AB0379 EFFICACY OUTCOMES FOR ORIGINATOR TNF INHIBITORS AND BIOSIMILARS IN RHEUMATOID ARTHRITIS AND PSORIASIS TRIALS: A SYSTEMATIC LITERATURE REVIEW

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Background: Regulatory approval of biosimilar versions of innovator biotherapeutics requires that new biological products be highly similar to innovator products, with no clinically meaningful differences in safety, purity, and potency.[1,2] Pre-specified margins for equivalence in efficacy have been met in comparative trials of biosimilars of tumour necrosis factor inhibitors (TNFis) in rheumatoid arthritis (RA)[3] and plaque psoriasis (PsO),[4] supporting biosimilarity, but differences in treatment responses between originator pivotal trials and biosimilar trials have posed some interesting questions.
Objectives: To compare American College of Rheumatology 20% response (ACR20) and Psoriasis Area Severity Index 75% (PASI75) responses to originator TNFis in pivotal trials with those to originator TNFis and TNFi biosimilars in biosimilar trials in RA and PsO.
Methods: Historical data from originator pivotal trials (averaged across trials) were obtained from published systematic literature reviews. Searches were conducted to identify comparative randomized clinical trials of approved or proposed biosimilars of adalimumab (ADA), etanercept (ETN), and infliximab (INF) using Embase®, MEDLINE®, the Cochrane Central Trials Register and Database of Systematic Reviews, and other Cochrane Library databases, and 2015/16 congress abstracts. To reduce variability, only studies conducted in disease-modifying antirheumatic drug-experienced patients treated with the same biologic dosages and assessed at the same time points were selected for analysis.
Results: Of 83 publications initially identified, 16 publications were included for analysis (RA: originators, n=4; biosimilars, n=6; PsO: originators, n=3; biosimilars, n=3). Higher proportions of ACR20 responders were found among RA patients receiving the originator biologics and biosimilars in biosimilar trials, than among patients receiving the originator biologics in pivotal trials (Table). Insufficient data were available from ADA and INF biosimilar studies in PsO; in ETN studies in PsO, a difference was also observed in the proportions of PASI75 responders between biosimilar and pivotal trials.

Table: ACR20 and PASI75 responders in pivotal vs biosimilar trials and differences in response rates

Product	RA trial type	Time point (wk)	ACR20 responders, %	Difference, pivotal vs biosim, %
ADA	Pivotal[5,6]	24	65	—
ADA	Biosim[7]	24	72	10
	Biosim[8]	24	72	9
ABP 501	Biosim[7]	24	75	13
SB5	Biosim[8]	24	73	10
ETN	Pivotal[9]	24	71	—
ETN	Biosim[3]	24	80	12
	Biosim[10]	24	91	22
SB4	Biosim[3]	24	78	9
CHS-0214	Biosim[10]	24	91	22
INF	Pivotal[11]	30	50	—
INF	Biosim[12]	30	59	15
	Biosim[13]	30	59	15
CT-P13	Biosim[12]	30	61	18
SB2	Biosim[13]	30	56	10
Product	**PsO trial type**	**Time point (wk)**	**PASI75 responders, %**	**Difference, pivotal vs biosim, %**
ETN	Pivotal[14,15]	12	43	—
ETN	Biosim[4]	12	72	40
GP2015	Biosim[4]	12	70	39

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Conclusions: Differences were observed in treatment response rates between originator pivotal trials and more recent trials of originator biologics and their respective biosimilars. Such differences in outcomes may be attributable to fundamental differences in study design and/or baseline patient characteristics, which require further analysis. Additional research is also needed to explore the clinical relevance of these differences.
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AB0380 RESULTS FROM A RANDOMIZED, SINGLE-BLIND, SINGLE-DOSE, PARALLEL-GROUP STUDY IN HEALTHY SUBJECTS DEMONSTRATING PHARMACOKINETIC SIMILARITY BETWEEN ABP 710 AND INFLIXIMAB

