AB0690 CLINICAL EXPERIENCE WITH INFLIXIMAB BIOSIMILAR (BOW015) IN ANKYLOSING SPONDYLITIS- EFFICACY AND SAFETY ANALYSIS FROM AN INDIAN PERSPECTIVE

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Background: The regulatory phase III trial supporting the approval of biosimilar infliximab (BOW015) in India included only rheumatoid arthritis patients. Consequently there is paucity of data on the effectiveness of BOW015 in Ankylosing Spondylitis (AS).[1,2,3] Hence, we decided to objectively quantify the effectiveness and safety of BOW015 in AS patients.
Objectives: To determine safety, efficacy and tolerability of BOW015 in Indian AS patients.
Methods: We retrospectively collected data from seven centres to get a comprehensive picture of the Indian population. The protocol along with data collection form was designed by the investigators and ethics committee approval was obtained. Biologic naïve patients diagnosed with AS as per Assessment of Spondylo Arthritis International Society criteria who were having six months of follow up data during January-November 2016 were included in the study. Percentage of patients achieving major clinical improvement (Ankylosing Spondylitis Disease Activity Score C-reactive protein ($ASDAS_{CRP}$) >2 from the baseline to six months of follow up) was the primary variable. Secondary variables included; clinical improvement criteria ($ASDAS_{CRP}$>1.1 from the baseline to six months of follow up), change in $ASDAS_{CRP}$, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), CRP and Erythrocyte Sedimentation Rate (ESR) from the baseline to six months. Variables were reported as mean ± Standard Deviation (SD), absolute change in variable were reported along with their Confidence Interval (CI) and data was analyzed using Statistical Package for the Social Science V-22.
Results: A total of 68 patients treated with BOW015 having follow-up data for six months were analyzed. Mean age of patients was 32.63±11.73 (SD) years with mean body mass index of 25.72±7.48 (SD) kg/m^2 and about 32 (47%) patients had peripheral arthritis. Of the treated patients, 52 (76%) patients were administered four doses while 6 (9%) patients administered three doses, 3 (5%) patients administered two doses and 7 (10%) patients administered single dose as they were loss to follow up. As per the primary variable, 67.9% patients achieved major clinical improvement, 9.4% patients achieved clinical improvement and 22.6% were non-responders. There was an absolute change of -2.54 (95% CI -1.92, -3.17) in BASDAI and -1.77 (95% CI -1.43, -2.11) in $ASDAS_{CRP}$ right from first follow up corresponding to post 1st dose visit which was statistically significant (see Table-1). This trend was observed in the subsequent visits in BASDAI, $ASDAS_{CRP}$, ESR and CRP which continued till the end of six months. One patient developed pulmonary tuberculosis and marginally elevated liver enzymes were seen in two patients.

Table 1: Change in the primary and secondary variables

	Baseline (mean±SD)	Δ Baseline to 1st follow up (Mean Difference; 95% CI)	Δ Baseline to 2nd follow up (Mean Difference; 95% CI)	Δ Baseline to 6 months follow up (Mean Difference; 95% CI)	p value compared to previous visit and baseline vs. 6 months FU
BASDAI	5.83±1.90	-2.54 (95% CI -1.92, -3.17)	-3.44 (95% CI -2.79, -4.09)	-3.77 (95% CI -3.05, -4.48)	<0.05
$ASDAS_{CRP}$	3.88±0.80	-1.77 (95% CI -1.43, -2.11)	-2.212 (95% CI -1.86, -2.55)	-2.13 (95% CI -1.78, -2.47)	<0.05
ESR (mm/h)	39.45±27.04	-20.82 (95% CI -14.08, 27.55)	-26.137 (95% CI -19.05, -33.22)	-26.087 (95% CI - 17.89, 34.28)	<0.05
CRP(mg/L)	25.06±22.84	-18.408 (95% CI -12.01, 24.80)	-18.918 (95% CI -12.69, -25.14)	-15.702 (95% CI -9.38, 22.02)	<0.05

