1 STUDY REPORT TITLE PAGE

Reckitt Benckiser

EudraCT/IND Number:	2009-018018-21
Study Number:	NL0910
Protocol Title:	A randomised, double-blind, multi-centre, placebo controlled parallel group study to evaluate the efficacy and tolerability of a new Ibuprofen patch in patients with acute sports-related traumatic blunt soft tissue injury/contusion.
Study Phase:	III
Date First Patient Enrolled:	31 July 2010
Date Last Patient Completed:	14 December 2010
Report Date:	15 April 2011
Co-ordinating Investigator:	Professor Dr. med., HGP, Hans-Georg Predel, Deutsche Sport-hochschule Köln, Am Sportpark Müngersdorf 6, D-50933 Köln, Germany
Study Conduct Statement:	This study was conducted in accordance with ICH Good Clinical Practice and the ethical principles contained within the Declaration of Helsinki (South Africa, 1996), as referenced in EU Directive 2001/20/EC. Documents defined by ICH GCP as “essential documents” will be archived in the RB company archive in Hull, UK

Sponsor: Reckitt Benckiser Healthcare Ltd.	Study No.: NL09010
Ibuprofen 200 mg patch in patients with blunt soft tissue injury/contusion.	EudraCT/IND No.: 2009-018018-21

Reviewed and Agreed by:

Clinical Project Manager function:

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Statistician:

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Reviewed and Approved by:

R&D Manager - Clinical (Healthcare) in the EU:

Dr Sue Aspley BSc (Hons), PhD — Date: 21 April 2011

Global Medical Director:

Dr P Berry MB ChB, MPH — Date: 21 April 2011

Study Sponsor:

Reckitt Benckiser Healthcare (UK) Limited, Dansom Lane, Hull HU8 7DS, United Kingdom

2 SYNOPSIS

Name of Sponsor/ Company: Reckitt Benckiser Healthcare (UK) Limited	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only**)
Name of Finished Product:	**Volume:**	
Name of Active Ingredient(s):	**Page:**	
Title of Trial: A randomised, double-blind, multi-centre, placebo controlled parallel group study to evaluate the efficacy and tolerability of a new Ibuprofen patch in patients with acute sports-related traumatic blunt soft tissue injury/contusion.		
Investigator(s): Professor Dr. med., HGP, Hans-Georg Predel		
Trial Site(s): Four sites in Germany		
Publication (reference): None.		
Studied Period: 6 months **Date first patient enrolled:** 31 July 2010 **Date last patient completed:** 14 December 2010		**Phase of Development:** III
Objectives: The primary objective of the study was to assess the efficacy of a new ibuprofen patch versus placebo in the topical treatment of acute sports impact injuries/contusions. The secondary objective was to evaluate the tolerability of the patch in comparison to placebo.		
Methodology: Randomised, double-blind, multi-centre, placebo controlled parallel group study.		
Number of Patients: **Planned:** 132 for recruitment, 120 evaluable **Analysed**: 130 (Ibuprofen 200 mg: n=66, placebo: n=64)		
Diagnosis and Main Criteria for Inclusion: • Male or female patients aged 18-60 years with normal general health. • Fresh sports-related blunt soft tissue injury/contusion. • Baseline value of the algometric measurement at injured site ≤ 50% of the respective value at the contralateral site. • Pain on movement at baseline of at least 50 mm on a VAS (0-100 mm). • The absolute sensitivity to pain on the contralateral site is at least 2.5 N/cm^2. • Size of the trauma at least 25 cm^2 and maximal 150 cm^2.		
Test Product: Ibuprofen 200 mg, topical application, batch number: A08061		
Duration of Treatment: 5 days		
Reference Therapy: placebo, topical application, batch number: A07061		
Criteria for Evaluation: **Efficacy:** Primary endpoint was the area under the VAS assessment of pain on movement (POM) curve over Days 0-3 (VAS AUC_{0-3d}). Secondary variables were: VAS $AUC_{0-12h,}$ VAS POM at Hour 12, VAS AUC_{0-24h}, algometry AUC_{0-3d}, algometry and VAS POM at Hour 24, algometry AUC_{0-5d}, AUC_{0-3d} and AUC_{0-5d} of ratios of algometry injured/contralateral sites, time to resolution of pain, use of rescue medication, global assessment of treatment efficacy by patients and Investigators		

Name of Sponsor/ Company: Reckitt Benckiser Healthcare (UK) Limited	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only**)
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Name of Active Ingredient(s):	**Page:**	

Safety: Adverse events, physical examinations, vital signs, global assessment of local tolerability of the patch.

Statistical Methods: The primary variable VAS AUC_{0-3d} was compared between treatment groups using Analysis-of-Covariance (ANCOVA) with terms in the model for treatment group, total sum of RICE (Rest, Ice, Compression and Elevation) duration, and baseline VAS assessment of pain on movement. The level of significance was stipulated as α=1 % for the primary efficacy variable. Treatment effects were estimated using the least squares (LS) means and the mean square error from the ANCOVA. The two-sided 99%-confidence interval for treatment difference was calculated for the primary variable. All other variables were analysed by means of descriptive statistical methods.

SUMMARY & CONCLUSIONS

EFFICACY RESULTS

A total of 130 patients: (Ibuprofen n=66; placebo n=64), 88 male (Ibuprofen n=44; placebo n=44) and 42 female (Ibuprofen n=22; placebo n=20), with a mean age of 34.09 years (Ibuprofen) and 30.08 years (placebo) with acute sports-related traumatic blunt soft tissue injury/contusion were included in the trial to assess pain on movement over Days 0-3 and secondary efficacy variables, respectively.

The resolution of pain (algometry of injured site returns to algometry of contralateral site) was achieved for 17.7% of patient, the time taken to achieve this was proved statistically superior for the Ibuprofen patch (p=0.0071).

The results for VAS are summarised below:

AUC_{0-3d} differed significantly between Ibuprofen 200 mg and placebo (ANCOVA: p=0.0011) at a two-tailed significance level of 1%. The mean treatment effect was 662.82 mm*h in favour of Ibuprofen 200 mg.

Patients treated with the Ibuprofen patch were shown to have significantly lower VAS pain scores both in terms of the AUC after 12 hours, 24 hours, 3 hours and 5 hours (all p<0.01) and also the actual VAS scores after 12 (least square mean difference = -8.12 mm, p=0.0184) and 24 hours (least square mean difference = -10.76 mm, p=0.0007).

Tenderness:

Algometry values (AUC_{0-3d} and AUC_{0-5d}) were statistically significantly higher in the Ibuprofen 200 mg group than in placebo group at the injured site (p<0.001), indicating less pain or tenderness with the Ibuprofen patch versus placebo. This was also seen for the ratio scores (injured/contralateral) AUC after 3 and 5 days (p<0.001).

Use of Rescue Medication:

Throughout the trial, there was low usage of rescue medication and there was no statistically significant difference in the amount of time to use of rescue medication between the treatment groups.

Name of Sponsor/ Company: Reckitt Benckiser Healthcare (UK) Limited	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only**)
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Global Assessment:

At all time points both the patient and investigator rated the Ibuprofen patch more efficacious than placebo ($p<0.01$).

The results confirm that the new Ibuprofen patch has a clinically relevant favourable impact on the outcomes of patients suffering from fresh blunt injuries. Patients treated with the Ibuprofen patch had statistically significant and clinically relevant reductions in pain scores and tenderness values than patients in the placebo group.

SAFETY RESULTS

All documented adverse events (AEs) were classified into treatment-emergent AEs (TEAEs) or non-treatment-emergent AEs. A total of 15 patients (Ibuprofen 200 mg: n=7, Placebo: n=8) had at least one TEAE during the course of the clinical trial. The total number of TEAEs was lower in the Ibuprofen 200 mg treatment group than in placebo group. All TEAEs in this clinical trial were non-serious and of mild severity. The System Organ Classes most commonly affected by all non-serious TEAEs during the study were “General Disorders and Administration Site Conditions” (Ibuprofen 200 mg: n=7, Placebo: n=8) and “Infections and infestations” (Ibuprofen 200 mg: n=0, Placebo: n=2). The most frequent non-serious treatment-emergent adverse events were “Nasopharyngitis” (Ibuprofen 200 mg: n=0, Placebo: n=2), “Headache” (Ibuprofen 200 mg: n=1, Placebo: n=1), “Application site pruritus” (Ibuprofen 200 mg: n=1, Placebo: n=1), “Application site reaction” (Ibuprofen 200 mg: n=0, Placebo: n=2), and “Application site hypersensitivity” (Ibuprofen 200 mg: n=2, Placebo: n=0). A total of nine non-serious TEAEs were classified as drug-related (probable, possible, definite) in the treatment groups (Ibuprofen 200 mg: n=4, Placebo: n=5). Most cases were probably drug-related. Other than a total of eight adverse events at the site of application in both treatment groups, Ibuprofen 200 mg: n=3, Placebo: n=5, (application site reaction, pruritus, hypersensitivity, erythema and discomfort) there was no pattern indicating any specific adverse effect related to the study drug. The investigation of vital signs and physical examinations that were documented at the start and the end of the clinical trial did not detect any relevant safety concern. It is therefore concluded that the new Ibuprofen patch is a safe option for the treatment of acute sports-related traumatic blunt soft tissue injury/contusion.

CONCLUSION

The results confirm that the Ibuprofen 200 mg patch has a clinically relevant favourable impact on the outcome of patients suffering from fresh blunt trauma injuries.

Patients treated with the new Ibuprofen patch had statistically significant and clinically relevant reductions in pain scores and tenderness values than patients in the placebo group. All documented adverse events (AEs) were classified into treatment-emergent AEs (TEAEs) or non-treatment-emergent AEs. All documented AEs were TEAEs with a comparable proportion of TEAEs in both treatment groups.

