Objectives: To assess treatment patterns and DMARD discontinuation in RA patients with comorbid lung disease in comparison with other RA patients.

Methods: The study included RA Patients enrolled in the Forward Databank with ≥ 1 year observation after 2000 initiating a DMARD. Forward is a large longitudinal rheumatic disease registry in the US. RA patients' diagnoses were rheumatologist-confirmed, and every 6 months participants completed comprehensive questionnaires regarding symptoms, disease outcomes, medications, and clinical events. Lung disease (LD+) was defined as at least one of the following: emphysema, asthma, bronchitis, COPD, pleural effusion, fibrosis of the lung, "RA lung", or ILD, the later classified by ICD9 codes (England 2019). DMARDs were categorized hierarchically into four groups: csDMARDs, TNFi and NTNFi (bDMARDs), and tsDMARDs. Percentage of patients who initiated different DMARDs were reported for pts with LD+/LD-. Discontinuation was analyzed by Kaplan Meier (KM) curves, log-ranks tests, and Cox regression models using time-varying covariates. Best models were created using backward selection models (10% probability of removal) and pre-defined clinical models.

Results: Of the 21,525 eligible RA patients, 13.8% had LD+ at the time they initiated a DMARD (follow-up: 69,597 pt-yrs (median 1.9 yrs/pt)). LD+ patients tended to have more severe RA outcomes and comorbidities. MTX-monotherapy (48% vs 44%, $p < 0.001$) and NTNFi were initiated more frequently in LD+ pts with lower use of TNFi (Figure). DMARD discontinuation rates were higher among LD+ patients for all DMARD groups, but KM curves were only significantly different for csDMARDs and TNFi. Different HRs for LD+ were found depending on the model used ranging from 1.18 to 1.28, and all models revealed an increased risk of discontinuation for LD+ patients. Compared to csDMARDs, TNFi were more often discontinued (Table). Other variables associated with an increased risk of discontinuation included: HAQ, Rheumatoid Disease (RD) comorbidity index, pain, prior bDMARDs, and csDMARDs.

Conclusion: Different DMARD treatment patterns were found for LD+ patients, who tended to initiate more csDMARD and NTNFi and less likely to initiate a TNFi. LD+ patients were at a higher risk of discontinuation irrespectively of the DMARD treatment, but with greater risk for TNF users.

References:

[1] England BR, et al. Arth Care Res. doi:10.1002/acr.24043.

Figure. DMARD treatment initiators by disease group

Table. Cox models for DMARD discontinuation by stepwise (removal probability 10%) and clinical models including DMARD treatment.

Model of DMARD persistence* LD+ vs LD-	Model 1- Stepwise- Without drugs	Model 2 - Stepwise	Model 3 - Clinical
	1.18 (1.08 - 1.29)	1.28 (1.13 - 1.45)	1.20 (1.08 - 1.34)
TNF vs csDmard		1.32 (1.08 - 1.63)	1.22 (1.04 - 1.44)
NTNF vs csDmard		1.13 (0.83 - 1.52)	1.13 (0.90 - 1.41)
tsDmard vs csDmard		1.30 (0.65 - 2.60)	1.02 (0.64 - 1.62)

*Best models searched/Clinical adjusted for LD+/LD-, DMARDs, age, sex, education, HAQ disability, RD comorbidity index, smoking, pain, glucocorticoids, year of entry, prior bDMARDs and csDMARDs counts and MRC breath scale.

Disclosure of Interests: Sofia Pedro: None declared, Ted Mikuls Grant/research support from: Horizon Therapeutics, BMS, Consultant of: Pfizer, Joe Zhuo Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Kaleb Michaud: None declared

DOI: 10.1136/annrheumdis-2020-eular.5452

FRI0073

SEROLOGICAL PREDICTORS OF THE SEVERITY OF RHEUMATOID ARTHRITIS RELATED INTERSTITIAL LUNG DISEASE

S. Rajalingham¹, S. S. Shaharir¹, R. Sridharan¹. ¹Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia

Background: The most common extra-articular manifestation of rheumatoid arthritis(RA) is interstitial lung disease (ILD). Although pulmonary manifestations in RA encompass the main airway, parenchyma, vasculature and pleura, ILD in particular, is associated with reduced survival. Up to 10% of RA patients suffer from clinically significant ILD while a substantial proportion have abnormal CT chest findings despite being asymptomatic. There are various biochemical and serological markers to predict the severity of the joints in RA. However, the clinical and laboratory determinants of RA related ILD (RA-ILD) are not well defined owing to the paucity of research data in this regard.

