stopped treatment during 5 months follow-up. Higher patient's global score and no use of methotrexate were associated with withdrawal. Longer follow-up will offer additional understanding of the potential efficacy and safety consequences of the non-medical switch.

References:
[1] Glintborg et al. Arthritis Rheumatol. 2016; 68 (suppl 10): Abstract no 951.

Acknowledgements: Data analysis was partly financially supported by Biogen.

Disclosure of Interest: B. Glintborg Grant/research support from: Abbvie, Biogen, I. Sørensen: None declared, A. G. Loft: None declared, J. Esbesen: None declared, H. Lindegaard: None declared, D. Jensen: None declared, K. Danebod: None declared, S. Dieperink: None declared, O. Hendricks: None declared, I. M. Hansen Grant/research support from: Roche, A. Linauskas: None declared, S. Kristensen: None declared, L. Andersen: None declared, M. Hossein: None declared, H. Nordin: None declared, B. Andersen: None declared, S. Chrysidis: None declared, J. Raun: None declared, N. Manilo: None declared, J. Grydehøj: None declared, E. Dalgaard: None declared, D. Pedersen: None declared, N. Krogh: None declared, M. Hetland Grant/research support from: Orion, BMS, AbbVie, Biogen, Pfizer, MSD, Eli Lilly

DOI: 10.1136/annrheumdis-2017-eular.1703

FRI0191 INCIDENCE OF DISEASE WORSENING IN INFLAMMATORY ARTHRITIS PATIENTS ON LONG-TERM INNOVATOR INFLIXIMAB THERAPY

A.M. Marrache[1], E. Psaradellis[2], J. Vaillancourt[2], E. Rampakakis[2], F. Nantel[1]. *[1]Medical Affairs, Janssen Inc., Toronto; [2]JSS Medical Research, Montreal, Canada*

Background: A recent randomized controlled study in a single country reported rates of disease worsening over a one-year follow-up period for innovator infliximab (REMICADE®, IFX) and a comparator in various diseases including AS and RA. After a mean duration of treatment of 6.7 years of innovator IFX, rates for disease worsening post-one year follow-up were 39.5% in AS and 36.7% in RA[1]. Other such data reporting disease worsening rates are rare.

Objectives: Using data from a longitudinal database, the objective was to determine the incidence of disease worsening in AS and RA patients on long-term therapy with innovator IFX. PsA patients were not included in this study due to low numbers (n=49).

Methods: BioTRAC is an ongoing, prospective registry of inflammatory arthritis patients initiating treatment with infliximab, golimumab or ustekinumab that has been ongoing since 2002 in Canada. We included AS and RA patients who had been on innovator IFX therapy for at least two, four or six years. Disease worsening endpoint was defined as follows: for AS patients; an increase in ASDAS $\geq$1.1 from baseline and a minimum score of 2.1. For RA patients; an increase in DAS28 $\geq$1.2 from baseline and a minimum score of 3.2.

Results: This analysis included a total of 196 AS and 425 RA patients. Among AS patients, 36.1% were female, 90.8% were bio-naïve at IFX initiation and 50% were on concomitant NSAID(s) at the 2-year index. The mean (SD) ASDAS score was 2.17 (1.05). As for the RA patients, 75% were female, 88.5% were bio-naïve, and 93% were on concomitant DMARD(s) while 35% were on corticosteroids at the 2-year index. The mean (SD) DAS28 ESR and DAS 28 CRP were 3.37 (1.40) and 3.00 (1.24), respectively.

As shown in table 1, the incidence of disease worsening in AS and RA patients on stable IFX for 2–6 years was low and varied from 2.7% to 11.5% at the subsequent 12 and 24 months visit.

Table 1. Incidence of disease worsening in AS and RA patients at the 2, 4, and 6-year index

Disease	Outcome	Index date post IFX initiation	Disease worsening at subsequent visits, n/N (%)	
			12 months	24 months
AS	ASDAS	2 years	9/79 (11.4%)	6/59 (10.2%)
		4 years	2/42 (4.8%)	1/37 (2.7%)
		6 years	1/25 (4.0%)	2/18 (11.1%)
RA	DAS28 ESR	2 years	20/184 (10.9%)	17/148 (11.5%)
		4 years	9/121 (7.4%)	7/106 (6.7%)
		6 years	8/73 (11.0%)	5/47 (10.6%)
	DAS28 CRP	2 years	16/160 (10.0%)	11/124 (8.9%)
		4 years	8/115 (7.0%)	6/104 (5.9%)
		6 years	6/80 (7.5%)	4/54 (7.4%)

Conclusions: In this prospective longitudinal cohort, patients on long-term innovator IFX therapy show low rates of disease worsening of 2.7% to 11.5% at 1 and 2 years in AS and RA. Additional studies may elucidate the true rate of and reasons for disease worsening in rheumatologic populations.