The Ibuprofen 200 mg patch is an efficacious and safe option for the treatment of acute sports-related traumatic blunt soft tissue injury/contusion.

Date of the report: 15 April 2011

3 TABLE OF CONTENTS

3.1 LIST OF TABLES AND FIGURES IN THE BODY OF THE TEXT

4 LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Abbreviation in Full
ABPI	Association of the British Pharmaceutical Industry
AE	Adverse Event
AMG	German Medicines Law
ANCOVA	Analysis-of-covariance
ANOVA	Analysis of variance
AR	Adverse Reaction to an Investigational Medicinal Product
ATC	Anatomical, therapeutical, chemical
AUC	Area under the curve
BfArM	German Federal Institute for Drugs and Medical Devices
BL	baseline
BNF	British National Formulary
c.i.	Confidence interval
CA	Competent Authority
CFR	Code of Federal Regulations
cm	centimetres
COX	Cyclooxygenase
CPM	Clinical Project Manager
CRA	Clinical Research Associate
CRF	Case report form
CRO	Contract Research Organisation
CTA	Clinical Trial Application
CV	Curriculum Vitae
d	days
EC	Ethics Committee
ECG	Electrocardiogram
EU	European Union
FAS	Full Analysis Set
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GP	General Practitioner
i.e.	id est (that is)
ICH	International Conference on Harmonisation
ICH	International Conference on Harmonisation
IEC	Independent ethics committee
IMP	Investigational Medicinal Product (Study Drug)

Abbreviation	Abbreviation in Full
IND	Investigational New Drug
IRB	Institutional Review Board
ITT	Intent-to-treat
LOCF	Last-observation-carried-forward
LS	Least squares
MAX	Maximum
MedDRA	Medical Dictionary for Regulatory Activities
MHRA	Medical and Healthcare Products Regulatory Agency
MIN	Minimum
mm	millimetres
n	Sample size
N	Newton
NCR	No carbon required
NSAID	Non steroidal anti-inflammatory drug
OR	Odds ratio
OTC	Over–the-counter
PG	Prostaglandins
POM	Pain on movement
PP	Per Protocol
Q1	Lower quartile
Q3	Upper quartile
QA	Quality assurance
QC	Quality control
R & D	Research and Development
RB	Reckitt Benckiser Healthcare (UK) Limited
RICE	Rest, Ice, Compression and Elevation
SA	Statistical Analysis Plan
SAE	Serious adverse event
SAF	Safety
SAP	Statistical Analysis Plan
SD	Standard deviation
SDV	Source Data Verification
SmPC	Summary of Product Characteristics
SNRI	Serotonin and noradrenalin reuptake inhibitors
SOC	System Organ Class
SOP	Standard operating procedure
SSRI	Selective serotonin reuptake inhibitors
TEAE	Treatment-emergent adverse event
UK	United Kingdom (of Great Britain and Northern Ireland)

Abbreviation	Abbreviation in Full
V	Visit
VAS	Visual Analogue Scale
WHO	World Health Organisation

5 ETHICS

5.1 INDEPENDENT ETHICS COMMITTEE (IEC) OR INSTITUTIONAL REVIEW BOARD (IRB)

The name and full address of the three IECs consulted are provided in Appendix 16.1.3.

The study Protocol together with patient information and consent documents were reviewed and approved by three Independent Ethics Committees.

5.2 ETHICAL CONDUCT OF THE STUDY

This study was conducted in accordance with the Declaration of Helsinki (South Africa, 1996), as referenced in EU Directive 2001/20/EC. It complied with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) and applicable regulatory requirements.

5.3 PATIENT INFORMATION AND CONSENT

Copies of a representative patient information sheet and a blank consent form are provided in Appendix 16.1.3.

Patients who were considered by the Investigator to be suitable for entry into the study were given the opportunity to read the patient information sheet and consent form, and to ask questions. If they were happy with, and understood the information, they were asked to sign the consent form. The Investigator also signed the form. The patient was given a copy of the information sheet and signed consent form. No Protocol-related procedures were performed prior to the patient signing the consent form.

6 INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

Appendix 16.1.4 contains a table listing the names and affiliations of the individuals whose participation materially affected the conduct of the study, together with their roles. The list of investigators is provided in Appendix 16.1.4.1. Other important participants of the clinical trial are presented in Appendix 16.1.4.2. The curriculum vitae (CV) of the Co-ordinating Investigator and the other Investigators at each site are also included in the Appendix 16.1.4.3.

The following Contract Research Organisations were involved in the clinical trial:

- CRM Pharmaberatung GmbH, Marie-Curie-Str. 2, D-53359 Rheinbach, Germany, for planning, monitoring, and project management of the study.
- CRM Biometrics GmbH, Marie-Curie-Str. 2, D-53359 Rheinbach, Germany, for statistical planning, data management, data entry, biometrical evaluation, and reporting.

7 INTRODUCTION

Reckitt Benckiser Healthcare (UK) Limited (RB) is developing a new topical analgesic patch containing ibuprofen. This study was carried out to assess the efficacy of this new patch in the topical treatment of patients with acute sports related traumatic blunt soft tissue injury/contusion.

The study was double-blind and placebo-controlled in order to ensure that data generated were unbiased and that the study met the standards required by key regulatory authorities. The study site and staff selected for this study had extensive experience with this pain model [12]. The study was carried out in accordance with the CPMP/EWP/612/00 Note for Guidance on the clinical investigation of medicinal products for treatment of Nociceptive Pain adopted November 2002[23].

8 STUDY OBJECTIVES

The primary objective of the study was to assess the efficacy of a new ibuprofen patch versus placebo in the topical treatment of acute sports impact injuries/contusions.

The secondary objective was to evaluate the tolerability of the patch in comparison to placebo.

9 INVESTIGATIONAL PLAN

9.1 OVERALL STUDY DESIGN AND PLAN – DESCRIPTION

The study Protocol and Amendment No. 1 are included as Appendix 16.1.1. Unique pages from the case report form (CRF) are included as Appendix 16.1.2.

The clinical trial was carried out as a Phase III randomised, double-blind, multi-centre, placebo controlled, parallel group study with two independent treatment groups “Ibuprofen 200 mg” and “placebo”. A total of 130 patients with acute sports-related traumatic blunt soft tissue injury/contusion were enrolled and assessed for efficacy and safety. The patients were allocated to the study drugs by means of block randomisation (Block size 4) on Visit 1 (Day 0). Each patient attended the clinic on five separate occasions during the clinical trial:

- Visit 1 (Day 0)
- Visit 2 (Day 1)
- Visit 3 (Day 2)

- Visit 4 (Day 3)
- Visit 5 (Day 5)

An interim analysis of the clinical trial was neither planned nor carried out. Therefore, no safety or data monitoring or special steering or evaluation committees were involved.

Changes made during the course of the study due to the Protocol Amendment No. 1 are described in Section 9.8 of this report.

9.2 DISCUSSION OF STUDY DESIGN, INCLUDING THE CHOICE OF CONTROL GROUPS

For scientific reasons, a parallel-group design was selected as the most suitable method. An observation period of 5 ± 1 days was thought to be sufficient to prove efficacy based on previous experience.[33, 34, 35, 36, 37]

A double-blind design was chosen to avoid bias in the assessment of treatment success. Treatment was allocated according to a randomisation schedule to avoid a bias of treatment allocation.[23]

A placebo patch was included in the trial to determine the efficacy of the Ibuprofen 200mg patch in patients with acute sports-related traumatic blunt soft tissue injuries/contusions. As the patients to be included in this clinical trial were treated for a limited period of time, placebo treatment was justified; in addition a rescue medication was available if required.

All efficacy variables were carefully selected with respect to available international guidelines and clinical relevance for this indication and have been used in several other recently published clinical trials. The Visual Analogue Scale (VAS) is, internationally, a well documented and widely accepted method for the assessment of pain. The method is cited in the CPMP/EWP/612/00 Note for Guidance on the clinical investigation of medicinal products for treatment of Nociceptive Pain adopted November 2002.[23]

In addition this methodology was accepted as appropriate for use during discussions with Scientific Advise.

9.3 SELECTION OF STUDY POPULATION

To enable treatment within 3 hours of the injury occurring, patients were enrolled at sporting events in the locality of the study centres.

9.3.1 INCLUSION CRITERIA

- Age: 18-60 years.
- Sex: Either male or female patients
- Normal general health.
- Primary diagnosis: fresh sports-related blunt soft tissue injury/contusion. (Time elapse between traumatic event and inclusion not longer than 3 hours).
- Injury not requiring hospitalisation.
- The baseline value of the algometric measurement on the injured site was less than or equal to 50% of the respective value at the contralateral site.
- Pain on movement at baseline at least 50 mm on a VAS (0-100 mm).
- The absolute sensitivity to pain on the contralateral site was at least 2.5 N/cm^2.
- Written informed consent.
- Size of trauma between $25cm^2$ and $150cm^2$.

9.3.2 EXCLUSION CRITERIA

Patients to whom any of the following conditions applied had not be randomised:

- History of blood coagulation disorders.
- A history of significant disease deemed by the Investigator to render the patient unsuitable for inclusion.
- Any significant ongoing painful condition other than that associated with the sports-related injury/contusion.
- Any other treatment or medication that may interfere with the trial (e.g. corticosteroids) up to 3 days prior to the trial, except RICE (***R****est,* ***I****ce,* ***C****ompression and* ***E****levation*).
- Any ongoing condition that might interfere with the absorption, distribution, metabolism, or excretion of the study medication.
- A history of psychotic illness, attempted suicide, or neurosis.

