were younger and had higher levels of hip-related pain and disability. The LBP group also had a higher number of painful spinal levels and pelvic pain provocation tests. Results should be interpreted with caution due to the low sample size. Further research is warranted to explore the cause and effect relationship and underlying pain mechanisms associated with co-existing hip OA and LBP.

Conclusions: Treatment with DSPCC 35 mg TID and BID resulted in clinically meaningful improvements in pain in this study in patients with OA of the hip or knee.

### 712

**LOWER-DOSE DICLOFENAC CAPSULES DEVELOPED USING SOLUMATRIX FINE PARTICLE TECHNOLOGY RESULT IN CLINICALLY MEANINGFUL IMPROVEMENTS IN PAIN IN A PHASE 3 STUDY OF PATIENTS WITH OSTEOARTHRITIS**

**C. Young**, D. Parenti, M. Hochberg, Iroko Pharmaceuticals, LLC, Philadelphia, PA, USA; *Univ. of Maryland, Baltimore, MD, USA

**Purpose:** Osteoarthritis (OA) is characterized by acute and chronic pain and reduced physical function. Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently prescribed for the management of OA pain. As a class, NSAIDs are associated with dose-related serious gastrointestinal, cardiovascular, and renal adverse events which has prompted international health authorities and the United States Food and Drug Administration to recommend that NSAIDs be used at the lowest effective dose for the shortest possible duration. Diclofenac submicron particle containing capsules (DSPCC) consisting of submicron drug particles and a proprietary combination of excipients were developed using Solumatrix Fine Particle Technology to provide efficacy at lower doses than commercially available diclofenac drug products and are licensed for treatment of mild-to-moderate acute pain in adults. As previously reported, DSPCC 35 mg three times daily (TID) significantly reduced the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) pain subscale score compared with placebo (P = 0.0024) in a phase 3 study in adults with OA pain of the hip or knee. There was some evidence of improvement in the WOMAC pain subscale score compared with placebo for DSPCC 35 mg twice daily (BID), although this did not achieve statistical significance (P = 0.08). We report the results for measures of clinically meaningful pain relief following treatment with low-dose DSPCC in the phase 3 study.

**Methods:** This multicenter, randomized, double-blind, placebo-controlled study enrolled patients ≥40 years with clinically and radiographically confirmed (Kellgren-Lawrence grade II-III) hip or knee OA pain. Eligible patients were chronic NSAID and/or acetaminophen users with baseline WOMAC pain subscale scores ≥40 mm (based on 100-mm Visual Analog Scale) and a documented OA flares (≥15-mm increase in WOMAC pain subscale score from screening). Patients were randomized to receive DSPCC 35 mg TID, DSPCC 35 mg BID, or placebo for 12 weeks. Efficacy parameters included responder rates for patients who achieved a reduction of ≥10 mm in pain intensity from baseline based on the WOMAC pain subscale score at week 2, 6, and 12; the proportion of patients with a reduction (0%-100%) in WOMAC pain subscale score at week 12 (continuous responder analysis); and the proportion of patients who discontinued from the study due to lack of efficacy. Results: Overall, 305 patients were randomized. The mean (SD) age of patients was 61.6 (8.9) years and 66.6% were female. Both DSPCC 35 mg TID (86/96, 89.6% [P = 0.007]) and BID (86/102, 84.3% [P = 0.0148]) resulted in significantly more patients achieving ≥10-mm reductions in the WOMAC pain subscale score from baseline compared with placebo (67/96, 69.8%) at week 12. Similar effects were noted at week 2 (DSPCC 35 mg TID: 73/94, 77.7% [P = 0.0130]; DSPCC 35 mg BID: 78/100, 78.0% [P = 0.0098]; placebo: 56/92, 60.9%) and week 6 (DSPCC 35 mg TID: 76/96, 80.4%; [P = 0.0031]; DSPCC 35 mg BID: 76/91, 83.5% [P = 0.0338]; placebo: 61/87, 70.1%). The DSPCC 35 mg TID and BID groups achieved greater reductions in pain intensity compared with placebo. More than two-thirds of patients in the DSPCC 35 mg TID and BID groups achieved a reduction of ≥30% in the WOMAC pain subscale score from baseline and a majority of patients achieved a reduction of ≥50% at week 12 based on continuous responder analysis (Table). No patients in the DSPCC 35 mg TID group and 2 patients (1.9%) in the DSPCC 35 mg BID group withdrew from the study due to lack of efficacy compared with 6 patients (5.8%) in the placebo group.

<table>
<thead>
<tr>
<th></th>
<th>DSPCC 35 mg TID (n = 98)</th>
<th>DSPCC 35 mg BID (n = 102)</th>
<th>Placebo (n = 103)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with ≥30% reduction from baseline to week 12</td>
<td>75 (78.1%)</td>
<td>70 (68.6%)</td>
<td>61 (61.8%)</td>
</tr>
<tr>
<td>P value</td>
<td>0.0078</td>
<td>0.2271</td>
<td>0.9575</td>
</tr>
<tr>
<td>Subjects with ≥50% reduction from baseline to week 12</td>
<td>60 (62.5%)</td>
<td>57 (55.9%)</td>
<td>44 (43.8%)</td>
</tr>
<tr>
<td>P value</td>
<td>0.0205</td>
<td>0.1575</td>
<td></td>
</tr>
</tbody>
</table>

P-values are compared with placebo.

