8mg 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 ≤6mg/dL at 12 weeks. Secondary endpoints included 24-week durability of SU ≤6mg/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 9.2mg/dL. 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 (41% vs. 70%), BMI>30 (86% vs 70%), and renal insufficiency (defined as eGFR < 90mL/min; 73% vs. 70%). At 12 weeks, 19 of 22 (86%) in the MMF arm achieved SU ≤6mg/dL compared to 4 of 10 (40%) in PBO arm (p-value = 0.01). At 24 weeks, the SU was ≤6mg/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 infusion 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 <6mg/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 ≤6mg/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) ≤6mg/dL over 24 weeks study 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 [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 much higher in the AG group than in the IG and HC groups (p<0.05), while the ATG7 mRNA level was much 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 much higher in the AG group than in the other groups, while those of ATG5, ATG12, ATG16L1 and ATG4B were far lower in the AG group than in the other groups (p<0.05). In GA 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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