remained significant even after adjusting for age, gender, comorbidities, disease activity, smoking, education, seropositivity, symptom duration and steroid use in adjusted survival models (Table 2).

Table 1. Unadjusted survival model: Association of each variable with all-cause mortality

Baseline Variable	Unadjusted Hazard OR	95% CI
Socio-Demographic		
Age (years)	1.10	1.07 – 1.13
Female	0.37	0.22 – 0.62
Caucasian (white or European)	1.01	0.46 – 2.24
Aboriginal	1.71	0.61 – 4.76
Education > high school degree	0.48	0.28 – 0.82
Current Smoker	1.81	1.01 – 3.24
Rheumatic Disease Comorbidity Index (0-9)	1.60	1.36 – 1.87
RA Characteristics		
Symptom duration (months)	0.99	0.91 – 1.08
Seropositivity in first year	1.11	0.55 – 2.23
DAS28 ESR or CRP if ESR is missing	1.26	1.06 – 1.51
Oral Steroid use	1.75	1.03 – 2.98

Table 2. Multivariable discrete-time survival models: HAQ baseline vs 1 year

Model	Model 1: Crude (Time + HAQ-DI)	Model 2: Adjusted for age + sex	Model 3: Adjusted for Model 2 + DAS28 + RDCI	Model 4: Adjusted for Model 3 + edu- cation, smoking, seropositivity, symptom duration and oral steroids use	Model 5: Adjusted for Model 3 + smoking, symptom duration only
HAQ-DI (0-3) (at baseline)	1.46 – 2.09	1.02 – 1.95	1.37 – 1.94	0.81 – 1.94	1.30 – 2.00
HAQ-DI (0-3) (at 1 year)	2.58 – 3.72	1.78 – 3.52	1.63 – 2.77	1.10 – 3.02	1.09 – 2.74

*Hazard OR, 95% CI

~HAQ-DI: (Health Assessment Questionnaire Disability Index); RDCI: Rheumatic Disease Comorbidity Index; DAS28: Disease Activity Score

Conclusion: Higher HAQ at 1 year was significantly associated with all-cause mortality in a large early RA cohort suggesting that poorer disease control and function in the first year of RA contributes to higher mortality.

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FRI0038

THE RELATIONSHIP BETWEEN ABATACEPT EXPOSURE AND EFFICACY MEASURES IN EARLY MTX-NAIVE ANTI-CITRULLINATED PROTEIN ANTIBODY-POSITIVE PATIENTS WITH RA DURING THE DE-ESCALATION PERIOD OF A PHASE IIIB STUDY

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Background: Although EULAR/ACR guidelines suggest tapering biologic treatment for RA following sustained remission in patients (pts), specific de-escalation (DE) regimens are not defined. The Phase IIIB Assessing Very Early Rheumatoid arthritis Treatment (AVERT)-2 trial (NCT02504268) is evaluating SC abatacept (ABA) + MTX versus ABA placebo (PBO) + MTX in Anti-Citrullinated Protein Antibody (ACPA)-positive pts with early (ACR/EULAR 2010 criteria; disease duration ≤6 mths), active RA (SDAI >11). AVERT-2 was designed to investigate achievement of SDAI remission and a clinically meaningful dose DE strategy among pts in sustained remission who completed induction with ABA + MTX. In moderately to severely active RA and JIA patients, a relationship between ABA Cmin and efficacy was observed. Therefore, this analysis in very early RA patients, reports on the pharmacokinetics (PK) and immunogenicity of ABA and the maintenance of remission during the DE period of AVERT-2.

Objectives: To assess the relationship between changes in ABA exposure and the maintenance of remission and the effect of immunogenicity on exposure during the DE period of AVERT-2.

Methods: Pts received blinded SC ABA (125mg once wky [QW]) + MTX or ABA PBO + MTX induction treatment for 56 wks. Pts who completed induction with ABA + MTX and had sustained SDAI remission (≤3.3 at Wks 40 and 52) were re-randomized 1:1:1 to ABA QW + MTX for 48 wks (Arm C), ABA every other wk (EOW) + MTX for 24 wks followed by ABA PBO + MTX for 24 wks (Arm D), or ABA QW + MTX PBO for 48 wks (Arm E) in the DE period. ABA trough (Cmin) and anti-drug antibody (ADA) samples were collected in all subjects during the DE period. Serum ABA concentrations and ADA were measured using a validated enzyme immunoassay method and an electrochemiluminescence assay, respectively. Efficacy endpoints included change from DE Day 1 in SDAI score, HAQ-DI score, Physician's Global Assessment (PhGA), and tender (TJC) and swollen (SJC) joint counts. The relationship between ABA Cmin and efficacy endpoints were assessed. Additionally, the impact of immunogenicity on ABA Cmin was explored.

