therapy. Clinical response was assessed using the European League Rheumatism (EULAR) response criteria [2]. Serum etanercept levels were measured by sandwich ELISA based on the ability of etanercept to bind TNF. Antibodies against etanercept were measured by bridging ELISA (Promonitor).

Results: The 47 female and 11 male were of a mean age 52.1±11.2 years (22–87) and have been living with RA for a mean of 13.2±8.2 years (2–24). At baseline the DAS28-$_{ESR}$ mean score was 6.1±1.0. After six months of etanercept treatment, 20 (34.5%) patients were in remission, 20 (34.5%) were in low disease activity and 18 (31%) were in moderate disease activity. The serum etanercept levels were significantly higher in patients in remission compared with patients in moderate disease activity (p=0.05). According to the EULAR response criteria, RA patients were divided into responders (52pts, 89.7%) and non-responders (6 pts, 10.3%). Median etanercept levels in all patients were 3.937mcg/ml. There were no statistical differences in etanercept levels between responders and non-responders patients (p=0.41). In addition, we stratified all patients into quartiles according to height of the etanercept level. The percentage of EULAR good responders was significantly different between the highest and the lowest quartiles ($p<0.05$).

Anti-etanercept antibodies were not found in any of the studied patients (0/58).

Conclusions: Patients with RA who did not respond to etanercept treatment achieved lower etanercept levels compared with responding patients. Higher concentrations of the drug were associated with a better response to treatment. Further studies are needed to provide evidence for this approach.

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FRI0207 INDUCTION OF SUSTAINED REMISSION IN EARLY INFLAMMATORY ARTHRITIS WITH THE COMBINATION OF INFLIXIMAB PLUS METHOTREXATE, METHOTREXATE ALONE OR PLACEBO: THE DINORA TRIAL

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Background: Rheumatoid arthritis is a chronic form of inflammatory arthritis that is thought to have an early stage or reversibility with effective therapy ("window of opportunity").

Objectives: In the present study, we explored the effects of induction therapy with anti-TNFα antibody infliximab (IFX) plus methotrexate (MTX) compared with MTX alone and with placebo (PL) in patients with very early inflammatory arthritis.

Methods: In an investigator-initiated, double-blind, randomized, placebo-controlled, multi-center trial, patients with synovitis of 12–16 weeks duration in at least 2 joints underwent one year of treatment with IFX in combination with MTX, MTX monotherapy or PL randomized in a 2:2:1 ratio. The primary endpoint was clinical remission after 1 year (sustained for at least two consecutive visits 8 weeks apart including week 54) with remission defined as no swollen joints, 0 - 2 tender joints and a C-reactive protein (CRP) level within the normal range (<0.5 mg/dl) or a normal ESR (<25 mm/h). Further, sustainability of remission was assessed during the second year of the study, during which patients received no treatment. The trial was registered at www.isrctn.com (ISRCTN21272423).

Results: See Table 1.

Table 1. Number of patients in clinical remission at 6 months, one year and two years

	1: IFX+MTX (N=38)	2: MTX (N=36)	3: PL (N=16)
6 Mo	10 (26%)	6 (17%)	0
1 Year*	12 (32%)	5 (14%)	0
2 Years*	9 (24%)	1 (3%)	3 (19%)

*$p<0.05$ across the three groups.

90 patients participated in the present study. At week 54 (primary endpoint), 32% of the patients in the IFX+MTX group achieved sustained remission compared with 14% on MTX alone and 0% on PL (Table). This difference was statistically significant for all three groups ($p<0.05$) and for IFX+MTX vs PL ($p<0.05$) separately, but not for IFX+MTX vs MTX (p=0.10), nor for MTX vs PL (p=0.31). Remission was maintained during the second year on no therapy in 75% of the IFX+MTX patients but was lost in 80% of the MTX-only-patients (Table). The analysis of radiographic progression did not reveal significant differences between the three treatment groups. The number needed to treat (NNT) to achieve one additional sustained remission at 52 weeks with IFX+MTX was 3 compared to placebo; the NNT for MTX alone versus placebo was 7 (NNT=6 for IFX+MTX vs MTX alone).

Conclusions: These results indicate that patients with early arthritis can benefit from induction therapy with anti-TNF plus MTX compared to MTX alone, suggesting the existence of a window of opportunity where intensive treatment can alter the disease evolution

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FRI0208 COMPARISON OF EFFICACY, SAFETY AND PHARMACOKINETICS OF INFLIXIMAB BIOSIMILAR (BCD-055) AND INNOVATOR INFLIXIMAB

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Background: Infliximab (IFX) was one of the first genetically engineered biologics successfully applied for medical use in patients with active RA and patients with AS. Previous preclinical studies showed that BCD-055 is highly similar to innovator IFX.

