

Comparative Study for Efficacy and Safety of Biosimilar Infliximab in Patients with Active Rheumatoid Arthritis on a stable Dose of Methotrexate

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Abstract

Background: The present study evaluated the efficacy and safety of biosimilar infliximab in patients with active rheumatoid arthritis on a stable dose of methotrexate.

Methods: Subjects were assigned randomly to either study infliximab or reference infliximab product in approved dose of 3 mg/kg as an intravenous infusion at week 0, followed by similar doses at Weeks 2, 6 and 14. Primary efficacy endpoint was the proportion of subjects achieving ACR20 criteria at week 16 and secondary efficacy assessment included proportion of subjects achieving ACR20, ACR50 and ACR70 at week 16. In the open-label phase, all responders were followed till week 54. The non-responders entered a follow-up phase for immunogenicity and safety for an additional 3 months.

Results: Responders achieving ACR20 response were 106 (89.83%) in study arm and 51 (86.44%) in the reference arm at week 16 in the PP population. There was no significant difference ($p \leq 0.05$) in ACR20, ACR50 and ACR70 responders at Weeks 2, 6, 14 and 16 in the number of responders in both the treatment arms for PP population. The mean changes in HAQ-DI scores and DAS28 scores showed clinically significant improvement from baseline. There were 55 (43.31%) subjects in the biosimilar arm and 31 (50.00%) subjects in the reference arm with at-least one adverse event in the study and no deaths were reported.

Conclusions: Primary and the secondary endpoint assessments and the safety analysis showed comparable response in biosimilar and reference infliximab and the two treatments were considered clinically equivalent.

Keywords: Infliximab; Rheumatoid Arthritis; Tumor Necrosis Factor; Methotrexate; ACR; DAS28

List of abbreviations: TNFI: Tumor Necrosis Factor Inhibitor; ACR: American College of Rheumatology; DAS28: Disease Activity Score 28; HAQ-DI: Health Assessment Questionnaire Disease Index; MTX: Methotrexate, CRP: C Reactive Protein; RF: Rheumatoid Factor

Introduction

In RA pathogenesis, TNF plays a central role in the pro-inflammatory cytokine cascade. TNF α over-expression was shown to be arthritogenic [1]. TNFR1 receptor is responsible for most cellular responses to TNF α and TNFR2 has been shown to be important for cytotoxicity as well as NF κ B activation [2,3]. Infliximab was the first monoclonal antibody to human tumor necrosis factor alpha (TNF α). This chimeric antibody binds with high affinity to both soluble and trans-membrane TNF and is able to reduce synovial inflammation, bone resorption and cartilage degradation [3]. The efficacy of infliximab has been observed in active RA despite treatment with multiple disease modifying anti-rheumatic drugs (DMARDs), and in early disease with no prior treatment by methotrexate (MTX). Infliximab has been shown to reduce joint inflammation and to slow radiographic progression, in both clinical and non-clinical responders [4]. Recent data suggests that using infliximab early in RA treatment increases the percentage of clinical remission and allows MTX discontinuation. Sustained clinical benefit occurs when the TNF α –neutralizing agents like infliximab were administered alone or concomitantly with methotrexate, the current standard disease-modifying therapy for patients with rheumatoid arthritis [5-7].

A biosimilar is highly similar to the reference product and that no clinically meaningful differences exist between the biosimilar and reference product in terms of safety, purity and potency [8]. Biosimilars offer access to an alternative treatment option and compliance for the chronically ill subjects [9].

The study drug, biosimilar infliximab, was developed as biosimilar to innovator infliximab with comprehensive establishment of physicochemical and biological similarity [10,11]. The aim of the present study was to establish clinical similarity of the biosimilar infliximab with the reference or innovator infliximab product in terms of efficacy and safety in moderate to severe RA on stable dose of methotrexate [10].

Materials and Methods

The study was a prospective, multi-centre, randomized, double-blind, two-arm, parallel group, active-control, comparative clinical study to evaluate efficacy and safety of biosimilar infliximab, BOW015 (study arm)/ innovator infliximab (reference arm) in patients with active rheumatoid arthritis on a stable dose of methotrexate (CTRI/2012/05/002660). This was a multicenter study conducted at 22 centers across India. The study was conducted in compliance with the ethical principles that originated in the declaration of Helsinki and ICH-GCP and Indian Schedule-Y regulations [11,12].