Objectives: The main objective of this study is to determine the correlation between the rheumatoid factor (RF) serotypes and the severity of RA-ILD based on computer tomography (CT) findings.

Methods: We recruited a total of 100 RA patients who were tested for IgA RF, IgG RF and IgM RF and had high resolution CT chest performed. Participants were aged above 18 years, met the 2010 ACR/EULAR RA criteria, had RA for more than 6 months, were non-smokers, not pregnant and had no known chronic lung disease or lung malignancy based on their medical records. Seventy-two patients had ILD changes on HRCT of the chest and were included in this study. The CT images were scored based on a scoring system proposed by Kazerooni et al. Ground glass opacities represented the alveolar findings whereas honeycombing and septal thickening were the interstitial findings. The ground glass and fibrosis scores were on a scale of 0-5, with higher scores for greater involvement of the lobes. For each subject, the maximum ground glass and fibrosis scores were 25, respectively.

Results: The frequency of RF positivity was comparable across the 3 serotypes (83.33-84.72%). The correlation between the clinical variables and the CT scores are listed in Table 1. We found that the the CT scores for ground glass showed significant positive correlation with disease duration ($p=0.047$) and IgA RF levels ($p<0.050$) whereas the fibrosis scores had significant relationship with multiple clinical covariates i.e age ($p=0.004$), disease duration ($p=0.042$), IgA RF levels ($p<0.050$), IgG RF levels ($p=0.041$) and anti-CCP levels ($p=0.006$). On multivariate analysis, only IgA RF levels remained significantly ($p<0.05$, standardized beta coefficient =0.604) associated with the ground glass scores. As for the fibrosis scores, IgA RF levels and age were independent predictors based on multivariate analysis after adjusting for confounders, with p scores of <0.05 and 0.02, respectively.

Table 1. Correlation of CT scores with clinical covariates and antibodies

Parameters	Ground glass		Fibrosis	
	r	p value	r	p value
Age	0.229	0.053	0.334	0.004
Disease duration	0.235	0.047	0.240	0.042
Total MSS	0.058	0.628	0.224	0.145
Cumulative Methotrexate dose	0.039	0.748	0.098	0.413
Ig A	0.608	<0.05	0.576	<0.05
Ig M	0.053	0.660	0.019	0.873
Ig G	0.183	0.124	0.241	0.041
Anti CCP	0.117	0.328	0.319	0.006

Conclusion: The IgA RF was the only serotype which was independently associated with the severity of RA-ILD.

References:

- [1] Bongartz, T., Nannini, C., Medina-Velasquez, Y. F., Achenbach, S. J., Crowson, C. S., Ryu, et al. (2010). Incidence and mortality of interstitial lung disease in rheumatoid arthritis: a population-based study. *Arthritis and rheumatism*, 62(6), 1583-1591.
- [2] Dawson, J. K., Fewins, H. E., Desmond, J., Lynch, M. P., & Graham, D. R. (2001). Fibrosing alveolitis in patients with rheumatoid arthritis as assessed by high resolution computed tomography, chest radiography, and pulmonary function tests. *Thorax*, 56(8), 622-627.
- [3] Kazerooni, E. A., Martinez, F. J., Flint, A., Jamadar, D. A., Gross, B. H., et al. (1997). Thin-section CT obtained at 10-mm increments versus limited three-level thin-section CT for idiopathic pulmonary fibrosis: correlation with pathologic scoring. *AJR Am J Roentgenol*, 169(4), 977-983.
- [4] van der Helm-van Mil, A. H., & Huizinga, T. W. (2012). The 2010 ACR/EULAR criteria for rheumatoid arthritis: do they affect the classification or diagnosis of rheumatoid arthritis? *Annals of the rheumatic diseases*, 71(10), 1596-1598.

