hematoxylin and eosin (H and E) staining, Van Gieson staining, Masson's tri-chrome and fluorochrome labelling indicated PTEN inhibition provided protective effects against ethanol on bone tissue. Interestingly, our data revealed that the mRNA of PTEN, paralleled with PTENp1, was increased in a time-dependent manner upon ethanol stimulation, which resulted in increasing PTEN protein level. In addition, ethanol increased PTEN expression while decreased p-PTEN expression in a time-dependent manner, which indicated the generation of more functional PTEN.

Conclusions: Taken together, dual regulations of PTEN by ethanol via transcriptional and post-transcriptional process impaired the downstream signalling of Akt/PI3K/β-catenin and osteogenic differentiation of hBMSC. Therefore, we propose that PTEN inhibition treatment for Akt/PI3K/β-catenin activation could be tested in the clinic as a potential therapeutic approach to prevent the development of alcohol-induced osteopenia.

REFERENCES:

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Disclosure of Interest: None declared

SAT0048
ANALYSIS OF DIFFERENT THERAPEUTIC REGIMES IN PATIENTS WITH HEMOPHILIC ARTHROPATHY
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Background: The greater morbidity of the patient with haemophilia is due to hematrhrosis. The treatment is based on the administration of deficient coagulation factor (FC). The treatment is divided into prophylactic (TP) and on demand (AD). Prophylaxis consists in the administration of FC in order to maintain adequate levels of factor to prevent or reduce spontaneous bleeding and AD is the application of the factor when there is clinical evidence of bleeding. The TP is the recommended treatment in severe haemophilia, plasma and recombinant concentrates are used, safe and effective, but with a short half-life, which requires frequent intravenous infusions, being a barrier to compliance. Another drawback of the current treatment in haemophilia A (HA) is that up to 30% develop inhibitor (antibodies that neutralise the activity of a CF).

New subcutaneous drugs (NSD) have begun to be used in clinical trials, such as:
- Emicizumab: Bispecific anti–IXa/X monoclonal antibody.
- Concizumab: Anti–TFPI antibody.

This new therapeutic strategy can have implications both from a clinical and economic point of view.

Objectives: To analyse the different treatment regimens and their economic implications in a cohort of patients with hemophilic arthropathy (HA).

Methods: Consecutive patients in the Haemophilia Unit of our hospital (regional reference), in patients with HA (Haemophilia A and moderate-severe B), followed in consultation with episodes of joint bleeding, from January 2007 to October 2017. Gravity of the haemophilia determined by the percentage of FC activity (VIII and IX), moderate from 1% to 5%, severe <1%. The number of joint bleeds was analysed 6 months before and after the start of treatment with the NSD in patients who have participated in a multicenter phase III study and continue with the treatment.

Conclusions: This study demonstrated that there is a relationship between impaired catabolic pathways of tissue destruction, local GC activation by 11b-HSD1 is critical in within sites of inflammation and surrounding tissues, such as synovium and bone. Whilst this greatly increases local bioavailability of cortisol, which supports resolution of inflammation, in chronic disease, GCs drive may drive catabolic pathways that contribute to joint destruction and systemic bone loss.

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Disclosure of Interest: None declared

SAT0049
11BETA-HYDROXYSTEROID DEHYDROGENASE TYPE 1 REGULATES CHRONIC SYNOVITIS WITH LOCAL AND SYSTEMIC COMPLICATIONS
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Background: Inflammation, local joint destruction and systemic bone loss are common complications in patients with rheumatoid arthritis (RA). We have identified that localised pre-receptor activation of glucocorticoids (GC) by the enzyme 11beta-hydroxysteroid dehydrogenase type 1 (11b-HSD1) is increased within sites of inflammation and surrounding tissues, such as synovium and bone. Whilst this greatly increases local bioavailability of cortisol, which supports resolution of inflammation, in chronic disease, GCs drive may drive catabolic pathways that contribute to joint destruction and systemic bone loss.

Objectives: To determine the contribution of 11b-HSD1 activated glucocorticoids to joint destruction and inflammatory bone loss, we crossed an 11b-HSD1 null mouse onto a transgenic murine model of chronic polyarthritis (TNF-Tg) to generate TNF-Tg11bKO mice.

Methods: Clinical measures of joint inflammation, mobility and behaviour were collected between 4 and 9 weeks of age. Paw swelling was determined using caliper measurements. Histology was assessed in formalin fixed sections following staining with haematoxylin and eosin, saratin or TRAP staining. Juxta articular and systemic bone losses were measured by micro-CT. synovitis was determined by micro-CT analysis of histology sections following staining with haematoxylin and eosin. It was also assessed by Image J analysis of histology sections.

Results: 11b-HSD1 was completely knocked out within sites of inflammation in the TNF-tg11bKO mouse. At 9 weeks, both clinical and inflammation scores were markedly exacerbated in TNF-tg11bKO relative to TNF-tg counterparts inflammation score; TNF-tg, 4.3±2.26 versus TNF-tg11bKO, 11.0±8.06; p<0.001). This was supported by marked increases in joint swelling and juxta articular bone loss from these animals (erosion scores, TNFg, 5.2±0.61 versus TNF-tg11bKO, 9.0±0.66; p<0.005). Closer examination of joint destruction revealed that the pannus was larger and more extensive within subchondral bone, whilst evidence of cartilage degradation was significantly worse in the TNF-tg11bKO mouse (synovitis size, TNFg, 26.763 (AU) ±200 versus TNF-tg11bKO, 530±276 ±3225; p<0.005). Systemic bone loss determined by bone volume to tissue volume (BV/TV), trabecular thickness (TT) and trabecular number (TN) was also greatly exacerbated within the TNF-tg11bKO mouse (TNFg-BV/TV, 5.7±0.73, TT 73.5±6.4, TN 0.00077±0.0004 versus TNF-tg11bKO BV/TV 1.8±0.36, TT 7359.77 ±3.7, TN 0.00030±0.0005; p<0.001, p<0.005, p<0.001 respectively).

Conclusions: This study demonstrates that rather than contributing to catabolic pathways of tissue destruction, local GC activation by 11b-HSD1 is critical in mediating the suppression inflammation, joint destruction, synovitis and inflammatory bone loss in this murine model of chronic polyarthritis.

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