Randomization to treatment arm and study medication assignment was carried out programatically within the electronic case report form (eCRF) by ArisGlobal. All subjects who had given written informed consent to participate in the study were assigned a sequential subject number at the screening visit. Subjects who were eligible to continue in the study were assigned a randomisation number at Baseline (Week 0). Randomisation was centrally applied and stratified by site. Subjects were randomized in a double-blind fashion. In order to maintain a blinded study through Week 16, an unblinded pharmacist and unblinded monitoring team were arranged on a site-by-site basis. The unblinded pharmacist prepared the Study Medication for infusion, which was then supplied to the treating physician as a labeled infusion bag for administration to the subject. Pharmacy records were kept blinded and were monitored independently at the sites.

Male or female subjects, aged 18 to 65, with diagnosis at least 2 years prior to screening, of RA according to the criteria based on the revised 2010 ACR/European League Against Rheumatism (EULAR) RA Classification criteria, with ACR/EULAR diagnostic criteria score ≥ 6 and having active disease were included. Subjects were on treatment with MTX (10 to 20 mg/week) taken orally, for at least 3 months with no break(s) in treatment of more than 2 weeks in total during this period and stable dose between 10 and 20 mg/week for at least 4 weeks prior to screening were enrolled. Subjects using oral corticosteroids on a stable dose of ≤ 5 mg/day prednisolone or equivalent, for at least 4 weeks prior to screening were enrolled. Pregnant women, nursing mothers or those who had planned pregnancy within 18 months of randomization were excluded. Subjects with prior use of infliximab, adalimumab, certolizumab, golimumab, tocilizumab, rituximab, or etanercept (or any biological treatment of RA) and prior use of DMARDs, other than MTX within 4 weeks prior to screening were excluded. Subjects who had a history of serious infection, which caused hospitalization within 6 months prior to randomization or other severe or chronic infection (such as sepsis, abscess or opportunistic infections, invasive fungal infection such as histoplasmosis, or a history of recurrent herpes zoster or other chronic or recurrent infection) or a past diagnosis without sufficient documentation of complete resolution and subjects who had an infection requiring parenteral antibiotic treatment within 4 weeks of randomization were also excluded. Subjects with active TB or evidence of latent TB without adequate therapy for TB completed were excluded (evidence of TB based on chest X rays, tuberculin skin [Mantoux] test, QFT-TB Gold test and TB tests performed during screening). Additionally, subjects who had completed treatment for active TB within the previous 2 years were explicitly excluded from the study. Subjects with opportunistic infections including, but not limited to, evidence of active cytomegalovirus, active pneumocystis carinii, aspergillosis, or atypical mycobacterial infection, within the previous 6 months were also excluded.

In the double-blind phase, subjects were assigned randomly in a 2:1 ratio to receive either study infliximab or reference product. Infliximab approved dose of 3 mg/kg was given in both the arms as an intravenous infusion at week 0, followed by similar doses at Weeks 2, 6 and 14. The primary efficacy endpoint was the proportion of subjects achieving clinical response according to the ACR20 criteria at week 16. The per-protocol population was the primary efficacy analysis population.

Secondary efficacy assessment included proportion of subjects achieving ACR20, ACR50 and ACR70 at scheduled assessment visits of weeks 2, 6, 14 and 16. The same assessments were conducted in the open-label phase at Weeks 22, 30, 38 and 54. In the open-label phase, all responders received study product at a dose of 3 mg/kg administered IV at Weeks 22, 30, 38, and 46. Subjects in the open-label phase were then followed untreated for an additional 3 months up-to week 54. Long-term efficacy was assessed during the open-label phase based on ACR components assessments. Safety assessments for subjects in both the open-label phase as well as those in the safety follow-up phase included monitoring of AEs, clinical laboratory parameters, vital signs, and 12-lead ECG. The non-responders entered a follow-up phase for immunogenicity with evaluation of anti-drug antibodies (ADA) and safety for an additional 3 months. The immunogenicity was evaluated by ELISA at Eurofins Pharma Bioanalysis Services UK using immunogenicity assays specific for BOW015 and reference infliximab.