Results: Mean ABA Cmin values remained stable throughout the DE period for subjects in Arms C and E. ABA Cmin values decreased by ~50% in subjects in Arm D for the first 24 weeks from the start of DE and were ~0 for weeks 24-48 consistent with the change in the frequency of ABA dosing from EOW to ABA withdrawal (Figure 1 top).

The incidence of immunogenicity appeared to increase upon withdrawal of ABA in Arm D. ADA formation did not appear to affect ABA Cmin, as ABA Cmin remained consistent between pts with and without ADA.

Upon withdrawal of ABA in Arm D, there appeared to be an increase in the mean change from baseline (Day 1 of DE) in SDAI over time, which followed a similar time course as the washout of ABA (Figure 1 bottom). Similar results were observed for other efficacy endpoints such as HAQ-DI, PhGA, TJC, and SJC.

Conclusion: The PK data in these early onset, MTX-naive, ACPA+ RA pts correlated well with the maintenance of remission in Arms A and E. Tapering of ABA from EOW to MTX only in Arm D results in a corresponding decrease in ABA Cmin, an increase in positive antibody response, and loss of remission.

References:

[1] Emery et. al. ACR [Abstract L11]. Nov. 2019. Atlanta GA USA

[2] Li et. al. J Clin Pharmacol. Vol 59(2). Feb 2019.

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Figure 1: Mean (SD) ABA Cmin values (top) and Mean Change From Baseline in SDAI (bottom) in Subjects in DE Arm C (ABA QW + MTX), D (ABA EOW + MTX followed by ABA placebo + MTX), and E (ABA QW + MTX placebo)

Squibb, Employee of: Bristol-Myers Squibb, Kuan-Hsiang Gary Huang Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Robert Wong Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Shannon Chlewski Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Bindu Murthy Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

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FRI0039 LUNG ULTRASOUND UTILITY IN INTERSTITIAL LUNG DISEASE DETECTION IN RHEUMATOID ARTHRITIS

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Background:

Objectives: To analyze the diagnostic utility of lung ultrasound (US) to detect interstitial lung disease (ILD) in Rheumatoid arthritis (RA) patients comparing with high-resolution computed tomography (HRCT).

Methods: Study design: We performed a cross-sectional, observational study in patients with RA-ILD (cases) controlled with a group of RA patients without ILD (controls) paired by sex, age and time of disease evolution.

Protocol: Patients were selected between May and September 2019. Patients were interviewed by two rheumatologist for the protocolized collection of clinical data. The patients were assessed using HRCT, Pulmonary Function Test (PFT) and lung US. The rheumatology who performed the lung US were blinded to patients clinical data. Variables: (1) B-lines number; (2) evaluation of the lung-ultrasound score already described: L. Gargani, Gutiérrez comprehensivo, Gutiérrez reducido and Mohammadi; (3) pleural irregularities; (4) A pattern US lost; (5). Other variables included demographic, clinical-analytical, therapeutic and ILD-type description. Statistical analysis: descriptive, bivariate analysis. We applied Pearson's correlation coefficient between B-lines, PFT and clinical variable. Furthermore, to establish the cut-off point of the US B-lines number for detecting the presence of significant RA-ILD in relation to HRCT, we used the receiver operating characteristic (ROC) curve analysis. A logistic regression analysis was performed to identify the intercostal spaces (IV: B-lines number in each space) which were independently associated with ILD (DV: ILD in HRCT).

Results: 71 patients were included, 37 (52.1%) with ILD-RA and 34 (47.9%) RA controls. The main characteristics are shown in Table 1. RA-ILD presented more B-lines number than control without ILD (median IQR) 91.0 [31.0-149.0] vs 6.5 [1.5-30.5]; $p < 0.001$ and more pleural irregularities (PI) [PI-median(IQR) 41.0