- A positive history of drug or alcohol abuse within the past year.
- Those taking any concomitant medications that might confound assessments of pain relief, such as psychotropic drugs, antidepressants, sedative –hypnotics taken within fives times of their elimination half lives.
- Selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs) were permitted if the patient had been on a stable dose for at least four weeks prior to Visit 1 (screening) and remained on this dose throughout the study.
- Any other treatment or medication, that interfered with the conduct of the trial, except RICE (***R****est,* ***I****ce,* ***C****ompression and* ***E****levation)*.
- Women of childbearing potential, who were pregnant or lactating, seeking pregnancy or failing to take adequate contraceptive precautions, (i.e. an oral or injectable contraceptive, an approved hormonal implant or topical patch, an intrauterine device, abstinence [should the patient become sexually active, she had to agree to use a double barrier method] or condoms/diaphragm and spermicide). A woman of childbearing potential was defined as any female who was less than 2 years post-menopausal or had not undergone a hysterectomy or surgical sterilisation, e.g. bilateral tubal ligation, bilateral ovariectomy (oophorectomy).
- Any previous history of allergy or known intolerance to any of the drugs or formulation constituents which, in the Investigator's opinion, might preclude use of an NSAID, including aspirin sensitive asthma or a previous allergic response to a NSAID, including bronchospasm, urticaria, angioedema and rhinitis.
- Those previously randomised into this study.
- Patients who had received any analgesic, anti-inflammatory, antispasmodic or other therapy (except RICE) within 24 hours prior to taking the study medication.
- Those who had participated in a clinical trial in the previous 30 days calculated from time of last dosing in the prior trial to time of anticipated dosing in this trial.
- Injured area is too hairy.
- Current skin disorders in the area to be treated.
- Open wounds to the area to be treated.
- Suspected fractures.
- Suspected torn ligaments.
- Head injuries.

- Pre-treatment of injury (any other therapy, except RICE (***R****est,* ***I****ce,* ***C****ompression and* ***E****levation*).
- Anticipated poor compliance by the patient.
- Patients with a known sensitivity to any of the materials/ drug/excipients in the patch respectively Paracetamol.
- Relevant consumption of alcohol 24 hours prior to randomisation.

Criteria concerning the size and the severity of the pain of the trauma at Visit 1:

Size of injury

The size of injury was measured by the Investigator. The size of the trauma had to be at least 25 cm^2 and a maximum of 150 cm^2 on the basis of the largest perpendicular diameters. Injuries smaller then 25 cm^2 were in general of too little clinical relevance to be treated. Injuries larger then 150 cm^2 might cause symptoms and impairment requiring additional treatments.

Severity of the pain of injury

The pain assessment on movement by patient had to be ≥ 50 mm on a 100 mm VAS at baseline (Visit 1).

The severity of pain (i.e. tenderness) was determined by measurement of pressure intensity by means of an algometer. The basic value of the algometric measurement on the injured site was required to be less than or equal to 50% of the respective value at the contralateral site. Furthermore, the absolute sensitivity to pain on contralateral, not injured site was required to be at least 2.5 N/cm².

Over the age of 60 years, there can be an increased risk in oedema regression, possibly caused by latent cardiac insufficiency. As age may introduce bias in the baseline values, patients over the age of 60 years must not be included.

Since injuries in sport activities are more common in the male population, it was anticipated that more males than females were enrolled. Nevertheless, efforts were made to try and ensure an approximately equal gender distribution. Possible gender specificities were analysed at the end of the trial.

9.3.3 REMOVAL OF SUBJECTS FROM THERAPY OR ASSESSMENT

Participation in the trial was strictly voluntary. A patient had the right to withdraw from the trial at any time, for any reason. Should a patient have decided to withdraw from the study, the Investigator had to make all reasonable effort to determine the reason for withdrawal and to complete the investigations for the final visit.

The Investigator was also able to withdraw the patient from the study at any time. Reasons for removing a patient from the study included, but were not limited to:

- Adverse events that in the judgement of the Investigator may have caused severe or permanent harm (significant clinical deterioration is an adverse event).
- Prerequisites for the participation in the trial were not fulfilled.
- Intake of non-permitted medication during the trial.
- Severe deviation from the planned execution of the trial.
- Poor compliance.
- Non-appearance at follow-up examinations.
- Other reasons (e.g. pregnancy).

The primary reason for withdrawal had to be documented as one of the following: adverse events; lack of efficacy; lost to follow-up; no further need for study medication (unless this is a study end point); unauthorised concomitant medication; poor compliance; protocol violation; death or other reasons (e.g. pregnancy, randomisation code broken and other). The Investigator had to make reasonable attempts to contact patients who were lost to follow-up - a minimum of two documented telephone calls or a letter is considered reasonable.

If a patient was withdrawn prematurely from the study, the following assessments should be carried out and documented in the CRF under the Final Visit section (Visit 5):

Vital Signs

- Blood pressure (after sitting for 5 minutes; mmHg).
- Heart rate (radial pulse counted for 30 seconds after resting for 5 minutes; beats/minute).
- oral temperature (ºC).

Physical examination

- a standard physical examination.

Pregnancy testing

- women of child-bearing potential underwent urine pregnancy testing.

Study specific assessments

- Pain on movement. (VAS).
- Global assessment of local tolerability.
- Global assessment of treatment efficacy.

Review of adverse events

Review of concomitant and rescue medication as well as therapies (including RICE)

Withdrawn patients were not replaced. Sufficient patients were randomised to ensure completion of the required number.

9.4 TREATMENTS

9.4.1 TREATMENTS ADMINISTERED

The trial medication was for topical administration. Patients were randomised to receive one of the following treatments:

- Ibuprofen 200 mg patch
- Placebo patch.

Patches were to be administered once daily (once every 24 hours). The applications on assessment Days 0-3 were performed by the study staff. On Visit 4 trial medication was handed out to the patient for self application on Assessment Day 4. The Investigator instructed patients how to use the patch. The correct position of the patch was always marked with a water resistant pen to ensure that the patch was applied at the same site. Patients were advised that should the patch become detached from the test site, it should be re-applied. The contact of the applied patch with any humidity or water should be avoided.

As rescue medication Paracetamol 500 mg tablets (for oral administration) were allowed during the trial. The maximum dose per day (24 hr period) was 4000 mg Paracetamol, single dose maximal 500-1000 mg equivalent to 10-15 mg/kg body weight) which was provided by RB with the manufacturer's label as sold. Rescue medication was dispensed at Visit 1. The consumption of rescue medication was recorded by the patient in the diary and was then documented by the Investigator in the CRF. At the final visit (Visit 5) the unused rescue medication and all used or unused medication packages were collected by the Investigator.

9.4.2 IDENTITY OF INVESTIGATIONAL PRODUCT(S)

The following medication was supplied.

Study medication consisted of:

- Active patch 200 mg ibuprofen
- Placebo patch.

Study medication was manufactured and primary packed according to Good Manufacturing Practice (GMP) standards by LEAD CHEMICAL Co., LTD. Address: 77-3 Himata, Toyama city, Toyama pref, 930-0912, Japan.

All drug supplies were secondary packed to Good Manufacturing Practice (GMP) standards by RB Investigational Material Supply Unit, Hull. The rescue medication provided for this study (described in Section 12.5.2 of the Protocol) was provided as open-label.

9.4.3 METHOD OF ASSIGNING SUBJECTS TO TREATMENT GROUPS

A detailed description of the randomisation method, including how it was executed, is presented in Appendix 16.1.7.

Matching drug supplies were randomised by the RB Investigational Material Supply Unit, according to a computer-generated randomisation schedule with an allocation ratio of 1:1 for active and placebo. The block (Block size = 4) randomisation schedule was generated by RB statistician (John Sykes) on 2 March 2010 using SAS® Version 9.1. The randomisation schedule was checked by a statistician not involved in the analysis of the study. On entry, patients were allocated a unique patient number in numerical sequence. Issue of the study drug in this sequence ensured randomisation.

The procedure for blinding is described in Section 9.4.6.

9.4.4 SELECTION OF DOSES IN THE STUDY

Trial medication was for topical administration. Patients were randomised to receive one of the following treatments:

- Ibuprofen 200 mg patch
- Placebo patch.

Ingredients of the active patch: Ibuprofen 200 mg, Polyethylene Glycol (PEG) 20000, PEG 400, Styrene-Isoprene-Styrene (SIS), Block Copolymer Polyisobutylene (PIB), Hydrogenated Rosin Glycerol Ester (HRGE), levo menthol and Liquid Paraffin.

Ingredients of the placebo patch: Polyethylene Glycol (PEG) 20000, PEG 400, Styrene-Isoprene-Styrene (SIS), Block Copolymer Polyisobutylene (PIB), Hydrogenated Rosin Glycerol Ester (HRGE), levo menthol and Liquid Paraffin.

The posology of the new patch in adults is one 200mg patch applied every 24 hours. This represented a maximum daily topical dose of 200mg of ibuprofen, less than the maximum dose allowed topically (500mg/day in UK, no limit in Germany) and considerably less than the maximum allowable daily dose of oral ibuprofen in non prescribed medicines (1200 mg per day in Germany and the UK).

9.4.5 SELECTION OF TIMING OF DOSE FOR EACH SUBJECT

Patients were treated with the authorised dose and route of administration. The duration of treatment corresponded to the average duration of treatment for acute sports-related traumatic blunt soft tissue injury/contusion and was therefore sufficient for recording the primary and secondary efficacy variables.

9.4.6 BLINDING

The clinical trial was carried out as a double-blind clinical trial. Matching drug supplies were randomised by RB Investigational Material Supply Unit, according to a computer-generated randomisation schedule with an allocation ratio of 1:1 for active and placebo. On entry, patients were allocated a unique patient number in numerical sequence. Issue of the study drug in this sequence ensured randomisation.

The RB Clinical Trials Supply Unit held the master code for the randomisation schedule and supplied the Investigator with the randomisation code for each patient in sealed code break envelopes.