### 713

**INTRA-ARTICULAR INFILTRATION THERAPY FOR PATIENTS WITH GLENOHUMERAL OSTEOARTHRITIS: A SYSTEMATIC REVIEW OF THE LITERATURE**


**Purpose:** Conservative treatments are especially in patients with GH-OA important, since shoulder arthroplasty has its limitations. In this systematic review we will evaluate the current evidence regarding the efficacy of intra-articular infiltration treatment options in patients with glenohumeral osteoarthritis (GH-OA).

**Methods:** The following databases are searched: Pubmed/Medline, Cochrane Clinical Trial Register, Embase and the WHO clinical trial register. All intra-articular injection products used for the treatment of shoulder OA in humans are included.

**Results:** A total of 8 studies could be included in this review. Hyaluronic acid (HA) showed effect sizes of 2.07, 2.02 and 2.11 at 6, 12 and 26 weeks follow-up, respectively. Placebo (1.60, 1.82 and 1.68) also showed stable effect sizes at the same time points. The efficacy of corticosteroids (CS) decreased rapidly at follow-up (1.08, 0.43 and 0.19). Although statistical significant, the maximum difference in effect sizes between HA and placebo was only 0.43 with absolute values between 2.0 and 6.4 on a 100-point VAS for pain.

**Conclusion:** Intra-articular treatment with HA has a good efficacy at follow-up compared to baseline. However, the difference in efficacy between HA and placebo never reaches the minimal clinically important difference at any of the follow-up points. We are not able to give clear recommendations for the use of intra-articular CS injections in patients with GH-OA. In future research we recommend to focus on sufficiently powered randomized trials to compare the efficacies of HA, CS, placebo and other intra-articular treatment options in patients with GH-OA.

### 714

**IMPROVEMENT IN CARTILAGE FOLLOWING INTRA-ARTICULAR INJECTION OF TG-C, A CELL MEDIATED GENE THERAPY FOR OSTEOARTHRITIS**


**Purpose:** A randomized single-blind phase IIa trial was conducted in 28 patients with knee OA to determine both safety and efficacy of TG-C. TG-C is a cell mediated gene therapy that contains non-transduced (hChon) and transduced (hChonJb#7) human allogeneic chondrocytes. hChonJb#7 cells were transduced with TGF-β1 gene using retroviral vector, while hChonJ cells were not modified. The hChonJb#7 cells were
then irradiated with gamma-ray for preventing a replication of the cell and went to a cell death.

**Methods:** MR images acquired at baseline (pre-treatment), as well as 6 and 12 months post-treatment, were evaluated by two experienced musculoskeletal radiologists in a blinded fashion using a modified WORMS (Whole Organ Magnetic Resonance Imaging Score) method. After this scoring, the images were presented to the two radiologists again, in time sequence, and radiological impressions were generated for cartilage, and any significant visible trends or changes were identified. During the un-blinded radiological evaluation, a set of patients was noted to have improvements in the cartilage.

**Results:** The following improvements were observed: full thickness cartilage defect filling, generalized cartilage thickening in the defect area, and improvement or resolution of cartilage blisters. One patient showed several of these findings, and additionally showed considerable bone regeneration (bone remodeling) and cartilage regeneration in the trochlea, restoring the trochlea shape. Although these patients demonstrated many areas of improvement, in some patients there was evidence of progression of OA as well.

**Conclusions:** Based on these findings, there was an indication that in certain cases this treatment induced cartilage regeneration.

715 ASPIRIN IS ASSOCIATED WITH REDUCED CARTILAGE LOSS IN KNEE OSTEOARTHRITIS: DATA FROM A COHORT STUDY

A. Whuka 1, C. Ding 1, Y. Wang 1, G. Jones 1, F. Cicutini 1, 1 Monash Univ., Melbourne, Australia; 1 Menzies Res. Inst. Tasmania, Hobart, Australia

**Purpose:** Inflammation and vascular disease are important in the pathogenesis of osteoarthritis. Low dose aspirin has anti-inflammatory and vasculoprotective effects. This study examined whether use of low dose aspirin affects change in knee cartilage volume in osteoarthritis.

**Methods:** Participants from the Melbourne osteoarthritis cohort were classified as users and non-users of aspirin based aspirin use (<300 mg/day) at baseline. Participant’s knees were imaged twice over 2 years. Medial and lateral tibial cartilage volumes were measured and change in cartilage volume was calculated.

**Results:** Twenty one (18%) of participants were aspirin users at baseline. After adjustment for age, gender, body mass index and severity of radiographic change, annual change in medial tibial cartilage volume was -0.43 mm³ (95% confidence intervals (CI) – 0.46 to 0.39) in aspirin users and -0.10 mm³ (95% CI – 0.124, -0.077) in non-users (P = 0.048 for difference).

Similar results were seen for annual percentage loss (1.9% vs. 5.4%, p = 0.03). No difference was observed for lateral tibial cartilage change (p = 0.88).