Statistical methods

The sample size was based on an overall proportion of ACR20 responders of 70% with an absolute equivalence margin of + 23% for a power of 80% and a two-sided significance level of 0.05 with an adjustment for unequal allocation. Statistical analyses were performed using the SAS® system. Analysis was performed in per-protocol (PP) and safety populations as defined in the study.

Subject disposition

A total of 407 subjects were screened for this study and 199 subjects were found to be eligible and were randomized. Remaining 208

subjects were considered as screen failures. As depicted in figure 1, out of 199 randomised subjects, 189 subjects were dosed in the study as per the study plan. All 189 subjects were considered for safety analysis. Out of 189 subjects, 127 subjects were randomized in the study infliximab arm and 62 subjects were randomized in the reference arm. In the study arm, 120 subjects completed the double blind phase and seven subjects prematurely discontinued the study. Five subjects prematurely discontinued because of adverse events, one subject discontinued due to protocol non-compliance and one due to consent withdrawal. In the reference arm, 61 subjects completed the double blind phase and one subject prematurely discontinued the study due to adverse event. A total of 181 subjects (120 subjects from study arm and 61 subjects from reference arm) completed the double-blind phase of the study and entered the open-label follow-up phase of the study. For the primary efficacy assessment at week 16, eight subjects (7 in study arm and 1 in reference arm) were prematurely discontinued before week 16 and were considered to be ACR20 non-responders for primary endpoint assessment.

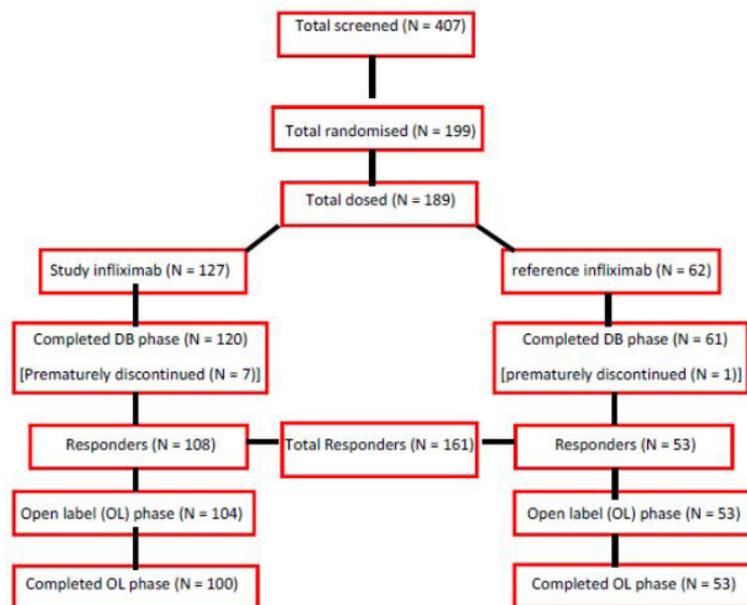


Figure 1: Subject disposition

Out of the remaining 181 subjects, 161 subjects (108 in study arm and 53 in reference arm) were responders and were eligible for open label phase. However four subjects from the study arm developed TB and were followed up only for safety. Hence 157 subjects (104 in study arm and 53 in reference arm) entered open label phase (157 subjects) and were continued on study infliximab dosing in this phase. Total 153 subjects completed the open label phase (100 in the study arm and 53 in reference arm). Four subjects were discontinued before completion of open label phase (1 due to AE, 1 due to investigator discretion and 2 due to consent withdrawal).

Results

Demographic and Other Baseline Characteristics

Out of 127 subjects randomized in the study infliximab arm, 110 subjects were female (86.6%) and 17 (13.4%) subjects were male. The mean age of subjects was 45.6 years and the mean weight was 58.8 kg. The mean duration of disease in the study arm subjects was 4.3 years. The mean CRP, ESR and Rheumatoid factor values were 25.3 mg/L, 59.2 mm/h and 156.5 IU/mL respectively in the study arm. Out of 62 subjects randomized in the reference arm, 56 (90.3%) subjects were female and six (9.7%) subjects were male. The mean age of subjects randomized in the reference arm was 43.1 years and mean weight was 55.8 kg. The mean duration of disease in the reference arm subjects was 3.8 years. The mean CRP value, ESR and RF values were 29.0 mg/L, 59.8 mm/h and 158.6 IU/mL respectively. The treatment groups were similar with respect to mean age, body mass index, CRP, ESR, and RA Factor. All study subjects were on treatment with MTX (10 to 20 mg/week) taken orally.

