antagonist, tocilizumab (TCZ), on NT-proBNP levels and systolic heart function is yet to be obtained.

Objectives: Access the effect of 12 months TCZ therapy on NT-proBNP levels, transthoracic echocardiography results and analyze the association between congestive heart disease progression and RA activity.

Methods: 37 RA patients (pts) (31F/6M); median age 56,5 [48; 63,5] years; disease duration 48 [6; 348] months; DAS28 score 6,15 [5,44; 6,45]; rheumatoid factor (RF)+100%; anti-citrullinated protein antibody (ACPA) + 79,6% were treated in an open-label study with TCZ (8mg/kg every 4 weeks). Identification of NT-pro-BNT in blood serum, transthoracic ultrasound evaluation of left ventricular ejection fraction (LVEF), E/A ratio performed at baseline and 12 months.

Results: 11 (29,7%) pts had congestive heart disease (CHD) (II functional class of NYHA), 7 (18,9%) pts having signs of mild left ventricular dysfunction (LVD) as dyspnea, shortness of breath, cardiotropic treatment remained the same in the course of the study. After 12 month TCZ treatment as RA activity lowered (DAS28 2.32 [1,75; 3,15], $p < 0,05$), NT-proBNP levels decreased (100,95 [57,9; 117,6] pg/ml to 90,46 [33,62; 106,6] pg/ml), along with elevation of LVEF (60,75 [60; 70]% to 67,68 [62,5; 73,5], $p = 0,001$). Increase of E/A (0,97 [0,8; 1,17] to 1,04 [0,7; 1,42] correlated with decrease of NT-proBNP level ($r = -0,63$, $p = 0,036$). Raise of LVEF over 12 months correlated with decrease of RA activity according to SDAI scale ($r = -0,670$, $p < 0,05$). No significant relationship between NT-proBNP levels, LVEF, E/A and other scales measuring RA activity was found. Clinically all patients had improvement in evaluation of their health and no signs of CHD or RVD progression were found.

Conclusion: Use of TCZ in patients with active RA showed none to positive influence on heart condition, specifically, lowering NT-proBNP levels, improving LVEF and reducing clinical signs of LVD.

References:

- [1] Pan Y, Li D, Ma J, Shan L, Wei M. NT-proBNP test with improved accuracy for the diagnosis of chronic heart failure. *Medicine (Baltimore)*. 2017 Dec;96(51):e9181.
- [2] D Novikova, I Kirillova, E Markelova et al. The first report of significantly improvement of NT-proBNP level in rheumatoid arthritis patients treated with tofacitinib during 12-month follow-up, *European Heart Journal*, Volume 40, Issue Supplement 1, October 2019, ehz745.0836.
- [3] Pappas DA, Nyberg F, Kremer JM et al. *Clin Rheumatol*. 2018 Sep;37(9):2331-2340.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5361

AB0309

MEASURING THE DIFFERENCE: COMPARISON OF MEASUREMENT OF FREE INFLIXIMAB ANTI-DRUG ANTIBODIES

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Background: Infliximab (IFX) was one of the first TNF alpha inhibitors to be licenced in inflammatory arthritis and is still commonly used today. Studies have shown that approximately 50% of primary IFX responders will suffer from secondary loss of response within the first 12 months of treatment (1). The development of Anti-Drug Antibodies (ADAs) plays a significant role in this treatment failure (2).

Monitoring of ADAs helps identify those patients who fail to respond to treatment due to low IFX trough levels. In this scenario the presence of ADAs can aid decision-making regarding increasing IFX dosing or switching biologic therapy to optimise treatment. (3).

Objectives: Despite their potential importance the detection of ADAs varies widely depending on the type of assays used. The aim of this study was to determine the qualitative concordance of three commercially available ELISA kits for measurement of free ADAs to IFX on the Grifols Triturus analyser.

Methods: 150 patient samples from patients with inflammatory conditions and low IFX trough drug levels ($\leq 0,6\mu\text{g/ml}$) were analysed for free ADAs using Promonitor, Lisa Tracker and IDKmonitor kits on the Grifols Triturus automated ELISA analyser.

