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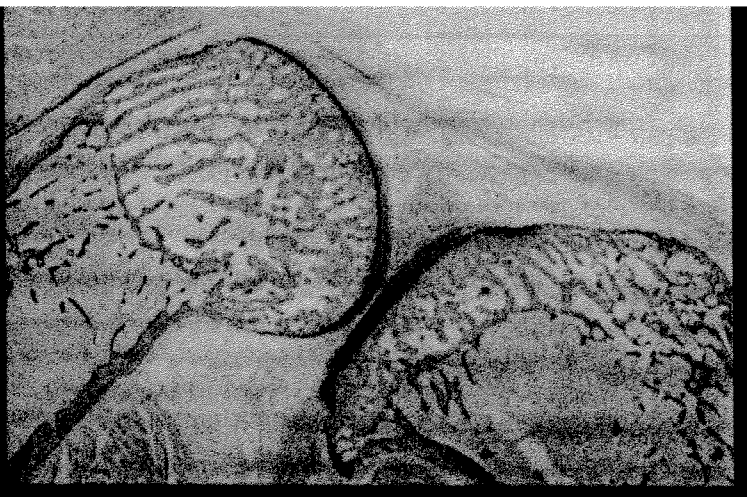

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OSTENIL HYALURONAN FOR INOPERABLE ARTHRITIS OF THE SHOULDER

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Aim: The aim of this study was to assess the efficacy of Ostenil in the treatment of shoulder arthritis in patients not suitable for shoulder replacement surgery.
Methods: Seven patients presenting to a busy shoulder service over a 2 year period were found to have disabling arthritis of the shoulder, but were too medically unfit or refused shoulder replacement surgery. All patients received a course of three Ostenil injections into the glenohumeral joint at weekly intervals. Patients were assessed pre-injection and at 3 months post-injection using the Constant Score and additional quality of life questions.
Results: The mean patient age was 83 years (range 72 to 93), including six females and one male. Five patients had osteoarthritis, one rheumatoid arthritis and one cuff arthropathy.
The mean pre-injection Constant Score was 15.5 (10–25). The mean Constant Score at 3 months was 49.5 (25–84). Pain was improved significantly by the injections from 11.6 (10–14) to 4.7 (0–9). All patients had their sleep disturbed by pain prior to the injections. Only three had some disturbance of sleep at 3 months post-injection, with none having their sleep disturbed at all times after the injections. Subjective shoulder elevation improved from chest level to hand above head, whilst objectively it improved from 61.8° (30–90) to 92.1° (60–130). Patient satisfaction (on a scale of 0 to 10) improved from 1.3 (0–2) pre-injection to 8.4 (4–10) following the injections (Table I).
Conclusions: Ostenil Hyaluronan appears to reduce pain and improve patient satisfaction in patients with advanced arthritis of the shoulder.

	Pre-injection	3 months post-injection
Constant score	15.5 (10–25)	49.5 (25–84)
Pain (VAS:0–15)	11.6 (10–14)	4.7 (0–9)
Subjective range of motion	Chest level	Above head
Shoulder elevation	61.8° (30–90)	92.1° (60–130)
Patient satisfaction (%)	13 (0–20)	84 (40–100)

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PD-0200347, AN ALPHA 2 DELTA LIGAND, CAN REDUCE THE PROGRESSION OF EXPERIMENTAL OSTEOARTHRITIS BY INHIBITING A MAJOR CATABOLIC SIGNALING PATHWAY

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The aim of this study was to examine the effect of PD-0200347, an $\alpha 2\delta$ ligand of voltage-activated Ca^{2+} channels and a member of the gabapentin family, in the ACL dog experimental model of osteoarthritis (OA) and investigate its mechanism of action on the major signaling pathways implicated in OA.
OA was surgically induced in dogs by sectioning the anterior cruciate ligament. OA dogs were divided into three groups and treated orally with (1) placebo, (2) 15 mg/kg/day of PD-0200347, or (3) 90 mg/kg/day of PD-0200347. Dogs were sacrificed 12 weeks after surgery. The severity of lesions was scored macroscopically and histologically. Cartilage specimens from femoral condyles and tibial plateaus were processed for quantitative PCR and immunohistochemistry. Specific probes and antibodies were used to study iNOS, MMP-1, MMP-3 and MMP-13 mRNA and protein levels, respectively. Specific phospho-antibodies were also used to study the level of activity of PKCα, Ras and Raf, the MAP kinases, JNK, P38 and ERK1/2 and the transcription factors CREB and Elk-1.
No clinical signs of drug toxicity were noted in the treated animals. PD-0200347 treatment at both dosages tested (15 or 90 mg/kg/day) reduced the development of cartilage lesions. Quantitative PCR and immunohistochemical analyses showed that PD-0200347 treatment also reduced key OA mediators, iNOS, MMP-1, MMP-3 and MMP-13 gene expression and synthesis. PD-0200347 decreased dose-dependently the activity of PKCα, Raf, ERK1/2 and Elk-1.
This study demonstrated the efficacy of PD-0200347 at reducing the progression of cartilage structural changes in experimental OA. It also showed that this effect is linked to the inhibition, at the transcriptional level, of the major pathophysiological mediators. The mechanism of action could be related to a significant reduction of Ca^{2+} current amplitude via voltage gated calcium channels, which in turn down-regulates the downstream PKC, Raf and ERK1/2 signaling pathway.

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LUMIRACOXIB 100 MG ONCE DAILY IS EFFECTIVE IN TREATING OSTEOARTHRITIS AS ASSESSED BY OMERACT-OARSI CRITERIA

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Aim: To assess the efficacy of lumiracoxib 100 mg qd vs placebo and celecoxib 200 mg qd over 13 weeks in patients with primary knee osteoarthritis (OA) using OMERACT-OARSI criteria, a single measure of OA treatment response incorporating three variables: pain intensity, functional status and patient's global assessment of disease activity.
Methods: Patients (1551) with primary knee OA and pain intensity in the target knee $\geq$ 40 mm on a 100 mm visual analog scale after a 3–7-day washout for NSAIDs were randomized to lumiracoxib 100 mg qd (n = 391), lumiracoxib 200 mg qd for 2 weeks followed by 100 mg qd (200/100 mg qd; n = 385), celecoxib 200 mg qd (n = 393) or placebo (n = 382) at centers in the US and Canada. Efficacy was assessed according to OMERACT-OARSI criteria at Weeks 2 and 13 in which patients were considered responders if they had a reduction of: $\geq$ 50% from baseline and an absolute reduction of $\geq$ 20 in either OA pain intensity or the WOMAC™ Difficulty in Performing Daily Activities (DPDA) subscale (rescaled to 0–100); or $\geq$ 20% from baseline and an absolute reduction of $\geq$ 10 in $\geq$ 2 of the following: OA pain intensity, WOMAC™ DPDA subscale (rescaled to 0–100) or patient's global assessment of disease activity.
Results: Lumiracoxib (100 mg qd and 200/100 mg qd) was an effective treatment for OA in terms of the proportion of patients meeting the OMERACT-OARSI criteria at Week 13 (64.7% and 66.8%, respectively, vs 49.3 for placebo; both $P < 0.001$). There was no significant difference between lumiracoxib groups, or between either lumiracoxib group or the celecoxib group (responders: 61.6%). Lumiracoxib was effective from the first assessment (Week 2), where the proportion of responders in the lumiracoxib 100 mg qd and lumiracoxib 200/100 mg qd groups was 60.6% and 64.2%, respectively, vs 39.4% for placebo (both $P < 0.001$). Neither lumiracoxib group was significantly different from the