Objectives: This abstract presents results from three clinical trials of infliximab biosimilar, BCD-055, including comparative data on pharmacokinetics (PK), efficacy and safety in a variety of patient populations.
Methods: All three studies were conducted as international multicenter randomized double-blind studies in direct comparison with innovator IFX. ASART-1 study (Phase 1, PK study) and ASART-2 study (Phase 3, efficacy and safety study) were conducted in patients with AS. After the screening patients were stratified by CRP and BASDAI score, randomized (1:1 ratio in ASART-1; 2:1 ratio in ASART-2) into 2 arms and received BCD-055 or innovator IFX at a dose 5 mg/kg IV on day 1 wk 0, 2, 6 and then every 8 wks (up to wk 54). LIRA study (Phase 3 study) was conducted in patients with active RA who were stratified by age and DAS28 score, randomized (2:1) into 2 arms and received BCD-055 or innovator IFX at a dose 3 mg/kg IV on day 1 wk 0, 2, 6 and then every 8 wks (up to wk 54).
Results: A total of 91 patients were enrolled in ASART-1 study, 198 patients - in ASART-2 study and 195 patients - in LIRA study in Russia and Belarus.
PK characteristics were equivalent for BCD-055 and innovator IFX. After the single administration 90%CI for the ratio of geometric means for $AUC_{0–336}$ was 86.40% – 110.09%, for C_{max} – 82.70% – 109.83%. After multiple-dose administration 90%CI for the ratio of geometric means for $AUC_{0\text{-}tau}$ was 81.35% – 121.13%, for $C_{max,ss}$ – 90.16% – 117.32%.
Efficacy: BCD-055 is non-inferior to innovator IFX both in RA and AS patients: ACR20 at wk 14 was reached by 75.83% of patients in BCD-055 group and 74.19% in innovator IFX group (p=0.951, 95% CI for difference in proportion [-12.90%; 16.18%], margin -20%), ASAS20 at wk 30 - by 81.30% and 67.74% respectively (p=0.061, 95% CI for difference in proportion [-1.18%; 28.28%], margin -17.5%).
Safety: BCD-055 and innovator IFX showed highly similar safety profiles in all three studies without cases of unexpected toxicity. The rates of AEs were equivalent for both drugs and varied from 47% in patients with AS to 53% in patients with RA. Immunogenicity assessment didn't find any significant difference between BCD-055 and innovator IFX, anti-drug antibodies occurred at the same rate irrespectively to the group.
Conclusions: BCD-055 is highly similar to innovator IFX in patients with active RA and in patients with AS in terms of efficacy, safety and PK.
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FRI0209 REAL-LIFE SAFETY PROFILE OF BIOSIMILAR ADALIMUMAB IN PATIENTS WITH INFLAMMATORY ARTHRITIC CONDITIONS

