 weeks, administered at the investigator's discretion as mono or in combo with a csDMARD. Stable oral corticosteroids (CCS), ≤10 mg/day prednisone or equivalent (eq.pred), were allowed.