THU0037 IMMUNOGENICITY IN A TERTIARY CARE HOSPITAL: OUR EXPERIENCE

A.G. Valle[1], M. Garijo Buffort[2], M. Retuerto Guerrero[2], C. Iñiguez[2], E. Díez[2], C. Moriano[2], A. López[2], M. Martín[2], C. Álvarez[2], T. Pérez Sandoval[2].
[1]Rheumathology, Hospital Can Misses, Ibiza; [2]Rheumathology, Complejo Asistencial Universitario, León, Spain

Background: The drugs called Anti-TNF inhibitors are capable of inducing an immune response (immunogenicity) Its effectiveness may be affected by the development of Anti-Drug Antibodies (Ab)
Objectives:
- To assess the frequency of appearance of Anti-Drug Antibodies: Infliximab (IFX), Adalimumab (ADA), etanercept (ETN)
- To classify the failures of response
- To analyse the relationship between anti-TNFα antibodies and concomitant treatment with DMARDs
- To observe whether there is a link between risk factors and drug levels

Methods: This is a retrospective, descriptive, observational study of patients with Rheumatoid Arthritis (RA), Spondyloarthritis (SpA), Psoriatic arthritis (PsA), Seronegative arthritis (SA) and Enteropathic arthritis (EA) with active disease and that were treated in the "University Health Care Hospital of León" between Jan-2015 and Jan-2016. Using ELISA Technology and the kits Promonitor®, it was possible to detect serum levels of IFX ADA, ETN (reference values>2.5μg/mL, 5–8μg/mL and 0.8–1.2μg/mL respectively) and of anti-drug antibodies. The samples were collected the same day of the administration, prior to it, always in a trough level. The gathered data was: demographic data, activity, time-to-disease progression, prior treatment with biologics, concomitant DMARDs, duration of the biologic treatment and dosage, quantization levels, anti-TNF antibodies, cardiovascular risk factors (CVRF) and smoking habits.
Results: Variables to study:
N=40: IFX 50%, ADA 30%, ETN 20%.
Age 53.6±3.7 years old [95% CI], Women: 55%, time-disease progression: 12.3±2.7 years old.
Type of disease: RA 47.5%, SpA 15%, PsA 20%, SA 7.5%, EA 10%.
DAS28: 3.5±0.4, BASDAI 4.7±0.5, BASFI 4.3±1.4.
Prior treatment with biologics (30%): IFX 15%, ADA 66%, ETN 12.5%.
Frequency of administration: IFX 8.6±0.36 weeks, ADA 2.25±0.36 weeks, ETN 1.1±1.0 weeks.
Reasons for requesting the levels:
- Secondary failure (82%): IFX 90%, ADA 66.7%, ETN 75%
- Primary failure (17%): IFX 5%, ADA 33%, ETN 25%
- Infusion reactions (2.5%)

Drug levels within the therapeutic range: IFX 10%, ADA 41%, ETN 50%.
Formation of anti-TNF Ab of the sample: IFX 30%, ADA 16%, ETN 0%.
DMARDs: presence of 62.5% (MTXsc 64%, MTXvo 20%, Leflunomide, Sulfasalazine e Hydroxychloroquine 16%).
Conclusions: We found the following conclusions:
- In the data collected, we observe that the IFX (30%) is the most immunogenic drug, followed by the ADA (16%) and being the ETN (0%) the one that so far has not presented anti-drug Ab, outcomes in agreement with the medical literature
- The main reason for requesting has been the secondary failure (90%)
- The suboptimal levels of the drug and the presence of specific ab are correlated with the loss of clinical response. In our case, the proper range of drug is only objective in 10% of the patients treated with IFX, 41% with ADA and 50% with ETN
- The concomitant use of DMARDs in our study has not been shown to decrease levels of Ab, being the MTX the most used in our patients (84%). We observed no correlation between the occurrence of Ab, the use of DMARDs or the type of disease
- The monitoring of the levels of anti-TNF drug may be useful to individualize the treatment, to avoid possible side effects and to make decisions regarding the continuation or change of therapy.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2800

THU0038 BIMEKIZUMAB DUAL INHIBITION OF IL-17A AND IL-17F PROVIDES EVIDENCE OF IL-17F CONTRIBUTION TO CHRONIC INFLAMMATION IN DISEASE-RELEVANT CELLS

A. Maroof[1], R. Okoye[1], T. Smallie[1], D. Baeten[2], S. Archer[1], C. Simpson[1], M. Griffiths[1], S. Shaw[1]. *[1]UCB Pharma, Slough, United Kingdom; [2]UCB Pharma, Brussels, Belgium*

