Objectives: The aim of this work was to compare the clinical and biological response to biotherapy with the presence of ADA and the residual dose rate.

Methods: We analysed the medical records of 69 patients treated with biotherapy between September 2017 and October 2018. 3 pathologies were considered: rheumatoid Arthritis (RA) diagnosed by ACR/EULAR 2009 criteria, Spondylarthritis (SPA) according to Assessment of Spondylarthritis international Society (ASAS) And crohn's disease (CD) classified upon the 2006' Montreal classification. We did search the presence of anti-body anti-drugs (ADA) and the residual dose for the following therapies: Etanercept (ETN), Infliximab (IFX), Adalimumab (Ada) or Rituximab (RTX).

Results: The mean age was 43.33 ± 11.4 year. The sex ratio M/F was 1.57.

Regarding the RA: they were 13 patients. 10 had positive (ACPA) and seven positive (RF). All the patients had an initial treatment by conventional synthetic disease modifying antirheumatic drugs (csDMARDs) before moving to bDMARDs. 14 were in concomitant disease modifying therapy. The DAS28-ESR average was at 4.12 [2.67 à 5.79]. we found positive ADA in only one patient analysis. There were 8 responding versus five non-responding patients, according to the clinical and biological evaluation of disease activity.

28 patients were in the SPA group: 13 with an axial spondylarthritis. 14% had the HLAB 27. It was an active disease in 15 cases. ASDAS-CRP average was 4.87 ± 0.17 [4.7; 5]. The received biotherapy was IFX 50%, ETN 28.6% and Ada 21.4%. 10 patients had a positive ADA and 8 of them had a rate superior to 100 UI. 19 patients were considered as non-Responding.

In the CD group, 28 patients were enrolled. All of them had a previous immunosuppressor treatment. Same patients in association with biotherapy. It was positive ADA in 7 cases. And 7 patients were non-responding to the treatment.

The residual dose of drugs was calculated for each drug and it is explained in the following table :

	IFX		Ada		ETN		RTX	
	%	N	%	n	%	n	%	n
High Residual dose	60%	21	52.9%	9	90.9%	10	66.7%	4
Low residual dose	40%	14	47.1%	8	9.1%	1	33.3%	2

Positive ADA was associated with therapy failure in all type of biotherapy ($p=0.001$). A low residual dose was associated to therapy failure only in the case of IFX ($p=0.005$).

In multivariate analyses, the predictive factors associated with therapeutic failure were : positive ADA ($p=0.008$) and advanced age at diagnosis, below 30 years old age ($p=0.020$). Hosmer index=0.452.

Conclusion: Immune response induced in patients treated with biotherapy can be quantified now thanks to ADA dosage and the residual dose assessment.

REFERENCES

- [1] Kristensen LE, Kapetanovic MC, Gülfe A, Söderlin M, Saxne T, Geborek P. Predictors of response to anti-TNF therapy according to ACR and EULAR criteria in patients with established RA: results from the South Swedish Arthritis Treatment Group Register. *Rheumatology (Oxford)*. 2008;47:495-9.
- [2] Lanfant-Weybel K, Lequerré T, Vittecoq O. Anti-TNF alpha dans le traitement de la polyarthrite rhumatoïde et de la spondylarthrite ankylosante. *Presse Med*. 2009;38:774-87.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.8230

AB1309

QUANTIFICATION OF MINIMAL RESIDUAL DOSE ASSOCIATED WITH BIOLOGICAL THERAPEUTIC RESPONSE ANTI DRUG ANTI BODIES: ARE THEY ALL NEUTRALIZING?

Salma Athimni¹, Rim dhahri¹, Maroua Slouma¹, Leila Metoui¹, Imen Gharsallah¹, Bassem Louzir¹, ^{2,2}Maroua Meddeb^{2,2}, Mahdi Dridi². ¹Military Hospital, rheumatology, Teboulbou, Tunisia; ²Military Hospital, pharmacology, Teboulbou, Tunisia

Background: The use of biological was associated to the capacity of inducing an immune response in patients that could neutralize the drug.

The anti-body anti-drug (ADA) assay was a revolutionary tool to prevent treatment failure.

Objectives: The aim of this work was to assess if the presence of ADA in patients system is sufficient to predict failure and indicates the switch of treatment.

Methods: We enrolled 69 patients treated with biotherapy between September 2017 and October 2018. 3 pathologies were considered: rheumatoid Arthritis (RA) diagnosed by ACR/EULAR 2009 criteria, Spondylarthritis (SPA) according to Assessment of Spondylarthritis international Society (ASAS) And crohn's disease (CD) classified upon the 2006' Montreal classification. We did search the presence of anti-body antidrugs (ADA) and the residual dose for the following therapies: Etanercept (ETN), Infliximab (IFX), Adalimumab (Ada) or Rituximab (RTX).

Results: The mean age was 43.33 ± 11.4 year. The sex ratio M/F was 1.57. there were 13 patients with RA, 28 SPA and 28 CD. The Majority of patients were receiving IFX 50.7% (n=35) with same doses. There were 20 responding versus 15 non-responding patients. 40% of them had a high residual dose. Regarding Ada 24.6% (n=17). There were 9 non-responding patients and low residual doses were found in 47.1%. 11 patients were using ETN. The ADA was positive in only one patient who was non-responding and having a low residual dose.

Concerning the RTX, it was used for 6 patients. The ADA was negative in all patients. Two non-responding cases having a low residual dose.

The following table explains the repartition of patients according to ADA rates:

		ADA Positifs	ADA Négatifs
IFX	Responding patients	4	16
	Non-responding patients	9	6
ETN	Responding patients	0	6
	Non-responding patients	1	4
Ada	Responding patients	0	8
	Non-responding patients	4	5
RTX	Responding patients	0	4
	Non-responding patients	0	2

Positive ADA was associated with therapy failure in all type of biotherapy ($p=0.001$). A low residual dose was associated to therapy failure only in the case of IFX ($p=0.005$).

Positive ADA was associated to a low rate of residual dose in the case of IFX and Ada.

This association couldn't be evaluated for RTX (none) and ETN (just one positive rate).

Conclusion: The ADA assay is a revolutionary tool allowing the evaluation of treatment response but it cannot be considered without the clinical assessment of patient. The evaluation residual dose should be concomitant to valorize and guide the therapeutic decision

REFERENCES

- [1] Kristensen LE, Kapetanovic MC, Gülfe A, Söderlin M, Saxne T, Geborek P. Predictors of response to anti-TNF therapy according to ACR and EULAR criteria in patients with established RA: results from the South Swedish Arthritis Treatment Group Register. *Rheumatology (Oxford)*. 2008;47:495-9.
- [2] Lanfant-Weybel K, Lequerré T, Vittecoq O. Anti-TNF alpha dans le traitement de la polyarthrite rhumatoïde et de la spondylarthrite ankylosante. *Presse Med*. 2009;38:774-87.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.8271

AB1310

PROSPECTIVE USE OF THE GLUCOCORTICOID TOXICITY INDEX (GTI) IN A COHORT OF VASCULITIS PATIENTS

Lisa Ehlers¹, Edgar Wiebe¹, Desiree Freier¹, Sandra Hermann¹, Eli Miloslavsky², Yuqing Zhang², Frank Buttgerit¹, John H. Stone². ¹Charité – Universitätsmedizin Berlin, Berlin, Germany; ²Division of Rheumatology, Allergy, and Immunology, Medicine, Boston, United States of America

Background: The Charité Rh-GIOP is a prospective study of disease- & bone-related data from patients with chronic inflammatory diseases treated with glucocorticoids (GCs). The Glucocorticoid Toxicity Index app (GTI 2.0) measures changes in GC-associated morbidity. The GTI captures

improvement as well as worsening in GC toxicity, and consists of two subscores. With the Cumulative Worsening Score (CWS), only worsening toxicities are counted. The CWS is always a positive number or, if no toxicity has occurred, 0. With the Aggregate Improvement Score (AIS), both improvement and worsening are considered. If the overall GC toxicity has improved, the AIS is negative.

Objectives: To evaluate the GTI in a prospective cohort of GC-treated vasculitis patients.

Methods: Vasculitis patients were included if starting GC or having a flare requiring increased GC. Doses were calculated in prednisone (PRED) equivalents. Nearly all patients had received GC (often for years) baseline (V1). Data for the 9 GTI domains were collected at V1 and follow-up (V2). These included: medications for hypertension, hyperglycemia, and hyperlipidemia; body mass index; bone mineral density; and data pertaining to muscle strength, skin toxicity, neuropsychiatric effects, and infections. Data for the blood pressure, glucose control, and lipid domains were inferred from treatment changes. We used multivariate logistic regression models to examine the relationship of PRED dose to the likelihood of CWS worsening and AIS improvement.

Results: 37 patients (25F; 12M) of mean age 66.6 years (range: 40.5-81.7) were included. Diagnoses: GCA (n=7), PMR (14), AAV (10), EGPA (4), and PAN (2).

Table 1. Prednisone Dosing

Mean Cumulative PRED Dose V0 & V1 (mg)(range)	7888 (30-55,800)
Mean Cumulative PRED Dose V1 & V2 (mg)(range)	3762 (108-14,207)
Days Between V0 & V1 (range)	1095 (2-7,443)
Days Between V1 & V2 (range)	613 (335-1,111)
Mean Daily PRED Dose Before V1(mg)(standard deviation, SD)	6.1 (6.2)
Mean PRED dose V1 (mg)(SD)	34.2 (36.5)
Mean PRED dose V2 (mg)(SD)	3.1 (2.9)

Thirty-four (92%) patients had changes in GC toxicity between V1-V2. The mean CWS & AIS were 34.8 and 11.1, respectively. Twenty-eight patients (76%) had CWSs >0, indicating worsening toxicity. Twenty-one (57%) had AISs >0, also consistent with overall GC toxicity worsening. However, 13 (35%) had negative AISs, indicating improvements in GC toxicity. BMD measurements worsened by at least 3% in 16 (43%) patients and improved by at least 3% in 9 (24%). Cumulative PRED doses correlated strongly with the CWS. For every 1000mg of PRED between V1 & V2, the risk of CWS increase – worsening of GC toxicity – rose by 79% (Table 2).

Table 2. GTI Score Relationships to PRED Dose

PRED Dose	Total (n=37)	CWS		AIS	
		Did not worsen (n=9)	Worsened (n=28)	Improved (n=13)	Did not improve (n=24)
V1-V2 (mg/d)(SD)	6.3 (4.5)	4.8 (5.9)	6.9 (4.0)	5.5 (4.6)	6.8 (4.5)
Cumulative PRED V1&V2 (mg; SD)	3761 (2660)	2027 (2165)	4319 (2592)	3147 (2047)	4094 (2925)
		OR (95% CI)*		AIS	
Daily Mean Dose V1-V2** (per 1mg)		1.15 (0.92-1.43)		0.93 (0.78-1.11)	
Cumulative PRED V1&V2 (per 1000mg)**		1.79 (1.06-3.03)		0.85 (0.63-1.16)	

V0 = Date when PRED was started, before baseline (V1)

*OR for CWS refers to risk of worsening. OR for AIS refers to risk of improvement.

**Adjusted for age, sex.

Conclusion: The GTI captured changes in GC toxicity over time well, both improvement and worsening. Cumulative PRED dose correlated strongly with increase in the Cumulative Worsening Score.

Acknowledgement: Rh-GIOP is supported by a joint funding of Amgen, Bristol-Meyers Squibb, MS, Celgene, Chugai, Generic Assays, Glaxo-Smith Kline, Hexal AG, Horizon, Lilly, Medac, Mundipharma, Novartis, Pfizer, Roche, and Sanofi.

Disclosure of Interests: Lisa Ehlers: None declared, Edgar Wiebe Grant/research support from: Rh-GIOP is supported by a joint funding of Amgen, BMS, Celgene, Generic Assays, Chugai, Hexal AG, Horizon, Lilly,

medac, Mundipharma, Novartis, Pfizer, Roche, and Sanofi., Desiree Freier: None declared, Sandra Hermann: None declared, Eli Miloslavsky: None declared, Yuqing Zhang: None declared, Frank Buttgeriet: None declared, John H. Stone Grant/research support from: F. Hoffmann-La Roche, Genentech, Xencor, Consultant for: Chugai, F. Hoffmann-La Roche, Genentech, Xencor

DOI: 10.1136/annrheumdis-2019-eular.876

AB1311

NEUTROPHIL-, MONOCYTE-, EOSINOPHIL- AND BASOPHIL-LYMPHOCYTE RATIOS: ASSOCIATIONS WITH TRADITIONAL INFLAMMATORY MARKERS AND DISEASE ACTIVITY MEASURES AT BASELINE AND 6 MONTHS AFTER A bDMARD AMONG BIOLOGIC-NAÏVE RHEUMATOID ARTHRITIS PATIENTS

Bruno Miguel Fernandes, Salomé Garcia, Raquel Ferreira, Sara Ganhão, Miguel Bernardes, Lúcia Costa. *Centro Hospitalar Universitário São João, Rheumatology, Porto, Portugal*

Background: Neutrophil-lymphocyte (NLR) and monocyte-lymphocyte (MLR) ratios have been not only suggested as systemic inflammatory markers, but also associated with disease activity in some inflammatory diseases. Eosinophil-lymphocyte (ELR) and basophil-lymphocyte (BLR) ratios have been studied to a lesser extent.

Objectives: To correlate NLR, MLR, ELR and BLR with inflammatory markers, other laboratory markers and disease activity measures in a portuguese sample of rheumatoid arthritis (RA) patients.

Methods: We conducted a retrospective study including all RA patients under the first bDMARD (*biological disease-modifying antirheumatic drug*), followed in a tertiary university hospital and registered in the Rheumatic Diseases Portuguese Register (*Reuma.pt*). Results of blood tests (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], serum amyloid A [SAA], rheumatoid factor [RF], anti-citrullinated protein autoantibodies [ACPA], haemoglobin, platelets, 25-hydroxide-vitamin D [25OHvitD]), leukocyte formula ratios (NLR, MLR, ELR, BLR) and disease activity and function measures (disease activity score 28 [DAS28 4V, 3V, 4V-CRP, 3V-CRP], clinician and simple disease activity scores [CDAI, SDAI], swollen and tender joint count [SJC, TJC], physician and patient visual analogical scale [VAS]) at baseline and at 6 months of bDMARD therapy were collected. Correlations between variables were evaluated by Spearman rank test (significance level at $p < 0.05$), using SPSS 25.0 software.

Results: 435 patients were included: 81.2% female, mean age at baseline 53.3 ± 11.4 years, mean disease duration 12.6 ± 8.8 years, 72.2% RF positive, 77.1% ACPA positive, 52.5% erosive disease.

At baseline, NLR correlated positively with CRP ($r = 0.343$; $p < 0.001$), ESR ($r = 0.124$; $p = 0.031$), RF title ($r = 0.185$; $p = 0.009$), platelets count ($r = 0.137$; $p = 0.018$), DAS28(4V) ($r = 0.183$; $p = 0.002$), DAS28(3V) ($r = 0.159$; $p = 0.007$), DAS28(4V-CRP) ($r = 0.235$; $p < 0.001$), DAS28(3V-CRP) ($r = 0.222$; $p < 0.001$), SDAI ($r = 0.178$; $p = 0.024$), SJC ($r = 0.120$; $p = 0.040$), TJC ($r = 0.139$; $p = 0.018$) and patient VAS ($r = 0.133$; $p = 0.026$). At baseline, we also found a negative correlation between NLR and 25OHvitD levels ($r = -0.286$; $p = 0.012$). Baseline MLR showed a positive correlation with baseline CRP ($r = 0.138$; $p = 0.017$), RF ($r = 0.156$; $p = 0.027$) and patient VAS ($r = 0.135$; $p = 0.023$). Similarly, at baseline, ELR correlated with CRP ($r = 0.115$; $p = 0.048$) haemoglobin levels ($r = 0.126$; $p = 0.029$) and DAS28(4V-CRP) ($r = 0.126$; $p = 0.037$); and BLR associated positively with DAS28(4V-CRP) ($r = 0.138$; $p = 0.022$), TJC ($r = 0.121$; $p = 0.038$) and patient VAS ($r = 0.131$; $p = 0.028$). At six months of a bDMARD, NLR correlated positively with: CRP ($r = 0.340$; $p < 0.001$), ESR ($r = 0.140$; $p = 0.018$), SAA ($r = 0.350$; $p = 0.008$) and physician VAS ($r = 0.186$; $p = 0.023$). MLR also exhibited a positive association with CRP ($r = 0.161$; $p = 0.007$). Similarly, at six months, ELR correlated positively with CRP ($r = 0.120$; $p = 0.043$), RF ($r = 0.135$; $p = 0.046$), CDAI ($r = 0.180$; $p = 0.027$) and SDAI ($r = 0.183$; $p = 0.025$); and BLR correlated positively with platelets count ($r = 0.139$; $p = 0.020$).

Conclusion: Although weak to moderate in strength, we found significant correlations, between leukocyte formula ratios (NLR, MLR and ELR) and, not only, inflammatory markers but also disease activity measures, predominantly at baseline but also at 6 months of bDMARD. Interestingly, is of note the negative association between NLR and 25OHvitD at baseline. This study reinforced the suggested place of NLR and MLR (but also of ELR) as inflammatory markers and possible disease activity measures in RA. More studies are needed to validate this data.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.1549