Disclosure of Interests: Sakthiswary Rajalingham Speakers bureau: Pfizer (500USD), Syahrul Sazliyah Shaharir: None declared, Radhika Sridharan: None declared

DOI: 10.1136/annrheumdis-2020-eular.218

FRI0074

UNDERLYING PROBLEMS AND IMPACT OF DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS: PRELIMINARY RESULTS OF A CROSS-SECTIONAL CASE-CONTROL STUDY

N. M. T. Roodenrys¹, M. C. Van der Goes^{1,2}, P. Welsing¹, J. Tekstra¹, F. Lafeber¹, J. W. G. Jacobs¹, J. M. Van Laar¹. ¹University Medical Center, Department of Rheumatology & Clinical Immunology, Utrecht, Netherlands; ²Meander Medical Center, Department of Rheumatology, Amersfoort, Netherlands

Background: Difficult-to-treat (D2T) RA is defined here by signs and symptoms, suggestive of active/progressive RA, which are perceived as problematic by rheumatologist and/or patient, and are present despite treatment according to EULAR recommendations including ≥ 2 b/tsDMARDs with different mechanisms of action.¹ Its treatment is generally based on trial-and-error and challenged by several underlying problems (Figure 1),²⁻⁴ of which the exact impact is unknown.

Objectives: To obtain insight into the potential problems underlying D2T RA and into its impact.

Methods: Consecutive RA patients fulfilling the 2010 ACR/EULAR classification criteria, treated according to current standard of care for ≥ 1 year, are being enrolled, and categorised as D2T or not (controls). Potential problems underlying D2T RA (Figure 1) and its impact on quality of life and physical functioning were assessed and compared between the two patient groups.

Results: In this preliminary analysis, 45 patients are classified as having D2T RA and 100 are controls (Table 1). Fibromyalgia (33 vs 9%), depression (18 vs 4%), a mismatch between patient and rheumatologist in wish to adapt treatment (51 vs 15%) and DMARD discontinuation because of adverse events (96 vs 57%), were statistically significantly more frequent in D2T RA patients than in controls. Higher levels of threatening illness perception and helplessness, and more comorbidities according to EULAR domains were found in D2T RA patients (Figure 2). Other potential problems did not differ significantly.

Table 1. Patient characteristics

	D2T RA (n=45)	Control RA (n=100)	p-value
Demographics			
Age [†]	60.9 (10.8)	64.5 (10.9)	0.06 ¹
Female, %	76	72	0.66 ²
Disease characteristics			
Disease duration, years	17.0 (10.0-27.5)	14.0 (8.0-24.0)	0.18 ³
RF positivity, %	76	65	0.21 ²
ACPA positivity, %	71	65	0.47 ²
DAS28-ESR	4.0 (3.4-5.7)	2.5 (1.8-3.3)	<0.001 ³
Drugs			
Number of previous DMARDs	7 (5-10)	2 (1-4)	<0.001 ³
Number of current DMARDs	2 (1-2)	1 (1-2)	0.03 ³
Current conventional synthetic DMARDs, %	74	86	0.07 ²
Current biological DMARDs, %	57	39	0.06 ²
Current targeted synthetic DMARDs, %	22	0	<0.001 ²
Glucocorticoid therapy, %	53	16	<0.001 ²
Dose, mg/day prednisone or equivalent daily, in users	7.5 (5.0-13.8)	5.0 (5.0-7.5)	0.03 ³

ACPA: anti-citrullinated protein antibodies; D2T: difficult-to-treat; DAS28-ESR: disease activity score assessing 28 joints using erythrocyte sedimentation rate; DMARD: disease-modifying antirheumatic drug; mg: milligram; n: number; RF: rheumatoid factor. Numbers are median (interquartile range), unless stated otherwise; [†] mean (standard deviation). Differences between groups were analysed using: 1. Independent T-test; 2. Chi-square Test; 3. Mann-Whitney U Test.

