an overall EQ-5D health status index score. SF-36 and EQ-5D data from the 2 OA studies and the low back pain study were also pooled for analysis; comparisons versus placebo were prespecified.

Results: The intent-to-treat populations contained the following numbers of patients: low back pain study, n = 965; OA study 1, n = 1023; OA study 2, n = 987; DPN study, n = 389; pooled analysis, n = 2968. In the low back pain study and OA study 1, mean changes in SF-36 scores from baseline to endpoint were statistically significant for tapentadol PR compared with placebo for physical functioning, role-physical, bodily pain, and the physical component summary scores ($P \leq 0.029$ for all comparisons). In OA study 2, numerically greater improvements were observed with tapentadol PR compared with placebo for the SF-36 physical functioning, bodily pain, social functioning, role-emotional, and physical component summary scores. In the DPN study, mean changes in SF-36 scores from baseline to endpoint were statistically significant for tapentadol PR compared with placebo for role-physical, bodily pain, social functioning, and physical component summary scores (all $P \leq 0.012$). In the pooled analysis of SF-36 data from the 2 OA studies and the low back pain study, significant improvements were observed for tapentadol PR compared with placebo for physical functioning ($P < 0.001$), role-physical ($P = 0.001$), bodily pain ($P < 0.001$), vitality ($P = 0.041$), and physical component summary ($P < 0.001$) scores; no significant improvements were observed for oxycodone CR compared with placebo. In the low back pain study, OA study 1, and the DPN study, significantly greater improvements from baseline to endpoint were observed in the EQ-5D health status index score with tapentadol PR compared with placebo (all $P \leq 0.020$). In the pooled analysis of EQ-5D data from the 2 OA studies and the low back pain study, a significantly greater improvement from baseline to endpoint in the EQ-5D health status index score was seen with tapentadol PR compared with placebo ($P < 0.001$) and compared with oxycodone CR ($P < 0.001$); a significant improvement was not observed for oxycodone CR compared with placebo.

Conclusions: Treatment with tapentadol PR (100-250 mg bid) was associated with significant improvements in overall health and physical health status compared with placebo across nociceptive and neuropathic pain conditions.

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ASSESSMENT OF OPIOID WITHDRAWAL IN PATIENTS TREATED WITH TAPENTADOL PROLONGED RELEASE DURING AN OPEN-LABEL EXTENSION STUDY

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Purpose: Opioid withdrawal following treatment with tapentadol prolonged release (PR) was evaluated in this 1-year open-label extension study (ClinicalTrials.gov Identifier: NCT00487435).

Methods: Patients were eligible for enrollment if they completed 1 of 4 phase 3 studies: two 15-week studies that evaluated the efficacy of tapentadol PR and oxycodone controlled release (CR) compared with placebo for chronic osteoarthritis pain (NCT00421928) or low back pain (NCT00449176), a crossover study (two 2-week periods following a 3-week titration with tapentadol immediate release) to assess dose conversion between the immediate-release and prolonged-release tapentadol formulations in patients with chronic low back pain (NCT00594516), or a 1-year controlled long-term safety study of tapentadol PR and oxycodone CR in patients with chronic osteoarthritis or low back pain (NCT00361504). Patients who successfully completed one of the efficacy or crossover studies or who received oxycodone CR in the 1-year safety study were titrated to their optimal therapeutic dose of tapentadol PR (100-250 mg bid) during a titration period of up to 4 weeks then continued on their optimal dose for up to 48 weeks during the maintenance period. Patients who received tapentadol PR in the 1-year safety study continued on their optimal dose determined in the parent study. The Clinical Opiate Withdrawal Scale (COWS; 11-item scale scored from 0-48; <5 = no withdrawal, 5-12 = mild, 13-24 = moderate, 25-36 = moderately severe, and >36 = severe) and the Subjective Opiate Withdrawal Scale (SOWS; 15-item scale, possible score of 0-60; 60 = severe withdrawal) were used to assess opioid withdrawal in patients who did not take opioids after study drug discontinuation. COWS and SOWS scores were summarized according to the time of the last study drug intake. For the COWS, the categories were ≥2 days to <5 days and ≥5 days, and for the SOWS, the categories were 1, 2, 3, 4, and ≥5 days. Treatment-emergent adverse events (TEAEs) were recorded throughout the study.

Results: Of the 384 patients who had a COWS assessment from ≥2 to <5 days after study drug discontinuation, 88.8%, 10.7%, and 0.5% experienced no withdrawal, mild withdrawal, or moderate withdrawal, respectively. Of the 321 patients who had a COWS assessment ≥5 days after discontinuation of tapentadol PR, 90.7% had no withdrawal; mild and moderate withdrawal were observed in 8.7% and 0.6% of these patients, respectively. Based on results of COWS assessments, no patients experienced moderately severe or severe withdrawal. Mean (standard deviation) SOWS scores were as follows: 1 day (n = 2), 4.5 (2.12); 2 days (n = 536), 8.8 (9.48); 3 days (n = 556), 9.3 (9.99); 4 days (n = 561), 7.8 (9.24); ≥5 days (n = 552), 5.6 (7.20); mean SOWS scores for all time periods were low (<10), indicating minimal opioid withdrawal. The most common TEAEs (reported by ≥10% of patients [N = 1154]) were headache (13.1%), nausea (11.8%), and constipation (11.1%).

Conclusions: Results of COWS assessments completed by investigators ≥2 to <5 days following study drug discontinuation indicate that the majority of patients experienced no opioid withdrawal. SOWS assessments completed by patients each day immediately following study drug discontinuation also indicate a low incidence of withdrawal and suggest that opioid withdrawal peaks between Days 3 and 5. These results are similar to those shown previously following tapentadol PR treatment and are similar to those shown for placebo in previous placebo-controlled studies of tapentadol PR for chronic pain. Together, these results indicate that long-term treatment with tapentadol PR (100-250 mg bid) for up to 1 year in this open-label extension trial was associated with a low incidence of opioid withdrawal following treatment discontinuation without tapering in patients with moderate to severe chronic painful osteoarthritis or chronic low back pain.

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TREATMENT OF CARTILAGE DEFECTS IN THE KNEE USING ALGINATE BEADS CONTAINING HUMAN MATURE ALLOGENIC CHONDROCYTES: CLINICAL RESULTS AT 3 YEARS OF FOLLOW-UP

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Aim: The present study was designed to evaluate the implantation of alginate beads containing human mature allogenic chondrocytes for the treatment of symptomatic cartilage defects in the knee.

Methods: A biodegradable, alginate-based biocompatible scaffold containing human mature allogenic chondrocytes was used for the treatment of chondral and osteochondral lesions in the knee. Twenty-one patients were clinically prospectively evaluated with use of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and a Visual Analogue Scale (VAS) for pain preoperatively and at 3, 6, 9, 12, 24 and 36 months of follow-up.

Results: A statistically significant clinical improvement became apparent after 6 months and patients continued to improve during the 36 months of follow-up. Adverse reactions to the alginate/fibrin matrix seeded with the allogenic cartilage cells were not observed. Two of the procedures failed. One of the patients had loosening of the periosteal flap, which was attributed to a failure of the surgical procedure. The other failure case was the result of the poor quality and quantity of the repair tissue itself.

Discussion: The results of this pilot study show that the alginate-based scaffold containing human mature allogenic chondrocytes is feasible for the treatment of symptomatic cartilage defects in the knee. The described technique provides clinical outcomes equal to those of other cartilage repair techniques.