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

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 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 $\geq$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: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Oliver Medzihradsky Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Yizhao Li Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Ann Qin Employee of: Gilead Sciences, Inc., Brian Kearney Employee of: Gilead Sciences, Inc., Anita Mathias Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc.
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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

MIWA YUSUKE, Nobuyuki Yajima, Sakiko Isojima, Ryo Yanai, Mika 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 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 m^2) decreased from 88.5 ± 21.8 to 86.1 ± 21.5 and 83.7 ± 21.0 at 6 months and 1 year, respectively, in the combination treatment group and from 86.3 ± 37.9 to 79.5 ± 19.1 and 78.5 ± 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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