References:
[1] Goll et al. Biosimilar Infliximab (CT-P13) Is Not Inferior to Originator Infliximab: Results from a 52-Week Randomized Switch Trial in Norway. Arthritis Rheum 2016;68(S10). Abstract 19L.

Disclosure of Interest: A. M. Marrache Employee of: Janssen Inc., E. Psaradellis Employee of: JSS Medical Research, J. Vaillancourt Employee of: JSS Medical Research, E. Rampakakis Employee of: JSS Medical Research, F. Nantel Employee of: Janssen Inc.

DOI: 10.1136/annrheumdis-2017-eular.4545

FRI0192 CLINICAL PRACTICE GUIDE FOR THE TREATMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA). SYSTEMATIC REVIEW: IN PATIENTS WITH RA, WHICH IS THE SAFEST THERAPY FOR PATIENTS WITH PREVIOUS CANCER?

M.B. Nishishinya[1], C.A. Pereda[2], P. Diaz del Campo[3], A. Balsa[4] on behalf of GUIPCAR, Evidence based Rheumatology Working Group (SER) and GUIPCAR Working Group. *[1]Traumatology Institute Quirón, Barcelona; [2]Rheumatology, Hospital Mediterraneo, Almeria; [3]Investigation Unit, Spanish Rheumatology Society; [4]Rheumatology, Hospital Universitario la Paz, Madrid, Spain*

Background: Anti TNF therapy, has been used for the treatment of RA patients for several years. Yet, cancer and infections are among the most serious adverse effects described. Unfortunately, little is known about the effect of anti TNF therapy amongst patients with RA and previous cancer, mainly when synthetic DMARds treatment fails.

Objectives: To review the evidence on the safety of biological therapy in RA patients with previous neoplasia.

Methods: we performed a systematic review through Medline, Cochrane Library, and EMBASE databases. Studies written in English, French and Spanish were considered. Patients 18 years or older, with RA diagnosis (ACR 1987 o ACR/EULAR 2010 criteria), and cancer diagnosis before starting biologic therapy were included. While Systematic reviews, clinical trials and or observational studies with a minimal follow –up of 6 months were considered; case reports or narrative reviews were excluded.

Results: 1077 studies were potentially identified, and 6 cohort studies were finally included, (Aaltonen 2015, Dixon 2010, Phillips 2015, Raaschou 2015, Silva-Fernández 2016, Stranfeld 2010). Studies were based on registries of patients with RA treated with DMARds and biological therapy. Registries evaluated between 3.762 and 14.168 patients. The number of patients with documented previous cancer was around 122 to 425 as a whole. Biological therapies evaluated were: IFX, ETN, ADA, RTX, certolizumab pegol, Golimumab, ANAKinRA and synthetic DMARDs. Studies results were organized as anti TNF vs. DMARDs. All studies assessed were cohort trials, SIGN 2+ (Quality Scale). They included solid tumours as breast cancer, lymphoproliferative tumours, skin cancer, neck and brain tumours, as well as in situ uterus cancer.

There was no increment in the risk of incidence of previous cancer in patients treated both with synthetic DMARDs and with anti TNF therapy in all studies assessed.

We point out, that 1 SR (LaForest Divonne 2016) evaluated biological therapy safety in patients with RA. It included 124 trials, while in 27 metanalysis was performed. From these 27, only 3 (Dixon 2010, Mercer 2013 and Strangfeld 2010) where the only studies which assessed risk of recurrence of previous cancer in patients with RA. The RR 0, 77 (IC 95% 0, 29–2,03), did not exhibit an increment in the risk of cancer in these patients.

Conclusions: - Studies showed no differences in the incidence of previous cancer in patients treated either with synthetic DMARds or with anti TNF. However, we suggest precaution in the use of these therapies, as the real risk in this population is still unknown.

