does not normally occur in end-stage OA) during the course of treatment.

The aim was to describe the core differences in regard to image acquisition and radiologic assessment in OA efficacy studies and studies assessing a-NGF compounds.

**Methods:** The current standards in image acquisition and assessment in OA efficacy studies will be reviewed based on the authors' long-standing involvement in OA trials and the available literature. In particular, the role of radiography vs. MRI will be briefly reviewed. These findings will be contrasted to past and future a-NGF studies applying radiography and MRI for patient eligibility and safety monitoring. Differences between expected JSN in OA vs. rapid progression will be discussed. In addition, the role of MRI as an adjunct instrument to detect early findings of relevance will be emphasized.

**Results:** In regard to eligibility, OA efficacy studies require semi-quantitative assessment of screening radiographs to define disease severity. Similarly in a-NGF studies, subjects may be included based on screening radiographs. In addition to standard semiquantitative assessment, additional pre-defined diagnoses of exclusion have to be considered, such as atrophic OA, which potentially indicate increased risk of more rapid progression. In regard to on-study radiologic assessment, the focus in traditional OA efficacy studies is on maximized sensitivity to change over time to detect differences in JSN, while in a-NGF studies the focus lies on maximized sensitivity to detect early adverse findings that potentially result in withdrawal from treatment. Especially in cases of discrepant clinical and radiographic findings additional MRI examinations are needed to increase sensitivity to detect early changes.

**Fig. 1.** Osteoarthritis efficacy study. A. Baseline image shows medial joint space narrowing (JSN) (arrows). B. At 2-year follow-up there is an increase in JSN that is definite but does not suggest rapid progression.

**Fig. 2.** a-NGF study. A. Baseline image shows definite medial JSN (arrows) and no osteophytes consistent with atrophic OA. B. At the 9-month follow-up rapid progression in JSN is seen with new bone-to-bone appearance (arrows). Finding is consistent with RPOA Type I.

**Fig. 3.** a-NGF study. A. Baseline image shows definite osteoarthritis Kellgren-Lawrence Grade III with presence of osteophytes and medial JSN. B. At the 12-month follow-up severe disintegration of the medial compartment including collapse of the tibial plateau is observed. Finding is consistent with RPOA Type II.

**Conclusions:** The role of radiologic assessment differs in traditional efficacy and a-NGF studies. While in traditional efficacy studies image acquisition and evaluation is optimized for sensitivity to detect minor changes between treated and non-treated subjects, in a-NGF studies the focus is on early detection of diagnoses that either puts a subject at increased risk for an adverse outcome (eligibility) or may result in withdrawal from treatment (safety).

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**Purpose:** Stiffness and pain from osteoarthritis (OA), is often more pronounced in the morning than later in the day. When testing treatment of OA symptoms this circadian variation is rarely recognized. The aim of this study, therefore, was to evaluate the size of change in stiffness and pain scores from early morning until noon in OA patients. We also tested if the reduction in stiffness and pain from treatment, if any, was more pronounced in the morning than later in the day.

**Methods:** Stiffness and pain from osteoarthritis (OA), is often more pronounced in the morning than later in the day. When testing treatment of OA symptoms this circadian variation is rarely recognized. The aim of this study, therefore, was to evaluate the size of change in stiffness and pain scores from early morning until noon in OA patients. We also tested if the reduction in stiffness and pain from treatment, if any, was more pronounced in the morning than later in the day.