**Conclusions:** Low dose aspirin use was associated with reduced medial tibial cartilage loss over 2 years in people with knee osteoarthritis. This data should be considered hypothesis generating and clinical trials are required to confirm efficacy.

716 DYSLIPIDEMIA IN PATIENTS WITH OSTEOARTHRITIS AND TYPE 2 DIABETES MELLITUS

M. Olinyuk, Kharkov Natl. Med. Univ., Kharkov, Ukraine

**Purpose:** To investigate influence of dyslipidemia to articular syndrome and glycosylated hemoglobin (HbA1c) in patients with osteoarthritis (OA) and type 2 diabetes mellitus (T2DM).

**Methods:** We examined 60 patients with knee OA and T2DM (28 males, age 58.7 ± 4.7 years). Baseline characteristics of patients included history of OA (6.2 ± 2.1 years), T2DM (7.3 ± 2.7 years). All patients were divided into 2 groups: 1st group – patients with OA, T2DM and concomitant dyslipidemia (n = 31), 2nd group (n = 29) – patients with OA, T2DM and without concomitant dyslipidemia. The levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL), very LDL (VLDL), triglycerides (TG), high-density lipoprotein cholesterol (HDL), of HbA1c, C-reactive protein were determined. All patients were made X-ray examination of knees.

**Results:** Among the 1st group of patients the level of HbA1c was significantly correlated with TC level (r = 0.58; p < 0.05), LDL (r = 0.48; p < 0.05), TG (r = 0.42; p < 0.05), HDL (r = -0.46; p < 0.05). The study found that the level of C-reactive protein was significantly higher in patients with concomitant dyslipidemia (p < 0.05). The degree of radiographic changes was significantly more increased in patients in the 1st group. We also noticed the severity of radiographic changes were significantly correlated with duration of T2DM (r = 0.41, p < 0.05).

**Conclusions:** Dyslipidemia can negatively affect the severity of articular syndrome and HbA1c in patients with OA and T2DM. We recommend to determine the level of lipid metabolism in patients with OA and T2DM for prescribing adequate lipid-lowering therapy that can minimize the risk of possible complications.

Pain and Disability

717 ASSESSMENT OF CHRONIC PAIN AFTER TOTAL KNEE REPLACEMENT: DEVELOPMENT OF A CORE OUTCOME SET

V. Wykle 1, J. Bruce 1, F. MacKichan 1, R. Gooberman-Hill 1, 1 Univ. of Bristol, Bristol, United Kingdom; 1 Univ. of Warwick, Warwick, United Kingdom

**Purpose:** Total knee replacement (TKR) can be a successful operation for providing pain relief; however approximately 20% of patients continue to experience chronic pain after TKR. The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) includes pain in its recommendations for core outcomes to assess in clinical trials of pain treatment. However, pain is multidimensional and there are no recommendations about which aspects of pain should be assessed. In this project, we aim to develop a core outcome set for the assessment of chronic pain after TKR using a Delphi survey. This core outcome set will represent the minimum pain information that should be measured and reported in clinical trials focusing on chronic pain after TKR.

**Methods:** This project is funded through a National Institute for Health Research Programme Development Grant on the treatment and management of chronic pain after TKR (the STAR programme). Phase I: identification of pain features

A Delphi survey requires that a long-list of possible domains has been developed, which adequately reflects previous research and the views of patients and clinicians. A list of pain feature that can be assessed after TKR has been developed through three studies:

1) Systematic review of 1,164 articles which assessed pain at a minimum of 3-months after TKR.

2) Three focus groups with 14 health care professionals.

3) Brief interviews with 50 patients experiencing chronic pain after TKR.

**Phase II: Delphi survey**

A 3-round Delphi survey with patients and clinicians is being undertaken to achieve consensus in the reduction of the long-list of pain features to a core outcome set. In round 1, participants are asked to rate the importance of assessing each pain feature from 1–9 (very important to very unimportant). Those pain features given an importance rating of 7–9 by at least 70% of each of the two panels (patients and clinicians) and rated as 1–3 by less than 15%, or given an important rating of 7–9 by 90% or more members of one panel, are retained and carried forward to round 2. In round 2, participants are provided with group feedback and asked to re-rate the pain features. In round 3, participants are asked to rate their level of agreement that each pain feature should be included in a core outcome set.

**Results:** Phase I: identification of pain features

A long-list of 56 pain features was developed from the systematic review, focus groups and brief interviews with patients. The features identified focused on pain intensity, temporal aspects of pain, pain with activities/movements, pain interference, recovery and pain after TKR, emotional aspects of pain and use of pain medications.

**Phase II: Delphi survey**

123 participants have been recruited into the Delphi survey (80 patients with chronic pain after TKR and 43 clinicians with relevant experience).

In round 1, participants rated the importance of the 56 pain features identified in Phase I. Of these 56 pain features, 33 were retained and carried forward to round 2. Rounds 2 and 3 of the Delphi survey are currently ongoing and will be completed by January 2014. The core outcome set will be finalised by March 2014 and ready for presentation at the OARSI conference in April 2014.