Efficacy analysis

The total number of responders achieving ACR20 response were 106 (89.83%) in study arm and 51 (86.44%) in the reference arm at week 16 in the PP population (Table 1). The difference between the two groups was not significant and hence, the two treatments were considered to be clinically equivalent ($P=0.6151$).

The total number of responders achieving clinical response as per ACR20 criteria at week 2, 6, 14 and 16 was 40 (33.90%), 70 (59.32%), 89 (75.42%) and 106 (89.83%) in the study arm. In the reference arm, the total number of responders at respective weeks were 22 (37.29%), 36 (61.02%), 43 (72.88%) and 51 (86.44%). There was no significant difference ($p \leq 0.05$) at weeks 2, 6, 14, 16 in the number of responders in both the treatment arms (Table 1).

Variable	Study INFX (N=118) n%	Reference INFX (N=59) n%	Difference in Proportions Between treatment groups	95% CI of treatment difference	P-Value
ACR20					
Visit**					
Week 2	40(33.90)	22(37.29)	3.39%	(-12.60%, 19.27%)	0.7386
Week 6	70(59.32)	36(61.02)	1.69%	(-14.28%, 17.61%)	0.8718
Week 14	89(75.42)	43(72.88)	-2.54%	(-12.60%, 13.44%)	0.7177
Week 16	106(89.83)	51(86.44)	-3.39%	(-19.27%, 12.60%)	0.6151
ACR50					
Visit					
Week 2	5(4.24)	3(5.08)	0.85%	(-15.11%, 16.78%)	1.0000
Week 6	17(14.41)	7(11.86)	-2.54%	(-18.44%, 13.44%)	0.8165
Week 14	40(33.90)	16(27.12)	-6.78%	(-22.58%, 9.25%)	0.3954
Week 16	57(48.31)	28(47.46)	-0.85%	(-16.78%, 15.11%)	1.0000
ACR70					
Visit					
Week 2	1(0.85)	1(1.69)	0.85%	(-15.11%, 16.78%)	1.0000
Week 6	4(3.39)	2(3.39)	0.00%	(-15.95%, 15.95%)	1.0000
Week 14	14(11.86)	4(6.78)	-5.08%	(-20.93%, 10.93%)	0.4296
Week 16	28(23.73)	13(22.03)	-1.69%	(-17.61%, 14.28%)	0.8521

** - Subjects who discontinued prior to week 16 were classified as non-responders. Subjects with ACR component information missing due to reasons other than discontinuation had last observation carried forward to calculate ACR20

Table 1: ACR20, ACR50 and ACR70 responders at week 2, 6, 14 and 16

In the secondary analysis, summary of responders by the ACR50 criteria is presented in Table 1 in the PP population. The total number of responders achieving ACR50 response at week 2, 6, 14 and 16 were 5 (4.24%), 17 (14.41%), 40 (33.90%) and 57 (48.31%) respectively in the study arm. In the reference arm the ACR50 responders at the same evaluation periods were 3 (5.08%), 7 (11.86%), 16 (27.12%) and 28 (47.46%) respectively. There was no significant difference ($p \leq 0.05$) at weeks 2, 6, 14 and 16 in the number of responders in both the treatment arms.

The total number of responders achieving ACR70 response at week 2, 6, 14 and 16 (Table 1) were 1 (0.85%), 4 (3.39%), 14 (11.86%) and 28 (23.73%) in the study infliximab arm. In the reference arm the ACR70 responders at week 2, 6, 14 and 16 were 1 (1.69%), 2 (3.39%), 4 (6.78%) and 13 (22.03%) for respective weeks. There was no significant difference ($p \leq 0.05$) at Weeks 2, 6, 14 and 16 in the number of responders in both the treatment arms for PP population.

In the open label phase, 157 subjects (104 subjects in the study arm and 53 in the reference arm during the double-blind phase) who achieved an ACR20 response to infliximab (study or reference) were considered. All subjects during this phase received study infliximab. Table 2 presents ACR20, ACR50, and ACR70 responders at week 54 by visit and treatment for the open-label phase which were similar for both arms without any significance difference.

