Improvements in OA signs and symptoms in response to valdecoxib were dose-dependent, with the greatest improvements in primary efficacy measures observed at 5 mg BID, 10 mg QD, and 10 mg BID, compared with placebo ($p \leq 0.004$). Valdecoxib doses of 5 mg BID, 10 mg QD, and 10 mg BID were also as effective as naproxen 500 mg in the treating signs and symptoms of OA. There were no statistically significant differences between any of the treatment groups in the number of adverse events or in vital signs or clinical laboratory measurements.

Abstract OP0048 Table 1

	Least Square Mean Change from Baseline at Week 2	Least Square Mean Change from Baseline at Week 6
Placebo	-11.46*	-10.44*
Valdecoxib 0.5 mg BID	-13.84*	-15.74*
Valdecoxib 1.25 mg BID	-19.09**	-24.32**
Valdecoxib 2.5 mg BID	-24.30**	-28.08**
Valdecoxib 5 mg BID	-28.12**	-29.42**
Valdecoxib 10 mg QD	-27.77**	-29.50**
Valdecoxib 10 mg BID	-30.28**	-29.24**
Naproxen 500 mg BID	-27.76**	-30.05**

Patient's Global Assessment of Arthritis at Weeks 2 and 6 (* $p \leq 0.05$ vs naproxen, ** $p \leq 0.05$ vs placebo).

Conclusion Valdecoxib is an effective therapy among patients with symptomatic OA of the knee. Valdecoxib doses of 5 mg BID, 10 mg QD, and 10 mg BID are maximally efficacious, as they are superior to placebo and comparable to naproxen 500 mg BID in all primary efficacy measures. Valdecoxib is well tolerated at all doses.

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OP0049 A POOLED INDEX TO ASSESS SEVERITY OF OSTEOARTHRITIS OF THE HIP OR KNEE. PERFORMANCE IN A RANDOMISED, DOUBLE BLIND, MULTICENTER, CROSSOVER CLINICAL TRIAL OF DICLOFENAC/MISOPROSTOL (ARTHROTEC) COMPARED TO ACETAMINOPHEN IN PATIENTS WITH OSTEOARTHRITIS OF THE HIP OR KNEE

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Background A pooled index of various measures, such as the disease activity index (DAS) in rheumatoid arthritis, can provide advantages over individual measures to assess disease severity, analyse responses to therapy, and improve statistical power in a clinical trial or observational study.

Objectives To apply an index of four measures of severity of osteoarthritis of the hip or knee, the Western Ontario McMaster (WOMAC) scale, visual analogue scale (VAS) for pain, Kellgren-Lawrence radiographic stage, and number of joints involved among two hips and two knees, in analyses of results of a

randomised, controlled clinical trial of diclofenac/misoprostol (Arthrotec, ARTH) compared to acetaminophen (ACET).

Methods 227 patients with radiographic stage 2–4 osteoarthritis of the hip or knee received either 6 weeks of ARTH 75 mg twice a day or ACET 1,000 mg four times a day after a washout period, and then the other drug for 6 weeks, in a randomised, double-blind, multicenter, crossover clinical trial. A pooled index to recognise patients who had mild osteoarthritis was developed according to 4 criteria: location in only one knee, Kellgren-Lawrence stage 2, lowest tertile at screening for the WOMAC, and lowest tertile at screening for the pain VAS. The value of the pooled index was 0 (mildest) if 3 or 4 of the indicators applied to a patient; the value was 1 if 2 indicators applied to a patient, 2 if only one indicator applied to a patient, and 3 (most severe) if no indicator applied to a patient.