Results: Kappa coefficient (κ) analysis indicated a moderate agreement between the Promonitor and IDKmonitor assays ($\kappa = 0,484$ (95% CI, 0.357 to 0.611)) and the IDKmonitor and Lisa Tracker assays ($\kappa = 0,485$ (95% CI, 0.348-0.621)) as well as substantial agreement between the Promonitor and Lisa

Tracker assays ($\kappa = 0,768$ (95% CI, 0.667-0.870)). Figure 1 shows the distribution of samples identified as free ADA positive by each kit.

Figure 1. Distribution of samples identified as free ADA positive by Promonitor, Lisa Tracker, and IDKmonitor assays. Fifty samples were considered positive by all assays. Three samples were considered positive by Promonitor and Lisa Tracker, and eight samples were considered positive by Lisa Tracker and IDKmonitor. No samples were considered positive by Promonitor and IDKmonitor. One sample was considered positive by Promonitor only, seven samples were considered positive by Lisa Tracker only, and twenty-six samples were considered positive by IDKmonitor

Conclusion: All kits appear amenable for utilisation in a high-throughput laboratory though a true quantitative comparison between these kits was precluded by the absence of any certified reference material for free ADAs to IFX.

Although broad qualitative agreement was found between the three kits, they should not be used interchangeably for patient management.

Further research is required to estimate the impact of free ADAs on efficiency of IFX treatment and patient management.

References:

- [1] Quistbrecht J, Hässler S, Bachelet D et al. *Incidence and risk factors for adalimumab and infliximab anti-drug antibodies in rheumatoid arthritis: A European retrospective multicohort analysis*. *Seminars in Arthritis and Rheumatism* Volume 48, Issue 6, June 2019, Pages 967-975 2.
- [2] Moots RJ, Xavier RM, Mok CC, Rahman MU, Tsai W-C, Al-Maini MH, et al. (2017) *The impact of anti-drug antibodies on drug concentrations and clinical outcomes in rheumatoid arthritis patients treated with adalimumab, etanercept, or infliximab: Results from a multinational, real-world clinical practice, non-interventional study*. *PLoS ONE* 12(4): e0175207. <https://doi.org/10.1371/journal.pone.0175207>
- [3] Smolen JS, Landewé R, Bijlsma J, et al. *EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update*. *Annals of the Rheumatic Diseases* 2017;76:960-977.

Disclosure of Interests: Rhona Hamilton: None declared, Stephanie Shields: None declared, Andrew McGucken: None declared, Jonathan MacDonald: None declared, Martin Perry Grant/research support from: Grifols, Abbvie, Sandoz unrestricted educational grant, Consultant of: Abbvie, Gilead, Celltrion Advisory Board, Speakers bureau: Sandoz, Allan Dunlop: None declared, Elaine Gribben: None declared, Peter Galloway: None declared

DOI: 10.1136/annrheumdis-2020-eular.665

AB0310

TROUGH CONCENTRATION AND ESTIMATED CLEARANCE CAN DETECT IMMUNOGENICITY TO ADALIMUMAB IN RA PATIENTS: A PROSPECTIVE LONGITUDINAL MULTICENTRE STUDY

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Background: Anti-Drug Antibodies (ADA) to adalimumab increase drug clearance in rheumatoid arthritis (RA).

Objectives: To study the ability of drug concentration or estimating clearance to identify ADA to adalimumab.

Methods: Adalimumab concentration was measured with a validated ELISA. ADA was measured using a capture ELISA (Theradiag®) and the Meso scale discovery (MSD) platform. Using a bayesian PK model, adalimumab clearance was estimated at 1, 3, 6 and 12 months. Predictions for ADA presence were calculated, and the correlation between ADA and adalimumab clearance was analysed.

Results: We analyzed 108 samples from 53 RA patients. Serum concentrations and clearance estimates showed good prediction performance for ADA presence (Table 1). There was a correlation between adalimumab clearance and ADA (Figure 1).

Table 1. Immunogenicity prediction of adalimumab, using trough concentration or estimated clearance

Time of visit	ADA method	Adalimumab trough concentration		Adalimumab estimated clearance	
		AUC ROC	p-value	AUC ROC	p-value
Month 1	THER	.55	.6411	.52	.8358
	MSD	.65	.0821	.61	.1872
Month 3	THER	.89	.0006	.91	.0003
	MSD	.73	.0096	.72	.0131
Month 6	THER	.95	.0035	.95	.0035
	MSD	.85	.0004	.84	.0006
Month 12	THER	.87	.0045	.86	.0057
	MSD	.88	.0002	.88	.0002

Figure 1. correlation between adalimumab estimated clearance and ADA as provided by the Meso scale discovery (MSD) platform

Conclusion: Adalimumab concentration and clearance should be considered as reliable predictors for ADA presence in RA patients.