Conclusions: BOW015 showed significant improvement in $ASDAS_{CRP}$ and BASDAI in patients with AS on a six month follow up period and the clinical benefits were apparent as early as first dose of BOW015.
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Disclosure of Interest: I. Agrawal: None declared, A. Roy: None declared, R. Kiran: None declared, V. Rao: None declared, R. Sarkar: None declared, S. Naorem: None declared, A. Ray: None declared, M. Shamil Employee of: Sun Pharma Laboratories Ltd, Mumbai, India
DOI: 10.1136/annrheumdis-2017-eular.5865

AB0691 METFORMIN THERAPY CAN RESTORE THE BALANCE OF TH17 AND TREG CELLS IN PATIENTS WITH SPONDYLOARTHRIT

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Background: Spondyloarthrit (SpA) is a chronic autoimmune disease and is associated with immunological function disorder. Previous studies have observed that increased number of T17 cells and decreased number of Regulatory T (Treg) cell in patients with S [1,2]. However, the current therapy for SpA, focusedon NSAID, biological agents and glucocorticoid, can't correct the imbalance of Th17 and Treg cells. Metformin has been demonstrated a reducing effect on Th17 cells but an increasing effect on Treg cells, regulating the Thl7/Treg ratio [3].
Objectives: The study is to explore the effect of metformin therapy on the balance of Th17 and Treg cells in patients with SpA.
Methods: SpA patients (n=27) (from August 1st to November 30th in 2016, both outpatients and inpatients in our department, according to American-European Consensus Group criteria for SpA), who were given metformin (750mg/day for 6 weeks). Laboratory indicators were compared before and after metformin treatment.
Results: The number of Treg cells [25.37 (18.31,45.78) vs.34.43 (25.91,50.31), P=0.015] significantly increased after the treatment. At the same time, there was a significantly decrease in the ratio of Th17/Treg cells [0.26 (0.15,0.48) vs. 0.22 (0.1,0.33), P+0.037]. Besides, Th17 cells were also decreased [7.85 (4.95,10.65) vs. 6.42 (3.7,10.63)].
Conclusions: Metformin can restore and maintain the balance of Th17 and Treg cells in the patients with SpA. And it may be a potential therapy for SpA.
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Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4554

AB0692 EFFECTS OF INTRAVENOUS GOLIMUMAB ON PATIENT-REPORTED OUTCOMES IN ACTIVE ANKYLOSING SPONDYLITIS: 28-WEEK RESULTS OF THE PHASE III GO-ALIVE TRIAL

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Objectives: To evaluate patient-reported outcomes (PRO) of physical functioning, mental health functioning, health state, and health-related quality of life (HRQoL) in patients (pts) w/active Ankylosing Spondylitis (AS) treated w/intravenously administered (IV) golimumab (GLM), an anti-TNFα monoclonal antibody.
Methods: GO-ALIVE is a Phase 3, multicenter, randomized, double-blind, placebo-controlled trial. Pts (aged ≥18 years) had a diagnosis of definite AS (per modified New York criteria) and BASDAI ≥4, total back pain visual analogue scale ≥4, and CRP ≥0.3mg/dL. At baseline, 208 pts were randomized either to IV GLM 2mg/kg (N=105) at Wks 0, 4, and every 8 wks or placebo (PBO, N=103) at Wks 0, 4, and 12, w/crossover to GLM at Wk 16.
Three PRO instruments were included: 1) SF-36, a generic instrument designed to measure physical & mental health functioning, 2) EQ-5D visual analogue scale (VAS), a generic measure of current health state & 3) Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire, a disease-specific instrument designed to measure the impact of AS on HRQoL. The scores for SF-36 range from 0–100 w/higher scores indicating better functioning. It has Physical (PCS) and Mental Component Summary (MCS) and eight subscales (physical functioning, role-physical, body pain, general health, vitality, social functioning, role-emotional, & mental health). EQ-5D has a scale of 0–100 (0=worst health you can imagine to 100=best health you can imagine). ASQoL assesses sleep, mood, motivation, ability to cope, activities of daily living, independence, relationships, & social life in pts w/AS. The scores range from 0–18 w/higher scores indicating worse HRQoL. Unadjusted p-values of least square mean differences (LSMD) between treatment groups were based on analysis of covariance (ANCOVA) controlling for prior anti-TNF therapy.
Results: Table 1 summarizes the mean changes from baseline at Wks 8, 16, & 28. Improvements from baseline in SF-36 PCS & MCS were greater in the GLM group than PBO at Wk 8 (6.83 vs. 2.07, p<0.001; 5.56 vs. 1.67, p=0.006, respectively) and maintained through Wk 16 (8.52 vs. 2.87, p<0.001; 6.47 vs.

