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

KIELY Patrick1,2, Amanda Busby3, Elena Nikiphorou1, Keith Sullivan1, Adam Young1,2, St George’s University Hospitals NHS Foundation Trust, Rheumatology, London, United Kingdom; 1University of Hertfordshire, Center for Health Services and Clinical Research and Post Graduate Medicine, Hatfield, United Kingdom; 3King’s College, London, Academic Rheumatology, London, United Kingdom

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, 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.

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.

Disclosure of Interests: All recruiting ERAS and ERAN centers

Abstract THU0115 – Figure 1. Cox proportional hazards regression model showing time to 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.

THU0116 COMPARATIVE SAFETY OF BIOLOGIC DMARDS AND ABATACEPT IN RHEUMATOID ARTHRITIS WITH COPD: A REAL-WORLD POPULATION-BASED OBSERVATIONAL STUDY

Samy Suissa1, Marie Hudson1, Pierre Ernst1, Sophie Shen2, Teresa Simon2, Samy Suissa1, Marie Hudson1, Pierre Ernst1, Sophie Shen2, Teresa Simon2, 1McGill University, Montreal, Canada; 2Bristol-Myers Squibb, New Jersey, United States of America

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.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-conditioned propensity scores. 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
PHARMACOKINETICS AND SHORT-TERM SAFETY OF TREATMENT OF RHEUMATOID ARTHRITIS WITH FILGOTINIB, AN INHIBITOR OF JANUS KINASE 1, IN SUBJECTS WITH MODERATE HEPATIC IMPAIRMENT

Kacey Anderson, Hao Zheng, Oliver Medzihradsky, LI Yizhao, Ann Qin, Brian Kearney, Anita Mathias. Gilead Sciences, Inc., Foster City, United States of America

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 logarithm of FK 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 (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.


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

MIWA YUSUKE, Nobuyuki Yajima, Sakiko Isejima, Ryo Yanai, Mikako Hatano, Yoko Miura, Nao Oguro, Tomoki Hayashi, Kosuke Sakurai, Tsuyoshi Kasama. Showa University School of Medicine, Division of Rheumatology, Department of Medicine, Tokyo, Japan

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 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 non-nephrotoxic 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 (eGFIR) was calculated using the following factors: age, sex, prednisolone dosage, MTX dosage, SDAI, Cr level, eGFIR, diabetes status, hypertension status, dyslipidemia status, and serum creatinine (Cr) level.

Results: The decrease in eGFIR 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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