established.¹ Selective inhibitors of COX-2 are thought to reduce pain, fever and inflammation without causing the gastrointestinal or renal injury associated with inhibition of COX-1.² SVT-2016 is a new COX-2 inhibitor being developed for the treatment of pain and inflammation associated with osteoarthritis and rheumatoid arthritis.

Objectives Evaluate the safety and tolerability of rising doses (16 mg, 32 mg and 64 mg) of SVT-2016, in healthy male volunteers. In addition, the pharmacokinetics (PK) of SVT-2016 following a single oral dose was examined.

Methods Three groups of 6 healthy male volunteers, aged 23–43 years, were exposed to a single oral dose of SVT-2016 or matching placebo (Group 1: 16 mg SVT-2016, Group 2: 32 mg SVT-2016 and Group 3: 64 mg SVT-2016). For each group, subjects were randomised to receive either SVT-2016 or matching placebo (2:1 active to placebo). All volunteers provided informed written consent prior to participation. The study was approved by the Simbec Independent Ethics Committee. Following administration of SVT-2016, blood samples were taken for the determination of plasma SVT-2016 levels at the following time points: Pre-dose, 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 8, 10, 12, 16, 24, 36 and 48 h post dose. Vital signs were measured and a 12-lead ECG performed throughout the 48 h post dose. Continuous ECG monitoring took place until 4 h after dosing. Laboratory safety tests were conducted prior to dosing and at 24 h and 48 h post dose. Adverse events were monitored throughout the study. Validated LCMS method was used for the determination of plasma SVT-2016 concentrations.

Results There were no clinically significant changes in vital signs, ECG or laboratory safety tests during the study. A total of three adverse events were recorded (2 events of mild headache and 1 event of mild dizziness). No serious or severe adverse events were recorded. All events were considered to be mild in severity. The pharmacokinetic profile obtained following a single oral dose of SVT-2016 demonstrates that, SVT-2016 was absorbed in a dose dependent manner, C_{max} increasing with increasing dose level administered. This peak plasma concentration occurs at approximately 1.7 h (range: 1.5 h ? 1.9 h) following administration of SVT-2016, suggesting a rapid onset of action. The elimination half-life of SVT-2016 appears to increase with increasing dose level and would support the suitability of this compound for the treatment of patients with osteoarthritis and rheumatoid arthritis.

Conclusion SVT-2016 was considered to be safe and well tolerated at the dose levels investigated. The PK obtained favour the development of SVT-2016 as a novel COX-2 inhibitor for the treatment of pain and inflammation associated with osteoarthritis and rheumatoid arthritis. To further examine the safety, tolerability and PK of SVT-2016, it is proposed that further dose levels be investigated.

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SAT0083 ULTRASONOGRAPHIC EVIDENCE OF INTRA-ARTICULAR INJECTIONS IN THE HIP

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Background In order to validate intra-articular medical treatment of osteoarthritis in the hip joints it is imperative to have documentation of the correct placement of the injection.

Radiographic methods imply a radiation load, while ultrasound (US) is harmless.

Objectives Our goal was to evaluate the use of US as guidance when performing injections in osteoarthritic hips using air as contrast medium.^{1–3}

Methods A total of 30 injections were given to 11 Patients with hip-osteoarthritis (ACR criteria)(Mean age 60 years (Range 44–86)).

The femoral head and neck was scanned with a 8–13 MHz linear transducer.

The probe was placed below the inguinal ligament in parallel with the axis of the femoral neck.

Placement of a gauge 21 needle into the hip joint (anterior/inferior capsule below the femoral head) was monitored with a B mode (grey scale) scanning allowing a continuous visual guidance.

Preceding the treatment, a small (0,5–2 ml) amount of atmospheric air was injected.

Results The position of the needle was evident on the screen in all cases. The injections of air into the joint was demonstrated in 29 cases presenting a small hyperechoic brim inside the joint capsule. However, in one case in spite of a seemingly correct placement of the needle the hyperechoic air brim was clearly positioned outside the joint. Placement of the needle was subsequently corrected.

Still picture of the setting as documentation revealed the presence of air without difficulty, however the needle tended to be less recognisable when not in motion.

Conclusion The sole use of grey scale US as guidance device gives a good view of the intra-articular placement of a needle. However use of air as US contrast before an injection or aspiration, enhances the precision and allows photographic documentation of the set-up.

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SAT0084 DEVELOPMENT AND INITIAL PSYCHOMETRIC VALIDATION OF THE ARTHRITIS TREATMENT SATISFACTION QUESTIONNAIRE (ARTS)

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Background

Objectives To develop and examine the reliability and validity of a questionnaire assessing patient satisfaction with their osteoarthritis treatment.

Methods Item generation: Semi-structured interviews were performed among 20 French patients (6 suffering from arthritis of the knee, 6 of the hip and 8 of the hand), and 10 clinicians (5 rheumatologists and 5 general practitioners (GPs)). Interviews were recorded, transcribed and analysed. The first version of the questionnaire was produced in French and reviewed by 5 rheumatologists and 5 GPs. Content validity and cognitive debriefing

were performed on 10 arthritis patients. The resulting arthritis treatment satisfaction (ARTS) questionnaire comprised 24 items.