The code was to be broken only in an emergency situation, such as a serious adverse event (SAE), which required knowledge of the study drug taken in order to treat the SAE appropriately. If the code for a patient was broken, the Investigator was to withdraw the patient from the study, document the details of the event in the patient's case report form and promptly inform the RB Clinical Project Manager. The date and reasons for code break was to be noted on the code envelope by the Investigator.

The study monitor checked the randomisation codes on a regular basis at monitoring visits, to ensure the above procedures were being followed at the study site. All codes, whether sealed or opened, were returned to RB at the end of the study.

RB broke the code for all patients only after all data queries had been answered and the database had been locked.

The certificates of analysis for each product were reviewed to ensure comparability of active and placebo products.

9.4.7 PRIOR AND CONCOMITANT THERAPY

Concomitant therapies were defined as prescribed medications, physical therapy including cooling measures and over-the-counter preparations, including herbal preparations (including but not limited to Arnica cream for bruising) licensed for medicinal use, other than study medication and supplementary medication (rescue medication) that the patient receives during the course of the study.

The Investigator recorded any medications/ therapies given in treatment of adverse events on the concomitant medication page in the patient's case report form. Any medication taken by the patient during the course of the study was to be recorded on this form. Any changes in concomitant medication/ therapy during the study were documented, including cessation of therapy, initiation of therapy and dose changes.

Since R I C E (***R**est, **I**ce, **C**ompression and **E**levation*) technique was allowed before and during the trial the investigator noted down any of these treatments on page for recording concomitant medications and non-drug therapies in the patient's case report form at each visit.

The use of the following treatments was not permitted:

- Analgesic or anti-inflammatory drugs (by any route of administration) within 24 hours prior to study entry.
- Analgesic or anti-inflammatory drugs (by any route of administration) during the entire clinical phase of the study, except for the rescue medication.
- Psychotropic drugs, antidepressants, or sedative-hypnotics (other than those permitted for conscious sedation) taken within five times of their elimination half lives prior to Visit 1 (screening) and during the entire in-clinic post-dosing assessment period.
- SSRIs and SNRIs can be used during the study if the patients have maintained a stable dose for at least four weeks prior to Visit 1.
- Physical therapy or other comfort measures (e.g. heat, infrared heat, shortwave, ultrasound massage), except RICE.
- Herbal preparations for treatment of bruises.
- Patients were required to refrain from applying sunscreen, moisturisers, or any other skin treatments to the target area for the whole treatment period.

9.4.8 TREATMENT COMPLIANCE

If a patient did not comply with the treatment schedule, it was deemed a protocol deviation and documented appropriately. Patients were to continue in the study if considered appropriate by both the Investigator and the sponsor.

Treatment compliance was checked by means of Drug Accountability. The patients were asked to return the trial medication (used or unused) at Visit 5 and the rescue medication at each visit. The returned unused/empty packages were counted and the number recorded in the CRF and on the drug accountability form by the Investigator. The rescue medication was also counted and documented in the CRF.

9.5 EFFICACY AND SAFETY VARIABLES

9.5.1 EFFICACY AND SAFETY MEASUREMENTS ASSESSED AND FLOWCHART

The primary endpoint was the area under the VAS assessment of pain on movement curve over Days 0-3 (VAS AUC_{0-3d}). The area under the curve was calculated using the trapezoidal rule.

The secondary efficacy variables were:

Area under the VAS assessment of pain on movement curve over Hours 0-12 (VAS AUC_{0-12h}).

VAS assessment of pain on movement at Hour 12.

Area under the VAS assessment of pain on movement curve over Hours 0-24 (VAS AUC_{0-24h}).

Area under the tenderness/algometry assessment curve (pressure required to produce the first tenderness reaction) over Days 0-3 (AUC_{0-3d}).

Tenderness/algometry assessment at Hour 24.

VAS assessment of pain on movement at Hour 24.

Area under the tenderness/algometry assessment curve over Days 0-5 (AUC_{0-5d}).

AUCs over Days 0 to 3 and Days 0 to 5 for the ratio of the tenderness/algometry assessments, injured/contralateral sites (RATIO AUC_{0-3d} and RATIO AUC_{0-5d}).

The time taken to reach the contralateral (healthy) values of tenderness (time to resolution of pain).

Use of rescue medication and time of use of rescue medication.

Global assessment of treatment efficacy by patients and Investigators using a 5-point scale (0 = excellent, 1 = good, 2 = fair, 3 = poor, and 4 = none). Assessments were made on Assessment Days 1 (Visit 2), 3 (Visit 4), and 5 (Final Visit).

Safety was evaluated by monitoring general physical examinations and vital signs as well as the occurrence of adverse events. In addition, patients and Investigators made a global assessment of local tolerability of the patch under double-blind conditions using a 4-point scale (3 = excellent, 2 = good, 1 = fair, and 0 = poor) assessments were made on Assessment Days 1 (Visit 2), 3 (Visit 4) and 5 (Final Visit).

Baseline Visit/ Visit 1/ Assessment Day 0

Screening/Enrolment Procedures

In most cases outpatients suffering from fresh impact injuries/contusions were recruited by attending sports events. Patient information and informed consent forms were made available at events. Time elapsed between injury and randomisation was not to exceed 3 hours.

Each patient had to meet all requirements for inclusion and exclusion criteria and give written informed consent before any trial related activities.

Patients were screened for eligibility and then asked to consent to screening procedures before they were performed. The Investigator or medical designee discussed the purpose and nature of the study with the patient. The Investigator then signed to confirm that the patient had been provided with a copy of the patient informed consent form including a copy of the patient insurance and the patient travel accident insurance, written in German, and that a full explanation of the study had been given. The patients were required to confirm their willingness to participate in the study by signing and dating the consent form.

RB procured patient insurance and a patient travel accident insurance for every patient enrolled in the clinical study.

Each patient was allocated a screening number. This was different from the randomisation number that was issued to the patient when randomised.

The physician assessed patients for eligibility according to the stated inclusion and exclusion criteria and conducted a physical examination, recorded medical history, including relevant allergies and surgeries, current medical and prior medication and therapies (taken/ performed within 30 days of baseline visit) and current concomitant medication and therapies. Patients were asked if they were currently experiencing any adverse events other than the injury.

Following screening and confirmation of eligibility, patients were provided with rescue medication (Paracetamol), a patient diary and a patient card.

Patient Diary

A patient diary was handed out to the patient at Visit 1 to record information about the consumption of rescue medication, concomitant medications, VAS on movement and adverse events after 1, 2, 4, 6, 12, and 96 (±1) hours of first application.

The patient had to document:

- Pain on movement: The pain on movement was recorded by the patient on a 100 mm VAS scale with anchors at 0 mm = no pain and 100 mm = unbearable pain.
- Adverse events.
- Concomitant medications and therapies (RICE).
- Use of rescue medication: Time of consumption (not less than 6 hours before the next visit), the number of tablets taken and the reason for intake (for pain related to the injury or for other reasons).

At each visit the Investigator reviewed the diary and transferred the relevant information into the CRF. VAS entries were measured and the values noted in the CRF.

At the end of the study the diary was collected and regarded as source data.

Patient Card

The patient card was approximately the size of a credit card and contained the following details in German:

- Study name and number.
- EudraCT number.
- Statement that the patient was participating in a clinical trial.
- Patient Name.
- Name and telephone number of the study physician.
- Any restrictions with which they must comply.
- Paracetamol as rescue medication is allowed.

At the end of the study the patient card was collected by the Investigator or study staff and will be kept with source data.

Clinical Assessments Performed at Baseline

The following baseline assessments were conducted:

Demographic Data Collection

- sex

- race (categorised as: Caucasian, Asian, Afro-Caribbean and Other)
- date of birth
- height (cm)
- weight (kg)
- body mass index (kg/m^2)
- smoking/alcohol/drugs of abuse history/use.

Vital Signs

- systolic and diastolic blood pressure (after resting for 5 minutes; mm Hg);
- heart rate (radial pulse counted for 30 seconds after resting for 5 minutes; beats/minute)
- oral temperature (ºC).

Medical history and current status

- primary diagnosis: size of injury, location of injury
- medical history, including relevant allergies and surgeries, and current status.

Medication and therapy history

- current medication/therapy usage (including RICE)
- medication/ therapy (including RICE) taken in the previous 30 days was recorded.

Physical examination

- a standard physical examination.

Pregnancy testing

- women of child-bearing potential had urine pregnancy testing
- patients with a positive urine pregnancy test were not to be randomised

Study Specific assessments

- algometric measurement of the injured site was not to exceed 50% of the respective measurement on the contralateral site.
- absolute sensitivity to pain on the contralateral site of at least 2.5N/cm^2
- pain on movement at baseline of at least 50 mm (VAS) at the injured site.

All patients were randomised within 3 hours of sustaining the injury, baseline assessment as described above were carried out. Patients were randomised to treatment (if applicable). Each patient was issued with a diary, instructed how to complete, and a patient card to take home. After the clinical assessments were performed the Investigator applied the study medication according to the directions below:

Instructions for patch application:

1. Wipe the affected area clean and dry.
2. Remove one patch from the pouch.
3. Remove the central release liner marked.
4. Place the adhesive strip over the desired application area i.e. over the middle of the pain.
5. Carefully remove the release liner marked (2) and stretching slightly smooth the patch onto your skin.
6. Carefully remove the release liner marked (3) and stretching slightly smooth the patch onto your skin. When first applied the product may feel cool.

Patients returned to the study centre the following day (24 hours following first product application).

Next Visits/ Visits 2-4/ Assessment Days 1-3

Patients were asked about any changes to concomitant medication/therapy (including RICE) as well as rescue medication and any adverse events since their previous visit, any concomitant medication/therapy (including RICE) and any adverse events recorded in the diary by the patient was copied to the patient's case report form. The study specific assessments (algometric measurement and pain on movement) were carried out for all patients. Compliance was checked by the Investigator and a new patch applied.

