Methods: We are recruiting 25 controls, 25 non-tophaceous and 25 tophaceous gout patients, 45-80 years old. Exclusion criteria include CPPD disease, RA, spondyloarthritis or spinal malignancy. All gout subjects meet ACR gout classification criteria with entry serum urate (sU) of >6.8 mg/dL, or sU >6.0 mg/dL on ULT for <6 months. Demographics, gout history, Aberdeen back pain scale, sU, ESR, and CRP are collected. DECT of the lumbosacral spine is used to assess MSU deposition and osteoarthritic changes.

Results: 63 subjects are enrolled and analyzed to date (25 control, 23 non-tophaceous and 15 tophaceous gout). Control, non-tophaceous gout, and tophaceous gout subjects have similar mean age in years (controls 61.8 ± 3.8 , non-tophaceous 64.0 ± 6.2 , tophaceous 63.5 ± 9.2 , $p=0.45$), but differ in BMI (controls 28.3 ± 6.5 kg/m², non-tophaceous 32.1 ± 6.7 kg/m², tophaceous 29.1 ± 4.3 kg/m², $p=0.01$) and creatinine (controls 1.0 ± 0.2 mg/dL, non-tophaceous 1.4 ± 0.6 mg/dL, tophaceous 1.7 ± 0.9 mg/dL, $p=0.048$). Mean sU and ESR are higher in gout subjects (sU-controls 5.3 ± 1 mg/dL, non-tophaceous 8.3 ± 1.4 mg/dL, tophaceous 8.4 ± 2.0 mg/dL, $p<0.05$; ESR-controls 13.7 ± 13.8 mm/h, non-tophaceous 25.2 ± 18.7 mm/h, tophaceous 22.5 ± 15.1 mm/h, $p<0.05$). Using default threshold settings for MSU visualization, greater MSU deposition is observed in the spine of gout patients (controls 2.2 ± 1.2 cm³, non-tophaceous 4.5 ± 4.3 cm³, tophaceous 8.5 ± 12.5 cm³, $p<0.05$; Table 1). Reanalysis of several scans using narrower threshold settings to limit possible artifact confirms increased MSU signal among gout patients. Although many subjects in each group do not have excessive MSU deposition, deposition is more common in both gout groups. No subject demonstrated a frank spinal tophus.

Conclusion: Based on preliminary results, gout patients have higher inflammatory markers and greater spinal MSU deposition than controls. Preliminary analyses with more stringent DECT threshold settings suggests these differences are not artifact, but analysis is ongoing. These data suggest that MSU deposition in the spine occurs in a subset of gout patients.

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Figure 1. DECT of the spine. (A) Patient with tophaceous gout (SU 8.9mg/dL, DECT volume 39.76cm³). (B) Control patient (SU 4.5mg/dL, DECT volume 0.70cm³).

Table 1. Baseline characteristics and mean DECT deposition volumes. Bold font indicates statistical significance.

Characteristic	Control	Non-tophaceous Gout	Tophaceous Gout	P-value
Number of subjects	25	23	15	
Age in years, mean $\pm$ SD	61.8 $\pm$ 3.8	64.0 $\pm$ 6.2	63.5 $\pm$ 9.2	0.45
Male sex, n (%)	23 (92.0)	23 (100.0)	13 (86.7)	0.23
Race:				0.52
-White, n (%)	18 (72.0)	14 (60.9)	7 (46.7)	
-Black, n (%)	6 (24.0)	6 (26.1)	6 (40.0)	
-Hispanic, n (%)	1 (4.0)	3 (13.0)	2 (13.3)	
BMI, mean $\pm$ SD	28.3 $\pm$ 6.5	32.1 $\pm$ 6.7	29.1 $\pm$ 4.3	0.01
Chronic kidney disease, n (%)	0 (0.0)	6 (26.1)	3 (20.0)	0.03
Diabetes mellitus type II, n (%)	3 (12.0)	5 (21.7)	2 (13.3)	0.62
Hyperlipidemia, n (%)	14 (56.0)	15 (65.2)	7 (46.7)	0.52
History of myocardial infarction, n (%)	1 (4.0)	2 (8.7)	1 (6.7)	0.80
Mean sU, mg/dL $\pm$ SD	5.31 $\pm$ 0.98	8.25 $\pm$ 1.4	8.42 $\pm$ 2.0	<0.001
Mean ESR, mm/hr $\pm$ SD (normal 0-10)	13.7 $\pm$ 13.8	25.2 $\pm$ 18.7	22.53 $\pm$ 15.1	0.04
Mean CRP, mg/L $\pm$ SD (normal 0-5)	2.7 $\pm$ 4.7	7.6 $\pm$ 12.5	4.1 $\pm$ 5.0	0.13
Mean serum creatinine, mg/dL $\pm$ SD	0.97 $\pm$ 0.18	1.36 $\pm$ 0.58	1.70 $\pm$ 0.88	0.048
Mean DECT volume, cm ³	2.2 $\pm$ 1.2	4.5 $\pm$ 4.3	8.5 $\pm$ 12.5	$p<0.05$