Validation study: Psychometric analysis was performed to establish the structure (Principal Component Analysis (PCA) and multi-trait analysis) and the internal consistency (Cronbach alpha) of the questionnaire on a cross-sectional sample of 797 arthritis patients recruited by their clinicians. Patients were on average 67.5 years old (sd = 10.4), 64.5% were women, 26% had arthritis of the hip, 58% had arthritis of the knee, and all patients had suffered from arthritis for an average of 7 years (sd = 6.4).

Results PCA revealed a clear four dimensional structure. In order to reduce the number of items, 6 out of the 24 items were discarded because of moderate to low item convergent validity, and because they did not modify the internal reliability coefficient and content validity of the questionnaire. The final questionnaire comprised 18 items consisting of 4 dimensions measuring treatment advantages, treatment convenience, apprehensions about treatment and satisfaction with medical care. Item convergent and discriminant validity and the internal consistency reliability were satisfactory (Cronbach alpha of 0.84 for the global questionnaire which varied between 0.63 and 0.88 per dimension). PCA and multitrait analysis were reproduced on an independent sample of 137 patients, thus confirming the relevance of the 4 dimensional structure and internal consistency reliability of the questionnaire.

Conclusion Psychometric validity of this first treatment satisfaction questionnaire specific to arthritis is promising and further psychometric validation (clinical validity and reproducibility) is presently underway.

SAT0085 MELOXICAM HAS A LOW RISK OF SERIOUS GASTROINTESTINAL COMPLICATIONS: POOLED ANALYSIS OF 27,039 PATIENTS

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Background Gastrointestinal (GI) complications are the most common adverse events associated with nonsteroidal anti-inflammatory drugs (NSAIDs). Although serious gastrointestinal complications, such as perforated ulcers and catastrophic bleeding, are uncommon, these events are.

Objectives We reviewed the incidence of serious upper GI (UGI) complications, including perforations, obstructions and hemodynamically-significant bleeds in a pooled data analysis of Meloxicam clinical trials that were at least 3 weeks in duration and included at least 20 patients per arm.

Methods Thirty-five trials with 27,309 patients on Meloxicam, comparator NSAID's, or placebo were included in the analysis. Nearly 39% (8109) patients were over age 65, and 1002 patients (4%) had a previous history of perforation, ulcer or bleed. Cases of suspected GI events were ascertained based on pre-defined criteria. Case report forms and supporting details were blinded and submitted to an independent Endpoint Committee for adjudication.

Results A total of 448 potential cases were identified and sent for adjudication. The Endpoint Committee determined that 54 of these cases met the predefined criteria for a clinically significant event.

Abstract SAT0085 Table 1

	No. Patients	Mean Exposure (Days)	Cummulative Pt Years	No. Events	Rate per 100 pt years
Placebo	736	56	113	0	0
Meloxicam 7.5	10158	33	918	3	0.3
Meloxicam 15	2960	179	1451	9	0.6
Meloxicam 22.5	910	241	600	6	1.0
Diclofenac	5464	35	524	9	1.7
Naproxen	243	117	78	1	1.3
Piroxicam	5371	41	603	16	2.7

Conclusion The risk of clinically significant UGI events with meloxicam is dose-dependent and low at the recommended doses of 7.5 mg and 15 mg.

SAT0086 CARTILAGE DERIVED SEROLOGIC MARKERS AND RADIOGRAPHIC PROGRESSION OF KNEE OSTEOARTHRITIS

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Background

Objectives To determine relation between serum levels of cartilage derived markers (cartilage oligomeric matrix protein ? COMP, human gp 39 – chondrex, YKL-40) and radiographic progression in knee osteoarthritis (OA) patients.

Methods A cohort of 202 patients with symptomatic knee OA was introduced into the study and followed-up over the period of 3 years. Serum levels of markers were measured at the baseline and at the end of the study. COMP was measured using monoclonal antibodies, developed in our institute. Chondrex was measured using chondrex-kit (Biometra, USA). Radiographic progression was defined as reduction of joint space width (JSW) > 0.5 mm over the 3 years follow-up. Baseline serum COMP and chondrex levels were compared in patients with and without radiographic progression and correlated with maximal JSW reduction (one knee) and a total of JSW reductions from both knees.

Results Totally 118 patients completed the 3 years follow-up; 22 of them showed JSW reduction at least in one knee joint. The levels of both markers in progressive and non-progressive groups are summarised in the Table 1.

Abstract SAT0086 Table 1

		Progressive (n = 22)	Non-progressive (n = 96)	p
COMP (entry)	ug/ml	1.36 ± 0.38	1.18 ± 0.41	< 0.05
COMP (3 years)	ug/ml	1.76 ± 0.59	1.18 ± 0.35	<0.05
Chondrex (entry)	ng/ml	93.35 ± 81.59	77.97 ± 47.36	NS
Chondrex (3 years)	ng/ml	98.03 ± 85.04	83.35 ± 52.81	NS