Visit	OL Study IFLX		
	Treated with Study IFLX in DB (N=104) n %	Treated with Ref. INFX in DB (N=53) n %	Treated with Study IFLX in OL (N=157) n %
ACR20			
Week 54/22	85(81.73)	46(86.79)	131(83.44)
ACR50			
Week 54/22	57(54.81)	26(49.06)	83(52.87)
ACR70			
Week 54/22	30(28.85)	13(24.53)	43(27.39)

Table 2: ACR20, ACR50 and ACR70 responders at week 54

The durability of response over 54 weeks was assessed by comparing the proportion of subjects with ACR20 response during the double-blind and open-label phases in 189 subjects (127 in study arm and 62 in reference arm). As shown in Table 3, the proportion of responders was similar for the treatment groups, and relatively stable from Week 14 to Week 54.

Phase	Visit	Study arm in DB (N=127) n %	Reference arm in DB (N=62) n %
Double Blind	Week 2	41(32.28)	24(38.71)
	Week 6	73(57.48)	39(62.90)
	Week 14	91(71.65)	45(72.58)
	Week 16	108(85.04)	53(85.48)
Open-Label	Week 22	94(74.02)	44(70.97)
	Week 30	86(67.72)	46(74.19)
	Week 38	92(72.44)	43(69.35)
	Week 46	86(67.72)	45(72.58)
	Week 54	85(66.93)	46(74.19)

Table 3: ACR20 responders in double blind and open label phase (N= 189)

Figure 2 presents mean HAQ-DI and DAS28 scores for the double-blind phase of the study. The mean HAQ-DI scores were similar for the treatment arms at baseline (1.76 for the study arm, and 1.74 in the reference arm), as were the mean DAS28 scores (6.0 for the study arm, and 6.2 for the reference arm). A gradual reduction in mean HAQ-DI scores was noted from baseline to week 16 for both treatment arms (mean change -0.945 for the study arm, and -0.826 for the reference arm). Week 16 DAS28 scores showed clinically significant improvement (-2.6 in the study arm and -2.5 in the reference arm), as compared with baseline. The scores were comparable between treatment arms at any of the timepoints for either scoring system.