0.84, p<0.001, respectively). Improvements in all SF-36 subscales were observed in the GLM group at Wks 8 & 16 compared to PBO (p<0.01, with the exception of the role-emotional subscale [p=0.058]). The percentage of pts achieving clinically meaningful change (5 points or greater) in SF-36 PCS & MCS were higher in GLM than PBO in Wks 8 & 16 (PCS: 58.1 vs. 27.2, 67.6 vs. 35.9, respectively; MCS: 48.6 vs. 34.0, 54.3 vs. 29.1, respectively; p<0.05 for all). Mean EQ-5D VAS improvements were greater (p<0.001) in GLM than PBO at Wks 8 & 16 (17.61 vs. 6.63, 20.32 vs. 4.79, respectively). Greater improvements in ASQoL were observed in GLM compared to PBO at Wks 8 & 16 (-4.5 vs. -1.5, p<0.001, -5.4 vs. -1.8, p<0.001, respectively). By Wk 28, after PBO crossed-over to GLM, improvement in PCS, MCS, EQ-5D VAS, & ASQoL were similar between the two treatment arms.

Table: Summary of mean (standard deviation) changes in SF-36, EQ-5D, and ASQoL.

		IV GOLIMUMAB 2mg/kg	PLACEBO
Patients		105	103
Mean (SD) change from baseline in SF-36 PCS:	Week 8	6.83 (6.90) (p<0.001)	2.07 (5.66)
	Week 16	8.52 (7.54) (p<0.001)	2.87 (6.11)
	Week 28	9.08 (8.02)	9.29 (7.09)
Mean (SD) change from baseline in SF-36 MCS:	Week 8	5.56 (9.26) (p=0.006)	1.67 (8.80)
	Week 16	6.47 (9.12) (p<0.001)	0.84 (9.82)
	Week 28	6.16 (10.91)	5.60 (9.70)
Mean (SD) change from baseline in EQ-5D VAS:	Week 8	17.61 (24.02) (p<0.001)	6.63 (19.881)
	Week 16	20.32 (24.59) (p<0.001)	4.79 (23.47)
	Week 28	20.52 (27.86)	22.45 (23.08)
Mean (SD) change from baseline in ASQoL:	Week 8	-4.5 (4.71) (p<0.001)	-1.5 (3.90)
	Week 16	-5.4 (5.01) (p<0.001)	-1.8 (4.50)
	Week 28	-5.3 (5.24)	-5.3 (4.84)

Conclusions: Adult pts w/active AS treated w/IV GLM showed marked improvements in physical functioning, mental health functioning, health state, & HRQoL.