(5.0-57.5) vs 2.5 (0.0-7.2); $p < 0.001$. Furthermore, RA-ILD showed a negative correlation between B-lines and DLCO ($r = -0.337$, $p = 0.048$) and positive with DAS28 ($r = 0.347$, $p = 0.035$). Regarding US score, we found that the detection of 32.5 B-lines in 72 intercostal spaces, had a Sensitivity of 75.7%, Specificity=79.4%, PPV= 80% and NPV=75%, whilst in reduced score of 10 intercostal spaces, the detection of 5.5 B-lines had a sensitivity= 62.2%, Specificity= 91.3%, PPV=88.4%, NPV=69.5%. In multivariate analysis, the intercostal spaces which showed independent association with ILD were 3rd right anterior axillary space (OR [IC 95%] 19.0 [1.3-27.5]), 8th right posterior axillary space (OR [IC 95%] 0.04 [0.0-0.6]), 8th right subscapular space (OR [IC 95%] 16.5 [1.8-45.5]), 9th right paravertebral space (OR [IC 95%] 7.11 [1.0-37.1]) and 2nd left clavicular middle space (OR [IC 95%] 21.9 [1.26-378]).

Conclusion: Lung Ultrasound could be a useful tool for interstitial lung disease diagnosis associated with Rheumatoid Arthritis. A 10 space reduced score showed a similar total predictive capacity than 72-space score

References:

VARIABLE	RA-ILD n=37	RA n=34	P-VALUE
Epidemiological Characteristics			
Age in years, mean (±SD)	70.5 (9.1)	70.6 (7.5)	0.970
Sex, male, (%)	20 (54.1)	18 (52.9)	0.920
Body Mass Index, mean, (±SD)	27.5 (3.0)	29.2 (4.2)	0.106
Clinical-analytical characteristics			
Smoking			0.899
Smokers, n (%)	4 (11.8)	4 (10.8)	
RA evolution time, months, median, (p75-p25)	172.5 (100.4-234.4)	134.5 (106.5-211.9)	0.304
ILD evolution time, median, (p75-p25)	42.8 (21.3-101.3)	-	-
Rheumatoid Factor (RF)+ (>10), n (%)	35 (94.6)	27 (79.4)	0.055
RF (>60)	28 (77.8)	18 (52.9)	0.029
ACPA+ (>20), n (%)	34 (91.9)	26 (76.5)	0.073
ACPA (>340), n (%)	26 (72.2)	11 (32.4)	0.001
Erosive, n (%)	22 (59.5)	19 (55.9)	0.761
Clinical manifestation			
DAS28, mean (±SD)	3.1 (1.2)	2.7 (0.9)	0.151
Remission-LDA, n (%)	21 (56.8)	24 (72.7)	0.164
Mild-High activity actividad, n (%)	16 (43.2)	9 (27.3)	0.164
HAQ, mean (±DE)	1.1 (0.6)	0.7 (0.6)	0.021
Tratamiento			
sDMARDs, n (%)	32 (86.5)	34 (100)	0.026
bdMARDs, n (%)	11 (29.7)	11 (32.4)	0.811
Metotrexate, n (%)	19 (51.4)	28 (82.4)	0.060
Leflunomide, n (%)	4 (10.8)	4 (11.8)	0.899
Sulfasalazine, n (%)	5 (13.5)	2 (5.9)	0.281
Hidroxicloroquine, n (%)	4 (10.8)	2 (5.9)	0.456
Micofenolate, n (%)	4 (10.8)	0 (0.0)	0.048
Infliximab, n (%)	0 (0.0)	3 (8.8)	0.065
Etanercept, n (%)	3 (8.1)	4 (11.8)	0.606
Adalimumab, n (%)	0 (0.0)	1 (2.9)	0.293
Golimumab, n (%)	1 (2.7)	1 (2.9)	0.952
Certolizumab, n (%)	0 (0.0)	1 (2.9)	0.293
Tocilizumab, n (%)	2 (5.4)	0 (0.0)	0.169
Abatacept, n (%)	4 (10.8)	0 (0.0)	0.048
Rituximab, n (%)	1 (2.7)	0 (0.0)	0.334

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FRI0040 MULTI-VARIATE APPROACH INCLUDING SEROLOGY AND GENETICS FOR AN IMPROVED IDENTIFICATION OF PATIENTS AT RISK OF DEVELOPING RA

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Background: First-degree relatives of rheumatoid arthritis (RA) patients (FDR-RA) have a 3 - 5-fold increased prevalence of the disease [1]. RA development is triggered by an interaction between genetic and environmental factors. As the field is moving towards prevention in pre-clinical stages of RA, it is key to identify individuals with imminent RA, prior to onset of symptoms, which will presumably rely on both the measurement of autoantibodies and genetic risk markers.

Objectives: Assemble a pattern of serologic biomarkers in combination with genetics to improve the identification of individuals at high risk to develop RA.