Acknowledgments: Measurement of adalimumab serum concentrations was performed within the 'Centre pilote de suivi biologique des anticorps thérapeutiques' (CePiBac)– Pilot centre for therapeutic antibodies monitoring platform of Tours University Hospital, which was cofinanced by the European Regional Development Fund (ERDF). We thank Oscar Knight, Delphine Delord and Fabien Giannoni (ABIRISK lab technician), Caroline Brochon and Anne Claire Duveau (CePiBac), Alette Decock-Giraudaud (Centre de ressource-Biobank), Sophie Tourdot (ABRISIK Project manager), Aline Doublet (Assistance Publique Hopitaux de Paris, Agnès Hincelin-Méry (Sanofi, Chilly-Mazarin, France). This work has received support from the Innovative Medicines Initiative Joint Undertaking (IMI JU) under grant agreement no. 115303, the resources of which are composed of financial contributions from the European Union's Seventh Framework Programme (FP7/2007-2013) and European Federation of Pharmaceutical Industries and Associations (EFPIA) companies' in-kind contributions.

Disclosure of Interests: David Ternant Consultant of: Sanofi and Amgen., Jamal Elhasnaoui: None declared, Natacha Szely: None declared, Salima Hachein-Bey: None declared, Aude Gleizes: None declared, Christophe Richez Consultant of: Abbvie, Amgen, Mylan, Pfizer, Sandoz and UCB., Jessica Manson: None declared, Martin SOUBRIER: None declared, Olivier Brocq: None declared, Jérôme Avouac: None declared, Anna Fogdell-Hahn Grant/research support from: Biogen Idec and Pfizer., Consultant of: Pfizer, Biogen, Merck-Serono, and Sanofi-Genzyme., Pierre Dönnès: None declared, Gilles Paintaud Grant/research support from: Amgen, Genzyme (Sanofi), Lilly, Merck, Novartis, and Roche Pharma., Consultant of: Chugai, Novartis and Shire (Takeda), with remunerations received by his institution., Céline Desvignes: None declared, Florian Deisenhammer: None declared, Sebastian Spindeldreher Employee of: Novartis, Marc Pallardy: None declared, Xavier Mariette Consultant of: BMS, Gilead, Medimmune, Novartis, Pfizer, Servier, UCB, Denis Mulleman Grant/research support from: Non-governmental organisation Lions Club Tours Val de France, French Society for Rheumatology., Consultant of: Pfizer, Novartis.

DOI: 10.1136/annrhumdis-2020-eular.2809

AB0311 THE PROPER STUDY: RESULTS OF THE FIRST INTERIM ANALYSIS OF A PAN-EU REAL-WORLD STUDY OF SB5 BIOSIMILAR FOLLOWING TRANSITION FROM REFERENCE ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS, AXIAL SPONDYLOARTHRITIS OR PSORIATIC ARTHRITIS

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Background: SB5, a biosimilar to reference adalimumab (ADA), received EU marketing authorisation in August 2017, based on the totality of evidence from pre-clinical and clinical Phase I and III studies that demonstrated bioequivalence, similar efficacy, and comparable safety and immunogenicity to the reference. There are few published data on the transition from reference to biosimilar ADA outside the controlled, randomised, clinical trial setting.

Objectives: To evaluate candidate predictors of persistence on SB5 in EU patients across multiple indications.

Methods: This ongoing observational study will enrol approximately 1200 subjects with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) or psoriatic arthritis (PsA), who initiated SB5 as part of routine clinical practice following a minimum of 16 weeks' treatment with reference ADA, at clinics in Belgium, Germany, Ireland, Italy, Spain and the UK. Data are captured from clinic records retrospectively for the 24 weeks prior to transition, and prospectively and/or retrospectively for 48 weeks following transition. The primary objective is to evaluate candidate predictors of persistence, and primary outcome measures include baseline clinical characteristics, disease activity scores, clinical management and patient satisfaction over time. This interim analysis provides an overview of baseline characteristics for subjects enrolled and followed up by the data extract date of 20th December 2019.

Results: Of the 123 patients included in this interim analysis, 43 suffer from RA, 42 from axSpA and 38 from PsA.