Disclosure of Interest: J. Reveille Grant/research support from: Janssen Scientific Affairs, LLC., A. Deodhar Grant/research support from: Janssen, Amgen, Abbvie, GSK, Eli Lilly, Novartis, Pfizer, UCB, Consultant for: Janssen, Eli Lilly, Novartis, Pfizer, UCB, E. Chan Employee of: Janssen Global Services, LLC, S. Peterson Employee of: Janssen R&D, LLC, N. Li Employee of: Janssen R&D, LLC, E. Hsia Employee of: Janssen R&D, LLC, L. Kim Employee of: Janssen R&D, LLC, K. H. Lo Employee of: Janssen R&D, LLC, D. Harrison Employee of: Janssen R&D, LLC, C. Han Employee of: Janssen Global Services, LLC

DOI: 10.1136/annrheumdis-2017-eular.6145

AB0693 PATIENTS WITH CHRONIC INFLAMMATORY ARTHROPATHIES TREATED WITH GOLIMUMAB ACHIEVE A HIGHER SERUM LEVEL OF DRUG IF USED AS THE FIRST OR SECOND BIOLOGICAL DRUG

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Objectives: To know the influence of the order of introduction of Golimumab (GLM), on clinical efficacy in ankylosing spondylitis (AS), psoriatic arthritis (PSA) and rheumatoid arthritis (RA).

Methods: A prospective, observational study, in 46 consecutive patients with AS, APS and RA, treated with GLM. Data: epidemiological, concomitant DMARD, time of disease evolution, HLA-B27, RF and ACPA; from GLM: order of introduction, time in treatment, serum level and anti-GLM Ab. The clinical response was assessed in AS patients using BASDAI, BASFI, ASDAS-VSG. In patients with RA or peripheral APS, DAS28-VSG, DAS28-PCR and SDAI. Serum levels of GLM and anti-GLM Ab were determined by ELISA (Progenika, Grifols SA, Spain). Serum cutoff levels for serum GLM levels: 36 ng/mL and for anti-GLM Ab: UA>20 AU/mL. Samples were extracted just prior GLM administration (trough level) and stored frozen at -80ºC until analysis.

Results: Of 33 (72%) AS patients: 52% were males, mean age 53±12 years, mean BMI 28±4, disease mean evolution 16±12 years and in GLM: 1.3±1.1 years, 30% received DMARD, being GLM the first anti-TNF in 25%, second 37%, third 25% and fourth in 13%. The mean GLM level was 0.77±0.62 mg/mL and the prevalence of anti-GLM antibodies was 6%. In the 5 patients with RA and 8 with APS: 23% were men, mean age of 55±11 years, mean BMI 28±6, mean disease evolution of 10.5±8 years and in GLM of 2±1.5 years, the 85% of patients received DMARD, being GLM the first anti-TNF in 31%, second 15%, third 31% and fourth 23%. The mean GLM level was 0.703±0.53 mg/L. No anti-GLM Ab were detected.

Table 1. Characteristics of patients with receiving GLM, according to the order of introduction

Golimumab (GLM) RA-APS (n: 13)	1°–2° anti-TNF (n: 7)	3°–4° Anti-TNF (n: 6)	p
BMI, kg/m^2: mean (SD)	28,72 (6,62)	28,93 (6,66)	0,95
Disease evolution (years): mean (SD)	10,1 (7,64)	11,53 (10)	0,78
DMARD, n (%)	7 (100)	4 (67)	0,13
Years on GLM: mean (SD)	2,27 (1,86)	2,5 (2,04)	0,84
anti-GLM Ab, U/L, n (%)	0	0	–
DAS28-VSG, mean (SD)	1,74 (0,83)	2,12 (0,94)	0,47
DAS28-PCR, mean (SD)	1,82 (0,85)	2,28 (0,93)	0,39
SDAI, mean (SD)	3,92 (5,17)	7,67 (6,58)	0,30
Golimumab (GLM) AS (n: 33)	**1°–2° anti-TNF (n: 21)**	**3°–4° anti-TNF (n: 12)**	**p**
BMI, kg/m^2: mean (SD)	27,46 (4,20)	29,26 (3,09)	0,16
Disease evolution (years): mean (SD)	14,25 (10,55)	20,65 (14,27)	0,21
DMARD, n (%)	8 (38%)	2 (17)	0,57
Years on GLM: mean (SD)	1,75 (1,47)	1,13 (0,89)	0,14
GLM level, mg/dL: mean (SD)	0,919 (0,63)	0,448 (0,47)	**0,025**
anti-GLM Ab, U/L, n (%)	0	2 (17)	–
BASDAI: mean (SD)	5,96 (2,48)	6,10 (2,23)	0,86
ASDAS: mean (SD)	2,92 (0,87)	3,79 (2,68)	0,64

