OP0226 SOLID TUMOUR OUTCOMES IN PATIENTS WITH RA TREATED WITH ABATACEPT AND OTHER DMARDS: RESULTS FROM A 10-YEAR INTERNATIONAL POST-APPROVAL STUDY

Teresa Simon[1], Samy Suissa[2], Mary Lou Skovron[1], Thomas Frisell[3], Johan Askling[3], Kaleb Michaud[4,5], Sofia Pedro[5], Anja Strangfeld[6], Maarten Boers[7], Diane Lacaille[8], Marc Hochberg[9], Andres Gomez[1]. [1]*Bristol-Myers Squibb, Princeton, United States of America*; [2]*McGill University, Montreal, Canada*; [3]*Karolinska Institutet, Stockholm, Sweden*; [4]*University of Nebraska Medical Center, Omaha, United States of America*; [5]*FORWARD, The National Databank for Rheumatic Diseases, Wichita, United States of America*; [6]*German Rheumatism Research Centre, Berlin, Germany*; [7]*VU University Medical Center, Amsterdam, Netherlands*; [8]*Arthritis Research Center, Richmond, Canada*; [9]*University of Maryland, Baltimore, United States of America*

Background: The abatacept global post-marketing epidemiology programme includes observational studies based on biologic disease registries and healthcare claims database studies to evaluate infection and malignancy risks associated with abatacept treatment, as used in routine clinical practice.
Objectives: To assess the risk of solid tumour malignancies in patients with RA treated with abatacept vs conventional synthetic (cs)DMARDs and other biologic (b) or targeted synthetic (ts)DMARDs.
Methods: Data were analysed from four cohorts: two biologic registries (the Anti-Rheumatic Therapy in Sweden [ARTIS] register and the Rheumatoid Arthritis Observation of Biologic Therapy [RABBIT] German registry), a disease registry (FORWARD, The National Databank for Rheumatic Diseases in the USA) and a healthcare claims database (the population-based British Columbia Canadian RA Cohort [BC]). Exposure defined as "ever exposed" unless specified. Crude incidence rates (per 1000 patient-years of exposure) with 95% CIs were calculated for overall malignancy, breast cancer, lung cancer and lymphoma. Adjusted risk ratios (RRs) with 95% CIs were estimated using multivariate models adjusting for demographics, comorbidities and other potential cofounders within each database and were subsequently pooled using a random-effects model for meta-analyses.[1]
Results: Patients treated with abatacept (~5100), csDMARDs (~74K) and other b/tsDMARDs (~37K) were followed up for a mean of 3.0–3.7, 3.0–6.2 and 3.0–4.7 years, respectively. Patients were mainly female (71–86%), with a mean age ranging from 55–63 years, and 4–34% had a history of malignancy. A greater number of abatacept-treated patients had been treated with ≥2 prior biologics (abatacept, 44–85%; csDMARDs, 11% [FORWARD] and other b/tsDMARDs, 0–19%). The incidence rate of overall malignancy in abatacept-treated patients was low (Table). Adjusted RRs (95% CIs) for abatacept vs csDMARDs (range: 0.8 [0.2, 3.4] to 1.3 [0.5, 3.3]; pooled estimate: 1.1 [0.8, 1.5]) and abatacept vs other b/tsDMARDs (range: 1.0 [0.4, 2.6] to 1.2 [0.6, 2.3]; pooled estimate: 1.0 [0.8, 1.3]) showed no increased risk in overall malignancy. Although individual registries showed a slight increase in breast (BC), lung (RABBIT) and lymphoma (ARTIS) cancers in patients treated with abatacept, numbers were too low to make an accurate comparative risk assessment.
Conclusion: While the development of malignancy is a potential risk associated with the use of immunomodulators, data from this large, international, post-marketing epidemiology programme suggest that the risks of overall malignancy and breast, lung or lymphoma cancers were not significantly increased in patients treated with abatacept. These data are consistent with the established safety profile of abatacept.