Results Overall, WOMAC pain scores were improved by 7.8 of 100 units ($p < 0.001$), and pain VAS scores were improved by 14.6 of 100 units ($p < 0.001$), while taking ARTH versus ACET. Differences between changes in WOMAC scores while taking ARTH versus ACET were -0.8 (advantage to ACET) for 26 patients with a pooled index of 0 ($p = 0.86$), compared to 1.5 (advantage to ARTH) for 50 patients with a pooled index of 1 ($p = 0.70$), 6.8 for 74 patients with a pooled index of 2 ($p = 0.06$), and 14.7 for 77 patients with pooled index of 3 ($p < 0.001$). Differences between changes in pain VAS scores while taking ARTH versus ACET were 0.9 (advantage to ARTH) for patients with a pooled index of 0 ($p = 0.88$), compared to 8.8 for patients with a pooled index of 1 ($p = 0.11$), 14.0 for patients with a pooled index of 2 ($p = 0.002$), and 22.1 for patients with a pooled index of 3 ($p < 0.001$).

Conclusion A pooled index of four measures of severity of osteoarthritis of the hip or knee, the WOMAC, pain VAS, Kellgren-Lawrence radiographic stage, and number of joints involved can be applied to analyse results of a clinical trial, and may be useful to stratify patients in clinical trials and clinical care.

REFERENCE

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OP0050 IMMUNOGENETIC ASPECTS OF EROSIVE OSTEOARTHRITIS OF THE HAND

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Background Erosive osteoarthritis of hand (EOA) is believed to be a subset of generalised OA characterised by frequent inflammatory episodes and an aggressive clinical course.

Objectives Since rare studies are available on the risk factors of EOA, we investigated its immunogenetic predisposition.

Methods In 47 patients with EOA (42 F, mean age 62.8 ± 8 years), HLA typing for A, B, C, DRB1 loci was performed. In the same patients we also evaluated the number of active joints (NAJ), the number of X-ray erosions (NEJ), the radiographic score (RS, Kallman), along with ESR and CRP.

Results The HLA antigens most frequently found in the 47 patients with EOA were A2 (16 = 34%), B5 (13 = 27.7%), Cw4 (13 = 27.7%), and DRB1011 (11 = 23.4%) and DRB103 (8 = 17%). Interestingly, the frequency of these two latter antigens were higher in EOA than in non-EOA patients (DRB1011

= 10%; DRB103 no found). NAJ ($p < 0.01$), RS ($p < 0.001$) and ESR ($p < 0.01$) were higher in EOA than in non-EOA. No differences were observed (ANOVA test) in NAJ, NEJ, RS, ESR and CRP, among the various HLA antigens found in EOA.

Conclusion EOA seems characterised by a high frequency, higher than in non-EOA, of some HLA antigens, in particular DRB103 and DRB1011, thus suggesting an immunogenetic predisposition in these patients. HLA antigens do not seem to be associated with the disease severity of EOA. However, more information may derive from an adequately long follow-up of these patients.

OP0051 SYNOVITIS PREDICTS THE ARTHROSCOPIC PROGRESSION OF MEDIAL TIBIOFEMORAL KNEE OSTEOARTHRITIS (OA)

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Background

Objectives To evaluate the prevalence of synovitis in painful medial tibiofemoral knee OA and to evaluate correlations between such synovitis and the structural severity of medial knee OA.

Methods Multicenter, prospective, one year duration study; primary painful knee OA (ACR criteria) of the medial compartment; medial joint space width $>$ or $=$ 2 mm; at least 10% of one cartilage surface of the medial compartment affected by superficial fibrillation or worse. Arthroscopy under local anaesthesia performed and videorecorded at entry and after one year; medial chondropathy scored by using SFA score (0–100) and reader's overall assessment (VAS score 100 mm); medial perimeniscal synovial scored as normal (few villi, fine vascular network), reactive (proliferation of opaque villi), inflammatory (hypervascularization and/or proliferation of hypertrophic and hyperemic villi). Progression of medial chondropathy defined by an increase in SFA and VAS scores of at least 4.5 and 8.0 after one year, respectively, as previously reported;¹ assessment of severity of chondropathy by a single reader blind to chronology of paired videotapes.