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Background: ABP 710 is being developed as a biosimilar with the same amino acid sequence as infliximab, an anti-tumor necrosis factor therapy. Analytical and functional comparisons between ABP 710 and infliximab have been conducted and completed.
Objectives: This report describes the results of analyses comparing the pharmacokinetics (PK), safety, and immunogenicity of ABP 710 and infliximab sourced from the European Union (EU).
Methods: This was a single-blind, single-dose, parallel-group study among healthy adults, 18 to 45 years of age and with a body mass index of 18 to 30 kg/m^2. Subjects were randomized to receive a 5 mg/kg intravenous infusion of either ABP 710 or infliximab. The primary objective of this analysis was demonstration of PK similarity of ABP 710 to infliximab based on area under the serum concentration-time curve from time 0 extrapolated to infinity (AUC_{inf}; primary endpoint). PK equivalence was deemed achieved if the geometric mean (GM) ratio and its 90% confidence interval (CI) for AUC_{inf} was within the range of 0.80 and 1.25. Secondary endpoints included maximum observed serum concentration (C_{max}), area under the serum concentration-time curve from time 0 to last quantifiable concentration (AUC_{last}), safety, and immunogenicity.
Results: *Pharmacokinetics:* A total of 49 subjects received ABP 710 and 49 subjects received infliximab. Following a single dose, the adjusted least square (LS) GM of AUC_{inf}, AUC_{last}, and C_{max} for ABP 710 was 33559 μg·h/mL, 31789 μg·h/mL, and 123 μg/mL, respectively. The adjusted LS GM of AUC_{inf}, AUC_{last}, and C_{max} for infliximab was 33706 μg·h/mL, 31847 μg·h/mL, and121 μg/mL, respectively. Ratios of adjusted LS GMs (90% CIs) between ABP 710 and infliximab for AUC_{inf}, AUC_{last}, and C_{max} were 0.996 (0.904, 1.096), 0.998 (0.918, 1.086), and 1.021 (0.962, 1.083), respectively.
Safety: There was one subject in the infliximab group who developed polyarthritis that resolved with treatment and the subject completed the study. There were no deaths, other serious adverse events, or treatment-emergent adverse events (TEAEs) leading to discontinuation from the study. The incidence of TEAEs was similar in the two treatment groups (ABP 710: 83.7%; infliximab: 83.7%); the majority of TEAEs were mild or moderate. The most frequently reported TEAEs were somnolence, headache, nasopharyngitis, upper respiratory tract infection, nausea, and lethargy.
Immunogenicity: All subjects tested negative for antidrug antibodies (ADAs) prior to dosing. At the end of study (Day 57), 40% of subjects in the ABP 710 group and 27% in the infliximab group were positive for binding ADAs, and 13% of subjects in the ABP 710 group and 19% in the infliximab group were positive for neutralizing ADAs.
Conclusions: Results of this phase 1 study demonstrate PK similarity between ABP 710 and infliximab sourced from the EU among healthy subjects. The safety and immunogenicity profile were comparable between the treatment groups.
Disclosure of Interest: E. Krishnan Shareholder of: Amgen Inc., Employee of: Amgen Inc., V. Chow Shareholder of: Amgen Inc., Employee of: Amgen Inc., N. Zhang Shareholder of: Amgen Inc., Employee of: Amgen Inc., A. Kaliyaperumal Shareholder of: Amgen Inc., Employee of: Amgen Inc., P. Kaur Shareholder of: Amgen Inc., Employee of: Amgen Inc.
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AB0381 CHANGE IS GOOD, BUT WHAT IS BETTER? RETROSPECTIVE STUDY IN CLINICAL PRACTICE FIRST SWITCH WITH DIFFERENT BIOLOGICAL THERAPIES IN RHEUMATOID ARTHRITIS

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Background: The effectiveness of the switch when the first anti-TNF failure in patients with rheumatoid arthritis has been demonstrated in multiple studies. But what is more effective, if you make the switch to another anti-TNF or another molecule, is not clearly defined.
Objectives: A retrospective study was performed in clinical practice to determine if there is a response to DAS 28 at 6 months of change and whether there is a difference in response if the switch is performed on another anti-TNF or another biological.
Methods: From a total of 254 that met ACR 2010 criteria for RA, which have been biologically treated at Rheumatology of the Parc Salut Mar from 2000 to 2016, 61 (24%) were the first switch and the DAS 28 response at 3 and 6 months of follow-up. The following variables were analyzed: age, sex, years of evolution RA, erosions, FR, ACPA, type of biological treatment, DAS 28 at the start of the switch, 3 months and 6 months,% of patients presenting DAS 28 <2, 6 at 6 months.The statistical study was performed with SPSS 20 for paired and independent quantitative variables with Student's T and chi2 for qualitative variables
Results: Of the total of 61 first treatment changes, 27 (44.3%) were to another anti-TNF alpha, 23 (37.7) to tocilizumab (TCZ), 7 to abatacept (11.5%) and 4