Patients returned to the study centre for further assessments and further product application as per study assessment flow. The study specific procedures for follow up visits assessment Days 1-3 were exactly the same as those described for Assessment Day 0.

On Visit 4 (Assessment Day 3) the patient was provided with the trial medication for Assessment Day 4. Additionally, on Visit 2 and Visit 4 the patient and the investigator gave their global assessment of treatment efficacy and local tolerability:

Global Assessment of Treatment Efficacy

A global assessment of treatment efficacy was completed by patient and Investigator at Visits 2, 4 and 5 (Assessment Days 1, 3, and 5) and was classified according to the following 5-point Likert scale[27]

0 = excellent (hervorragend) – ideal response, virtually pain free,

1 = good (gut) – satisfactory effect with occasional episodes of pain,

2 = fair (mittelmäßig) – reasonable effect, but could be better,

3 = poor (gering) – some effect, but unsatisfactory,

4 = none (kein Effekt) – no good at all, ineffective.

The patient's global assessment of treatment efficacy was measured by the response to the following question:

"Wenn Sie bedenken, wie Ihre Verletzung Sie beeinträchtigt hat, wie beurteilen Sie den Behandlungserfolg heute?"

The English translation of which is "Considering all the ways your injury has affected you, how do you evaluate the effect of therapy today?"

The corresponding value was documented directly in the CRF by the Investigator.

The Investigator's global assessment of treatment efficacy was measured by the following question:

"Wenn Sie bedenken, wie die Verletzung Ihren Patienten beeinträchtigt hat, wie beurteilen Sie den Behandlungserfolg heute?"

The English translation of which is "Considering all the ways the injury has affected your patient, how do you consider the effect of therapy today?"

The corresponding value was documented in the CRF by the Investigator.

Global Assessment of Local Tolerability

A global assessment of local tolerability was completed by Investigator and patient according to the following scale[28, 29].

3=excellent (hervorragend)

2=good (gut)

1=fair (mittelmäßig)

(0=poor (gering/schlecht).

The patient's and Investigator's global assessment of local tolerability was measured by response to the following question:

"Wie würden Sie die lokale Verträglichkeit der Behandlung beschreiben?"

The English translation of which is "How do you consider the local tolerance of the treatment?"

The Investigator independently evaluated the local tolerability at the treated area after the removal of the plaster. The corresponding values were documented in the CRF. There was one scale for the patient and one scale for the Investigator.

Final Visit/ Visit 5/ Assessment Day 5

At the final Visit (Assessment Day 5) or earlier if the patient was withdrawn from the study; prematurely the following assessments were conducted:

Vital Signs

- blood pressure (after sitting for 5 minutes; mmHg)
- heart rate (radial pulse counted for 30 seconds after resting for 5 minutes; beats/minute)
- oral temperature (ºC).

Medication/Therapy

- changes to concomitant medication/therapy (including RICE) since last visit
- use of rescue medication.

Physical examination

- a standard physical examination.

Pregnancy testing

- women of child-bearing potential.

Study specific assessments

- algometric measurement
- pain on movement .
- global assessment of local tolerability (according to Visit 4)
- global assessment of treatment efficacy (according to Visit 4)

Adverse events

- any adverse events since last visit.

Used and unused trial medication, rescue medication, patient card and the patient diary were collected during this visit.

The flowchart of the study procedures is provided below.

Table 9.5 - 1 Flowchart of Study Procedures

Visit	**1**	**2**	**3**	**4**	**-**	**5**
Assessment Day	**0**	**1**	**2**	**3**	**4**	**5**
Hours since last visit	**0**	**24**	**24 (±1)**	**24 (±1)**	**24 (±1)**	**48 (±1)**
Time following 1st application	**-**	**24**	**48**	**72**	**96**	**120**
Demographic data	x	-	-	-	-	-
Previous diseases	x	-	-	-	-	-
Previous medication	x	-	-	-	-	-
Concomitant diseases	x	x	x	x	-	X
Concomitant medication	x	x	x	x	-	X
Concomitant therapy (including RICE)	x	x	x	x	-	X
Vital signs	x	-	-	-	-	X
Diagnosis	x	-	-	-	-	
General physical examination	x	-	-	-	-	X
Pregnancy test	x	-	-	-	-	X
Check of contraception	x	-	-	-	-	-
Inclusion criteria	x	-	-	-	-	-
Exclusion criteria	x	-	-	-	-	-
Randomisation	x	-	-	-	-	-
Pain on movement (VAS) recorded directly in CRF	x	x	x	x	-	X
Pressure algometry	x	x	x	x	-	X
Product application by study staff	x	x	x	x		
Product application by patient	-	-	-	-	x	-
Distribution of patient diary	x	-	-	-	-	-
Distribution of rescue medication	x	-	-	-	-	-
Check of consumption of rescue medication	-	x	x	x	-	X
Global assessment of local tolerability by patient and by Investigator	-	x	-	x	-	X
Global assessment of treatment efficacy by patient & Investigator	-	x		x	-	X
Review of patient diary and transfer relevant information to the CRF	-	x	x	x	-	X
Distribution of trial medication for Day 4	-	-	-	x	-	-
Collection of used and unused trial medication	-	-	-	-	-	X
Collection of patient diary and rescue medication	-	-	-	-	-	X
Compliance check	-	x	x	x	-	X
Adverse Events	-	x	x	x	-	X

Visit	**1**	**2**	**3**	**4**	**-**	**5**
Assessment Day	**0**	**1**	**2**	**3**	**4**	**5**
Hours since last visit	**0**	**24**	**24 (±1)**	**24 (±1)**	**24 (±1)**	**48 (±1)**
Time following 1st application	**-**	**24**	**48**	**72**	**96**	**120**
End of trial	-	-	-	-	-	x *

9.5.2 APPROPRIATENESS OF MEASUREMENTS

All efficacy variables were carefully selected with respect to available international guidelines and clinical relevance for this indication and have been used in several other recently published clinical trials.[12, 20, 34] The Visual Analogue Scale (VAS) is a well documented and internationally accepted method for the assessment of pain. The method is cited in the CPMP/EWP/612/00 Note for Guidance on the clinical investigation of medicinal products for treatment of Nociceptive Pain adopted November 2002.[23]

The documentation of AEs and the investigation of vital signs, physical examinations, as well the global assessment of tolerability by investigators and patients were the usual appropriate measurements for the assessment of safety and tolerability.

9.5.3 PRIMARY EFFICACY VARIABLE

The primary endpoint was the area under the VAS assessment of pain on movement curve over Days 0-3 (VAS $AUC_{0\text{-}3d}$). The area under the curve was calculated using the trapezoidal rule.

9.5.4 DRUG CONCENTRATION MEASUREMENTS

Drug concentrations were not measured in this study.

9.6 DATA QUALITY ASSURANCE

CRAs were trained on a regularly basis by the Clinical Project Coordinator (7 CRA-Trainings in total). Monitoring visits were performed approximately every four weeks by the CRAs and furthermore, irregular Co-monitoring visits were performed by the Clinical Project Manager (RB) as well as the Clinical Project Co-ordinator.

9.7 STATISTICAL METHODS PLANNED IN THE PROTOCOL AND DETERMINATION OF SAMPLE SIZE

9.7.1 STATISTICAL AND ANALYTICAL PLANS

A copy of the final Statistical Analysis Plan is presented as Appendix 16.1.9.

The statistical analysis was undertaken in collaboration with CRM Biometrics (CRMB).

All data recorded for all consented patients were listed in the appendices to the study report and summarised appropriately.

The following analysis populations were used for analysis of study data:

Safety population: all patients who were randomised to the study and received at least one dose of study medication. This population was used for summaries of demography and safety.

Full Analysis Set (FAS)/ Intention to treat (ITT) population: all patients who were randomised to the study and received at least one dose of study medication and had efficacy data for at least one post-baseline assessments. Any patients with treatment administration errors were analysed according to the treatment to which they were randomised. This population was used for summaries of efficacy data and was the primary analysis population in this superiority trial.

Per protocol (PP) population: all patients who were randomised to the study, satisfy all of the inclusion/exclusion criteria, received the correct study medication (as randomised) and had efficacy data for all assessments, and had no major protocol violations. Only the primary efficacy endpoint, the area under the VAS assessment of pain on movement curve over Days 0-3 ($AUC_{0\text{-}3d}$), was planned to be analysed using this study population. However, according to the decisions of the blind review meeting between CRM and RB, the FAS/ITT population and the PP population were identical.

Demographic and baseline characteristics were summarised for the Safety population, overall and by treatment group. Continuous variables were summarised using the mean, standard deviation, median, minimum, maximum values and lower and upper 95% confidence limits for the mean for the population were presented. Categorical variables were summarised using the cell frequencies and percentage of patients in each demographic category.

Concomitant medications were coded using the ATC level 2 categories from the WHO dictionary.

The primary endpoint was the area under the VAS assessment of pain on movement curve over Days 0-3 (VAS AUC_{0-3d}). The area under the curve was calculated using the trapezoidal rule.

The secondary efficacy variables were:

Area under the VAS assessment of pain on movement curve over 0-12 hours (VAS AUC_{0-12h}).

VAS assessment of pain on movement at 12 hours.

Area under the VAS assessment of pain on movement curve over 0-24 hours (VAS AUC_{0-24h}).

Tenderness/algometry assessment at 24 hours.

VAS assessment of pain on movement at 24 hours.

Area under the tenderness/algometry assessment curve over Days 0-5 (AUC_{0-5d})

AUCs over Days 0-3 and Days 0-5 for the ratio of the tenderness/algometry assessments, injured/contralateral sites (RATIO AUC_{0-3d} and RATIO AUC_{0-5d}).

