Methods Patients with symptomatic gout and elevated sUA (≥6 mg/dL) were treated with fixed doses of pegviscag (0.2 mg/kg or 0.4 mg/kg) alone or co-administered with SVP-R (0.05, 0.08, or 0.1 mg/kg). SEL-212 was infused in 28 day cycles x3 doses followed by challenge with pegviscag alone on 28 day cycles x2 doses. Safety, tolerability, sUA, and ADAs were monitored.

Results In the SEL-212 Phase 1b study, 70% of patients administered 0.4 mg/kg pegviscag with a mid-dose of 0.1 mg/kg SVP-R showed low or no ADA formation correlating with sustained low sUA levels for at least 30 days after a single dose, compared to 20% for patients treated with pegviscag alone. In the ongoing Phase 2 study, the majority of patients receiving 0.1 mg/kg SVP-R administered with either 0.2 or 0.4 mg/kg pegviscag also showed low or no ADAs and maintained low sUA levels after 3 monthly doses of SEL-212, indicating sustained activity with repeated doses of SEL-212. However after 2 subsequent doses of pegviscag alone, a drop in activity was noted. These data suggest that either a higher dose of SVP-R or the addition of SVP-R at the 4th and 5th dose may be required to sustain activity through 5 months. Currently patients are being dosed with 0.15 mg/kg SVP-R, a dose level which enabled sustained control of sUA levels in all patients in Phase 1b. SEL-212 was generally well tolerated and associated with a low rate of gout flare rates compared to those treated with pegviscag alone.

Conclusions SVP-R showed a dose-dependent reduction in ADAs and enabled sustained control of sUA with repeated dosing of SEL-212. SVP-R is a promising approach to prevent the formation of ADAs against immunogenic biologic therapies.

REFERENCE

Acknowledgements We thank the patients that participated in these studies, the clinical study site investigators, and the entire SEL-212 project team.

Methods Human adipose-derived stem cells (hASCs) were encapsulated via a micromolding method. We first manufactured polydimethylsiloxane chips containing 1600 micromolds with a circular shape, 150 μm in diameter and 100 μm in depth. For cell encapsulation, a solution of 2% alginate (w/v) containing 3 million of hASCs per mL polymer was deposited onto the chips, loaded in the moulds either by sedimentation or centrifugation and crosslinked using an agarose gel charged with CaCl2. The number of encapsulated cells was evaluated by a CyQUANT assay immediately and 24 hour after encapsulation. The impact of encapsulation on metabolic activity was determined by a presto blue assay 24 hours after encapsulation and 24 hour after their injection through a 26G needle.

Results We successfully obtained cylindrical alginate microparticles presenting a diameter of 103±0.7 μm. Using cell quantification, we determined that the centrifugation method allowed the encapsulation of 30 333 (±5552) cells within one chip versus 6056 (±2862) by sedimentation. Cell number and metabolic activity remained stable for 24 hours after encapsulation. We also demonstrated that injection through a 26G needle had no impact on the viability of encapsulated cells.

Conclusions Our results show that micromolding allows hASCs encapsulation into alginate particles injectable through a 26 G needle without impacting cell viability. Future work will focus on evaluating in vitro long-term encapsulated cell survival and functionality. In case of success, we will then consider intra-articular injection in an animal model of osteoarthritis.

Disclosure of interest None declared

P113 ARGINASE I AND THE METABOLIC CONTROL OF OSTEOCLASTOGENESIS

1JS Brunner*, 2M Hofmann, 3V Safdering, 4A Vogel, 5A Lercher, 6Y Cheng, 7G Schabbauer, 8S Blüml.
1Institute for Vascular Biology; 2Dpt. of Rheumatology, Medical University Vienna; 3FoMM, Vienna, Austria; 4Bio Cancer Treatment International Ltd, Hong Kong, China

Introduction Osteoclasts are giant, multi-nucleated cells that derive from the monocyte-macrophage lineage and are regulators of bone turnover. Availability and catabolism of L-Arginine have been implicated with immune cell biology, skewing inflammatory responses within myeloid cells in a pro- or anti-inflammatory manner. Objectives While the role of L-Arginine within certain myeloid lineages such as macrophages is well appreciated, its role within osteoclasts is relatively unknown. We therefore aim to investigate L-Arginine metabolism in the context of osteoclastogenesis. Methods We analysed osteoclastogenesis of C57BL/6J wildtype bone marrow cells in vitro in the presence and absence of recombinant Arginase 1 (recArg1). This approach was complemented with qPCR analysis of relevant osteoclast marker genes and an extracellular flux assay. We further investigated the