Results 506 patients were enrolled and 498 completed the one year longitudinal study (mean age: 61.2 ± 7.7 years, female sex: 58.9%, BMI: 30.4 ± 4.7 , mean disease duration: 3.8 ± 2.9 years). The Table 1 summarises cross-sectional and longitudinal correlations between synovitis and chondropathy.

Conclusion This study suggests that synovitis is a common feature of painful knee OA, associated with more severe

chondropathy, but it also suggests that synovitis could be considered as a predictive factor of subsequent chondrolysis.

REFERENCE

- 1 Ayral X, et al. Arthroscopic evaluation of chondropathy in osteoarthritis of the knee. *J Rheumatol.* 1996;**23**:698–706

OP0052 GLUCOSAMINE SULFATE AS AN OSTEOARTHRITIS DISEASE MODIFICATION AGENT: A CONFIRMATORY, LONG-TERM, RANDOMISED, PLACEBO-CONTROLLED, INDEPENDENT STUDY

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Background Recent data showed that glucosamine sulfate is an osteoarthritis disease modifying agent.¹ International guide-lines on clinical development of osteoarthritis drugs recommend to perform at least two independent studies to confirm the drug properties.

Objectives To confirm the effects of glucosamine sulfate as a disease modifying agent.

Methods Randomised, double-blind, placebo-controlled, study. 202 patients with knee-osteoarthritis (ACR criteria) were randomised to glucosamine sulfate 1500 mg once-a-day p.o., or placebo for 3 years. The minimum joint space width (JSW) of the narrowest medial compartment of the tibio-femoral joint at 3 years was the study structure primary endpoint, and a secondary endpoint at 1 and 2 years. JSW was measured visually by a 0.1 mm graduated magnifying glass, on standardised weight-bearing antero-posterior radiographs of each knee, in full extension. Symptoms were assessed by both the WOMAC LK 3.0 version and the Lequesne indices.

Results The two study groups were comparable for demographic and disease characteristics and represented the standard primary-knee-osteoarthritis population. The placebo group presented a progressive joint space narrowing (JSN) at each year of evaluation, while glucosamine sulfate presented no average JSN at any point of evaluation. Results at 3 years are shown in the Table 1 below. Glucosamine sulfate significantly improved symptoms as measured by both the Lequesne: (20–25% vs. $<10\%$ with placebo) and the WOMAC (15–20% vs. $<2\%$) indices. No significant differences were seen in the reported adverse events rate, while more patients on the placebo group prematurely left the study, without reaching a statistical significance.

Abstract OP0051 Table 1

	Medial perimeniscal Normal	Synovial membrane Reactive	At baseline Inflammatory
BASELINE	N = 252	N = 145	N = 109
SFA score	30 ± 19	$38 \pm 20^*$	$41 \pm 18^*$
VAS score	34 ± 17	$41 \pm 19^*$	$44 \pm 17^*$
CHANGES	N = 251	N = 144	N = 103
% SFA progressors	13.1%	14.6%	23.3%**
% VAS progressors	13.9%	13.2%	30.1%***

p-value vs Normal: * $p < 0.05$ ** $p = 0.003$ *** $p = 0.0005$.

Abstract OP0052 Table 1

	Placebo (N = 101)	Glucosamine Sulfate (N = 101)
JSW enrolment (mm)	3.59 (0.16)	3.97 (0.14)
JSN 3 years (mm)	-0.19 (0.05)	+0.02 (0.05)**
Lequesne enrolment (points)	8.9 (0.2)	9.0 (0.2)
Δ 3 years (points)	-0.8 (0.2)	-1.7 (0.2)**
WOMAC enrolment points	30.5 (1.4)	30.7 (1.4)
Δ 3 years (points)	-4.9 (0.8)	-8.0 (0.9)*

Data are mean (SE). * $p < 0.05$ and ** $p < 0.005$ vs. placebo. Intention-to-treat (ITT) population.