Table. IRs per 1000 PY (95% CI) for malignancies

	Overall malignancy			Breast			Lung			Lymphoma		
	Abatacept	csDMARDs	Other b/tsDMARDs	Abatacept	csDMARDs	Other b/tsDMARDs	Abatacept	csDMARDs	Other b/tsDMARDs	Abatacept	csDMARDs	Other b/tsDMARDs
ARTIS	11 (9, 14)	13 (13, 14)*	10 (9, 11)	2.5 (1.5, 4.1)	2.5 (2.4, 2.7)	2.3 (2.0, 2.7)	0.7 (0.2, 1.6)	2.0 (1.8, 2.1)	1.4 (1.1 1.6)	1.1 (0.5, 2.0)	0.9 (0.8, 1.0)	0.6 (0.4, 0.7)
BC	11 (6, 18)	10 (8, 13)	12 (10, 13)†	4.4 (1.6, 9.6)‡	2.3 (1.2, 4.0)‡	2.5 (1.9, 3.4)‡,§	NR	3.7 (2.4, 5.4)	2.9 (2.2, 3.6)‡	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)‡
FORWARD	8 (5, 12)	9 (6, 13)	5 (3, 7)	0.0 (0.0, 0.4)	0.0 (0.0, 1.3)	0.0 (0.0, 0.7)	0.1 (0.0, 0.7)	0.0 (0.0, 1.3)	0.0 (0.0, 1.0)	0.0 (0.0, 0.4)	0.0 (0.0, 1.3)	0.0 (0.0, 0.7)
RABBIT	9 (7, 13)	12 (10, 15)*	9 (8, 10)	1.3 (0.5, 2.8)	3.3 (2.1, 4.9)*	1.8 (1.4, 2.4)	2.8 (1.5, 4.8)	2.3 (1.3, 3.7)*	1.7 (1.3, 2.3)	0.2 (0.01, 1.2)	0.7 (0.2, 1.7)*	0.5 (0.3, 0.9)

*Biologic-naive patients (most of whom had been receiving csDMARDs)
†Other biologic group in BC only included anti-TNF inhibitors
‡Female only
ARTIS=Anti-Rheumatic Therapy in Sweden; b/tsDMARD=biologic/targeted synthetic DMARD; BC=British Columbia Canadian RA Cohort; csDMARD=conventional synthetic DMARD; FORWARD=FORWARD, The National Databank for Rheumatic Diseases in the USA; IR=incidence rate; NR=not reported; PY=patient-years; RABBIT=Rheumatoid Arthritis Observation of Biologic Therapy German registry

REFERENCE:

[1] DerSimonian R, Laird N. Control Clin Trials 1986;7:177–88.

Acknowledgement: Professional Medical writing: Claire Line, PhD, Caudex; funding: Bristol-Myers Squibb
Disclosure of Interests: Teresa Simon Employee of: Bristol-Myers Squibb, Samy Suissa Grant/research support from: Advisory board meetings, or as speaker, or received research grants from AstraZeneca, Bayer, Boehringer-Ingelheim, Bristol-Myers Squibb, Novartis, Speakers bureau: Advisory board meetings, or as speaker, or received research grants from AstraZeneca, Bayer, Boehringer-Ingelheim, Bristol-Myers Squibb, Novartis, Mary Lou Skovron Shareholder of: Bristol-Myers Squibb, Consultant for: Bristol-Myers Squibb, Thomas Frisell: None declared, Johan Askling Grant/research support from: Karolinska Institutet (JA) has or has had research agreements with the following pharmaceutical companies, mainly in the context of the ATRIS national safety monitoring programme for rheumatology biologicals: Abbvie, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and UCB., Consultant for: Karolinska Institutet has received remuneration for JA participating in ad boards arranged by Lilly, Novartis, and Pfizer., Kaleb Michaud Grant/research support from: Research grant funding in the last 2 years from Rheumatology Research Foundation and Pfizer, Sofia Pedro Employee of: FORWARD, The National Data Bank of Rheumatic Diseases, Anja Strangfeld Speakers bureau: Speakers fees from Bristol-Myers Squibb, MSD, Pfizer, Roche, Maarten Boers Consultant for: Bristol-Myers Squibb, Teva, Novartis, Pfizer, GlaxoSmithKline, Diane Lacaille Grant/research support from: Bristol-Myers Squibb and Eli Lilly Canada, Marc Hochberg Shareholder of: BriOri Biotech, Theralogix LLC., Consultant for: Bristol Myers Squibb, Eli Lilly, EMD Serono, Novartis Pharma AG, Pfizer Inc., Samumed LLC, Symic Bio Inc., Theralogix LLC, TissueGene Inc., TLC Biopharmaceuticals, Inc., Zynerba, Galapagos, IQVIA, Hoffman LaRoche., Andres Gomez Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb
DOI: 10.1136/annrheumdis-2019-eular.1663