Background: IL-17A and IL-17F share structural homology and have similar biological function[1]. Although the contribution of IL-17A to immune-mediated inflammatory diseases has been widely reported[1–3], the role of IL-17F is less well characterised in human tissue inflammation. Bimekizumab, a humanised monoclonal IgG1 antibody, was developed to neutralise both IL-17A and IL-17F potently and selectively, and is under clinical development as a treatment for psoriatic arthritis (PsA) and other immune-mediated conditions such as psoriasis.
Objectives: To assess the involvement of IL-17F in chronic inflammation in tissue from patients with PsA and disease-relevant cells, and to determine the effect of dual neutralisation of IL-17A and IL-17F in suppressing inflammation, compared with blockade of IL-17A.
Methods: Synovial and lesional skin tissue from patients with PsA was probed by immunostaining for expression of IL-17F protein. Normal dermal fibroblasts and synoviocytes, in the presence of TNFα, were stimulated with recombinant IL-17A and IL-17F to assess the inflammatory response. Using cytokine-specific blocking antibodies, the individual and combined effects of IL-17A and IL-17F were explored with: pro-inflammatory cytokine expression in a complex *in vitro* model (synoviocytes from patients with PsA and normal dermal fibroblasts were treated with pro-inflammatory mediators from supernatant [SN] of sorted Th17 cells), microarray and cell migration studies.
Results: IL-17F expression was observed in tissue biopsies from patients with PsA. In normal dermal fibroblasts, normal synoviocytes and synoviocytes from patients with PsA, stimulation with recombinant IL-17F promoted production of pro-inflammatory mediators, such as IL-6 and IL-8, though to a lesser extent than with recombinant IL-17A. Treatment of Th17 SN-stimulated synoviocytes from patients with PsA with bimekizumab (neutralising IL-17A and IL-17F) led to greater reductions of IL-6 (42% lower $p<0.05$) and IL-8 (35% lower $p<0.05$) production than IL-17A inhibition. Bimekizumab treatment of Th17 SN-stimulated normal dermal fibroblasts also reduced production of IL-6 (35% lower $p<0.0001$) and IL-8 (57% lower $p<0.0001$) more than IL-17A alone. Combining IL-17A + IL-17F monoclonal antibodies produced similar results to bimekizumab. Levels of expression of 27 inflammation-linked genes, including *CXCL1*, *CXCL2*, *CXCL3* and *IL-15RA*, were lower with dual neutralisation of IL-17A and IL-17F by bimekizumab versus inhibition of IL-17A. Suppression of migration of neutrophils (Fig.) and monocytes, both involved in tissue destruction in immune-mediated diseases, was substantially greater with bimekizumab treatment than with single blockade of IL-17A.

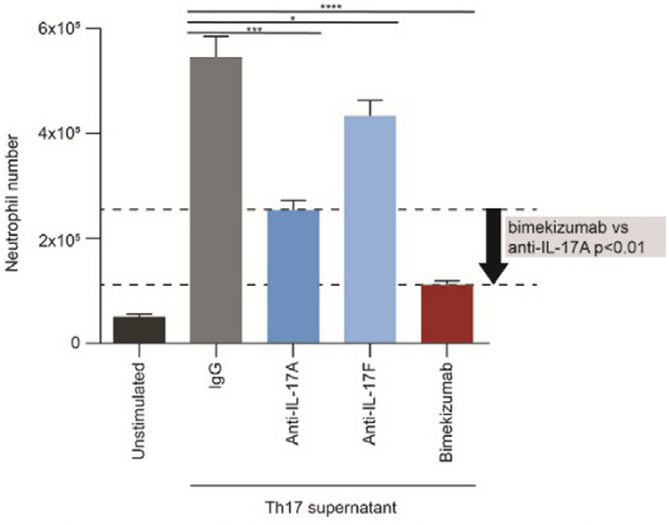

Fig. Quantification of neutrophil migration following treatment with cytokine-specific antibodies and bimekizumab. * represents a significant reduction of cell migration vs IgG control, *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001

Conclusions: Dual neutralisation of IL-17A and IL-17F provides evidence for the contribution of IL-17F to inflammation in joints and skin beyond IL-17A alone. As a result, dual inhibition of IL-17A and IL-17F by bimekizumab may provide an effective treatment for immune-mediated inflammatory diseases such as PsA.
References:
[1] C Johansen et al. Br J Dermatol 2009:160:319–24.
[2] AL Lima et al. Br J Dermatol 2016:174:514–21.
[3] C Doe et al. Chest 2010:138:1140–7.
Disclosure of Interest: A. Maroof Employee of: UCB Pharma, R. Okoye Employee of: UCB Pharma, T. Smallie Employee of: UCB Pharma, D. Baeten Grant/research support from: UCB Pharma, Consultant for: AbbVie, Pfizer, MSD, Roche, BMS, Novartis, Eli Lilly, Boehringer Ingelhaim and Glenmark, S. Archer Employee of: UCB Pharma, C. Simpson Employee of: UCB Pharma, M. Griffiths Consultant for: UCB Pharma, Employee of: UCB Pharma, S. Shaw Employee of: UCB Pharma
DOI: 10.1136/annrheumdis-2017-eular.4966

THU0039 LIPIDOMICS ANALYSIS OF HDL PARTICLE IN INFLAMMATORY RHEUMATIC DISEASES: ALTERATION OF PHOSPHOLIPID COMPOSITION AND ROLE OF INFLAMMATION

C. Giraud[1], F. Capel[2], F. Dutheil[3], B. Pereira[4], M. Soubrier[1], A. Kontush[5], M. Lhomme[6], J.L. Sebedio[2], A. Tournadre[1]. *[1]Rheumatology, CHU Gabriel Montpied; [2]Unité nutrition humaine, UMR 1019/Inra; [3]AME2P, Blaise Pascal University; [4]Biostatistic/ "Delegation Recherche Clinique et Innovation", CHU Gabriel Montpied, Clermont Ferrand; [5]INSERM UMR_s 1166 – Ican, Université Pierre et Marie Curie – Paris 6; [6]ICANalytics, ICAN, Paris, France*

Background: Rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylsosing