change from baseline to week 24, DAS28-CRP remission and ACR 20/50/70 at week 24. IPD mixed-effects meta-regressions were estimated with trial fixed effects, main effects and interaction of enrichment status and treatment type, trial-level random effects on the interaction, and baseline DAS28-CRP score for DAS28-CRP outcomes. These regressions were conducted in the full population and among ABA patients only. Sensitivity analyses defining enrichment using only criteria 3 and 4 were also conducted.

Results: 2,087 patients [1,328 (64%) enriched, 759 (36%) non-enriched] were included (AGREE 492 [24%], AMPLE 509 [24%], AVERT 339 [16%], AVERT-2 747 [36%]). Disease duration, RF+, and anti-CCP values differed as expected between the two groups, while DAS28-CRP was high regardless of enrichment status (Table 1). Among ABA-treated patients, outcomes were more favorable for enriched patients compared to non-enriched patients across all outcomes, either statistically or directionally (Figure 1, ABA treatment arm only analysis). The differences in outcomes between enriched vs. non-enriched patients were larger for ABA than for comparators across all outcomes with the exception of ACR 50, where the difference was directionally consistent (Figure 1, ABA vs. comparator analysis). The relative odds of improved efficacy of ABA vs. comparators ranged from 37% to 87% for remission and ACR responses. The results were consistent in the sensitivity analysis using only anti-CCP and RF seropositivity to define enrichment.

Table 1. Baseline characteristics

	All patients		Non-enriched patients		Enriched patients	
	Abatacept		Comparators		Abatacept	
	N = 2,087	N = 385	N = 374	N = 784	N = 544	
Demographics						
Age (years)	49.3 ± 12.9	49.4 ± 12.6	50.6 ± 12.9	48.6 ± 12.5	49.2 ± 13.5	
Female	79.3%	81.3%	83.4%	77.2%	77.9%	
Disease characteristics						
Disease duration (months)	8.5 ± 12.5	19.9 ± 15.9	18.3 ± 15.1	2.4 ± 2.8	2.4 ± 2.9	
RF Positive	91.0%	74.2%	76.1%	100%	100%	
Anti-CCP Positive	81.8%	52.2%	47.3%	100%	100%	
DAS28-CRP Score	5.71 ± 1.13	5.72 ± 1.19	5.66 ± 1.20	5.68 ± 1.09	5.76 ± 1.08	

Comparators included MTX and MTX+ADA.

Figure 1. Analysis results

Conclusion: This post-hoc study corroborates previous evidence of improved outcomes among ABA-treated, seropositive early RA patients by applying eAMPLE inclusion criteria retrospectively to ABA RCTs. The findings support a differential treatment effect for costimulation blockade using ABA among enriched and double antibody positive early RA patients, suggesting a potential for patient-tailored RA treatment approaches.

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POS0475 INTEGRATIVE CLINICAL, MOLECULAR AND COMPUTATIONAL ANALYSES ALLOW THE IDENTIFICATION OF DISTINCTIVE PHENOTYPES OF RHEUMATOID ARTHRITIS PATIENTS RELATED TO THE CLINICAL INVOLVEMENT AND THE RESPONSE TO TNF INHIBITORS

M. Luque-Tévar¹, C. Perez-Sanchez¹, N. Barroja Puerto¹, A. M. Patiño-Trives¹, I. Arias de la Rosa¹, M. D. C. Abalos-Aguilera¹, J. A. Marin-Sanz¹, D. Ruiz¹, R. Ortega Castro¹, C. López-Medina¹, F. U. Pilar¹, M. Romero-Gómez¹, C. Rodríguez-Escalera², J. J. Pérez Venegas³, D. Ruiz-Montesinos³, C. Domínguez³, C. M. Romero-Barco⁴, A. Fernandez-Nebro⁵, N. Mena-Vázquez⁶, J. L. Marengo⁶, J. Uceda⁶, M. D. Toledo-Coello⁷, M. Á. Aguirre-Zamorano¹, A. Escudero Contreras¹, E. Collantes Estevez¹, C. Lopez-Pedraza¹.
¹IMIBIC/Hospital Reina Sofía/Universidad de Córdoba (UCO), IMIBIC/Hospital Reina Sofía/Universidad de Córdoba (UCO), Córdoba, Spain; ²Hospital Universitario de Jaén, Hospital Universitario de Jaén, Jaén, Spain; ³Hospital Universitario Virgen Macarena, Hospital Universitario Virgen Macarena, Sevilla, Spain; ⁴Hospital Clínico Universitario, Hospital Clínico Universitario, Málaga, Spain; ⁵Hospital Regional Universitario de Málaga, Hospital Regional Universitario de Málaga, Málaga, Spain; ⁶Hospital Universitario Virgen de Valme, Hospital Universitario Virgen de Valme, Sevilla, Spain; ⁷Hospital Universitario de Jerez de la Frontera, Hospital Universitario de Jerez de la Frontera, Cadiz, Spain

Background: TNF inhibitors (TNFi) represent an extraordinary advance in the management of Rheumatoid Arthritis (RA). Despite their benefits, there is a percentage of patients (20–40%) that do not achieve clinical improvement. Therefore, it is necessary to search for new and easily accessible biomarkers predictive of therapeutic response that might guide precision medicine.

Objectives: 1. To explore changes in the molecular profile of RA patients following TNFi therapy in serum samples. 2. To search for new and reliable biomarkers predictive of TNFi response, based on clinical and molecular profiles of RA patients, by using machine learning algorithms.

Methods: In a prospective multicenter study, 79 RA patients undergoing TNFi and 29 healthy donors (HD) were enrolled. Twenty-two RA patients were further included as a validation cohort. Serum samples were obtained before and after 6 months of treatment, and therapeutic efficacy was evaluated. Patients' response was determined following EULAR response criteria. Serum inflammatory profile was analyzed by a multiplex immunoassay, along with oxidative and NETotic profiles, evaluated by commercial kits. A circulating miRNA array was also performed by next-generation sequencing. Clustering analysis was carried out to identify groups of patients with distinctive molecular signatures. Then, clinical and molecular changes induced by TNFi were delineated after 6 months of therapy. Finally, integrative clinical and molecular signatures as predictors of response were assessed at baseline by supervised machine learning methods, using regularized logistic regressions.

Results: Inflammatory, oxidative stress and NETosis-derived biomolecules were found altered in RA patients versus HD, closely interconnected and associated with several deregulated miRNAs. This altered molecular profile at baseline allowed the unsupervised division of three clusters of RA patients with distinctive clinical phenotypes, further linked to TNFi effectiveness. Cluster 1 included RA patients with low levels of pro-inflammatory cytokines, associated with a medium-low disease activity score and good clinical response. Clusters 2-3 comprised patients with high levels of pro-inflammatory cytokines, associated with a high disease activity and a non-response rate of 30%.

After 6 months of therapy the molecular profile found altered in RA patients was reversed in responder patients, who achieved a molecular phenotype similar to HDs. However, non-responder patients' molecular profile remained significantly deregulated, including alterations in inflammatory mediators (IL-6, L-8, TNF α , VEGF, IL-1RA, IL-5, IL-15, GM-CSF, G-CSF, FGFb), oxidative stress markers (LPO) and NETosis-derived products (Elastase), along with specific miRNAs (miR-199a-5p). These molecular changes further correlated with changes in disease activity score. Machine-learning algorithms identified clinical (Creatinine, IgM, Vitamin D, Swollen Joints, C4, Disease Duration and Tryglicerides) and molecular (Nucleosomes, IL-10, miR-106a-5p, IL-13, IL-12p70, IL-15 and

LPO) signatures as potential predictors of response to TNFi treatment with high accuracy. Furthermore, the integration of both features in a combined model increased the predictive value of these signatures (AUC: 0.91). These results were further confirmed in an independent validation cohort.

Conclusion: 1. RA patients display distinctive altered molecular profiles directly linked to their clinical status and associated with TNFi effectiveness. 2. Clinical response was associated with a specific modulation of the inflammatory profile, the reestablishment of the altered oxidative status, the reduction of NETosis and the reversion of related altered miRNAs. 3. The integrative analysis of the clinical and molecular profiles using machine learning allows the identification of novel signatures as potential predictors of therapeutic response to TNFi therapy.

Disclosure of Interests: None declared

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POS0476

CAN LOW-DOSE ASPIRIN DURING PREGNANCY PREVENT THE DEVELOPMENT OF ADVERSE PREGNANCY OUTCOMES IN WOMEN WITH ARTHRITIS? DATA FROM THE P-RHEUM.IT STUDY

D. Lini¹, M. C. Gerardi¹, A. Zanetti², G. Carrara², A. Bortoluzzi^{2,3}, F. Crisafulli¹, M. Filippini⁴, M. Fredi¹, R. Gorla⁴, M. G. Lazzaroni¹, C. Nalli⁴, M. Taglietti⁴, A. Lojaco⁵, S. Zatti⁵, C. A. Scirè^{2,3}, L. Andreoli¹, F. Franceschini¹, A. Tincani¹ on behalf of P-RHEUM.it. ¹ASST Spedali Civili and University of Brescia, Rheumatology Unit, Brescia, Italy; ²Italian Society for Rheumatology (Sir), Epidemiology Unit, Milan, Italy; ³University of Ferrara, Section of Rheumatology, Ferrara, Italy; ⁴ASST Spedali Civili, Rheumatology Unit, Brescia, Italy; ⁵ASST Spedali Civili and University of Brescia, Obstetrics and Gynaecology, Brescia, Italy

Background: In rheumatic diseases, specifically in chronic inflammatory arthritis (IA), there are no data about the effectiveness of LDA in preventing pregnancy complications.

Objectives: To assess the potential benefit of LDA administration during pregnancy to prevent adverse pregnancy outcomes (APO) in IA.

To compare pregnancy outcomes in IA pregnancies treated during pregnancy with LDA with those untreated.

Methods: Italian P-RHEUM.it register is designed as a nationwide, web-based longitudinal observational cohort study collecting data on pregnancies in inflammatory rheumatic diseases. At baseline, socio-demographic parameters, obstetric history, comorbidities and clinical/laboratoristic characteristics are registered. During pregnancy, the course of maternal disease, medications, development of fetus and complications are collected for each trimester.

Results: From May 2018 to May 2020, 349 patients were enrolled. Forty-five patients with IA had completed their pregnancy with known outcome (20 Rheumatoid Arthritis, 10 Psoriatic Arthritis, 6 Ankylosing spondylitis, 5 Juvenile Idiopathic Arthritis, 4 Undifferentiated Arthritis): 13 (28.89%) treated with LDA during pregnancy and 32 (71.11%) without LDA prophylaxis. LDA was used with a higher frequency in women with previous APO, anti-phospholipid positivity and on biological DMARDs even if it's not statistically significant (Table 1). All the LDA-treated women had a live-birth rate of 100%, whereas among women not

Table 1. Comparison between inflammatory arthritis pregnancies treated with low-dose aspirin and those untreated.

	LDA (n 19)	Not LDA (n 39)	p
Maternal age at conception, median (IQR)	33 (30.5 - 36.5)	33 (28.2 - 35)	
BMI, median (IQR)	25.4 (22.9 - 28.5)	22.5 (20.4 - 24.5)	
Smoking, n (%)	3 (15.8%)	4/36 (11.1%)	0.68
Previous APO, n (%)	7/11 (63.7%)	7/13 (56.1%)	0.34
aPL+, n (%)	3 (15.8%)	1/36 (2.8%)	0.1
CRP+, n (%)	5/15 (33.3%)	11/27 (40.7%)	0.75
GC at baseline, n (%)	9 (47.4%)	15/34 (44.1%)	0.82
cDMARDs at baseline, n (%)	1 (5.3%)	3/34 (8.8%)	1
bDMARDs at baseline, n (%)	6 (31.6%)	11 (28.2%)	0.79
Live-birth pregnancy, n (%)	18 (94.7%)	32 (82.1%)	0.25
Pregnancy loss, n (%)	1 (5.3%)	7 (17.9%)	0.25
Hypertensive disorders, n (%)	2/18 (11.1%)	6/38 (15.8%)	1
HELLP syndrome, n (%)	0 (0%)	0 (0%)	1
PROM, n (%)	0 (0%)	3/38 (7.9%)	0.54
Preterm delivery, 34-37 GW, n (%)	2 (10.5%)	2 (5.2%)	0.59
Preterm delivery, <34 GW, n (%)	1 (5.3%)	1 (2.6%)	1
IUGR, n (%)	0 (0%)	3 (7.8%)	0.54
SGA, n (%)	0 (0%)	0 (0%)	1
Pregnancy/Peripartum complications, n (%)	3 (15.8%)	11 (28.9%)	0.35

Legend: aPL, Antiphospholipid syndrome; bDMARDs, biological disease-modifying antirheumatic drugs; BMI, Body mass index; cDMARDs, Conventional disease-modifying antirheumatic drugs; CRP, C-reactive protein; GC, Glucocorticoids; GW, gestational week; HELLP, haemolysis, elevated liver enzymes, and low platelets; Hypertensive disorder defined as gestational hypertension, preeclampsia and eclampsia; IQR, Interquartile range; IUGR, intrauterine growth restriction; LDA, Low-dose Aspirin; Pregnancy loss defined as early fetal-loss, miscarriage and still-birth; PROM, Premature rupture of membranes; SGA, Small for gestational age.

treated with LDA the live birth rate was of 84.4% with 27 live-birth pregnancies, 3 early miscarriages, 1 fetal loss and 1 stillbirth observed. There were no significant differences between the LDA and the not LDA groups regarding pregnancy/peripartum obstetric complications (p=0.14), although less adverse pregnancy/peripartum outcomes were registered in LDA patients' group (Table 1).