- The final decision of treating or not treating these patients (risk factors, limitations etc.) needs to be performed in accordance with oncologists.
- There is no strong evidence that could identify the real risk of anti TNF therapies in RA patients, with previous cancer.
- The Individual impact risk of different anti-TNF therapies in this population could not be performed due to incomplete data. Yet, there is not real time schedule considering time since previous cancer and the start of anti TNF therapy.

Well design studies with long follow-up periods are needed to answer these questions

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5953

FRI0193 EFFECT OF VALENCY OF ANTI-TNFS ON ELIMINATION MEDIATED BY ANTI-DRUG ANTIBODIES

J. Silva, A. Nesbitt. *UCB Pharma, Slough, United Kingdom*

Background: There are five different anti-TNF biologics: three are bivalent full length (FL) antibodies (adalimumab, golimumab, and infliximab), one a bivalent fusion protein (etanercept), and one a univalent PEGylated Fab' (PF) (certolizumab pegol [CZP]). Administration of such protein biologics can induce anti-drug antibodies (ADAbs), of which the majority are anti-idiotypic antibodies (anti-ID).[1] The potential cross-linking of bivalent anti-IDs with bivalent biologics can result in the formation of large immune complexes (ICs), which are subsequently cleared by mechanisms using the multiple Fc domains, thereby resulting in a decrease in the efficacy of the biologic. Since univalent biologics, such as CZP, only have one binding Fab' arm, such large cross-linked anti-ID-mediated ICs are unlikely to form. Therefore, anti-IDs may have a different effect on the elimination and bioavailability of univalent and bivalent biologics *in vivo*.

Objectives: To determine if the valency of a biologic will affect the *in vitro* size and *in vivo* elimination from the plasma of ICs formed with an anti-ID following intravenous (IV) administration to BALB/c mice.

Methods: An anti-ID antibody to CZP was generated and used for subsequent studies to mimic an ADAb response. Univalent PF CZP was reengineered as a bivalent FL humanized IgG1 antibody (similar to adalimumab) to directly

compare the effect of valency on IC-mediated clearance. This FL antibody showed very similar TNF neutralization compared to the conventional PF molecule in a bioassay. To generate ICs, the anti-ID was incubated overnight with either PF or FL CZP, and the size of the resultant ICs determined by analytical ultracentrifugation (AU). The anti-ID complexes and PF and FL CZP alone were then administered IV to the mice, and the elimination of the anti-TNFs from the circulation was monitored by quantitative liquid chromatography-mass spectrometry (LC-MS) in serial plasma samples.

Results: AU analysis of the immune complexes formed between PF CZP and the anti-ID showed the presence of one peak corresponding in size to one anti-ID molecule bound to two PF molecules (~$3.5x10^5$ Da). In contrast, the FL CZP/anti-ID mixture showed ICs of various sizes up to very large molecular weights (>$1x10^6$ Da), with the predominant species corresponding to a complex of two anti-IDs bound to two FL CZP molecules (~$6x10^5$ Da). The *in vivo* studies showed that the FL CZP/anti-ID ICs were eliminated much faster ($t_{1/2}$=0.3 hours) than the FL CZP alone ($t_{1/2}$=44.5 hours), whereas the PF CZP/anti-ID ICs were eliminated more slowly ($t_{1/2}$=60.5 hours) than the PF CZP alone ($t_{1/2}$=19.7 hours).

Conclusions: The FL CZP molecule formed large ICs with the anti-ID, which led to much faster elimination than the FL molecule alone. This result suggests that an ADAb response to a FL antibody could lead to rapid elimination and loss of efficacy of the drug in patients. In contrast, the PF CZP/anti-ID complex had a longer half-life than the PF CZP alone, presumably because this molecule was not seen as an IC due to the presence of only one Fc. These results showed that an ADAb to a univalent biological reagent may not lead to elimination and instead, may actually increase the *in vivo* half-life of the molecule.

References:

[1] van Schouwenburg PA. Ann Rheum Dis 2013;72:104–9.

Acknowledgements: This study was funded by UCB Pharma. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: J. Silva Employee of: UCB Pharma, A. Nesbitt Employee of: UCB Pharma

DOI: 10.1136/annrheumdis-2017-eular.2241

FRI0194 USE OF GLORESPONSETM NF-κB-RE-LUC2P HEK293 CELLS TO MONITOR DRUG AND ANTI-DRUG ANTIBODY LEVELS IN SERUM

B. Hernandez-Breijo[1], L.Y. Bravo Gallego[2], A. Martinez-Feito[1], A. Jochems[1], E. Olariaga[1], J. Cheng[3], L. Delaurière[4], F. Fan[3], T. Schagat[3], C. Plasencia[1], A. Mezcua[2], P. Nozal[2], A. Balsa[1], D. Pascual-Salcedo[1].

