literacy, willingness to change treatment, or decisional conflict. We found a significant improvement in pre-post willingness to change treatment in intervention vs. control participants (0.5 vs 0.01, $p=0.01$). We calculated an effect size (Glass's delta) for the intervention of 0.48 (i.e. moderate). Moreover, decisional conflict about treatment change decreased; there was no significant difference in pre-post differences in decision conflict between groups.

Conclusion: This randomized trial testing a novel patient-directed intervention advocating for T2T strategy implementation in RA care increased self-reported willingness to change RA treatment. Further studies are needed to evaluate if this effect is sustained over time and if it translates into actionable behavior change.

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THU0115

IS INCIDENT RHEUMATOID ARTHRITIS INTERSTITIAL LUNG DISEASE ASSOCIATED WITH METHOTREXATE TREATMENT? RESULTS FROM A MULTIVARIATE ANALYSIS IN THE ERAS AND ERAN INCEPTION COHORTS:

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Background: Rheumatoid arthritis interstitial lung disease (RA-ILD) is a rare but significant manifestation of RA, with high mortality. Methotrexate (MTX) is known to cause hypersensitivity pneumonitis, but its effect on the onset of RA-ILD is less clear.

Objectives: To assess predictive factors for rheumatoid arthritis interstitial lung disease (RA-ILD) in two early RA inception cohorts with a focus on MTX exposure.

Methods: Patients with new diagnosis of RA recruited to the early RA study (ERAS) and the early RA network (ERAN). Standardised data including demographics, drug therapies and clinical outcomes including the presence of RA-ILD were collected at baseline, within 3-6 months, at 12 months and annually for up to 25 years thereafter. Primary outcome was the association of MTX exposure with incident RA-ILD. Secondary outcomes were the association of demographic, comorbid and RA specific factors on incident RA-ILD using univariate and multivariate analyses and the association of MTX exposure on time to RA-ILD diagnosis using time to event Cox proportional hazards analysis.

Results: Of 92 eligible ILD cases, 39 occurred in 1578 (2.5%) MTX exposed and 53 in 1114 (4.8%) non-MTX exposed cases. The primary analysis of incident RA-ILD cases only developing after any csDMARD treatment ($n=67$) showed MTX exposure not to be associated with incident RA-ILD (O.R. 0.85 CI 0.49, 1.49 $p=0.578$) and a non-significant trend for delayed ILD diagnosis (O.R. 0.54 CI 0.28, 1.06 $p=0.072$) (see Figure). In an extended analysis including all RA-ILD cases ($n=92$, including those present pre csDMARD exposure), MTX exposure was associated with a significantly reduced risk of incident RA-ILD (O.R. 0.48, CI 0.3, 0.79 $p=0.004$) and longer time to ILD diagnosis (O.R. 0.41, CI 0.23, 0.75 $p=0.004$). Other independent baseline associations with incident RA-ILD were higher age of RA onset, ever smoking, male gender, rheumatoid nodules and longer time from first RA symptom to first out-patient visit (see Table).

Table Multivariate logistic analysis showing co-variables independently associated with RA-ILD development

	Primary analysis, RA-ILD onset after any csDMARD exposure, $n=67$	Wald test	Extended cohort, including RA-ILD onset pre any csDMARD, $n=92$	Wald test
	O.R. (95% C.I.)	p value	O.R. (95% C.I.)	p value
Methotrexate exposure	0.85 (0.49, 1.49)	0.578	0.48 (0.3, 0.79)	0.004
Age RA onset	1.04 (1.02, 1.06)	<0.001	1.04 (1.02, 1.06)	<0.001

Smoking, ever, baseline	2.21 (1.21, 4.03)	0.01	1.91 (1.13, 3.25)	0.016
Male gender	1.44 (0.83, 2.48)	0.193	1.74 (1.05, 2.86)	0.03
RF positive, baseline	2.02 (1.07, 3.82)	0.029		n.s.
RA nodules, baseline		n.s.	2.19 (1.08, 4.41)	0.029
Onset - 1 st OPD	1.04 (1.00, 1.07)	0.027	1.03 (1.0, 1.07)	0.04
Baseline major co-morbidities	0.62 (0.40, 0.95)	0.027	0.67 (0.46, 0.98)	0.037
Baseline ESR	-	n.s.	1.01 (1.0, 1.02)	0.047

Abstract THU0115 – Figure 1. Cox proportional time to event analysis showing time of onset of RA-ILD from first joint symptoms of RA in MTX exposed and non-MTX exposed groups; primary analysis: cases with RA-ILD first recorded after any csDMARD exposure, $n=67$.

