independently associated with OA severity (KL score). WOMAC pain and elevations of biomarkers – PGE2 and COMP fragments. Our data suggest that increased iron (ferritin levels) may promote cartilage damage in patients with knee OA and merits further investigation as a biomarker of disease severity and progression.

311 SAFETY AND EFFICACY OF NSAIDs IN ELDERLY ARTHRITIS PATIENTS: A SUBGROUP ANALYSIS

H. Kelner1, M. Essex2, C. Li3, 1Div. of Rheumatology, Ctr. for Inflammatory Joint Diseases, Munich, Germany; 2Pfizer Inc, New York, NY, USA; 3Pfizer Inc., New York, NY, USA

Purpose: As increasing age is a well-known risk factor for gastrointestinal (GI) adverse events and may contribute to reduced compliance and discontinuation of therapy, we set out to compare the safety and efficacy of celecoxib vs diclofenac slow release (SR) plus omeprazole in elderly patients with arthritis.

Methods: Patients aged ≥65 years, with osteoarthritis and/or rheumatoid arthritis at increased GI risk who participated in the CONDOR trial (Celecoxib vs Omeprazole and Diclofenac in Patients With Osteoarthritis and Rheumatoid Arthritis) were included in this subgroup analysis. The CONDOR trial was a 6-month, prospective, double-blind, randomized clinical trial of celecoxib vs omeprazole and diclofenac SR. Eligible patients were expected to need nonsteroidal anti-inflammatory drugs (NSAID) therapy for at least 6 months; aspirin or antiplatelet users were excluded. Patients were Helicobacter pylori negative. The primary end point was a composite of clinically significant upper and lower GI events adjudicated by an independent blinded expert committee and analyzed using a life-table method. Patients were randomized to either celecoxib 200 mg bid or diclofenac SR 75 mg bid plus omeprazole 20 mg qd. Follow up visits were at 1, 2, 4, and 6 months from baseline. Efficacy was determined by Patients’ Global Assessment of Arthritis at each visit.

Results: 2446 patients aged ≥65 years comprised the intent-to-treat population (n = 1219 celecoxib; n = 1227 diclofenac SR). Mean (SD) age was 70.4 (4.5) years for both arms; 83.0% of celecoxib and 80.8% of diclofenac SR patients were female. The majority of patients were white (54.1% celecoxib; 52.2% diclofenac SR). The difference between the 2 incidence proportions of adjudicated primary GI end points in patients aged ≥65 years, controlling for region, history of gastroduodenal ulceration, and time-block was statistically significant (odds ratio, 6.27; P < 0.0001 favoring celecoxib). 76.9% of celecoxib and 72.0% of diclofenac SR patients completed the study. Among those treated, 9.5% and 14.3% of patients, respectively, discontinued treatment for reasons related to study drug, and there were 2 deaths in the celecoxib arm and 1 in the diclofenac SR arm. Patients’ Global Assessment of Arthritis was 3.2±0.7 at baseline and 2.4±0.8 at Month 6 for both celecoxib and diclofenac SR, respectively. Similar percentages of patients rated efficacy at good/very good at baseline and Month 6 for celecoxib (10.5%, 55.9%) and diclofenac SR (10.6%, 56.4%). Least squares mean (SE) at Month 6 (last observation carried forward) was −3.25 (0.034) and −2.521 (0.033) for celecoxib and diclofenac SR (P=NS), respectively.

Conclusions: The results of the CONDOR trial, in which celecoxib was superior to diclofenac SR plus omeprazole in reducing the risk of clinical outcomes across the entire GI tract, were confirmed in a subgroup analysis of patients ≥65 years. The safety and efficacy of both treatments was comparable in this population. These data may help physicians make more informed decisions in treating elderly patients with arthritis.

312 SAFETY AND EFFICACY OF RETREATMENT WITH A BIOENGINEERED HYALURONATE FOR PAINFUL OSTEOARTHRITIS OF THE KNEE: RESULTS OF THE OPEN-LABEL EXTENSION STUDY OF THE FLEXX TRIAL

R.D. Altman1, J.E. Rosen2, D.A. Bloch3, H.T. Hatoum4. 1Div. of Rheumatology, Ctr. for Inflammatory Joint Diseases, Munich, Germany; 2Pfizer Inc, New York, NY, USA; 3Pfizer Inc., New York, NY, USA

Purpose: Intra-articular (IA) injection of hyaluronate (HA) has been shown to be safe and effective for relieving pain in patients with osteoarthritis (OA) of the knee and is recommended for patients who cannot be treated with oral medication (OA) managed with non-pharmacologic interventions or simple analgesics. Although many studies support the safety and efficacy of single course IA-HA injections, fewer trials have evaluated the risks and benefits of repeated series of injections. This 26 week Extension Study of the FLEXX Trial was conducted to evaluate the safety of repeated intra-articular (IA) injections of Euflexxa® (1% sodium hyaluronate; IA-BioHA) for painful knee osteoarthritis (OA).

