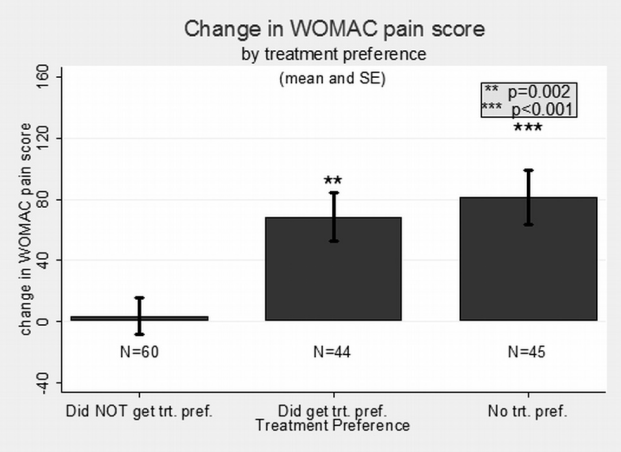

than men (75.5% vs 57.7%) and through randomisation got their preference more often (48.7% vs. 26.7%, p 0.04). The effects of patient preference on outcome was similar in men and women, furthermore the overall results of this study were independent of gender. Patients who had previously received an IS were more likely to express a preference (83.1% vs. 60.4%, p=0.003), but were less likely to receive it (32.7% vs. 50.9%, p=0.002). Adjusting for previous intra-articular injections did not significantly affect the overall results.

Conclusions: In this study, which demonstrated significant improvements for TI compared to IS, patient preference was also a strong independent predictor of outcome. Those who did not express a treatment preference obtained the best outcome and those did not receive their preference did not benefit from the treatments given. Previous studies suggesting that patient preference influences outcome have been conducted on treatments with long term therapies and as such differences have been attributed to adherence with treatment. This study of a single baseline intervention suggests that compliance is not the only reason and hence these findings have major implications for clinical practice and for the design of future RCT's.

P302

RETENTION ON TREATMENT WITH LUMIRACOXIB IN PATIENTS WITH OSTEOARTHRITIS

R. Fleischmann[1], H. Tannenbaum[2], N.P. Patel[3], M. Notter[4], P. Sallstig[4], J.-Y. Reginster[5]
[1]The University of Texas Southwestern Medical Center at Dallas, Dallas, TX, [2]Rheumatic Disease Center of Montreal, Montreal, PQ, Canada, [3]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [4]Novartis Pharma AG, Basel, Switzerland, [5]CHU Policlinique L Brull, Liège, Belgium

Purpose: Retention on treatment reflects the interrelated issues of efficacy, safety and tolerability in OA patients. Objective: To show that lumiracoxib 100 mg od and 100 mg bid are non-inferior to celecoxib 200 mg od with respect to the retention rate at week 52 in patients with OA.

Methods: In this 52 week, randomized, double-blind trial, 3036 patients with OA of the hip, knee, hand or spine were randomized to lumiracoxib 100 mg od, lumiracoxib 100 mg bid (2x recommended dose for OA) and celecoxib 200 mg od in a 1:2:1 ratio.

The primary efficacy variable was the retention rate at 52 weeks. Non-inferiority was tested by comparing pairwise differences in retention rates using a multiple testing procedure to adjust for multiplicity and a confidence interval approach with a pre-defined non-inferiority margin of -0.1. Secondary variables included efficacy using patient's assessment of OA pain intensity in the target joint, patient's and physician's global assessment of disease activity (defined as improvement by at least one grade in the Likert scale), usage of rescue medication and safety and tolerability.

Results: Patient disposition was similar across the treatment groups. Approximately 45% of patients in each group remained on treatment until study end. An amendment to the protocol following the announcement of possible increased CV risk with celecoxib excluded patients with CCV history and elevated CV risk (13%) and led to withdrawal of consent in 4% of the patients. Other major reasons for discontinuations were adverse events (12%), unsatisfactory therapeutic effect (11%) and withdrawal of consent (7%).

The results of the retention to treatment analysis are shown in Table 1.

Comparisons using an integrated measure of the overall level of OA pain intensity and patient's and physician's global assessments of disease activity showed no statistical significant differences between treatment groups.

Improvement rates at study end for OA pain intensity (51 - 54%), patient's and physican's global assessment and use of rescue medication were comparable between the treatment goups.