**Results:** Morning values for stiffness, group A (placebo first): 4.90 +/-2.30 vs 3.95 +/-1.82 at noon, a drop of 20% (p<0.000). Pain insignificantly declined by 5%. Testing the A group after a further 3 month on active therapy resulted in a similar pattern - a significant drop in stiffness comparing morning and noon (p<0.025) a drop but not significant in pain. Group B (active treatment first - then placebo): morning stiffness 4.56 +/-2.01 vs 3.68 +/-1.86 at noon. A drop of 20% (p<0.000). Pain: 4.27 +/-2.06 in the morning vs 3.60 +/-1.80 at noon, a 16% reduction (p<0.000). A similar pattern was seen testing after 3 month placebo. Lumping groups together (n=47) did not alter conclusions (data not given). When the A group was tested in the morning, active treatment resulted in a significant reduction of 20% (p<0.002) when compared to placebo. This reduction was 10% and still significant when testing at noon (p<0.037). The delta decline in stiffness in the morning caused by active treatment was 0.95 +/-1.46 as compared to noon, 0.39 +/-0.97 (p<0.046). Active treatment reduced pain by 15.5% (p<0.013) in the morning corresponding to a similar reduction at noon: 15.9% (p<0.055). No significant change comparing time of day. In the B group (active first) there were no significant changes in any of the parameters.
indicating carry-over. Lumping the groups together resulted in a significant drop in stiffness in the morning as well as at noon, (p<0.030) and (p<0.035), respectively, with no time difference in between. Pain showed identical pattern: p values morning <0.020 and noon <0.015, no time dependency. In accordance with the drop in stiffness and pain active treatment also resulted in an significant improved quality of sleep, improved mood and a better wellbeing (data not given).

Conclusions: Stiffness and to some degree pain was most pronounced in the morning. The present Rose-hip powder seems more potent, when symptoms are more pronounced. This may explain improved sleeping quality observed during active treatment. Circadian variation should be recognized in OA patients.

258 TISSUEGENE-C (INVOSSETM) IN PATIENTS WITH OSTEOARTHRITIS: A PHASE II TRIALS
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Purpose: TissueGene-C (TG-C) is a cell mediated gene therapy that contains non-transduced (hChonj) and transduced (hChonjβ7) human allogeneic chondrocytes. The hChonjβ7 cells were transduced with TGF-β1 gene by using retroviral vector and irradiated with gamma-ray. TG-C has been demonstrated its efficacy and safety in preclinical studies in vitro and in vivo. TG-C has been proven for its safety and efficacy in Phase I and Phase IIa clinical studies in osteoarthritis (OA) patients. The current placebo controlled phase llb study was conducted to determine both safety and efficacy of TG-C in patients with OA of the knee.

Methods: Participants (n = 54) with a confirmed diagnosis of knee OA by X-ray and MRI were randomized into the treatment group (TG-C, 1.8X107 cells/knee, n=27) and the placebo group (saline, n=27). The primary evaluation parameter was International Knee Documentation Committee (IKDC) which measures pain, sports activities, and daily function. The secondary evaluation parameters were Western-Ontario and MacMaster University (WOMAC) score, Knee Injury and Osteoarthritis Outcome Score (KOOS), and 100 mm Visual Analogue Scale (VAS). These parameters were assessed at 12 and 24 weeks post treatment. For TG-C treatment group, the evaluation was extended to 48 weeks post treatment.

Additionally, changes in biomarkers were assessed in serum and urine samples. Safety measures, including physical exams, complete blood count, and serum chemistry were included up to 6 months post treatment. Blood samples were screened to detect the replication competent retrovirus (RCR), retrovirally transduced cells, and TGF-β1 DNA and protein starting from 2 weeks up to 6 months post treatment.

Results: TG-C treatment group showed improvement in IKDC, WOMAC, KOOS and 100 mm VAS scores compared to placebo group, which was maintained up to the 1-year.

Conclusions: In summary, the Phase llb study indicated that TG-C (Invossa™) treatment improved pain, sports activities, and quality of daily life in patients with knee OA when compared to the placebo control.

259 ROSE-HIP INCLUDING SEEDS AND SHELLS REPORTED TO REDUCE SYMPTOMS OF OSTEOARTHRITIS, IMPROVES QUALITY OF THE SKIN BY MECHANISMS WHICH MAY INVOLVE COLLAGEN AND LONGEVITY OF CELL MEMBRANES