Methods: Participants who completed the randomized, double-blind, 26-week FLEXX Trial and who elected to participate in the Extension Study received acesone series of 3 weekly IA-BioHA injections and were followed for an additional 26 weeks. Adverse events (AEs) were recorded and the effect of treatment on knee pain was measured using a 50-foot walk test using a 100 mm visual analog scale (VAS). The 3 subscales of WOMAC, OARSI responder rate, Patient Global Assessment, SF-36, and intake of rescue medication was also evaluated.

Results: The FLEXX Trial included 588 subjects with painful knee OA who received 3 weekly IA injections of either BioHA or buffered saline (IA-SA). Results from the FLEXX Trial showed that IA-BioHA decreased mean pain 100 mm visual analog scale (VAS) scores immediately following a 50-foot walk test by −25.7 mm versus −18.5 mm for the IA-SA group. Both treatments were well tolerated with about 1% of subjects in each group reporting injection site reactions.

The Extension Study included 433 subjects, 219 who received IA-BioHA and 214 who received IA-SA during the FLEXX Trial. Safety results from the Extension Study indicate that 43.4% (188/433) of subjects had AEs, of which 4.8% (21/433) were deemed treatment-related AEs. Two AEs in the Extension study led to discontinuation, and no joint effusion was reported. Patients who continued with IA-BioHA in the Extension Study maintained their improvement from baseline, with an average further reduction in pain VAS score of −3.5 mm. Patients initially treated with IA-SA in the FLEXX Trial also had a reduction in pain VAS score of −9.0 mm. The OMERACT-OARSI responder rate for all subjects was 75.3% at the completion of the Extension Study. WOMAC Pain, Stiffness, and Disability scores decreased by 47.2%, 42.5%, and 44.1%, respectively. The Patient’s Global Assessment improved an additional −8.1 mm and there were 15.2% and 15.7% improvements for SF-36 physical functioning and bodily pain scores, respectively, from the beginning of the FLEXX Trial to the end of the Extension Study. Acetaminophen use was reduced from 14.6 to 9.5 tablets per week, representing an overall 34.9% reduction from the beginning of the FLEXX Trial.

Conclusions: Repeated injections of IA-BioHA were effective, safe, and well-tolerated, and were not associated with an increase in AEs such as synovial effusions. Additional symptom improvements during the Extension Study were noted for subjects who received either IA-BioHA or IA-SA during the FLEXX Trial.

313 A PHASE 2 STUDY EVALUATING THE EFFICACY AND SAFETY OF A NOVEL, PROPRIETARY, NANO-FORMULATED ORAL DICLOFENAC

S. Daniels1, G. Manvelian2, A. Gibofsky3. 1Premier Res. Group, Austin, TX, USA; 2Independent Clinical Res. Consultant, Poway, CA, USA; 3Hospital for Special Surgery, New York, NY, USA

Purpose: Nonsteroidal anti-inflammatory drugs (NSAIDs) are a common class of medication taken for acute arthritic pain. However, associated adverse events (AE) have prompted the development of new formulations that minimize AEs and maintain efficacy. The purpose of this clinical study was to evaluate the analgesic efficacy and safety of an investigational, proprietary, nano-formulated, oral diclofenac (diclofenac-N) compared with placebo in subjects with acute dental pain.

Methods: This was a phase-2, multisite, randomized, double-blind, single-dose, parallel-group, active- and placebo-controlled study. In total, 200 subjects who were 18–50 years of age, had extraction of ≥2 third molars (at least one of which had to be a fully or partially impacted mandibular third molar), and experienced moderate to severe pain intensity within 6 hours after surgery were enrolled. Subjects received either diclofenac-N 35 mg or 18 mg, celecoxib 400 mg, or placebo. The primary efficacy variable was the sum of total pain relief (TOTPAR) over 0–12 hours (TOTPAR-12) after Time 0. Higher scores indicated better pain relief. TOTPAR-8 and TOTPAR-4 were also evaluated.