Acknowledgements: Supported by an investigator-initiated grant from Horizon Therapeutics

Disclosure of Interests: Michael Toprover Consultant of: Horizon Pharmaceuticals, Michael Mechlin: None declared, Anastasia Slobodnick: None declared, Virginia C. Pike: None declared, Cheongun Oh: None declared, Claudine Davis: None declared, Theodore Fields Consultant of: Horizon Pharmaceuticals, Avion Pharmaceuticals, Fabio Becce Consultant of: Horizon Therapeutics, Michael H. Pillinger Consultant of: Horizon Pharmaceuticals, Grant/research support from: Horizon Pharmaceuticals

DOI: 10.1136/annrheumdis-2021-eular.2733

POS0135

REDUCING IMMUNOGENICITY OF PEGLOTICASE (RECIPE) WITH CONCOMITANT USE OF MYCOPHENOLATE MOFETIL IN PATIENTS WITH REFRACTORY GOUT: A PHASE II RANDOMIZED CONTROLLED TRIAL

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Background: Pegloticase is a recombinant, pegylated uricase, used for treatment of gout patients who fail oral urate lowering therapy (ULT). Its use has been limited due to immunogenicity leading to infusion reactions.¹

Objectives: We evaluated if co-administration of an immunomodulatory agent could prolong the efficacy of pegloticase.

Methods: Participants were recruited in a Phase II, double-blind, placebo-controlled trial over 18 months and randomized in a 3:1 ratio by site. Inclusion criteria were: a) Age ≥ 18 years who met 2015 ACR/EULAR gout classification criteria and b) chronic refractory gout defined as symptoms inadequately controlled with ULT or contraindications. After a 2-week run-in of mycophenolate mofetil (MMF) 1000mg twice daily or matching placebo (PBO), they received a combination of pegloticase

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 ≤ 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 (41% 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 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 < 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 week studyperiod in mycophenolate mofetil + pegloticase vs. placebo + pegloticase

Disclosure of Interests: Puja Khanna Consultant of: Horizon Pharmaceuticals, Swedish Orphan Biovitrum A, Grant/research support from: Selecta, 2)DYVE, Dinesh Khanna Consultant of: Horizon Pharmaceuticals, Gary Cutter: None declared, Jeff Foster: None declared, Josh Melnick: None declared, Sara Jaafar: None declared, Stephanie Biggers: None declared, Fazlur Rahman: None declared, Hui-Chen Kuo: None declared, Michelle Feese: None declared, Kenneth Saag Consultant of: AbbVie, Inc., Bayer, Daiichi Sankyo Company LTD, Gilead Services, Inc., Horizon Pharma plc, Mallinckrodt, Radius Health, Inc., Roche/Genentech, Shantou Pharma Co., LTD, Teijin, Dyve Bioscience, LG Chem, Regeneron Pharmaceuticals., Swedish Orphan Biovitrum AB, Takeda Pharmaceuticals America, Inc.,

DOI: 10.1136/annrheumdis-2021-eular.3111

POS0136

ROLES OF AUTOPHAGY IN THE PATHOGENESIS OF PRIMARY GOUTY ARTHRITIS

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Background: Gout is a chronic autoinflammatory 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 ATG4B, ATG5, ATG12, ATG16L1, ATG10 and LC3-2 mRNA were much lower 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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Disclosure of Interests: Yu-Qin Huang: None declared, Quan-Bo Zhang Grant/research support from: National Natural Science Foundation of China (General Program) (no.81974250) and Science and Technology Plan Project of Sichuan Province (no.2018JY0257), Jian-Xiong Zheng: None declared, gui-lin jian: None declared, tao-hong liu: None declared, Xin He: None declared, fan-ni xiao: None declared, qin xiong: None declared, Yu-Feng Qing Grant/research support from: Science and Technology Project of Nanchong City (no.18SXHZ0522)

DOI: 10.1136/annrheumdis-2021-eular.3592

POS0137

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

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