[1]Immuno-Rheumatology research group; [2]Immunology, University Hospital la Paz, Madrid, Spain; [3]Promega Corporation, Madison (WI), United States; [4]Promega Europe Training and Applications Laboratory (PETAL), Promega Corporation, Charbonnières-les-Bains, France

Background: Rheumatoid Arthritis (RA) is often treated with anti-TNFα such as infliximab (Ifx) which in a long-term treatment can lead to the development of anti-Ifx antibodies (ATI), resulting in an interference with the drug activity. The investigation of the bioactivity of the circulating drug and antibodies present in patients sera with inflammatory diseases will allow to harmonize the different published data using both bioassays as well as immunoassays.

Objectives: To evaluate the ability of the Promega bioassay in the quantification of both Ifx and ATI in serum from RA patients.

To compare the bioassay performance between capture- and bridging-ELISA.

Methods: Serum Ifx-trough levels were determined in 50 samples from patients with RA. To measure Ifx, the *bioassay* uses GloResponse™ NF-κB-RE-luc2P HEK293 cell line, which responses to TNFα resulting in modulation of NF-κB activity (Promega Corp., Madison, USA). This is an ease on performing reporter assay (add-mix-read) that detects the serum Ifx by inhibition of the luminiscent signal due to TNFα. The inhibition of the Ifx-driven luminescent signal is reverted by the presence of ATI in the serum. ATI concentration is determined using a standard curve obtained with a serial dilution of a serum sample known to have ATI. A relative luminescent unit (RLU) is arbitrarily defined. The *immunoassay* for Ifx (ELISA) captures recombinant TNFα, via a monoclonal antibody that does not interfere with the serum Ifx binding to TNFα. The reaction is developed with a biotinylated anti-idiotype antibody[1] (Cut-off for Ifx: 0.050 μg/ml). The ELISA to detect ATI takes advantage of the bivalency of most IgG subclasses, allowing the antibodies present in serum to bridge between Ifx-coated onto the plate with biotinylated Ifx in fluid phase[1] (Cut-off for ATI 50 AU/ml).

Results: Addition of TNFα on GloResponse cells induces the production of luciferase resulting in an increase of the luminescent signal in a dose-response. Addition of Ifx on GloResponse cells +TNFα decreases the production of luciferase and therefore the luminescent signal falls (r^2=0.99). Addition of anti-Ifx (in relative units) on GloResponse cells +TNFα + Ifx restore the production of luciferase resulting in an increase of the luminescent signal (r^2=0.98).

Serum Ifx concentrations were sorted into 3 groups (low, medium and high following ELISA levels). Similar number of positive Ifx results was found (30 samples, 55% by ELISA vs 28 samples, 52% by bioassay; κ=0.92; p=0.56) along with a significant Pearson correlation (r=0.8) between methods. The bioassay to measure ATI activity showed lower sensitivity than ELISA (9/31, 29% by ELISA vs 4/31, 13% by bioassay, κ=0.53, p=0.22) with a slightly less correlation for ATI levels by both methods (r=0.26).

Conclusions: Bioassay using GloResponse NF-κB cell line can be performed to monitor therapeutic drug of TNFα blocker and are useful to detect the presence of anti-drug antibody in serum samples treated with anti-TNFα antibodies. Comparison with ELISA method shows in most of the case the same data.

References:

[1] Pascual-Salcedo D. et al, Rheumatology, 2011.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6352

FRI0195 POINT-OF-CARE MONITORING OF ANTI-INFLIXIMAB ANTIBODIES IN PATIENTS TREATED WITH THE REFERENCE INFLIXIMAB OR CT-P13 IN ROUTINE CLINICAL PRACTICE

A. Ametzazurra[1], N. Rivera[2], A. Balsa[3], M.P. Arreba[4], E. Ruiz[2], C. Plasencia[3], J. Ortiz[4], D. Pascual-Salcedo[5], M.C. Muñoz[4], C. De Aysa[3], M.J. Allande[2], N. Torres[1], A.M. Hernández[1], X. Recalde[1], A. Martínez[1], D. Nagore[1]. *[1]R&D, Progenika-Grifols, Derio; [2]Rheumatology, Basurto University Hospital, Bilbao; [3]Rheumatology, la Paz University Hospital, Madrid; [4]Gastroenterology, Basurto University Hospital, Bilbao; [5]Immunology, la Paz University Hospital, Madrid, Spain*

Background: Loss of clinical response and infusion reactions to infliximab (IFX) are associated to the development of antibodies to IFX (ATI). ATI detection is a key step of patient management. However, current techniques may require additional patient appointments for sample collection, processing and batching in centralised facilities. Test reporting usually takes several days or weeks impairing effective decision making.

