from the knee joint cavity, in agreement with the previously observed hypocalcaemic effect after i.a. injection.

The efficacy of the HA-sCT treatment was tested in a rabbit OA model, where a chondroprotective effect of the high-dose test treatments was proven, in terms of synovial fluid and joint cartilage degradation, by macro- and microscopic assessments and histological findings. The cartilage surfaces of the weight-bearing parts, such as the medial tibial plateau and the lateral and medial femoral condyle, were evaluated and graded for degradation severity.

The average scores on the macroscopic assessment of sCT or HA-sCT treated group indicated a significant reduction in cartilage damage in comparison to controls. PAS staining of nuclei, indicating the maintenance of chondrocyte number, and Alcian blue staining of proteoglycan, indicating the matrix integrity of the cartilage, were significantly positive in the majority of the HA-sCT treated groups.

Conclusions: The in vivo PK and efficacy/safety profiles of sCT and HA-sCT were examined in this study in view of a potential application in the treatment of OA. Although the i.a. injection of the different sCT-based formulations showed to be comparably chondroprotective in a mechanical model of OA in vivo, the HA-peptide conjugate has the advantage of a sustained action and of a decrease in systemic exposure to sCT with consequent potential safety concerns. The promising results encourage further development and investigation on this therapeutic approach for OA.

869 HYALURONIC ACID ALKYL DERIVATIVE (HYADD®4) SHOWING INHIBITORY ACTIVITY ON HYALURONIDASES

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Purpose: Hyaluronic Acid (HA) homeostasis in the knee is based on a fine balance between synthesis and degradation; in pathological conditions, Hyaluronidases (specifically Hyal-2) play a key role in HA catabolism. The reduction of endogenous HA Molecular Weight (MW) and concentration in Synovial Fluid (SF) is one of the molecular signals that are common for the small molecule inhibitors. Since the HA alkylamide showed this unique property, in the second terms of Hyaluronidase inhibition, with the aim of verifying the in vitro action of HYADD®4, we tested the cross-linked HA and HA amidated with hexadecylamine, all formulated at 8%.</s>
871 EVALUATION OF A POLYACRYLAMIDE HYDROGEL IN THE TREATMENT OF INDUCED OSTEOARTHRITIS IN A GOAT MODEL: A RANDOMIZED CONTROLLED PILOT STUDY

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Purpose: Polyacrylamide hydrogel (PAAG) is an inert, non-degradable, non-immunogenic polymer gel with high viscoelasticity consisting of 97.5% sterile water and 2.5% cross-linked polyacrylamide. Its biocompatibility in soft tissues has been demonstrated. PAAG has recently been tested for the treatment of osteoarthritis (OA) in horses with highly encouraging results; however no standardized experimental studies have been done to explore its efficacy. The purpose of this study was to evaluate PAAG in the treatment of induced OA in a goat model.

Methods: A randomized controlled study was conducted involving goats with induced OA on the left stifle (knee) joint. OA was surgically induced by the transection of the medial collateral ligament, the bisection of the medial meniscus at its midpoint and partial-thickness incisions of the cartilage of the medial tibial plateau. Goats were allowed free exercise, and 3 months after surgery they were randomly divided into 2 groups: group 1 (n = 4); PAAG and group 2 (n = 2); saline solution (control). Treatments were injected intraarticularly. MRI of the left knee had been performed prior to surgery, at the time of injection (3 months) and 4, 5 and 7 months post-surgery. T1, T2/FL and Str weighted MRI images were used to assess OA. All goats were clinically evaluated on ground and on treadmill and videotaped for evaluation by 3 blinded observers. Haematology, biochemistry and acute phase proteins were also assessed. The goats were euthanized 7 months after surgery, and gross pathology and histopathology, including immunohistochemistry for nerve endings (n = 3 joints), were performed on both femorotibial joints. The hardness of the joint capsule was measured in both groups using Instron® 5564 testing system (HIS GlobalSpec, MA, USA).

Results: At the end of the study, 75% of the goats treated with PAAG were clinically sound, and 25% of them had not improved, whereas the 2 control goats were still lame. In both groups, the values of haematology, biochemistry, or acute phase proteins were within normal range. MRI showed that in group one, 2 out of 4 goats had a decrease followed by a stabilization of OA lesions, while 1 goat had a mild progression of the OA lesions. In group 2, both goats had a mild or marked increase of OA lesions. Gross pathology inspection in group 1 demonstrated that all the operated knees showed typical signs of OA. The inner synovial lining was thickened, and the cartilage surface was uneven in all cases. The gel was seen in various amounts adhering to the inner side of the joint capsule in all the goats of group 1. Gross inspection of both goats in group 2 also showed cartilage lesions and synovial thickening, but the histopathological investigations revealed this to be more prominent in group 1 than in group 2. It comprised angiogenesis, collagen and synovial cell increase, and in the injected goats, also the gel. The nerve endings were normal looking and in normal numbers. The investigation of the joint capsule hardness showed that in the treated knee of the goats of group 1, the medial side (injected with PAAG) was always less hard than the lateral side.

Conclusions: This study demonstrated the efficacy of a novel treatment of OA, with 75% of the goats treated with PAAG being clinically sound. Treatment with PAAG did not have any influence on haematology, biochemistry, or acute phase proteins. It induced a moderate synovial hyperplasia of the inner side of the capsule with trapped (integrated) gel, increased angiogenesis and collagen production. Preliminary pathology and joint capsule hardness data suggest that PAAG might act mainly on the joint soft tissue and especially the synovial membrane. PAAG might have 2 effects on OA joints. 1- Joint capsule was less hard on the treated (medial) than on the non-treated (lateral) side and had a lower hardness when compared to group 2. OA joints typically show joint stiffness - a major source of pain in OA. By decreasing the joint capsule hardness, and thus joint stiffness, PAAG might relieve the pain in the OA joint ("disease-modifying" effect). 2- MRI and pathology investigations have revealed a stabilization of OA lesions in the goats of group 1, which might be explained by the mechanical effect through the high viscosupplementation provided by PAAG that was still present in the joint cavity ("disease-stabilizing" effect). No adverse reaction was seen following intraarticular injection of PAAG. More investigations are needed to fully understand the mechanism of action of PAAG in improving clinical signs and in stabilizing OA. This pilot study may be used as a basis for further studies using larger animal numbers.

872 EVALUATION OF NONSTRUCTURED VECTORS FOR THE TREATMENT OF OSTEOARTICULAR PATHOLOGIES

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Purpose: One of the major problems in treatment of osteoarticular diseases is to reach cells inside the matrix to provide drug. Indeed, cartilage is an avascular tissue with a few cells feed by diffusion through a dense protein network (collagens, glycosaminoglycans). In this work we have designed polymeric nanoparticles (NPs) of poly (D, L-lactic)/glycolic acid)(PLGA) synthesized by a double emulsion method, which are biocompatible, biodegradable and can encapsulate water-soluble agents. Our NPs are labelled with BSA coupled to a fluorescent dye (Cyamine-3) to follow them by epifluorescent microscopy. As articular