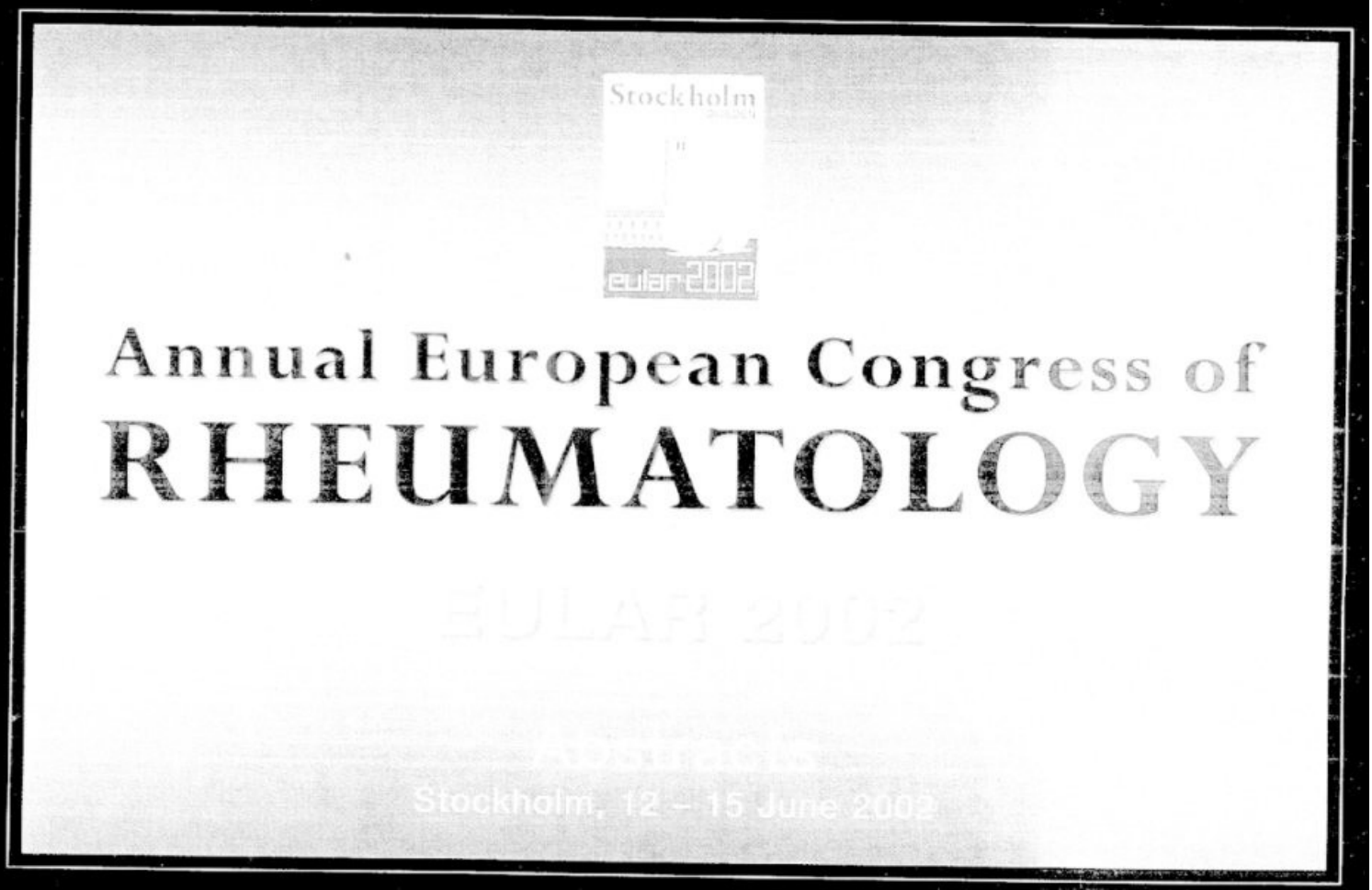
JULY 2002 VOL 61 SUPPLEMENT I

Annals of the Rheumatic Diseases



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THU0224 ETORICOXIB SHOWED RAPID ONSET OF EFFICACY AND SUSTAINED DURATION OF THERAPY OVER THE 24-HOUR DOSING INTERVAL IN PATIENTS WITH OSTEOARTHRITIS (OA) OF THE KNEE OR HIP

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Background: Etoricoxib (ETO), a selective COX-2 inhibitor, has demonstrated effects in the symptomatic treatment of OA. We present the results of an analysis of data from the OA clinical development program to assess the time to onset of treatment effects and the duration of these effects over the 24-hour dosing interval.