The safety and tolerability of both lumiracoxib doses and celecoxib were generally similar, with comparable overall incidences of AEs and SAEs. APTC events (stroke, MI, CV death) occurred in similar rates (0.7-0.8%). ALT/AST elevations > 3 x ULN occurred at a higher frequency in patients treated with lumiracoxib 100 mg bid (2x recommended dose) than with lumiracoxib 100 mg od or celecoxib 200 mg od.

Conclusions: Retention on treatment at 1 year of lumiracoxib 100mg od was non-inferior to celecoxib 200 mg od and all secondary efficacy parameters were comparable between these treatment groups. Lumiracoxib 100 mg od was shown to be as effective and safe as celecoxib 200 mg od.

P303

INTRA-ARTICULAR HYALURONIC ACID COMPARED WITH CORTICOID INJECTIONS FOR THE TREATMENT OF RHIZARTHROSIS

T.J. Heyse[1], C.O. Tibesku[1], R. Mönikes[2], A. Wohlmeiner[3], S. Fuchs[1]
[1]Academic Hospital of Marburg, Marburg, Germany, [2]Orthopaedic Practice, Unna, Germany, [3]Orthopaedic Practice, Havixbeck, Germany

Purpose: This trial is a prospective assessment of the efficacy and tolerability of intra-articular sodium hyaluronate (SH;

P302 – Table 1

Population treatment group	N	Retention rate n (%)	Contrasts	Estimated difference	97.5% CI of difference	Outcome
ITT						
LUM 100mg od	755	354 (46.9)	LUM 100mg od - CEL 200mg od	0.02	-0.04, 0.07	Non-inferiority shown
LUM 100mg bid	1519	722 (47.5)	LUM 100mg bid - CEL 200mg od	0.02	-0.03, 0.07	Non-inferiority shown
CEL 200mg od	758	343 (45.3)				

LUM = lumiracoxib; CEL = celecoxib.

Ostenil mini) and triamcinolone (TA; Volon A10) for treatment of osteoarthritis (OA) of the carpometacarpal (CMC) joint of the thumb in a 26-week, controlled, randomized, masked-observer study.
Methods: Patients were treated with three intra-articular injections of either SH (n=28) or TA (n=28). Primary assessments were pain according to VAS and extensive clinical and functional parameters such as swelling, grip power and range of motion. The population was analysed using one- and two-sided Mann-Whitney (MW) estimators.
Results: Maximum pain relief occurred at 2-3 weeks for TA and at week 26 for SH after the first intra-articular injection. At weeks 2-3 TA was significantly better than SH (MW: 0.3319 and 0.3063; p=0.9827 and 0.9929). At week 26 a slight superiority of SH could be observed (MW: 0.53; p=0.3624) and non-inferiority could be proven. After 26 weeks lateral pinch power was significantly better in the SH-group (MW: 0.6331; p=0.0226). In all, 88.0% of patients treated with SH and 79.2% of the TA-group described pain improvement after 26 weeks. No adverse events with causal connection to the investigational products occurred.
Conclusions: We conclude that a single course of three SH injections is effective in relieving pain and improving joint function in patients with OA of the CMC joint of the thumb. Although in comparison with triamcinolone its effects are achieved more slowly, the results indicate a superior long-lasting effect of hyaluronan at 6 months after end of treatment period.

P304

SUPPRESSION OF TNF-α, IL-1β, INOS, AND P38 EXPRESSION BY THE COMBINATION OF AVOCADO SOY UNSAPONIFIABLES, GLUCOSAMINE, AND CHONDROITIN SULFATE IN HUMAN MACROPHAGE-LIKE THP-1 CELLS