The time taken to reach the contralateral (healthy) values of tenderness (time to resolution of pain).

Use of rescue medication and time of use of rescue medication.

Global assessment of treatment efficacy by patients and Investigators using a 5-point scale (0 = excellent, 1 = good, 2 = fair, 3 = poor and 4 = none) assessments will be made on Assessment Days 1, 3 and 5 (Final Visit), respectively.

Safety – was evaluated by monitoring general physical examinations, vital signs as well as the occurrence of adverse events. In addition patients and Investigators made a global assessment of local tolerability of the patch under double blind conditions using a 4-point scale (3 = excellent, 2 = good, 1 = fair and 0 = poor) assessments will be made on Assessment Days 1, 3 and 5 (Final Visit), respectively.

All statistical tests performed were 2-tailed with significance at the 5% significance level, except the primary variable (see Section 9.8.2) which was analysed at the 1% level. The null hypothesis at all times was the equality of the treatments being compared.

Normality assumptions were evaluated by an examination of the residual plots and the Shapiro-Wilk test of normality. Depending on the degree of departure from these assumptions, alternative nonparametric approaches could be used for supportive purposes.

All area under curve analyses were based on actual rather than scheduled timings and were calculated using the trapezoidal rule.

For all non-AUC analyses, missing data were replaced using the last observation carried forward (LOCF) approach.

The primary efficacy endpoint, the area under the VAS assessment of pain on movement curve over Days 0-3 (VAS AUC_{0-3d}), was compared between treatment groups using Analysis-of-covariance (ANCOVA) with terms in the model for treatment group, total sum of RICE duration, and baseline VAS assessment of pain on movement. Treatment group differences were estimated using the least squares (LS) means and the mean square error from the ANCOVA.

The VAS assessments of pain on movement at 12 and 24 hours were compared between treatment groups using ANCOVA with terms in the model for treatment group, baseline tenderness/algometry assessment, total sum of RICE duration, and baseline VAS assessment of pain on movement.

The area under the tenderness/algometry assessment curve over Days 0-3 (AUC_{0-3d}), Days 0-5 (AUC_{0-5d}), the tenderness/algometry assessment at 24 hours and the AUCs over Days 0 to 3 and Days 0 to 5 for the ratio of the tenderness/algometry assessments, injured/contralateral sites (RATIO AUC_{0-3d} and RATIO AUC_{0-5d}), were compared between treatment groups using an ANCOVA model with terms in the model for treatment group, total sum of RICE duration, and the relevant baseline algometry assessment.

The time to first use of rescue medication was compared between treatment groups using survival analysis methods including Kaplan-Meier estimates and the log-rank test.

Use of rescue medication was compared between treatment groups using binomial logistic regression with terms in the model for treatment group and baseline tenderness/algometry assessment. The patients and Investigators global efficacy assessments were compared between treatment groups using ordinal logistic regression with terms in the model for treatment group and baseline tenderness/algometry assessment.

All adverse events were listed and tabulated by treatment, severity, relationship to therapy and Primary System Organ Class according to version 13.1 of MedDRA. In counting the number of events reported, a continuous event, i.e. an event reported more than once and which did not cease, was counted only once; non-continuous adverse events reported several times by the same patient were counted as multiple events. Events present immediately prior to the initial study medication dose that did not worsen in severity were not included. Events that occurred more than 10 hours after the last study medication dose were assigned to the post-treatment phase.

The incidence of adverse events (number and percent of patients reporting the adverse event at least once during the study) was summarised for all adverse events, by Investigator attribution of relationship to study medication and by severity. The incidence of adverse events was compared between treatment groups using Fisher's exact test for all adverse events, for those adverse events classified by the Investigator as probably or possibly related to study medication and for severe adverse events.

Summary statistics for the absolute vital sign value and the changes from baseline were presented using n, mean, standard deviation, median, minimum, maximum and lower and upper 95% confidence limits for the mean.

If appropriate the incidence of clinically meaningful changes, as designated by the Investigator, in blood pressure, heart rate and oral temperature were summarised.

The patients and Investigators global assessments of local tolerability of the patch, assessed under double blind conditions using a 4-point scale (3 = excellent, 2 = good, 1 = fair and 0 = poor) at Visit 4 and at the end of the study (Visit 5) were summarised by treatment group.

9.7.2 DETERMINATION OF SAMPLE SIZE

In a similar study in acute sports related traumatic blunt soft tissue injury/contusion using a diclofenac patch reported by Predel and co-workers[12], the mean (SD) scores for the absolute changes of pain on motion (mm VAS) over 3 days for an active patch (diclofenac) and for placebo were -46.62 (22.13) and -23.02 (14.47), respectively. Assuming that the efficacy of a 200 mg ibuprofen patch application every 24 hours would be only 50% of that of the 140 mg diclofenac patch used in the Predel study and that the difference in mean between active and placebo in the current study will therefore be only 50% of that shown in the previous study, and assuming also that the between patient variability would be of a similar magnitude to that in the previous study, then it was determine that a study with 60 completed patients in each treatment group would provide approximately 80% power to demonstrate that the topical ibuprofen patch provides statistically significantly greater pain relief in comparison to placebo, using a two-sided paired t-test at the 1% significance level.

9.8 CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSIS

9.8.1 CHANGES IN THE CONDUCT OF THE STUDY

No changes were made in the conduct of the study.

9.8.2 CHANGES IN THE PLANNED STATISTICAL ANALYSIS OF THE STUDY

In the confirmatory part of the analysis the level of significance for the evaluation of the primary variable was stipulated to α=1% ($p<0.01$) in the Statistical Analysis Plan before database lock.

Following database lock during data analysis it was noticed that study centre had being omitted in error from all planned analysis in the statistical analysis plan. As this was a multi-centre study, and following ICH E9 guidelines it was decided to include centre as a fixed effect in all primary and secondary analyses where possible. For ANOVA and logistic regression models, centre was added to the model. Log rank tests were stratified by centre. In all ANOVA and Logistic Regression models the centre x treatment interaction effect was also investigated as an exploratory analysis for each outcome. For VAS and algometry outcomes, the qualitative interaction was also assed using a one-sided Gail Simon test[39] (see Section 16.1.9, Appendix 16.1.9.34 for SAS code) to test the hypothesis that the outcome favoured the active treatment across centres.

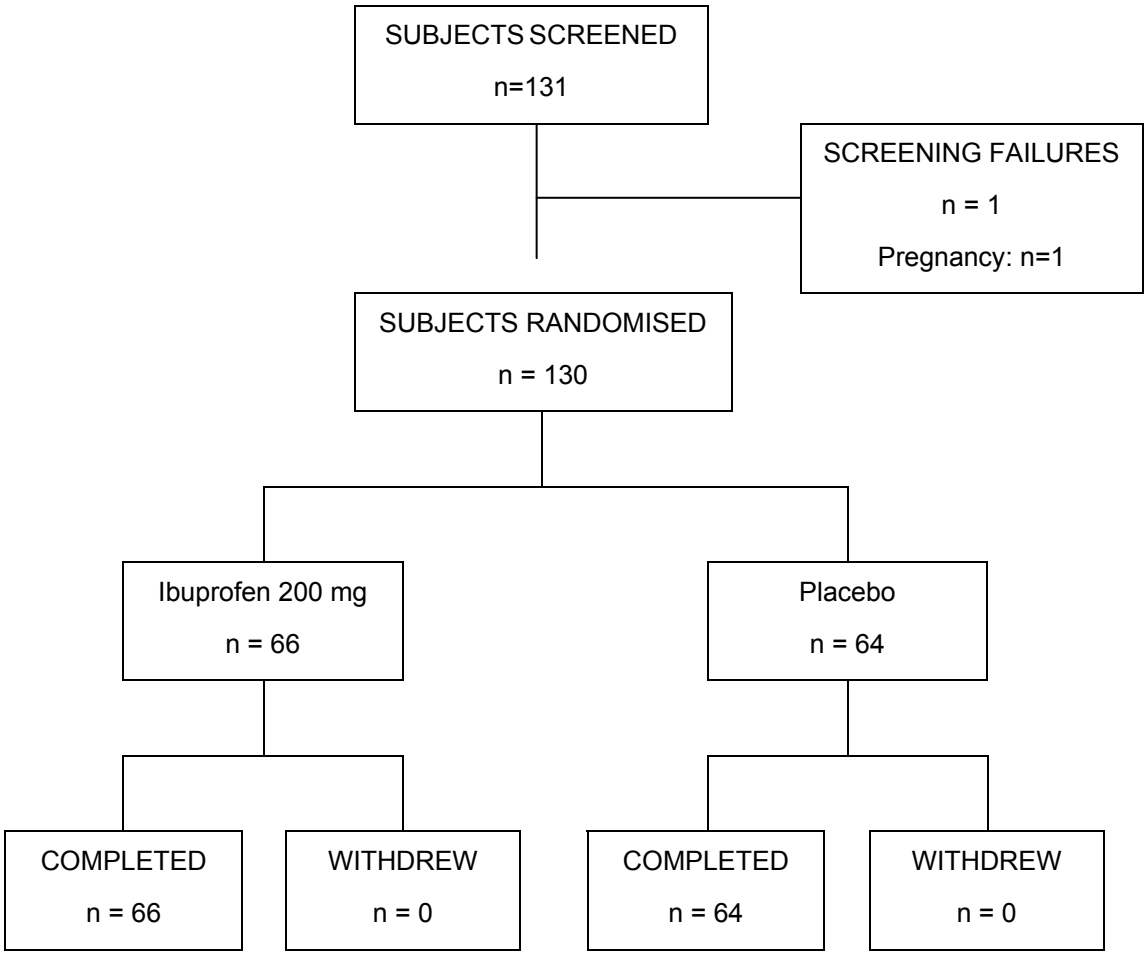
10 STUDY SUBJECTS

10.1 DISPOSITION OF SUBJECTS

In total, 130 male or female patients with acute sports-related traumatic blunt soft tissue injury/contusion were enrolled from 4 study centres in Germany between July 2010 (first patient in) and December 2010 (last patient out). All 130 patients were randomly assigned to double-blind treatment (Ibuprofen 200 mg: n=66; placebo: n=64). All randomized patients had given their written informed consent for the participation in the clinical trial (see Listing 16.2. 15). None of the patients terminated the clinical trial prematurely.