Purpose: Rose-hip powder, containing seeds and shells, rich in a galactolipid, GOPO, was shown to alleviate pain and stiffness in osteoarthritis and inhibit MMP-1, an enzyme breaking down collagen, in the cartilage of joints and in the subcutaneous tissue of the skin, causing wrinkles. Collagen is supported by anti-oxidants including Vitamin C. Anti-oxidants can also improve the longevity of cell membranes. Ani-

methods: A number of 34 healthy volunteers, 35 - 65 years of age, were randomly allocated to 2 month oral treatment with either the strong anti-oxidant Astaxanthin 4 mg daily, well known for its reduction of wrinkles, (p<0.01), or the present standardized rose-hip powder (Hyben-Vital™) 3 g daily (n=17) in a blinded manner. The depth of wrinkles was estimated initially and after 8 weeks, using a Skin Visioscan® VC98. Another group of 16 healthy volunteers were given either a single dose of 15 g of the present rose-hip powder, equivalent to 125 mg of natural vitamin C or a single dose of 250 mg of artificial vitamin C. Blood levels of vitamin C was estimated initially and after 1, 2, 4 and 6 hours using photometric methodology. Eighteen other healthy volunteers were treated with Rose-hip powder 45 g daily for 28 days. Red cells were isolated before and after 14 and 28 days of treatment, respectively, and again one month after stopping treatment. Each portion of blood was stored in a blood bank for 5 weeks. Then the leak of haemoglobin (HGB) from red cells into the surrounding medium, indicating cell membrane disintegration, was measured. The Wilcoxon test was used for statistical evaluation within groups. Mann-Whitney test for differences between groups. Data given is mean +/- s.d.

Results: Astaxanthin as well as Rose-hip significantly reduced the depth of wrinkles: Visioscan index initially: Astaxanthin 46.1 +/- 7.8 vs two month 42.2 +/- 5.5 (p <0.003). Rose-hip resulted in a similar and significant reduction of wrinkles: 45.9 +/- 9.9 vs 42.1 +/- 5.4 (p<0.034). No difference between groups (Mann-Whitney p value <0.095). Patients reported that they were equally satisfied by the two treatments (data not given). The lower dose of natural vitamin C (125 mg) given as rose-hip powder resulted in an improvement from 76.85 +/- 23.0 peaking after two hours 122.15 +/- 14.4 μmol/l (p<0.010). A similar pattern was seen when using the double dose of artificial vitamin C, initial level 71.7 +/- 25.6 peaking after 2 hours 119.1 +/- 21.0 μmol/l (p<0.010). No significant difference comparing groups. The leak of HGB, from erythrocytes, significantly declined during Rose-hip treatment. Initial value 57.2 +/- 13.9 vs 2 weeks treatment 49.2 +/- 16.2 (p<0.01). One month after stopping treatment, HBG levels were back to initial values (p<0.010).

Conclusions: The present data suggest that Rose-hip powder containing seeds and shells can have some impact on the protection of collagen and that vitamin C given in its natural form as a part of dried rose-hip powder is better absorbed than artificial vitamin C. The present rose-hip powder seems to improve the longevity of cell membranes

Epidemiology

260 THE PREVALENCE AND DIAGNOSTIC ACCURACY OF CLINICAL EXAM TESTS IN IDENTIFYING RADIOGRAPHIC FEMOROACETABULAR IMPINGEMENT (FAI): A PROSPECTIVE POPULATION-BASED STUDY
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Purpose: Femoroacetabular impingement (FAI) is common and sometimes associated with hip pain, labral and chondral pathology and osteoarthritis. The gold standard for diagnosis for bony FAI is specialized radiographic views and/or specific MRI sequences. Currently, no physical examination tests can accurately confirm or discard the presence of radiographic FAI. A recent systematic review found a critical absence of high quality studies and was unable to provide a clinical recommendation (Tijssen et al 2012). Almost all previous studies suffer from spectrum bias (most subjects had hip pathology) and the majority of studies from small samples. The objective was to undertake the largest, and first population-based study to estimate the prevalence and diagnostic accuracy of physical exam tests in identifying radiographic FAI in Caucasian and Chinese samples

Methods: A random population-based sample of 711 subjects (510 Caucasian and 201 Chinese) was recruited in Vancouver, Canada. The sample was stratified on the presence/absence of hip pain to recruit equal numbers of both. Individuals between 20 and 49 years were eligible if they reported both parents were of Caucasian or Chinese descent and could attend a two-hour session, consisting of physical