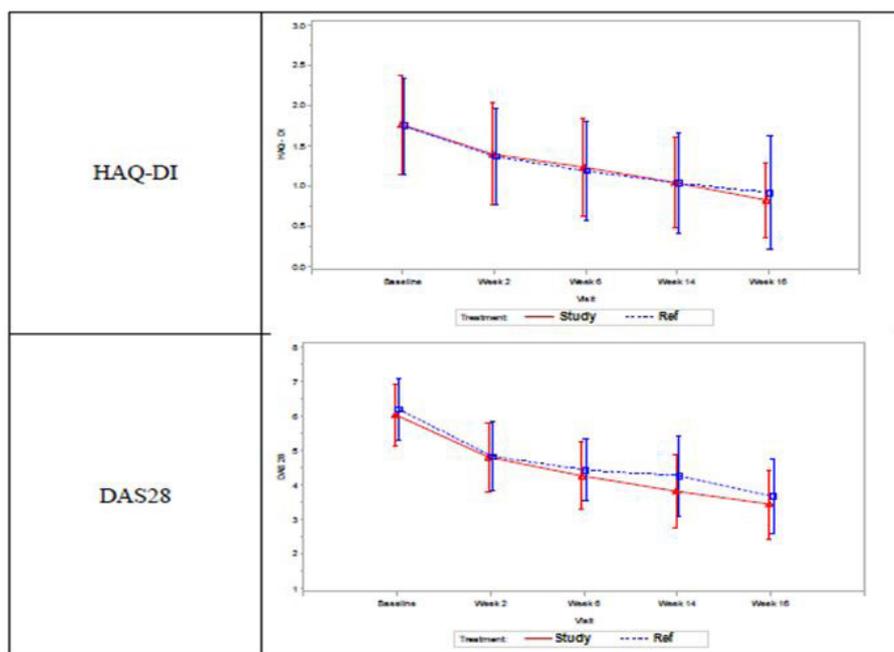


Figure 2: HAQ-DI and DAS28 up to week 16

The secondary efficacy parameters also included change observed in tender joint counts and swollen joint counts during double blind phase of the study. In the study infliximab arm, the mean tender joint count at baseline was 25.0 which reduced to 6.0 at week 16 and the mean swollen joint count of 15.0 at baseline reduced to 3.0 at week 16. In the reference arm, the mean tender joint count of 28.0 at baseline reduced to 17.0 and the mean baseline swollen joint count of 16.0 was reduced to 4.0 at week 16. In both the treatment arms, there was a gradual reduction in mean tender joint counts and swollen joint counts from week 2 to 16. There was no statistically significant difference observed in reduction of mean values of tender joint count ($p = 0.2720$) and swollen joint counts ($p = 0.5728$) between both the treatment arms during the double blind phase. In the open label phase, mean change in tender joint and swollen joint counts at week 54 remained approximately the same as those noted at week 16.

The mean baseline CRP value of 24.73 mg/L and ESR value of 58.7 mm/h in the study infliximab arm reduced to 11.34 mg/L and 31.9 mm/h at week 16 (double blind phase). In the reference arm, the mean CRP value at baseline was 28.41 mg/L which was reduced to 12.84 mg/L at week 16 and the mean ESR baseline value of 59.3 mm/h was reduced to 37.0 mm/h at week 16. In both the treatment arms, there was a gradual reduction in mean of CRP values from week 2 to week 16 (Table 4). Reduction of mean values of CRP between both the treatment arms were comparable ($P = 0.6532$). In the study arm, the mean Rheumatoid Factor value at baseline was 153.4 IU/ml which decreased to 112.4 IU/ml at week 16 and in the reference arm, the mean of Rheumatoid Factor

baseline value of 158.5 IU/ml decreased to 112.9 IU/ml at week 16. In both the treatment arms, there was a reduction in mean Rheumatoid Factor (Table 4).

	Study arm baseline value	Study arm week 16 value	P value	Reference arm baseline value	Reference arm week 16 value	P value
CRP	24.73 mg/L	11.34 mg/L	0.3240	28.41 mg/L	12.84 mg/L	0.6532
ESR	58.7 mm/h	31.9 mm/h	0.8780	59.3 mm/h	37.0 mm/h	0.1755
RF	153.4 IU/ml	112.4 IU/ml	0.8529	158.5 IU/ml	112.9 IU/ml	0.9841

Table 4: CRP, ESR and RF values at baseline and week 16

In the open label follow-up, mean CRP at week 54 was 11.14 mg/L for the study arm and 15.29 mg/L for the reference arm which was similar to that noted at week 16 and was similar between the two treatment arms. The same trend was noted for mean ESR at week 54 (33.7 mm/h for the study arm and 35.8 mm/h for the reference arm) and RA Factor (81.9 IU/mL for the study arm and 49.7 IU/ML for the reference arm).

Safety analysis

In the present study, in the double blind phase, a total of 52 subjects (40.94%) reported 97 TEAEs in the study arm and 30 subjects (48.39%) reported 45 TEAEs in the reference arm. Most TEAEs were mild to moderate in severity and reported by 3 or fewer subjects in either treatment group.

Thirty (23.62%) subjects in the study arm and 14 (22.58%) in the reference arm reported TEAEs that were considered to be related to study drug. Six (4.72%) subjects in the study arm and 2 (3.23%) in the reference arm reported TEAEs that were considered to be severe. Thirteen serious TEAEs (TESAEs) were reported, 9 (7.09%) in the study arm and 4 (6.45%) in the reference arm. Infusion reactions occurred with similar frequency in the treatment arms. There were no deaths reported in this study. In the open label phase, a total of 50 (48.08%) study arm responders reported 98 TEAEs and 28 (52.83%) reference arm responders reported 52 TEAEs. A total of 28 (17.83%) subjects reported 38 infections and infestations. The proportion of TESAEs was similar for the previous randomized treatment arms (6.73% in the study responders arm and 5.66% in the reference responders. There were no deaths reported in the study (Table 5).