The following figure summarizes the patients' disposition.

Figure 10.1 - 1 Disposition of Subjects



10.2 PROTOCOL DEVIATIONS

Three patients (Numbers 78, 80, and 195) showed time deviations between injury and inclusion of more than 3 hours. During a blind review meeting between CRM and RB, it was agreed that these time deviations were negligible and did not require further action.

No violations of exclusion criteria regarding past and concomitant diseases were detected. All previous and concomitant medications were reviewed by RB in order to find possible non-authorized medications described as exclusion criteria. However, no violations of such exclusion criteria were detected.

For patients 122-129, a VAS value after 88 hours rather than 96 hours was available. This resulted from a typing error in the documentation scheme for diary entries on page 5 of the patient diary (Final version 24 March 2010, rev. 10 May 2010), which was used at the beginning of the trial. In line 7 of the table of the documentation scheme wrong times were given and therefore the entries were done after 88 hours. After noticing this mistake, a Non-substantial Amendment No. 1 was created to correct the printing error in the diary.

AUC was calculated with planned time points. For patients Nos. 122 to 129 the VAS value after 88 hours was used in place of the missing value after 96 hours.

In the blind review meeting all protocol deviations were assessed as minor ones. Therefore, no patient was excluded from the efficacy analysis.

A listing of individual patients who deviated from the Protocol is presented in Appendix 16.2.2.

11 EFFICACY EVALUATION

11.1 DATA SETS ANALYSED

All enrolled and randomised patients were assessed with regard to efficacy in the Full Analysis Set (FAS). No patient was excluded from the analysis. Therefore, the FAS population and the per protocol population (PP) were identical in this clinical trial.

The strategy for the inclusion/exclusion criteria for each of the data sets analysed was included in the statistical analysis plan for the study and finalised following discussions of evaluability held after the database had been locked and prior to the blind being broken.

A FAS/intention-to-treat analysis, using all randomised patients with any on-treatment data has been conducted and the results are presented below. The outcome of this analysis is the same as for the per-Protocol analysis.

11.2 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

11.2.1 DEMOGRAPHICS

Full summaries relating to patient demographics, lifestyle and injuries are provided in Section 14.1, Tables 14.1.1 to 14.1.26. The by-patient displays of the demographic data are presented in Appendix 16.2.4.

The two treatment groups were relatively well balanced regarding demographic characteristics, although in the Ibuprofen 200 mg group, the patients were on average four years older than the patients in the placebo group (as shown in Table 11.2.1).

Table 11.2 - 1 Demographics (FAS/PP)

			Ibuprofen 200 mg (n=66)	**Placebo (n=64)**	**Overall (n=130)**
Sex	n (%)	male female	44 (66.7) 22 (33.3)	44 (68.8) 20 (31.3)	88 (67.7) 42 (32.3)
Ethnic origin	n (%)	Caucasian other	65 (98.5) 1 (1.5)	64 (100.0) 0 (0.0)	129 (99.2) 1 (0.8)
Age (yrs)	Mean SD Median		34.09 11.72 29.50	30.08 11.09 26.00	32.12 11.55 29.00
Height (cm)	Mean SD Median		178.47 9.98 178.00	178.78 9.71 178.00	178.62 9.81 178.00
Weight (kg)	Mean SD Median		79.68 14.26 78.00	80.75 17.06 79.00	80.21 15.65 78.00
BMI (kg/m^2)	Mean SD Median		24.95 3.49 24.00	25.19 4.57 24.00	25.07 4.04 24.00

Source: Table 14.1.2, Table 14.1.3, Table 14.1.4, Table 14.1.5, Table 14.1.6, Table 14.1.7

Table 11.2.2 presents information regarding demographic variables by centre.

In Centre 4 only male patients were enrolled and in addition patients in the active treatment group were on average approximately 10 years older than the patients in the placebo group.

On average, the male patients in Centre 4 were taller and heavier than patients at the other centres. The majority of patients in Centre 2 were also males.

Table 11.2 - 2 Demographics by centre (FAS/PP)

			Centre 1		Centre 2		Centre 3		Centre 4	
			Ibuprofen 20 mg	**Placebo**	**Ibuprofen 20 mg**	**Placebo**	**Ibuprofen 20 mg**	**Placebo**	**Ibuprofen 20 mg**	**Placebo**
Sex	male	n (%)	7 (46.7)	9 (60.0)	12 (75.0)	12 (80.0)	11 (52.4)	9 (45.0)	14 (100.0)	14 (100.0)
	female	n (%)	8 (53.3)	6 (40.0)	4 (25.0)	3 (20.0)	10 (47.6)	11 (55.0)	0 (0.0)	0 (0.0)
Ethnic origin	Caucasian	n (%)	14 (93.3)	15 (100.0)	16 (100.0)	15 (100.0)	21 (100.0)	20 (100.0)	14 (100.0)	14 (100.0)
	Afro-Caribbean	n (%)	1 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Age (years)		n Mean SD	15 34.37 11.92	15 30.07 12.14	16 34.25 10.95	15 34.40 11.71	21 34.71 13.33	20 31.75 11.64	14 32.29 10.84	14 23.07 3.56
Height (cm)		n Mean SD	15 173.60 9.85	15 179.53 10.65	16 178.13 9.59	15 176.27 8.50	21 178.57 10.46	20 174.95 8.68	14 183.93 7.73	14 186.14 7.62
Weight (kg)		n Mean SD	15 76.20 9.82	15 85.27 21.80	16 85.06 17.69	15 84.13 17.02	21 71.52 11.33	20 69.95 13.75	14 89.50 9.68	14 87.71 6.41
BMI (kg/m²)		n Mean SD	15 25.33 2.74	15 26.20 5.92	16 26.69 4.21	15 27.33 4.98	21 22.33 1.74	20 22.85 3.54	14 26.50 3.18	14 25.14 1.92

Source: Table 14.1.9, Table 14.1.10, Table 14.1.11, Table 14.1.12, Table 14.1.13, Table 14.1.14

Tables 11.2.3 and 11.2.4 summarise information regarding the history and current use of cigarettes, alcohol, and drugs. There were slightly more smokers in the Ibuprofen 200mg group compared to the placebo group.

Table 11.2 - 3 History and current use of cigarettes, alcohol, and drugs (FAS/PP)

			Ibuprofen 200 mg (n=66)	Placebo (n=64)	Overall (n=130)
Smoker	n (%)	yes no	18 (27.3) 48 (72.7)	12 (18.8) 52 (81.3)	30 (23.1) 100 (76.9)
Number of cigarettes/day	n (%)	≤ 10 11-30 >30	10 (15.2) 6 (9.1) 2 (3.0)	5 (7.8) 6 (9.4) 1 (1.6)	15 (11.5) 12 (9.2) 3 (2.3)
Ex-smoker	n (%)	yes	8 (12.1)	5 (7.8)	13 (10.0)
Consumption of relevant amounts of alcohol	n (%)	no	66 (100.0)	64 (100.0)	130 (100.0)
Alcohol abuse in past year	n (%)	yes, once in a while yes, regularly	41 (62.1) 2 (3.0)	37 (57.8) 2 (3.1)	78 (60.0) 4 (3.1)
Drug abuse in past year	n (%)	no	66 (100.0)	63 (98.4)*	129 (99.2)

* missing data n = 1

Source: Table 14.1.8

Table 11.2 - 4 History and current use of cigarettes, alcohol, and drugs by centre (FAS/PP)

			Centre 1		Centre 2		Centre 3		Centre 4	
			Ibuprofen 20 mg	Placebo	Ibuprofen 20 mg	Placebo	Ibuprofen 20 mg	Placebo	Ibuprofen 20 mg	Placebo
Smoker	n (%)	yes no	6 (40.0) 9 (60.0)	1 (6.7) 14 (93.3)	8 (50.0) 8 (50.0)	7 (46.7) 8 (53.3)	1 (4.8) 20 (95.2)	3 (15.0) 17 (85.0)	3 (21.4) 11 (78.6)	1 (7.1) 13 (92.9)
Number of cigarettes per day	n (%)	≤10 11-30 >30	4 (26.7) 2 (13.3) 0 (0.0)	1 (6.7) 0 (0.0) 0 (0.0)	2 (12.5) 4 (25.0) 2 (12.5)	1 (6.7) 5 (33.3) 1 (6.7)	1 (4.8) 0 (0.0) 0 (0.0)	2 (10.0) 1 (5.0) 0 (0.0)	3 (21.4) 0 (0.0) 0 (0.0)	1 (7.1) 0 (0.0) 0 (0.0)
Ex-smoker	n (%)	yes	5 (33.3)	3 (20.0)	1 (6.3)	1 (6.7)	2 (9.5)	1 (5.0)	0 (0.0)	0 (0.0)
Consump-tion of relevant amounts of alcohol	n (%)	no	15 (100.0)	15 (100.0)	16 (100.0)	15 (100.0)	21 (100.0)	20 (100.0)	14 (100.0)	14 (100.0)
Alcohol abuse in past year	n (%)	yes, once in a while yes, regularly	10 (66.7) 2 (13.3)	10 (66.7) 2 (13.3)	13 (81.3) 0 (0.0)	14 (93.3) 0 (0.0)	4 (19.0) 0 (0.0)	2 (10.0) 0 (0.0)	14 (100.0) 0 (0.0)	11 (78.6) 0 (0.0)
Drug abuse in past year	n (%)	no	15 (100.0)	14 (93.3)*	16 (100.0)	15 (100.0)	21 (100.0)	20 (100.0)	14 (100.0)	14 (100.0)

* missing data n = 1

Source: Table 14.1.15

Table 11.2.5 summarises information regarding baseline characteristics of the injury. The baseline characteristics of the injury were relatively well balanced between the two treatment groups.