Objectives: To clinically validate the use of a new rapid test to detect ATI in capillary blood in a real-life point-of-care (POC) setting where patients attend the infusion center for the reference IFX (Remicade®, RMC) or CT-P13 (Inflectra®, IFT, or Remsima®) infusions.

Methods: PQ-EF1 and PQ-EF2 are prospective, observational studies designed to evaluate and compare the performance of a rapid POC test (CE-marked Promonitor® Quick Anti-IFX, Progenika, Spain) to detect ATI in routine clinical practice in rheumatic and gastroenterology patients treated with the reference IFX or the biosimilar CT-P13 attending the infusion center with the ELISA technique as a reference. The POC test is a qualitative immunochromatographic assay based on lateral flow technology to detect ATI (including biosimilar CT-P13) in either fingerprick or serum or venous whole blood. Consecutive patients (initiating or under maintenance therapy) were recruited and tested in La Paz and Basurto University hospitals with the rapid test in capillary and venous whole blood specimens immediately before the infusion. ATI test results were read visually with the POC test in 30 min, just before the patient started the infusion. Trough sera were also collected for subsequent analysis with the rapid test and benchmarked with Promonitor®-Anti-IFX ELISA (Progenika, Spain). Follow-up time was 6 months. ELISA quantitative results were categorized as positive and negative to allow comparisons with the qualitative rapid test.

Results: Ninety consecutive patients were recruited (a total of 137 visits in the 6 months follow-up) accounting for a total of 137 sera, 137 fingerpricks and 71 venous whole blood samples. Overall, 8 (8.9%) patients developed ATI (5 ankylosing spondylitis, 1 Crohn's disease, 1 ulcerative colitis and 1 juvenile idiopathic arthritis). ATI were detected in 5 patients treated with Remicade® and 3 treated with Inflectra®. Overall agreements between fingerprick vs venous whole blood and fingerprick vs serum measured with the rapid POC test were 100% and 99%, respectively. Positive (PPA) and negative (NPA) agreements between the POC test and ELISA were 91% and 99%, respectively. PPA and NPA between the ELISA and the POC test in serum was 100% and 99%, respectively.

Conclusions: ATI can be reliably detected in either venous or capillary circulation. Results show an almost perfect agreement between specimens and with the reference ELISA technique. ATI measurement with the POC test allows the clinician to detect ATI in a quick and fully decentralised mode facilitating immediate POC decision making.

Disclosure of Interest: A. Ametzazurra Employee of: Employee of Progenika Grifols, N. Rivera: None declared, A. Balsa: None declared, M. Arreba: None declared, E. Ruiz: None declared, C. Plasencia: None declared, J. Ortiz: None declared, D. Pascual-Salcedo: None declared, M. Muñoz: None declared, C. De Aysa: None declared, M. Allande: None declared, N. Torres Employee of: Employee of Progenika Grifols, A. Hernández Employee of: Employee of Progenika Grifols, X. Recalde Employee of: Employee of Progenika Grifols, A. Martínez Employee of: Employee of Progenika Grifols, D. Nagore Employee of: Employee of Progenika Grifols

DOI: 10.1136/annrheumdis-2017-eular.5056

FRI0196 BIOSIMILARS IN THE UK: EARLY REAL WORLD DATA FROM THE BRITISH SOCIETY FOR RHEUMATOLOGY BIOLOGICS REGISTERS FOR RHEUMATOID ARTHRITIS

D. De Cock[1], K. Watson[1], K.L. Hyrich[1,2] on behalf of BSRBR-RA Control Centre Consortium. *[1]Arthritis Research UK Centre for Epidemiology, University of Manchester; [2]National Institute of Health Research Manchester Musculoskeletal Biomedical Research Unit, Central Manchester NHS Foundation Trust, Manchester Academic Health Science, Manchester, United Kingdom*

Background: Biosimilars, biopharmaceuticals assessed by regulatory agencies