	Study DB (N=127) n % E	Reference DB (N=62) n % E	Study OL (104) n % E	Reference OL (53) n % E
At least 1 TEAE	52 (40.94%) 97	30 (48.39%) 45	50 (48.08%) 98	28 (52.83%) 52
At least 1 TEAE Related to Study Drug	30 (23.62%) 37	14 (22.58%) 19	27 (25.96%) 39	17 (32.08%) 22
At least 1 Severe TEAE	6 (4.72%) 6	2 (3.23%) 2	6 (5.77%) 7	2 (3.77%) 3
At least 1 TEAE	9 (7.09%) 9	4 (6.45%) 4	7 (6.73%) 6	3 (5.66%) 3
At least 1 Infusion reaction	3 (2.36%) 4	4 (6.45%) 4	4 (3.85%) 6	1 (1.89%) 2
Death	0 (0.00%) 0	0 (0.00%) 0	0 (0.00%) 0	0 (0.00%) 0

Table 5: Summary of all adverse events (n = number of subjects; E = number of events)

The most commonly reported adverse events according to preferred term reported in this study was pyrexia 8 (6.30%) in the study arm and infusion related reaction 4 (6.45%) in the reference arm in this study. However, most commonly reported adverse events according to System Organ Class (SOC) reported was infection and infestation which occurred in 21 (16.54%) subjects in the study arm and 6 (9.68%) in the reference arm. A total of 6 cases of TB were reported in the study: 2 as TEAEs and 4 as TESAEs in the study arm. Subjects were started on anti-TB therapy at the discretion of the investigator and all subjects were withdrawn from the study. Given the high prevalence of TB in the India, this number of active TB cases on TNF therapy is considered low and supports the effectiveness of screening procedures employed in this study. The study drug was safe and well-tolerated, and similar to reference product with respect to overall TEAEs. The proportion of subjects with anti-drug antibodies (ADA) appeared to be lower in the study arm as compared with the reference arm at week 14 (22.1% versus 35.5%). In the responder population continuing to the open-label phase, the proportion of subjects with ADA was similar for the treatment groups, particularly at Week 58 (65.4% in the study arm versus 66.0% in the reference arm).

Discussion

It is known that the combination of infliximab and methotrexate improves the symptoms and signs of inflammation, physical function, and the quality of life and prevents radiographic evidence of progressive joint damage in a majority of patients with rheumatoid arthritis who have no response to methotrexate alone.

A biosimilar product must demonstrate that it has “no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product” [7]. In the present prospective, double-blind, randomized, comparator-controlled study in patients with active RA on a stable dose of MTX, the primary clinical objective of the study was met and the efficacy of study biosimilar infliximab was clinically equivalent to reference innovator infliximab as determined by ACR20 clinical response at Week 16 when administered with a background fixed dose of MTX. Results of all secondary efficacy variables supported the primary efficacy outcome. The totality of the efficacy data show clinical equivalence of biosimilar to that of reference infliximab. After Week 16, all subjects who were responders were switched to treatment with open-label study arm. These results indicate that the maintenance or sustainability of the clinical response was maintained up to 54 weeks.

In addition to therapeutic equivalence to reference product, the biosimilar infliximab was safe and well-tolerated, and similar to reference product with respect to overall TEAEs, clinical laboratories, vital signs, and ECGs. It was also interesting to observe that when subjects were switched from reference infliximab to study biosimilar in the open-label phase, the proportion of TEAEs and SAEs were broadly similar to those who were maintained on study infliximab from the randomized phase. The proportion of subjects testing positive for antibodies in both arms was similar, demonstrating similar immunogenicity of biosimilar to reference infliximab in both the comparative double-blind and the open-label phases of the study. The results of the present study are consistent with the conclusions that in patients with aggressive rheumatoid arthritis that is not responsive to methotrexate therapy, the combination of infliximab plus methotrexate can prevent progressive joint damage over a one-year period [8-10].

Conclusion

In the present study considering the clinical response rate using primary and the secondary endpoint assessments, the study data showed comparable response in both the treatment arms. Hence, the two treatments were considered clinically equivalent for the treatment of moderate to severe RA subjects on a stable dose of MTX. Infliximab, patients on stable chronic therapy can be switched to biosimilar infliximab without an increased risk for loss of response. With current therapy and use of biosimilar infliximab, RA patients can anticipate comfortable and productive lives on medical therapy [14].

Acknowledgement

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