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Background: Biologic therapies have dawned a new era in the management of patients with chronic inflammatory arthritis by nudging the goal post from control to induction of remission. Adalimumab, a TNF-α inhibitor, has proven to be safe and effective in improving the disease activity and quality of life in patients with conditions like rheumatoid arthritis (RA) and ankylosing spondylitis (AS).[1,2] A biosimilar adalimumab (developed by *Cadila Healthcare Ltd., India*) has been approved for clinical use in 2014 in India. While the initial biosimilarity has been established for physicochemical, functional as well as clinical efficacy and safety aspects;[3,4] ongoing evaluation of safety in real-life patients is crucial for such biosimilar therapies.
Objectives: We share our experience on the real-life safety profile of biosimilar adalimumab following its clinical use in patients with RA and AS.
Methods: Patients with RA or AS treated with biosimilar adalimumab in our outpatient clinic at Arthritis and Rheumatism Centre during the period of 17 Dec 2014 to 30 Mar 2016 were considered for this analysis. The patients were prescribed biosimilar adalimumab 40 mg subcutaneously every fortnight for a minimum of 6 months. The patients were followed up till the end of the treatment, and any safety signals or adverse events reported were collected and analysed.
Results: A total of 200 patients - 119 patients with AS and 81 patients with RA - who received biosimilar adalimumab therapy for a period of 6 months were included. The median age for the group was 36 (17–68 years); and 138 patients were males. The mean BMI was 25.74±3.83; and the median duration of disease for the entire group was 4.54 (0.5–13.5) years - 4.54 (0.5–9.58) years for the patients with AS, and 4.58 (2.5–13.5) years for the patients with RA. About 90% (181 out of 200 patients) received concomitant therapy with methotrexate. Biosimilar adalimumab therapy was well tolerated by all patients, with no serious adverse events. Adverse events were noted in only 2 patients - one patient had developed pulmonary tuberculosis in the 4th month of treatment, biosimilar adalimumab was discontinued and AKT treatment was started; while another patient experienced rise in transaminases for which, the dose of methotrexate was reduced. Overall assessment of tolerability as "Excellent" was 65.5% by the treating physician and 82% by patients.
Conclusions: To the best of our knowledge, this is the first report on "real-life" use of biosimilar adalimumab in such a large number of patients. The analysis reveals a safety and tolerability profile of biosimilar adalimumab comparable to that of the innovator product.
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FRI0210 REAL-WORLD HAWK STUDY: LONG-TERM SAFETY AND EFFECTIVENESS OF ADALIMUMAB WITH HIGHER-DOSE METHOTREXATE IN JAPANESE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: TNF inhibitors are first-line biologic therapy used in combination with MTX for treatment of RA. However, in Japan, limited real-world data exist on this combination with relatively higher doses of MTX (>8 to ≤16 mg/week).
Objectives: The HAWK study was designed to assess real-world, long-term safety and effectiveness of the TNF inhibitor ADA with MTX (≥12 mg/week) in Japan. Week 52 results are presented.
Methods: This multicenter, prospective, observational study, enrolled biologic-naïve, early (≤2 years) RA patients with DAS28-CRP>3.2 despite MTX therapy for ≥3 months. Eligible patients received ADA + MTX (≥12 mg/week at beginning of ADA) for 104 weeks. Primary endpoint was DAS28-CRP <2.6 at week 52. Secondary endpoints included CDAI, SDAI, HAQ-DI and inhibition of structural joint damage using the mTSS. ADRs and dosage of ADA and MTX were recorded.
Results: As of April 15, 2016, 346 patients were enrolled (safety set 301; effectiveness set 293). Effectiveness set comprised 73% women; mean (±SD) age, 54.3 (13.9) years; duration of RA, 12.1 (6.2) months; MTX dosage, 13.4 (1.8) mg/week; DAS28-CRP, 4.5 (0.9); and mTSS, 7.7 (10.0) at baseline. At week 52, DAS28-CRP <2.6 and low disease activity (<3.2) were achieved in 77% and 92% patients, respectively. Remission rates in CDAI (≤2.8), SDAI (≤3.3), and HAQ-DI (≤0.5) were 49%, 51%, and 82%, respectively. Although average MTX dosage was decreased (≤2 mg/week), unchanged, and increased (≥2 mg/week) from baseline in 19.6%, 78.9%, and 1.4% patients over 52 weeks, respectively, there was no significant difference in disease activity improvement across these MTX dosage groups at week 52 (p=0.350). Structural remission rate at week 52 was 86% (ΔmTSS ≤0.5) (Figure). A total 110 ADRs occurred in 80 (26.6%) patients, 23 were serious in 21 (7.0%) patients (Table).

	All (N=301)		Serious (N=301)	
ADR				
Total	80	26.6%	21	7.0%
ADRs by SOC				
Infections and infestations	29	9.6%	9	3.0%
Investigations	16	5.3%	1	0.3%
Respiratory, thoracic and mediastinal disorders	13	4.3%	3	1.0%
Hepatobiliary disorders	9	3.0%	0	
ADRs of particular interest				
Tuberculosis	0		0	
Pneumocystis jirovecii pneumonia	4	1.3%	4	1.3%
Pneumonia bacterial*	6	2.0%	4	1.3%
Herpes zoster	4	1.3%	0	
Malignancy (1)	4	1.3%	4	1.3%
Interstitial lung disease	2	0.7%	2	0.7%
Sepsis	0		0	
Pancytopenia	0		0	
Reactivation of hepatitis B	0		0	

*Pneumonia, Pneumonia bacterial, Pneumonia pneumococcal, Pneumonia legionella, Pneumonia streptococcal. (1) Colon cancer, diffuse large B-cell lymphoma, ovarian cancer metastatic, lung neoplasm malignant.

Conclusions: Results show that ADA with MTX (≥12 mg/week at the beginning) displayed a consistent safety profile and was effective with a DAS28-CRP remission rate of 77% in routine clinical practice. The ADR rate of 26% was similar to a previous, short-term (28 weeks) postmarketing surveillance report (1).
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