Methods: Data were collected during 2 double-blind studies in OA patients randomized to placebo (pbo), naproxen 500 mg twice daily (NAP) or ETO 60 mg once daily for 12 weeks, with a 40 week active comparator controlled safety and efficacy continuation period.

WOMAC pain walking on a flat surface (walking pain; 100-mm VAS), and patients global assessment of response to therapy (PGART; 5-point Likert scale) were used to assess the onset of treatment effect and the duration of effect over the 24-hour dosing interval. Patients provided information using take-home forms 4 hours after dosing for days 1 to 6 and predose on Days 2 to 6, corresponding to 24 hours postdose Days 1 to 5 of therapy. Information about night pain and stiffness on awakening (WOMAC pain and stiffness subscales; 100-mm VAS) were collected at each study visit to assess treatment response over the 24 hour dosing interval during the 12-week treatment period.

Results: Approximately 1000 patients enrolled. Data from 781 patients were available from take-home forms.

Data were analyzed for 84, 361, and 336 patients on pbo, ETO and NAP, respectively, for efficacy 4 hours postdose. Onset was observed as early as 4 hours postdose on Day 1 based on PGART ($p<0.05$ vs pbo); for walking pain effects were observed by 4 hours postdose on Day 2 ($p<0.001$ vs pbo).

For duration of therapy over the dosing interval, 274 patients; 32, 126, and 117 on pbo, ETO, and NAP, respectively, provided data on take-home forms prior to the morning dose. Treatment effects at the end of the 24-hour dosing interval were seen by the first measurement for each end point ($p<0.05$ vs pbo).

Data from 990 patients were included in an assessment of night pain and stiffness upon awakening over 12 weeks. Active treatments showed significant improvements in these manifestations of OA at the end of the dosing interval over the 12-week period ($p<0.001$ vs pbo).

Conclusion: Etoricoxib showed rapid onset in OA patients. The therapeutic benefits of etoricoxib were sustained over the 24-hour dosing interval.

THU0225 EFFECT OF SODIUM HYALURONATE INJECTIONS ON NITRIC OXIDE LEVELS IN SYNOVIAL FLUID FROM TEMPOROMANDIBULAR OSTEOARTHRITIS. A PILOT STUDY

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Background: Intra-articular (IA) sodium hyaluronate (HA) is increasingly used in the therapy of knee osteoarthritis (OA). Recently, HA has been also proposed for the treatment of OA of temporomandibular joint (TMJ-OA). Although no definitive data are still available on its mechanism of action, a possible anti-inflammatory effect has been suggested.

Objectives: To assess the effect of IA HA injections on nitric oxide (NO) levels in synovial fluid (SF) from patients with TMJ-OA.

Methods: SF was obtained from 12 patients with TMJ-OA diagnosed by clinical, radiographic and MR findings. Eight patients received a cycle of 3 injections of HA (Hyalgan (r) Fidia S.p.A. Italy, 10mg/1ml, once a week) (HA group), while a control group (4 patients) was randomly treated with 2 consecutive (once a week) sterile saline IA injections (1 ml). Before each TMJ injection, SF was collected by rinsing the joint space with 1 ml of Ringer lactate solution. SF samples were centrifuged to remove cells and then immediately stored at -20 °C. NO levels were measured by Griess colorimetric reaction (μM, mean $\pm$ SD).

Results: In the HA group, NO SF levels increased after the 1st injection (from 4.9 ± 2.8 μM to 5.7 ± 5.1 μM), then decreased progressively after the 2nd (5 ± 4 μM) and 3rd (3.7 ± 1.5 μM) injection, reaching, at final observation, levels lower than basal values, even if not significant. By contrast, in the control group NO levels lowered after the 1st and even increased after the 2nd injection (from 7.2 ± 4.9 μM at baseline to 4.8 ± 2.3 μM and 7.9 ± 8.1 μM, respectively).

Conclusion: This preliminary study confirms the possible influence of IA HA injections on synovial inflammation. In particular, the effects of HA on NO production, firstly stimulating and finally inhibiting, are similar to those observed on interleukin-1β (1), thus suggesting a possible cytomodulating effect of HA in SF inflammation. However, additional cases, in particular concerning controls, are necessary to further strengthen this hypothesis.

