8 mg biweekly with MMF or PBO for 12 weeks. Subsequent to this MMF or PBO were discontinued but pegloticase was continued for another 12 weeks. The primary endpoint was proportion of patients who sustained a serum urate (SU) level of ≤ 6 mg/dL at 12 weeks. Secondary endpoints included 24-week durability of SU ≤ 6 mg/dL and rate of adverse events (AEs). Fisher’s exact test and Wilcoxon two-sample test were used for analyses along with Kaplan-Meier estimates and log-rank tests to compare survival curves between groups. Hypothesis tests were two-tailed and p-value (p) < 0.05 indicated statistical significance.

Results: Of 42 subjects screened, 35 were randomized, and 32 who received at least one dose of pegloticase were included in modified intention to treat analyses. Subjects were predominantly men (88%), mean age of 55.2 years (SD=9.7). Mean duration of gout was 13.4 years (SD=9.0), mean baseline sUA was 9.2 mg/dL (SD=1.6). Tophi were present in 88% and majority were on optimized ULT - 59% on allopurinol and 16% on febuxostat, with 63% reporting > 1 flare in the past year. At baseline both arms (MMF vs. PBO) had similar comorbidities (~82% vs 70%), diabetes mellitus/metabolic syndrome (~14% vs 20%), coronary artery disease/peripheral vascular disease (~14% vs 70%), BMI<30 (86% vs. 90%) and renal insufficiency (defined as eGFR ≤ 90 mL/min; 73% vs. 70%). At 12 weeks, 19 of 22 (86%) in the MMF arm achieved SU ≤ 6 mg/dL compared to 4 of 10 (40%) in PBO arm (p-value = 0.01). At 24 weeks, the SU was ≤ 6 mg/dL in 68% of MMF arm vs. 30% in PBO (p-value = 0.06), and rates of AEs per month were similar between groups with the PBO arm having more infusions reactions (30% vs. 0%). The MMF arm had higher AEs compared to placebo: musculoskeletal (41% vs. 10%), gastrointestinal (18% vs. 10%), and infections (9% vs. 0%). Figure 1 shows that the percentage of subjects maintaining a SUA < 6 mg/dL at 12 weeks was significantly higher (p=0.02) in the MMF arm, and a significant difference (p=0.03) at 24 weeks indicates sustained benefit from MMF.

Conclusion: To our knowledge this is the first randomized-controlled proof of concept trial to demonstrate the ability of an immunomodulatory agent in prolonging the efficacy of pegloticase. Short-term concomitant use of MMF therapy with pegloticase was well tolerated and showed a clinically meaningful improvement in the targeted SU ≤6 mg/dL at 12 and 24 weeks. This study suggests an innovative approach to utilize pegloticase therapy in patients with chronic gout.

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Figure 1. Proportion of subjects maintaining serum urate (SU) ≤ 6 mg/dL over 24 weeks studied/period in mycophenolate mofetil + pegloticase vs. placebo + pegloticase


POS0136

ROLES OF AUTOPHAGY IN THE PATHOGENESIS OF PRIMARY GOUTY ARTHRITIS

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Background: Gout is a chronic inflammatory disease caused by monosodium urate (MSU) crystal deposition [1]. Acute gout is characterized by an acute inflammatory reaction that resolves spontaneously within a few days [2], which is one of the distinguishing features of gout compared to other arthropathies or self-inflammatory diseases. Autophagy is a lysosomal degradation pathway that is essential for cellular growth, survival, differentiation, development and homeostasis [3]. Studies have demonstrated that autophagy might play a key role in the pathogenesis of primary gouty arthritis (GA) [4-7]. However, the roles of autophagy in the development of gout have not yet been elucidated.

Objectives: The aim of our study was to investigate the changes in autophagy-related gene (ATG) mRNA and protein in patients and the clinical importance of these genes in primary gouty arthritis (GA) and to explore the roles of autophagy in the pathogenesis of GA.

Methods: The mRNA and protein expression levels of ATGs (ATG3, ATG7, ATG10, ATG5, ATG12, ATG16L1, ATG4B and LC3-2) were measured in peripheral blood mononuclear cells (PBMCs) from 196 subjects, including 57 acute gout patients (AG group), 57 intercritical gout patients (IG group) and 82 healthy control subjects (HC group). The relationship between ATG expression levels and laboratory features was analyzed in GA patients.

Results: The expression levels of LC3-2, ATG3, ATG7 and ATG10 were higher in the AG group than in the IG and HC groups (p<0.05). The protein expression levels of LC3-2, ATG3, ATG7 and ATG10 were far higher in the AG group than in the other groups (p<0.05). In AG patients, the levels of ATG mRNA and protein correlated with laboratory inflammatory and metabolic indexes.

Conclusion: Altered ATG expression suggests that autophagy is involved in the pathogenesis of GA and participates in regulating inflammation and metabolism.

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POS0137

CARDIOVASCULAR RISK ASSOCIATED WITH TREATMENT OF ALLOPURINOL AND BENZBROMARONE IN PATIENTS WITH GOUT

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Background: Studies have shown that cardiovascular risk is increased in patients with gout. There are many studies on the effect of uric acid lowering therapy on CV risk in gout patients, but few studies have compared allopurinol and benzbromarone.

Objectives: A nationwide population-based cohort study is designed to compare cardiovascular risk according to the treatment of allopurinol and benzbromarone in Korean gout patients.

Methods: We used South Korea’s database of the Health Insurance Review and Assessment service (HIRA) to identify gout patients 18 years of age or older who newly started allopurinol or benzbromarone between 2009 and 2015. The start date of allopurinol or benzbromarone is defined as the index date. We excluded patients who have been prescribed uric acid lowering agents or have been on dialysis for one year prior to the index date. During the study period, patients who used uric acid lowering agents other than allopurinol and benzbromarone or who used both drugs in combination were also excluded from the study. The primary outcome of the study was the occurrence of a composite cardiovascular endpoint, which included coronary revascularization, hospitalization due to MI, ischemic stroke, and transient ischemic attack (TIA). Cox proportional hazard regression analysis and Kaplan-Meier curves were used for the analysis.

Results: 257,097 allopurinol initiators and 7,868 benzbromarone initiators were included in the study. The mean age was 54.4 years, 88% were male. The mean administration of drugs for the period was 6.2±2.1 months in allopurinol initiators and 75.5% for benzbromarone initiators. In baseline, the benzbromarone initiator had more cardiovascular comorbidities and related drug administration than the allopurinol initiator. In allopurinol and benzbromarone initiators, the adjusted hazard ratio (aHR) of the composite CV endpoint was 1.01 (95% CI 0.83-1.21), which was not significantly different. No significant difference was found between the two groups in each of the items of the composite CV endpoint and hospitalization for heart failure. The results did not change even when 1:3 propensity score matching was performed for baseline characteristics. In subgroup analysis of high risk patients with cardiovascular disease, there was no significant difference between allopurinol and benzbromarone initiators. However, when the analysis was limited to the group taking allopurinol ≥200mg and benzbromarone ≤50mg, there was no difference in primary outcome and other outcomes, but the risk of coronary revascularization was higher in benzbromarone initiator (aHR 1.58; 95% CI 1.16-2.14).

Conclusion: In the study, there was no significant difference in cardiovascular risk between allopurinol initiator and benzbromarone initiator. In the high risk group of cardiovascular disease, there was no difference in risk between the two drugs.

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