Conclusion: In ERAS/ERAN, incident RA-ILD is significantly associated with older age of RA onset, ever smoking, nodules, RF positivity, male gender, ESR, and a longer time from first RA symptoms to first secondary care visit. There is no association between MTX treatment and incident RA-ILD. MTX may have a protective role in delaying the onset of RA-ILD.

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THU0116

COMPARATIVE SAFETY OF BIOLOGIC DMARDS AND ABATACEPT IN RHEUMATOID ARTHRITIS WITH COPD: A REAL-WORLD POPULATION-BASED OBSERVATIONAL STUDY

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Background: The biologic DMARD abatacept has been associated with respiratory adverse events in patients with RA who have chronic obstructive pulmonary disease (COPD) in the ASSURE trial (NCT00048932), based on only 54 patients with RA and COPD.¹ A large observational study of patients with RA and COPD, involving over 1,800 patients using abatacept did not find an increased incidence of respiratory adverse events with abatacept compared with other biologic DMARDs.² It remains uncertain, however, whether this potential respiratory risk affects all biologic DMARDs, including abatacept, when compared with non-biologic DMARDs.

Objectives: To assess in a real-world observational setting whether patients with RA and COPD treated with biologic DMARDs, including abatacept, have an increased risk of serious respiratory adverse events compared with similar patients treated with non-biologic DMARDs.

Methods: The Truven MarketScan® Commercial and Supplemental Medicare databases were used to identify patients diagnosed with RA and COPD, treated with a biologic or non-biologic DMARD between January 2007 and December 2015. A prevalent new-user cohort design was used to match each new user of a biologic DMARD with a new user of a non-biologic DMARD on time-conditional propensity scores.³ Patients were followed up from new use until the end of enrolment or 31 December 2015. The Cox model was used to estimate the hazard ratios (HRs) of respiratory adverse events associated with biologic DMARDs compared

with non-biologic DMARDs, further adjusted for confounders found to be unbalanced despite matching on propensity scores.

Results: The study cohort included 7,424 new users of biologic DMARDs matched to 7,424 new users of non-biologic DMARDs, followed for up to 9 years. The adjusted HR (95% CI) of the combined respiratory endpoint, including severe COPD exacerbation, bronchitis and severe pneumonia or influenza, with biologic DMARD use relative to non-biologic DMARDs was 1.06 (0.91-1.24). For severe COPD exacerbation it was 0.88 (0.64-1.21), 1.02 (0.82-1.27) for bronchitis, while for pneumonia or influenza it was 1.18 (0.90-1.54) if hospitalized and 1.01 (0.89-1.14) as outpatient. For users of abatacept relative to non-biologic DMARDs, the HR of the combined respiratory endpoint was 1.06 (0.80-1.42). Results remained unchanged with sensitivity analyses.

Conclusion: In this large real-world study of patients with RA and COPD, the risk of pre-specified serious respiratory adverse events was not significantly increased in patients using biologic DMARDs, and specifically abatacept, compared with those using non-biologic DMARDs. This study does not support the safety signal for abatacept from the ASSURE trial.

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THU0117 PHARMACOKINETICS AND SHORT-TERM SAFETY OF FILGOTINIB, A SELECTIVE JANUS KINASE 1 INHIBITOR, IN SUBJECTS WITH MODERATE HEPATIC IMPAIRMENT

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Background: Filgotinib (FIL) is an oral selective Janus kinase 1 (JAK1) inhibitor being developed to treat inflammatory diseases.

Objectives: This phase 1 study evaluated the pharmacokinetics (PK) and short-term safety of FIL in subjects with hepatic impairment (HI) to guide safe and appropriate dosing in the presence of this comorbidity.