OP0227 EFFECTS OF SUCCESSIVE SWITCHES TO DIFFERENT BIOSIMILARS INFLIXIMAB ON IMMUNOGENICITY IN CHRONIC INFLAMMATORY DISEASES IN DAILY CLINICAL PRACTICE

Ambre Lauret[1], Anna Moltó[1], Vered Abitbol[2], Loriane Gutermann[3], Ornella Conort[3], Francois Chast[3], Claire Goulvestre[4], Claire Le Jeunne[5], Stanislas Chaussade[2], Christian Roux[1], Frédéric Batteux[4], Maxime Dougados[1], Yannick Allanore[1], Jérôme Avouac[1]. [1]*Paris Descartes University, Cochin Hospital, Rheumatology, Paris, France*; [2]*Paris Descartes University, Cochin Hospital, Gastroenterology, Paris, France*; [3]*Paris Descartes University, Cochin Hospital, Pharmacy, Paris, France*; [4]*Paris Descartes University, Cochin Hospital, Immunology, Paris, France*; [5]*Paris Descartes University, Cochin Hospital, Internal Medicine, Paris, France*

Background:
Objectives: To determine whether the successive switches from innovator infliximab to a first then a second biosimilar infliximab increase the risk of immunogenicity during a 3-year observation period.
Methods: This is a usual care study performed in Cochin Hospital, Paris, France. First switch from innovator infliximab to a first biosimilar infliximab occurred in October/December 2015 and the second switch from the first to the second biosimilar infliximab started in December 2017. The end of the observation period was December 2018. Immunogenicity was defined by the detection of positive anti-drug antibodies (ADA >10 ng/mL), at least at two consecutive time points. The primary outcome of the study was the development of immunogenicity during the observation period. Secondary outcomes were i) the point prevalence of positive ADA at baseline, ii) the influence of the successive switches to biosimilars on the risk of immunogenicity and iii) the retention rate of biosimilar infliximab at the end of the observation period.
Results: Our prospective cohort consisted on 265 patients on maintenance therapy with innovator infliximab (135 axSpA, 64 with inflammatory bowel diseases, IBD, 31 with RA, 21 with PsA, 8 with uveitis and 6 with other chronic inflammatory diseases) who switched to biosimilar infliximab. Then, 140 patients switched to the second biosimilar infliximab, 26 remained treated with the first biosimilar, and innovator infliximab was re-established in 55 patients. 29 patients (15 females, 14 males) had positive ADA at baseline (point prevalence: 12.4%), before the switch to biosimilar infliximab. Among these 29 patients, 15 had axSpA (11%), 6 RA (19%), 6 IBD (9%) and 2 PSa (10%). Among the 236 patients with no ADA at baseline, 20 patients developed ADA during the observation period, corresponding to a rate of 3 for 100 patient years. The mean time to positive ADA detection was 21.2±13.7 months. Kaplan Meyer curve showed no influence of the number of biosimilars infliximab received on immunogenicity (Figure 1A). Among the 20 patients with positive ADA, 4 were back to innovator infliximab at the time of ADA detection, 10 patients were exposed to the first biosimilar and 6 to the second. The risk of treatment discontinuation was significantly higher in patients with positive ADA at baseline or during follow-up compared to patients without ADA (Figure 1B, Hazard Ratio 2.27, 95% confidence interval 1.33-3.89). No predictive factor of immunogenicity was identified (including type of disease, age, sex, BMI or concomitant DMARD intake). The retention rate of biosimilar infliximab (Figure 1C) was 58% (154/265) at the end of observation period, including 131 patients treated with the second biosimilar and 23 who remained treated with the first biosimilar.
Conclusion: In this usual care study with a 3-year observation period, the development of immunogenicity was low (3 for 100 patient years) and not favored by the switch to biosimilars infliximab. Thus, immunogenicity does not constitute a barrier to interchangeability between biosimilars infliximab in chronic inflammatory diseases.