R.Y. Au, A.Y. Au, C.G. Frondoza
Nutramax Laboratories, Inc., Edgewood, MD

Purpose: The present study determines whether the combination of Avocado Soy Unsaponifiables (ASU), glucosamine (Glu), and chondroitin sulfate (CS) was more effective in suppressing pro-inflammatory gene expression than ASU alone, or Glu and CS together.
Methods: Human monocyte/macrophage surrogate THP-1 cells (5 x 10^5 cells) were incubated for 24 hrs at 37°C and 5% CO_2 with: (i) control media alone, (ii) ASU (8.3 μg/ml; NMX1000™-ASU), (iii) Glu (15 mM; FCHG49®) and CS (20 μg/ml; TRH122®), or with (iv) a combination of ASU (8.3 μg/ml), Glu (15mM), and CS (20 μg/ml). All test materials were supplied by Nutramax Laboratories, Inc., Edgewood, MD. The cells were then activated with 20 ng/ml LPS for 1 hour. Total RNA was extracted and subjected to RT-PCR analysis using primers specific to TNF-α, IL-1β, iNOS, p38, and S14 as the housekeeping gene.
Results: Pre-treatment with the combination of ASU, Glu, and CS profoundly suppressed the expression of TNF-α, IL-1β, and iNOS by 50-80% in activated THP-1 cells. The combination treatment reduced TNF-α and IL-1β expression to levels similar to baseline non-activated controls and reduced iNOS expression to levels lower than baseline non-activated levels. The inhibitory effect of the combined preparation on TNF-α, IL-1β, and iNOS expression is more profound than ASU alone, or Glu and CS together. The inhibition of cytokine and iNOS expression is associated with a profound suppression of p38 expression.
Conclusions: In the present study, we demonstrate that the combination of ASU, Glu, and CS was more effective in suppressing pro-inflammatory gene expression than ASU alone, or Glu and CS together. The combined preparation suppressed TNF-α, IL-1β, and iNOS expression by downregulating p38, a key signal transduction molecule involved in inflammation. Our present findings suggest the utility of the combination product to alleviate pain and inflammation in OA patients who may not clinically respond to Glu and CS alone.

P305

EFFECTS OF HEAT STIMULATION VIA MICROWAVE APPLICATOR ON CARTILAGE METABOLISM AND HSP70 EXPRESSION IN RABBIT KNEE JOINT

K.A. Takahashi, H. Tonomura, Y. Arai, A. Inoue, K. Sakao, M. Saito, T. Kubo
Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

Purpose: Thermotherapy is widely used to conservatively treat joint diseases such as osteoarthritis (OA). While heat stimulation of joints increases pain threshold to alleviate pain, its effects on the articular cartilage have not been clarified. In the present study, heat stimulation was applied to rabbit knee joints to investigate the changes in expressions of heat shock protein 70 (HSP70) and cartilage matrix genes in the articular cartilage in vivo.
Methods: Heat stimulation (0-80 W) was applied to the knee joints of Japanese white rabbits for 20 min using a microwave applicator (2.45-GHz). After 8-72 hrs, the articular cartilage was removed from the knee joints and proteins and total RNA were extracted. As controls, the knee joints without heat stimulation were analyzed. Expression of HSP70 was confirmed by real-time PCR and Western blotting. Expression of proteoglycan core protein and type II collagen were quantified using real-time PCR to assess cartilage matrix metabolism.
Results: Compared to controls, expression of HSP70 mRNA was higher with not less than 40 W of heat stimulation in an intensity-dependent manner. Expressions of proteoglycan core protein and type II collagen mRNA were higher with not less than 20 W of heat stimulation and peaked with 40 W. When quercetin was used to block the increases in HSP70 expression, the expression of proteoglycan core protein mRNA did not increase.
Conclusions: External heat stimulation increased expression of HSP70 in the articular cartilage. This suggested that external heat stimulation reached the articular cartilage. Heat stimulation also increased expression of proteoglycan core protein and type II collagen mRNA in the articular cartilage, indicating increased cartilage metabolism. HSP70 might thus be involved in the increased expression of proteoglycan core protein. With some improvements, heat stimulation might be actively used to protect the cartilage in OA.

P306

THE EFFICACY AND SAFETY OF CRX-102 - A NOVEL SYNCRETIC DRUG CANDIDATE - IN HAND OSTEOARTHRITIS (HOA): RESULTS FROM A PLACEBO-CONTROLLED RANDOMIZED CLINICAL TRIAL (RCT)

T.K. Kvien[1], B. Slatkowsky-Christensen[1], E. Fjeld[2], A. Prøven[2], Ø. Palm[3], K. Mikkelsen[4], J. Anderson[5], Y. Zhang[5], M. Nichols[5], J. Lessem[5]
[1]Diakonhjemmet Hospital, Oslo, Norway, [2]Martina Hansens Hospital, Sandvika, Norway, [3]Dept. of Rheumatology, Østfold Hospital, Sarpsborg, Norway, [4]Lillehammer Hospital for Rheumatic Diseases, Lillehammer, Norway, [5]CombinatoRx Inc, Cambridge, MA

Purpose: A syncretic drug comprises two compounds that are designed to act synergistically through multiple pathways to provide a novel therapeutic effect, which neither component can achieve alone. The syncretic drug candidate CRx-102 comprises dipyramidole and low dose prednisolone and is in clinical de-