Methods: This study enrolled 20 subjects: 10 with moderate (Child-Turcotte-Pugh-B) HI and 10 healthy controls. All were matched for age, sex, and body mass index and received a single oral dose of FIL 100 mg followed by intensive plasma PK sampling over 120 hours. Plasma concentrations of FIL and its primary circulating metabolite were measured by validated LC-MS/MS methods; plasma protein binding was also evaluated. A parametric analysis of variance was applied to the natural logarithmic transformation of PK parameters (AUC and C_{max}) for FIL and its metabolite. Geometric least squares means (GLSM) ratios and 90% confidence intervals (CIs) of PK parameters were evaluated in subjects with moderate HI relative to controls, with clinically relevant exposure change defined as ≥ 2 -fold for FIL or its metabolite. Safety endpoints consisted of the incidence of adverse events (AEs), laboratory abnormalities, and vital sign and electrocardiogram changes monitored through day 15.

Results: All subjects completed the protocol-specified dosing and assessments. FIL and metabolite AUCs were increased by 1.6- and 1.2-fold, respectively, in subjects with moderate HI compared to controls. Protein bindings of FIL and its metabolite (f_u : 41%-44% and 55%-61%, respectively) were unchanged in subjects with moderate HI. FIL was well tolerated, with no serious AEs reported. All treatment-emergent AEs were Grade 1 in severity. Serum and plasma markers did not show evidence of treatment-emergent hepatotoxicity or worsened liver function and were consistent with the use of FIL in a population with moderate HI.

Conclusion: In the setting of moderate HI, a single oral dose of FIL 100 mg was well tolerated. FIL can be administered without predefined dose adjustment to patients with mild to moderate HI.

Disclosure of Interests: Kacey Anderson Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Hao Zheng Shareholder of:

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THU0118 TREATMENT OF RHEUMATOID ARTHRITIS WITH COMBINATION THERAPY USING A BIOLOGIC AGENT AND METHOTREXATE LOWERS THE RISK OF DECREASING KIDNEY FUNCTION COMPARED TO METHOTREXATE MONOTHERAPY

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Background: Rheumatoid arthritis (RA) is associated with reduced kidney function, possibly due to chronic inflammation or the use of nephrotoxic therapies. However, little is known about the effects of novel non-nephrotoxic biologic agents (biological disease-modifying antirheumatic drugs [bDMARDs]) on the risk of decreasing kidney function.

Objectives: To elucidate the effects of bDMARDs on decreasing kidney function.

Methods: We recruited a cohort of 1058 patients with RA from the All Showa University of RA database. The following background factors were analyzed: age, sex, type of bDMARD, methotrexate and prednisolone dosages, use of conventional synthetic DMARDs and nonsteroidal anti-inflammatory drugs, body mass index, smoking history, diabetes status, hypertension status, dyslipidemia status, serum creatinine (Cr) level, CRP level, and matrix metalloproteinase-3 level. Furthermore, we used the simplified disease activity index (SDAI) for the evaluation of the disease activity of RA. The estimated glomerular filtration rate (eGFR) was calculated using the serum Cr level, age, and sex. We divided the patients into two groups according to the treatment, as follows: bDMARD with methotrexate (MTX) treatment (combination) group (744 patients) and MTX monotherapy group (314 patients). The patients followed the same treatment plan for 1 year. Patients who had primary and secondary failures, adverse effects of drugs, and missing data and those who relocated or withdrew from the study were excluded. Propensity scores were calculated based on the following factors: age, sex, prednisolone dosage, MTX dosage, SDAI, Cr level, eGFR, diabetes status, hypertension status, and dyslipidemia status. Overall, 285 patients in each group were identified by propensity score matching. The primary end-points were the eGFR values before treatment and 6 months and 1 year after treatment. Significance was determined using the repeated-measures analysis of variance (ANOVA).

Results: The eGFR (mL/min/1.73 m²) decreased from 88.5 $\pm$ 21.8 to 86.1 $\pm$ 21.5 and 83.7 $\pm$ 21.0 at 6 months and 1 year, respectively, in the combination treatment group and from 86.3 $\pm$ 37.9 to 79.5 $\pm$ 19.1 and 78.5 $\pm$ 19.5 at 6 months and 1 year, respectively, in the MTX monotherapy group. No interaction was observed between the groups. A significant difference was observed between the groups ($p = 0.0066$) and even during the treatment period ($p < 0.001$) by repeated-measures ANOVA.

Conclusion: The decrease in eGFR was smaller in the combination treatment group than in the MTX monotherapy group. bDMARD use may lower the risk of decreasing kidney function in patients with RA.

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