moderate to high responsiveness according to OARSI criteria. After 3 weeks all subscales showed significant improvements compared to baseline (pain \( p<0.001 \)), stiffness \( p<0.001 \) and function \( p<0.001 \). No correlation where between the severity of OA (K&L) and improvement in WOMAC score. The only variable (age, gender, side, BMI, K&L, medial/lateral) which had a significant effect on WOMAC score was gender, women had higher score. Quality of life during the study time improved according to EQ-SD.

Conclusions: Conclusions: An Unloading knee brace did decrease pain and improve function as shown by significant improvement in WOMAC score for pain, stiffness, function and total score. An Unloader brace is a treatment alternative even in moderate and severe unicompartmental knee OA.

### 324

**CG100649, A TISSUE-SPECIFIC DUAL INHIBITOR OF COX-2 AND CARBONIC ANHYDRASE: PHASE 2A CLINICAL TRIAL IN HIP & KNEE OSTEOARTHRITIS**

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**Purpose:** The aim of the study was to evaluate the clinical efficacy and safety of CG100649 administered in different dosages. CG100649 is a first-in-class NSAID candidate with a new mode of “tissue-specific” activity designed to deliver sustained levels of drug to inflamed tissues while maintaining low systemic exposure by binding to carbonic anhydrase (CA) in red blood cells. Previous Phase I clinical studies have shown that CG100649 has a unique pharmacokinetic (PK) profile with 85-100x higher concentrations in whole blood (drug transport via erythrocytes that have high concentrations of CA) than in plasma (no CA). Synovial fluid has been shown to have little or no CA. Thus, CG100649 was hypothesized to achieve maximum efficacy in inflamed joints while minimizing its impact on the cardio-renal system or GI tract.

**Methods:** Clinical trial CG100649-2-01 was a randomized, double-blind study in male subjects, 18-75 years old, with a 3 month or longer history of primary osteoarthritis (OA) of the hip or knee. The study was conducted in 248 subjects at 25 investigative sites in Germany, Hungary, and Ukraine. The trial was designed to evaluate the safety and efficacy of three parallel dose regimens of CG100649 vs. placebo in the treatment of OA. After a 5-14 day washout period from other pain relief medications, all doses were administered orally, once a day in the morning. Initial loading doses (Day 0) and maintenance doses (Days 1-20) were: High Dose (8 mg + 1.2 mg/day), Medium Dose (4 mg + 0.6 mg/day), and Low Dose (2 mg + 0.3 mg/day). Subjects returned to the study center once a week on Days 7, 14, and 21 during the treatment period and on Days 28 and 35 during the follow-up period for safety and efficacy assessments. Efficacy assessments included the Western Ontario and McMaster Universities (WOMAC) OA index, Brief Pain Inventory (BPI), Subject's Global Assessment, Physician's Global Assessment, withdrawals due to lack of efficacy, and usage of paracetamol (acetaminophen) as a rescue medication. Blood pressure, ECG, and GI bleeding were monitored for potential adverse side effects.

**Results:** The CG100649 high dose group showed more than a 2-fold greater magnitude of improvement than the placebo group on the primary endpoint of change in the WOMAC score from baseline to Day 21 (median values were 37% vs. 17%), respectively; \( P<0.01 \). The study also met all key secondary endpoints, with the high dose demonstrating clinically and statistically significant superiority over the placebo group in the WOMAC OA score over the entire 21-day active treatment period \( P<0.01 \) and in the WOMAC subscales of pain, stiffness and physical function \( P<0.016, P<0.023, P<0.010 \), respectively over the entire 35-day treatment and follow-up evaluation periods. Weekly pain relief scores showed statistically significant improvements at Days 7, 14, 21, and 28 \( P<0.05 \) at all time periods which demonstrated that CG100649 had an early onset of activity and provided sustained treatment benefits over the entire treatment period. No treatment-related changes were observed in systolic, diastolic, or mean blood pressure in the entire subject population or after controlling for age (younger vs. older subjects). No relevant treatment group differences were noted for any other vital sign, clinical laboratory parameter, ECG parameter. No subject experienced gastrointestinal bleeding or other clinically relevant adverse GI side effects.

**Conclusions:** These data provide the first evidence of statistically and clinically significant analgesia and functional benefits produced by a dual COX-2/CA inhibitor without meaningful GI and CV side effects. All doses were well tolerated.Supported by a grant from CrystalGenomics and partially supported from the BioStar Program of MKE (Ministry of Knowledge Economy) of Korea.

### 325

**A RANDOMIZED TRIAL OF REALIGNMENT THERAPY FOR TREATMENT OF MEDIAL TIBIOFEMORAL OSTEOARTHRITIS**

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**Purpose:** Biomechanical studies of persons with medial tibiofemoral OA demonstrate that even with appropriate valgus knee bracing, large medial forces remain, suggesting that the addition of other interventions to further improve limb alignment may be of therapeutic value. The objective of this 30-week randomized crossover trial was to determine whether a multi-modal realignment therapy (consisting of valgus knee brace + motion control shoes + neutral foot orthoses) would be successful in relieving pain and improving function among persons with medial tibiofemoral OA.

**Methods:** We conducted a double blind, randomized crossover trial of a multi-modal realignment therapy for persons with medial tibiofemoral OA. Trial participants met ACR criteria for OA with knee pain, aching or stiffness on most of the past month and radiographic evidence of a definite osteophyte. We tested two different treatments: A) CONTROL TREATMENT consisting of a neutral knee brace (no valgus angulation), flat unsupportive foot orthoses, and shoes with a flexible midsole; and B) ACTIVE TREATMENT consisting of a valgus knee brace, customized neutral foot orthoses, and shoes designed for motion control. For each subject, the trial lasted 30 weeks, including 12 weeks each of active and control treatment separated by a 6-week washout period. The primary outcome was change in knee pain and function assessed by the WOMAC Osteoarthritis Index (VAS version). An unstructured correlation matrix for observations within subjects was used in generalized estimating equation fitting. The final linear regression model was conducted with exclusion of the differential carryover effect.

**Results:** 80 participants with medial tibiofemoral OA were randomized. 63% were female. Their mean age was 62 years and mean BMI was 34 kg/m². The main effects are depicted in Table 1. There was no evidence of a carryover effect in the initial analyses.