References

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THU0226 IMPROVED UPPER GASTROINTESTINAL (UGI) SAFETY AND TOLERABILITY OF A NEW COXIB, COX189 COMPARED WITH IBUPROFEN IN OSTEOARTHRITIS PATIENTS

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Background: Standard NSAIDs are commonly used for treating chronic pain associated with osteoarthritis (OA), but are associated with poor gastrointestinal (GI) safety and tolerability, due to non-selective inhibition of cyclooxygenase (COX). COX189 is a new highly selective COX-2 inhibitor with the potential to improve GI tolerability compared to non-selective inhibitors.

Objectives: To assess the general and GI safety and tolerability of COX189 as compared with ibuprofen in OA patients over 3 months with celecoxib as a control.

Methods: This multicentre, double-blind, parallel group study compared the safety and tolerability of COX189 200 mg OD and 400 mg OD, ibuprofen 800 mg TID and celecoxib 200 mg OD treatment in 1,042 consenting patients with OA (264, 260, 258 and 260 respectively) treated for 13 weeks. The cumulative incidence of gastroduodenal ulcers (greatest diameter$\geq$ 3 mm) was also determined by pre-treatment, Week-4 and Week-13 endoscopy. The frequences of adverse events (AEs) and of GI serious AEs (SAE) were recorded, as well as the rate of discontinuation due to AEs.

Results: The cumulative gastroduodenal ulcer rate showed no dose response, was significantly ($p<0.01$) lower with COX189 (4.3% and 4.0% in the 200 mg and 400 mg groups respectively) than with ibuprofen (15.7%), and similar to celecoxib (3.2%) in 1,011 evaluable patients. GI disorders were more frequently reported in the ibuprofen group (55.4%) vs. all other groups (46.5% - 50.4%), and specifically upper abdominal pain (28.8% with ibuprofen vs.16.7% and 23.1% in the COX189 groups, and 15.9% for celecoxib). More patients in the ibuprofen group discontinued due to AEs (12.7%) compared to other treatment groups (6.8%, 5.0% in the COX189 200, 400 mg groups, and 5.8% in the celecoxib group), and this difference was mainly driven by GI events. There were no other apparent patterns in discontinuations due to AEs.There were more GI SAEs in the ibuprofen group (1.6%) compared to the other treatment groups (0.4%, 0.4% and 0.8% in the COX189 200 mg, 400 mg and celecoxib groups, respectively). One patient in the COX189 200 mg group had an SAE of mild upper abdominal pain which resulted in hospitalization. One patient in the COX189 400 mg group had an SAE of severe abdominal pain not otherwise specified which led to discontinuation. Two patients in the celecoxib group had SAEs of severe rectal bleeding and moderate acute gastric ulcer, respectively. The GI SAEs reported by the 4 patients in the ibuprofen group were moderate worsening of inguinal hernia, mild duodenal ulcer hemorrhage, moderate pyloric ulcer and severe gastric ulcer.

Conclusion: Both doses of COX189 showed a superior safety and GI tolerability profile compared to ibuprofen, and generally similar to that of celecoxib. The difference between COX189 and ibuprofen was statistically significant for gastroduodenal ulcers and clinically meaningful in terms of discontinuation of treatment which was mainly driven by GI symptoms.

THU0227 EFFECTIVENESS OF HOME BASED EXERCISE THERAPY AND WALKING PROGRAM ON OSTEOARTHRITIS OF THE KNEE

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Background: Osteoarthritis of the knee(OA) is a very common rheumatological disease and there are various treatment modalities.

Objectives: The aim of this study is to investigate the effects of home based exercise and walking program in the treatment of OA.

Methods: A total of 90 patients with knee osteoarthritis were included in this study. Their ages ranged between 48-71. Patients were seperated in three groups. None of them had practiced a daily simple exercise program since one year. Group 1 (n=30) were given home based exercise program. Group 2 (n=30) had regular walking program three times per week, starting with 10 minutes. Patients were assessed according to pain, functional capacity and the quality of life parameters. Group 3(n=30) was accepted as control group. Pain was evaluated by Western Ontario McMaster Osteoarthritis index (WOMAC) pain score and Visuel Analogue Scale(VAS). Functional capacity was measured by WOMAC physical function index. Quality of life was assessed by Nothingham Health Profile questionnaire(NHP). All groups continued the program for 3 months.