Results: Diclofenac-N was significantly (p < 0.001) better than placebo for TOTPAR-12. Mean ± SD TOTPAR-12 values for diclofenac-N 35 mg, diclofenac-N 18 mg, celecoxib 400 mg, and placebo were 16.8±12.76, 17.76±13.76, 14.61±15.05, and 5.65±11.33, respectively. TOTPAR-4 and TOTPAR-8 values for diclofenac-N 35 mg and diclofenac-N 18 mg demonstrated comparable results when compared to placebo. The difference in time-to-onset of analgesia between each treatment
and placebo was also significant (p < 0.001) with the shortest times observed with diclofenac-N. Treatment-emergent AEs were similar across treatment groups with similar rates in subjects treated with placebo (52.9%), diclofenac-N 35 mg (60.8%) and diclofenac-N 18 mg (55.1%).

Conclusions: An investigational, proprietary, nano-formulated, lower dose, oral diclofenac demonstrated good efficacy, onset of action, and tolerability. As suggested by this phase-2 clinical trial, use of this lower dose formulation could maintain efficacy, shorten onset of action, and possibly result in an improved tolerability profile for patients with acute arthritic pain.

314
THE APPLICATION OF PLATELET-RICH PLASMA IN EARLY OSTEOARTHRITIS OF KNEE
S-C. Lang, Kosin Univ. Gospel Hosp., Busan, Korea, Republic of

Purpose: Platelet-rich plasma (PRP) is a natural concentrate of autologous blood growth factors experimented in different fields of medicine in order to test its potential to enhance tissue regeneration, and so emerged as a treatment option for tendinopathies and chronic wounds. In addition to release of growth factors, PRP also promotes concentrated anti-inflammatory signals including interleukin-1a, which has been a focus of emerging treatments for osteoarthritis. The primary objective is to compare a single, intra-articular injection of platelet-rich plasma (PRP) with hyruan injection in patients with early osteoarthritis of knee and to assess the clinical efficacy and safety of intra-articular platelet-rich plasma (PRP) injection in patients with low degree osteoarthritis (OA) of the knee.

Methods: Between June 2008 and October 2010, we reviewed the results of 86 consecutive primary osteoarthritic patients underwent intra-articular injection of PRP. In a group of early osteoarthritic patients, inclusion criteria was set to those who were able to be followed up for at least 6 months and showed as Kellgren-Lawrence grade I on simple radiograph or MRI, and exclusion criteria was set as severe obesity, infection, immunosuppressed patients, advanced osteoarthritis (K-L grade I, II, III), and severe deformity. PRP was injected once, in principle. Also, to compare the effects of PRP, hyruan injection was performed in 21 cases during the same period in a same target group, and the effect was compared by performing 3 times in an interval of 1 week. Results were evaluated at 4, 8, 12, 18, 24 weeks post-injection using radiologic study, visual analogue scale (VAS) and international knee documentation committee (IKDC) score for functional score.

Results: The mean preoperative VAS was 8.2 (range 7–10) and the mean postoperative score was 3.2 (range 1–4) and 2.9 (range 0–4) at 12 and 24 weeks of follow-up. In IKDC score, the mean preoperative knee score was 57.5 points (range 32–77), and the mean postoperative knee score was 77.3 points (range 60–95) and 88.9 points (range 69–98) at 12 and 24 weeks of follow-up, respectively. Patients receiving PRP experienced statistically significantly greater improvements in VAS (p = 0.032), and IKDC score measures, than patients receiving hyruan injection. There was no different between the safety results of the two groups. No increased risk of local adverse events was observed in the follow-up periods.

Conclusions: According to VAS, the mean preoperative scale was 8.2 (range 7–10) and the mean postoperative scale was 3.2 (range 1–4) and 2.9 (range 0–4) at 12 and 24 weeks of follow-up. In IKDC score, the mean preoperative knee score was 57.5 points (range 32–77), and the mean postoperative knee score was 77.3 points (range 60–95) and 88.9 points (range 69–98) at 12 and 24 weeks of follow-up, respectively. Patients receiving PRP experienced statistically significantly greater improvements in VAS (p = 0.032), and IKDC score measures, than patients receiving hyruan injection. There was no different between the safety results of the two groups. No increased risk of local adverse events was observed in the follow-up periods.

