tion (EC50=44.5nM) that was reversed by Dipyrindamole (IC50=0.3μM). When Pannexin-1 and Connexin-43 were absent, Tenofovir did not increase OC number. Tenofovir increases Cathepsin K and NFATc1 mRNA levels during OC differentiation, and the effect was reverted by Dipyrindamole. Tenofovir reduced bone formation *in vivo* (19±2μm bone apposition vs 35±4μm untreated $p<0.05$) and this effect was reverted in the presence of Dipyrindamole (30±3μm, $p<0.05$ vs Tenofovir alone). microCT revealed decrease BMD and altered trabecular bone in Tenofovir-treated mice, been reverted in the presence of Dipyrindamole. TRAP-staining showed increased OC *in vivo* in Tenofovir-treated mice (21±1 vs 16±1 OC/hpf in untreated, $p<0.005$) that was reverted with Dipyrindamole. Similar results were obtained for Cathepsin K.

Conclusions: These results indicate that Tenofovir enhances OC differentiation and inhibits osteoblast differentiation by an adenosine-dependent mechanism and suggests that treatment with agents that increase local adenosine concentrations, like Dipyrindamole, might prevent bone loss following Tenofovir treatment.

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OP0187 TRANSGENIC DISRUPTION OF GLUCOCORTICOID-SIGNALING IN MATURE OSTEOBLASTS AND OSTEOCYTES ATTENUATES STRUCTURAL BONE DAMAGE IN A LONG-TERM MURINE K/BXN SERUM-INDUCED ARTHRITIS MODEL

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Background: The role of endogenous glucocorticoids (GC) in bone metabolism in chronic inflammatory arthritis remains unclear. We have previously shown that disruption of GC-signaling in osteoblasts results in a marked attenuation of arthritis in the K/BxN serum-induced and CAIA mouse model with preservation of bone volume and structure^{1,2}.

Objectives: In order to investigate the impact of endogenous GCs on bone erosion and turnover in chronic inflammatory arthritis, we now studied the effects of disrupted osteoblastic GC-signaling in a long-term murine arthritis model.

Methods: Intracellular GC-signaling in osteoblasts was disrupted by transgenic overexpression of 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD type 2) under the control of a type 1 collagen promoter. Arthritis was induced in 5-week old male transgenic (tg) mice and their wild-type (WT) littermates. In order to maintain a chronically active arthritis, mice were boosted on day 14 and 28 by subcutaneous injection of K/BxN serum, controls (CTR) received PBS, respectively. Severity of arthritis was assessed daily by clinical scoring and ankle size measurements until the endpoint (day 42). Ankle joints were assessed by a histopathologic score and microfocus computed tomography (micro-CT). Systemic effects of inflammation on bone metabolism were quantified by histomorphometry and micro-CT of the tibia.

Results: Acute Arthritis developed in both tg and WT mice and remained active over the period of 42 days, with a reduced, yet non-significant, severity in tg compared to WT mice. Histological indices of inflammation, cartilage damage and especially bone erosion, additionally assessed by micro-CT, tended to be overall reduced in tg mice, yet not reaching a level of significance. Bone volume and bone turnover did not differ between tg and WT arthritic mice.

Conclusions: The modulating effect of disrupted GC-signaling in osteoblasts in serum-induced autoimmune-arthritis prevails in a chronic inflammatory setting, leading to less severe local inflammation and bone destruction. This supports the important role of endogenous GCs for an intact bone metabolism in inflammatory bone disease.

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Treat-to-target in axSpA: reality or utopy?

OP0188 DEFINING CLINICALLY IMPORTANT WORSENING BASED ON ASDAS-CRP FOR AXIAL SPONDYLOARTHRITIS: A DATA-BASED CONSENSUS BY THE ASSESSMENT IN SPONDYLOARTHRITIS INTERNATIONAL SOCIETY (ASAS)

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Background: Disease flares are increasingly used as outcomes in axial spondyloarthritis (axSpA) trials or observational studies.

Objectives: The objective of this initiative was to define a cutoff for the ASDAS score that best defines the concept of "worsening in axSpA", to be used in the context of clinical trials and longitudinal observational studies.

Methods: Various steps were followed between 2014 and 2017. (a) Initial expert opinion within the steering group to define the scope of the project; (b) systematic literature review to collect cutoffs used for worsening in published studies; (c) vignette-exercise among ASAS members: a theoretical 'paper' patient-vignette, in whom an initial and a final value of an outcome was provided, was judged by the physicians on whether or not the patient had worsened (defining phy-worsening) (ref); (d) real-life multicenter international study: data necessary to calculate different outcomes were collected from real patients at 2 consecutive visits (spaced 7 days to 6 months): external standard was defined as a patient's report that he/she had worsened and he/she felt there was a need for treatment intensification. (e) Testing of different changes in the outcomes against both external standards for worsening (phy-worsening and pt-worsening) followed by a consensus and voting procedure among ASAS members in January 2017.

Results: (a) There was consensus about worsening being an absolute change between 2 time-points (without defining time between the 2 time-points) and about exploring cutoffs for 3 outcomes: ASDAS-CRP, BASDAI and pain. (b) The literature review had yielded 27 different cutoffs in 38 studies indicating important heterogeneity (c) The vignette-exercise yielded 12 preliminary definitions for worsening to be tested (as previously reported). (d) In the prospective study the sensitivity and specificity of each cutoff was tested against pt-worsening and judged by the ASAS-community. (e) No consensus was reached for a BASDAI-based definition due to limited performance of all cut-offs, and it was decided to not define a value for a pain-based definition for worsening. Based on aggregated data (Table), a consensus was reached among the ASAS-members to define worsening as a deterioration in ASDAS of at least 0.9 points. While this cutoff led to only moderate sensitivity when tested against pt-worsening, the overall balance of sensitivity and specificity as well as the overall face validity of this cut-off value for ASDAS was deemed most acceptable.

Table. Sensitivity and specificity of different ASDAS cutoffs to define worsening, against phy-worsening and pt-worsening considered as external standards.

Cutoff values for change in ASDAS	Vignette exercise study (N=1150 physician judgments) against the external standard 'phy-worsening' (worsening in N=591)		Prospective real-life study (N=1169 patients), against the external standard 'pt-worsening' (worsening in N=127)	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
>=0.6	97	65	55	91
>=0.9	85	87	38	96
>=1.1	60	94	33	98

Conclusions: This data-driven ASAS consensus process has allowed to propose an ASDAS-based cutoff value defining worsening in axSpA. As has been observed in other settings, the change defining worsening (at least 0.9) is smaller than the change defining improvement which is 1.2 for ASDAS. This definition should now be applied in trials.

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