Conclusions: 1. The overall prevalence of anti-GLM Ab was 6% and 17% in AS patients. Not detecting in patients with RA or PSA. 2. Serum GLM level was higher among the patients receiving it as the 1st or 2nd anti-TNF. 3. In AS GLM as 3rd or 4th anti-TNF were able to achieve clinical remission, similar to that achieved as 1st or 2nd drug.

Acknowledgements: The study was supported by a grant from the Fundación Española de Reumatología (FVR/2012) and the Asociación para la Investigación en Reumatología de la Marina Baixa (AIRE-MB).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4308

AB0694 RHEUMATOLOGISTS' ATTRIBUTION OF PATIENT-REPORTED SYMPTOMS IN AXIAL SPONDYLOARTHRITIS (AXSPA): IMPACT ON RESPONSE TO TNF-INHIBITORS (TNFI) IN 508 PATIENTS

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Background: In axSpA, treatment decisions are mainly based on patient-reported symptoms: recommendations are to initiate TNFi in patients with active disease and with physician conviction that treatment is needed (ref). However, the attribution of symptoms to inflammation is difficult to establish in axSpA.

Objectives: The objective of the present analysis was to explore the link between physician-attributed causality for symptoms and treatment response to TNFi.

Methods: The PredictSpA study (ClinicalTrials.gov: NCT03039088) was a longitudinal observational multicenter study in France in 2015. Patients with physician-defined definite axSpA and starting a TNFi treatment were included, a TNFi was prescribed according to usual practice and efficacy was assessed at 12 weeks by BASDAI50 response. At baseline, symptoms levels including BASDAI and ASDAS were collected and the physician evaluated the causality of symptoms by answering the following 3 questions: how convinced are you that the symptoms of this patient are due to (A) inflammatory axSpA activity (B) to axSpA severity (eg syndesmophytes, kyphosis) and NOT to disease activity and (C) to other diseases and NOT axSpA. Each question was assessed 0–10 (not convinced at all to absolutely convinced). The link between a score ≥4/10 on each of the 3 questions and BASDAI50 response was assessed by univariate logistic regression. Patients interrupting the TNFi before 3 months were considered as non-responders and missing data were imputed using non-responder imputation.

Results: In all, 519 patients were included and 508 had data over 3 months: mean age 41.3 (SD 11.6) years, mean disease duration 6.1 (SD 8.4) years, 237 (46.7%) were women, 424 (83.5%) satisfied the ASAS criteria for axSpA of whom 379 (74.6%) were in the imaging arm and 45 (8.9%) in the clinical arm. Symptom levels were high: mean BASDAI was 5.7 (SD 1.8) and mean ASDAS-CRP was 3.3 (SD 0.9) with only 6 (1.2%) patients in inactive disease state according to ASDAS. The physician-attributed causality of symptoms was mostly related to inflammatory activity: mean scores for (A), (B) and (C) were respectively, 7.4 (SD 2.0), 2.3 (SD 2.5) and 2.1 (SD 2.2). When physicians attributed causality to non-axSpA (score (C) ≥4/10), BASDAI50 response was less frequent: 45/118 (38.4%) vs 213/390 (54.6%), odds ratio 0.5 [95% CI 0.3, 0.8].

Conclusions: In axSpA patients starting a TNFi with high symptom levels, physician-attributed causality of symptoms was mainly related to inflammatory activity of the axSpA. When physician-attributed causality was more oriented towards non-axSpA causes, BASDAI50 response after 3 months of a TNFi was lower. This confirms the validity of the ASAS-EULAR recommendations for starting a TNFi which rest on a level of symptoms but associated to physician conviction of the indication.

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