315
A PHASE 2 STUDY EVALUATING THE EFFICACY AND SAFETY OF A NOVEL, PROPRIETARY, NANO-FORMULATED ORAL INDOMETHacin
G. Manvelian1, S. Daniels2, 1Independent Clinical Res. Consultant, Poway, CA, USA; 2Premier Res. Group, Austin, TX, USA

Purpose: Nonsteroidal anti-inflammatory drugs (NSAIDs) are a common medication taken for acute pain relief. Indomethacin has a long-established efficacy and safety profile yet can have a variable and somewhat slow onset of action. Indomethacin also has the potential for gastrointestinal adverse events (AEs), suggesting the need for a new formulation which can safely provide fast onset of acute pain relief. Our objective was to evaluate the analgesic efficacy and safety of an investigational, proprietary, nano-formulated, oral indomethacin compared with placebo in subjects with acute dental pain.

Methods: This was a phase-2, multicenter, randomized, double-blind, single-dose, parallel-group, placebo-controlled study. In total, 203 subjects were enrolled who: were 18–50 years of age, had extraction of ≥2 third molars, and experienced moderate to severe pain intensity within 6 hours after surgery. Subjects received either nano-formulated indomethacin 20 mg, 40 mg, or placebo. The primary efficacy variable was the sum of total pain relief (TOTPAR) over 8 hours (TOTPAR-8). Higher scores indicated better pain relief.

Results: Nano-formulated indomethacin was significantly (p < 0.001) better than placebo for TOTPAR-8 (mean; 95% CI): 40mg (12.56; 2.64); 20mg (10.79; 2.66); placebo (3.02; 2.64). Nano-formulated indomethacin was also significantly (p < 0.001) better than placebo for TOTPAR-4 (mean; 95% CI): 40mg (6.16; 4.78); 20mg (5.47; 4.61); placebo (1.63; 2.83). The difference in time to onset of analgesia between each treatment and placebo was also significant (p < 0.001). Treatment-emergent AEs occurred less often in subjects treated with nano-formulated indomethacin (38.0%) than those treated with nano-formulated indomethacin 40mg (51.0%) or placebo (56.9%).

Conclusions: A proprietary, nano-formulated, lower dose, oral indomethacin demonstrated good efficacy, onset of action, and tolerability. The ability to utilize a lower dose and maintain efficacy could result in an improved tolerability and safety profile and in line with the FDA directive to use the lowest effective dose for the shortest duration.

316
CLINICAL EVALUATION OF A HERBAL FORMULATION, RHULIEF™, IN THE MANAGEMENT OF KNEE OSTEOARTHROSIS
B. Antony1, R. Kizhakedath2, M. Benny1, B.T. Kuruvilla1. 1Arjuna Natural Extracts Ltd., Aluva, India; 2Anugraha Med. Ctr., Kochi, India

Purpose: The study was conducted to evaluate the efficacy, safety and tolerability of Rhulief™, a unique mixture of acetyl boswellic acids with acetyl 11-keto beta boswellic acid (AKBA) content of 10% w/w and BCM 95™, a composition of curcumin which is about 7 times more bioavailable than conventional curcumin, compared with non-steroideal anti-inflammatory drug, Celecoxib in the management of knee osteoarthrotis.

Methods: Fifty four subjects were screened, 30 subjects were enrolled and 28 completed the study. Subjects of both sexes aged 18 to 65 years who were medically stable with moderate form of osteoarthritis were recruited. X-ray evidences of narrowing of the medial joint space with swelling were randomized into two groups and were treated for a period of 12 weeks. Gr I: Oral administration of Rhulief™ 500 mg capsule twice daily. Gr II: Oral administration of Celecoxib 100 mg capsule twice daily. Subjects with long standing and severe form of osteoarthritis, persons with history of rheumatoid or reactive arthritis and significant systemic diseases were excluded from the study. Symptom scoring and clinical examination were done during their each visit to find out the efficacy of the drug. Safety of the drug was assessed by recording the liver function test, renal function test and haemogram.

Results: The results of the symptom scoring revealed that there was a significant (p < 0.05) improvement in pain scores within the groups over a period of 12 weeks and the improvement was more with Gr I. Significant (p < 0.05) improvement in walking distance and joint line tenderness were also observed within the groups and the effects were greater with Gr I. Statistically significant difference between range of movements were observed within both the groups (p < 0.05). The differences in range of movements were comparable in both groups and there was no significant change between the two groups. Vital signs, haemogram, liver function test and renal function test were not adversely modified by Rhulief™. The results of the present study concluded that the treatment was well-tolerated and did not produce any adverse effect in patients.

Conclusions: Rhulief™ at 500 mg twice a day was better than Celecoxib 100 mg twice a day in symptom scoring and clinical examination. It was equally well tolerated and no dose-related toxicity was found. Efficacy and tolerability of Rhulief™ used in the current and