Conclusion: The preliminary data of this prospective cohort study show that LDA improve pregnancy outcome in IA even if women treated with LDA had more risk factors for APO. The extension of this cohort will allow us to further investigate these important results.

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POS0477

HIGH DISEASE ACTIVITY AT BASELINE AND SEROPOSITIVITY ARE ASSOCIATED WITH TREATMENT RESPONSE AT ONE YEAR POST SYNOVIAL BIOPSY IN RHEUMATOID ARTHRITIS PATIENTS

K. Murray¹, C. Low¹, F. Young¹, M. Bienicka¹, E. Mylod², U. Fearon², D. Veale¹. ¹Saint Vincent's University Hospital, Rheumatology, Dublin, Ireland; ²Trinity College, Trinity Biomedical Sciences Institute, Dublin, Ireland

Background: Despite recent therapeutic advances, our ability to predict prognosis and therapeutic response in RA remains imprecise.

Objectives: To determine biomarkers predictive of outcome at one year following arthroscopy.

Methods: RA patients were prospectively recruited and underwent knee arthroscopy performed under local anaesthetic. Each patient underwent a careful systematic assessment of demographic, clinical, and serologic factors on the day of arthroscopy and were reviewed at 2 weeks, 3, 6 and 12 months post arthroscopy. Erosive disease was defined based on plain-film radiographs of hands and feet. Disease activity at one year was used to define treatment response into responders (moderate/good EULAR Response) and non-responders.

Clinical characteristics, synovial tissue cell profiles and immunohistochemistry were analysed for T Cells (CD3), B Cells (CD20, CD138), macrophages (CD68) and vascularity (Factor VIII) to establish predictors of treatment response. All areas of each biopsy section were examined and the sub-lining layer independently scored by 2 observers using a well-validated semiquantitative scoring method, ranging from 0 to 4 (0=no staining, 1=<25%, 2=25-49%, 3=50-74%, and 4=75-100% staining). Factor 8 was scored by calculating the mean count of stained blood vessels per high-power field (at 20X magnification).

Results: There were no significant differences between responders and non-responders regarding gender, age, disease duration, medications, erosive status, ESR, CRP or synovitis or vascularity at arthroscopy (Table 1). Interestingly, rates of RF and ACPA positivity, tender and swollen joint counts, DAS28 and DAS28CRP were all higher amongst treatment responders. Immunohistochemistry was a very poor predictor of treatment response. There were no significant differences between the two groups in CD3, CD20, CD138, CD68 or Factor 8 score.

Table 1. Baseline Characteristics

	Responder (n=30)	Non-responder (n=18)	p value
Female	20 (66.7%)	14 (77.8%)	NS
Age	51.5 (11.2)	54.2 (10.9)	NS
Disease duration	0.5 (0-16)	0.5 (0-10)	NS
RF positive	22 (73.3%)	5 (27.8%)	0.003
ACPA positive	22 (73.3%)	8 (44.4%)	0.045
Erosions	8 (26.7%)	5 (27.8%)	NS
Medications			
No DMARD	23 (76.7%)	10 (55.6%)	NS
csDMARD only	4 (13.3%)	3 (16.7%)	NS
TNFi	2 (6.7%)	3 (16.7%)	NS
Other bDMARD	1 (3.3%)	2 (11.1%)	NS
Patient global health, VAS (mm)	54.2 (10-100)	51.5 (0-90)	NS
SJC (28 Joints)	4.5 (0-16)	1 (0-18)	0.001
TJC (28 Joints)	7 (1-25)	1 (0-15)	0.001
ESR, mm/hr	23 (2-120)	24 (2-81)	NS
CRP, mg/L	5 (1-95)	6.5 (1-64)	NS
DAS28	5.01 (1.95-7.36)	3.93 (1.40-6.62)	0.003
DAS28CRP	4.78 (2.82-7.13)	3.39 (1.21-6.26)	0.002
Synovitis, VAS	65 (10-100)	70 (30-100)	NS
Vascularity, VAS	60 (10-90)	70 (30-100)	NS