The drug management cycle is shown in green. Factors in pink, which influence (red arrows) the ideal drug management cycle and lead to difficulty in grading RA activity or drug effectiveness. All these factors may in different grades in individual patients contribute to D2T RA. CPD: calcium pyrophosphate deposition; D2T: difficult-to-treat; RA: rheumatoid arthritis. * Factors that might also hamper proper grading of disease activity. [†] Factors have not yet been determined. Adapted from: de Hair MJH et al. *Rheumatology* 2017;57:1135-44.

Quality of life and physical functioning were significantly lower in D2T RA patients than in controls (median (IQR) EQ-5D 2.6 (1.8-3.0) vs 1.6 (1.4-2.2) and HAQ 1.8 (1.3-2.1) vs 1.0 (0.5-1.4), $p<0.001$).

Conclusion: This first prospective study describing a cohort of D2T RA patients shows higher occurrences of potential underlying problems and a higher clinical impact. These should be recognised in daily practice and taken into account before considering another DMARD switch. More detailed research on disease state (biomarkers, radiographic damage) and use of medication (drug levels and in-depth interviews on treatment non-adherence) will follow.

References:

[1] Smolen JS et al. *Ann Rheum Dis* 2020. Epub ahead of print.
[2] Buch MH. *Ann Rheum Dis* 2018;77:966-9.
[3] de Hair MJH et al. *Rheumatology* 2017;57:1135-44.
[4] Roodenrys NMT et al. *Ann Rheum Dis* 2018;77:1705-9.

Disclosure of Interests: Nadia M. T. Roodenrys: None declared, Marlies C. van der Goes: None declared, Paco Welsing: None declared, Janneke Tekstra: None declared, Floris Lafaber Shareholder of: Co-founder and shareholder of ArthroSave BV, Johannes W. G. Jacobs Grant/research support from: Roche, Jacob M. van Laar Grant/research support from: MSD, Genentech, Consultant of: MSD, Roche, Pfizer, Eli Lilly, BMS
DOI: 10.1136/annrheumdis-2020-eular.369

FRI0075
DECREASED RISKS OF HOSPITALIZED INFECTION UNDER TARGETED THERAPIES VS METHOTREXATE IN ELDERLY AND OLDER ELDERLY PATIENTS COMPARED TO YOUNGER PATIENTS WITH RHEUMATOID ARTHRITIS USING JAPANESE HEALTH INSURANCE DATABASE

R. Sakai^{1,2}, E. Tanaka¹, M. Majima¹, M. Harigai¹. ¹Tokyo Women's Medical University School of Medicine, Department of Rheumatology, Tokyo, Japan; ²Tokyo Women's Medical University School of Medicine, Division of Epidemiology and Pharmacoepidemiology, Department of Rheumatology, Tokyo, Japan

Background: Recently, vital prognosis has been improved in patients with rheumatoid arthritis (RA)¹. In elderly patients, it is difficult to establish a treatment strategy due to multi-morbidities and treatment-related risks. Since older age is a significant risk factor of serious infections, one of the primary concerns during treatment of RA, rheumatologists should always strike a balance between efficacy and safety of the immunosuppressive treatment. However, infection data under the targeted therapy (TT) in elderly patients is still limited to date.

Objectives: To compare the risk of hospitalized infection (HI) under the TT among young, elderly, and older elderly patients with RA using the Japanese health insurance database.

Methods: This retrospective longitudinal population-based study was conducted using claims data in Japan provided by Medical Data Vision Co., Ltd. We defined individuals as RA cases if they met all of the following: 1) having at least one ICD10 code (M05x, M06x except for M061, or M08x except for M081 and M082); 2) having at least one prescription of disease-modifying antirheumatic drugs (DMARDs) including methotrexate (MTX) and TT (biological DMARDs and Janus kinase inhibitors) between April 2008 and September 2018; and 3)