Table 11.2 - 5 Baseline characteristics of injury (FAS/PP)

		Ibuprofen 200 mg (n=66)	Placebo (n=64)	Overall (n=130)
VAS (mm)	Mean	74.21	73.98	74.10
	SD	11.43	10.24	10.82
	Median	73.50	73.50	73.50
Pressure algometry injured site (N/cm^2)	Mean	1.37	1.46	1.42
	SD	0.86	0.96	0.91
	Median	1.10	1.10	1.10
Pressure algometry contralateral site (N/cm^2)	Mean	4.73	4.70	4.71
	SD	1.47	1.66	1.56
	Median	4.20	4.10	4.20
Tenderness ratio (injured/contralateral)	Mean	0.28	0.29	0.28
	SD	0.10	0.11	0.10
	Median	0.27	0.27	0.27
Time from injury to first treatment (min)	Mean	100.09	98.09	99.11
	SD	43.44	45.74	44.42
	Median	105.00	96.50	100.00
Size of injury/contusion (cm^2)	Mean	51.05	46.48	48.80
	SD	23.43	19.58	21.66
	Median	45.00	40.00	40.00

Source: Table 14.1.17, Table 14.1.22, Table 14.2.43, Table 14.2.65, Table 14.2.70, Table 14.2.71

However, there were differences between the centres regarding these variables (see Table 11.2.6). In Centre 4, the baseline values of the pressure algometry at the injured and the contralateral site and the corresponding tenderness ratios were on average much higher than in the other centres. The average size of the contusion was observed to be smallest at centre 1 and largest at centre 3.

Table 11.2 - 6 Baseline characteristics of injury by centre (FAS/PP)

		Centre 1		Centre 2		Centre 3		Centre 4	
		Ibuprofen 200 mg (n=15)	**Placebo (n=15)**	**Ibuprofen 200 mg (n=16)**	**Placebo (n=15)**	**Ibuprofen 200 mg (n=21)**	**Placebo (n=20)**	**Ibuprofen 200 mg (n=14)**	**Placebo (n=14)**
VAS (mm)	Mean	88.07	86.73	73.19	73.60	66.86	67.50	71.57	70.00
	SD	7.18	7.86	10.19	8.12	8.88	6.06	6.25	6.87
	Median	90.00	87.00	74.50	75.00	67.00	67.50	72.00	70.00
Pressure algometry at injured site (N/cm^2)	Mean	0.85	0.87	0.81	0.87	1.27	1.21	2.74	3.11
	SD	0.27	0.22	0.28	0.31	0.33	0.37	0.78	0.55
	Median	0.80	0.90	0.80	0.80	1.20	1.10	2.85	3.00
Pressure algometry at contralateral site (N/cm^2)	Mean	4.28	4.01	4.01	4.00	4.07	3.87	7.01	7.35
	SD	0.58	0.97	0.66	0.63	0.78	0.87	1.33	1.01
	Median	4.10	3.60	4.05	4.00	4.00	3.80	7.05	7.70
Tenderness ratio	Mean	0.20	0.22	0.20	0.21	0.32	0.32	0.38	0.42
	SD	0.06	0.07	0.04	0.06	0.08	0.09	0.06	0.04
	Median	0.18	0.23	0.21	0.22	0.32	0.32	0.40	0.43
Time from injury to first treatment (min)	Mean	98.00	120.33	146.56	124.00	79.29	80.00	80.43	72.36
	SD	34.27	34.61	24.75	49.03	37.02	30.95	39.70	47.91
	Median	95.00	135.00	152.50	135.00	75.00	80.00	65.00	72.50
Size of injury/contusion (cm^2)	Mean	33.07	33.67	48.44	42.33	64.52	55.25	53.07	52.14
	SD	6.08	13.37	15.02	11.00	27.11	22.74	25.19	20.45
	Median	30.00	30.00	45.00	40.00	60.00	50.00	49.00	47.50

Source: Table 14.1.19, Table 14.1.23, Table 14.2.24, Table 14.2.54, Table 14.2.76

Table 11.2.7 summarises injury location; the most common locations of the injury were “upper leg” (23.1 %), “upper arm” (20.8 %), and “lower leg” (18.5 %) in both treatment groups.

There were no marked differences between the two treatment groups with regard to the location of the injury.

Table 11.2 - 7 Location of injury (FAS/PP)

		Ibuprofen 200 mg (n=66)	Placebo (n=64)	Overall (n=130)
Feet	n (%)	1 (1.5)	4 (6.3)	5 (3.8)
Lower leg	n (%)	10 (15.2)	14 (21.9)	24 (18.5)
Knee	n (%)	6 (9.1)	2 (3.1)	8 (6.2)
Upper leg	n (%)	14 (21.2)	16 (25.0)	30 (23.1)
Hip	n (%)	4 (6.1)	3 (4.7)	7 (5.4)
Upper back	n (%)	1 (1.5)	0 (0.0)	1 (0.8)
Upper arm	n (%)	15 (22.7)	12 (18.8)	27 (20.8)
Forearm	n (%)	4 (6.1)	5 (7.8)	9 (6.9)
Chest	n (%)	3 (4.5)	3 (4.7)	6 (4.6)
Low back	n (%)	1 (1.5)	2 (3.1)	3 (2.3)
Shoulder	n (%)	7 (10.6)	3 (4.7)	10 (7.7)

Source: Table 14.1.24

Tables 11.2.8 and 11.2.9 show the location of injury by centre. Differences were noted between the four centres with regard to the locations of the injury. In Centre 4, no patients with injuries at the upper extremities were enrolled.

Table 11.2 - 8 Location of injury by centre (FAS/PP)

		Centre 1		Centre 2		Centre 3		Centre 4	
		Ibuprofen 200 mg (n=15)	Placebo (n=15)	Ibuprofen 200 mg (n=16)	Placebo (n=15)	Ibuprofen 200 mg (n=21)	Placebo (n=20)	Ibuprofen 200 mg (n=14)	Placebo (n=14)
Feet	n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (15.0)	1 (7.1)	1 (7.1)
Lower leg	n (%)	3 (20.0)	3 (20.0)	1 (6.3)	4 (26.7)	6 (28.6)	5 (25.0)	0 (0.0)	2 (14.3)
Knee	n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (9.5)	2 (10.0)	4 (28.6)	0 (0.0)
Upper leg	n (%)	1 (6.7)	1 (6.7)	6 (37.5)	6 (40.0)	3 (14.3)	2 (10.0)	4 (28.6)	7 (50.0)
Hip	n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.8)	2 (10.0)	3 (21.4)	1 (7.1)
Upper back	n (%)	1 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Upper arm	n (%)	7 (46.7)	6 (40.0)	6 (37.5)	4 (26.7)	2 (9.5)	2 (10.0)	0 (0.0)	0 (0.0)
Forearm	n (%)	2 (13.3)	4 (26.7)	0 (0.0)	0 (0.0)	2 (9.5)	1 (5.0)	0 (0.0)	0 (0.0)
Chest	n (%)	0 (0.0)	0 (0.0)	1 (6.3)	0 (0.0)	1 (4.8)	1 (5.0)	1 (7.1)	2 (14.3)
Low back	n (%)	0 (0.0)	1 (6.7)	0 (0.0)	0 (0.0)	1 (4.8)	1 (5.0)	0 (0.0)	0 (0.0)
Shoulder	n (%)	1 (6.7)	0 (0.0)	2 (12.5)	1 (6.7)	3 (14.3)	1 (5.0)	1 (7.1)	1 (7.1)

Source: Table 14.1.25

Table 11.2 - 9 Location categories of injury by centre (FAS/PP)

		Centre							
		1		2		3		4	
		Ibuprofen 200 mg (n=15)	Placebo (n=15)	Ibuprofen 200 mg (n=16)	Placebo (n=15)	Ibuprofen 200 mg (n=21)	Placebo (n=20)	Ibuprofen 200 mg (n=14)	Placebo (n=14)
Lower extremities	n (%)	4 (26.7)	4 (26.7)	7 (43.8)	10 (66.7)	11 (52.4)	12 (60.0)	9 (64.3)	10 (71.4)
	Overall n (%)	8 (26.7)		17 (54.8)		23 (56.1)		19 (67.9)	
Upper extremities	n (%)	9 (60.0)	10 (66.7)	6 (37.5)	4 (26.7)	4 (19.0)	3 (15.0)	0 (0.0)	0 (0.0)
	Overall n (%)	19 (63.3)		10 (32.3)		7 (17.0)		0 (0.0)	
Other	n (%)	2 (13.3)	1 (6.7)	3 (18.8)	1 (6.7)	6 (28.6)	5 (25.0)	5 (35.7)	4 (28.6)
	Overall n (%)	3 (10.0)		4 (12.9)		11 (26.8)		9 (32.1)	

11.2.2 PRIOR AND CONCOMITANT MEDICATION

Descriptive summaries regarding the prior and concomitant medications are presented in Tables 14.1.27 to Table 14.1.40 in Section 14.1. The corresponding casewise listings are provided in Listings 16.2.25 to 16.2.28 in Appendix 16.2.4.

Prior and/or concomitant medications were more prevalent in the Ibuprofen 200 mg group than in the placebo group (see Table 11.2.10 below).

Table 11.2 - 10 Frequency of prior and concomitant medications (FAS/PP)

			Ibuprofen 200 mg (n=66)	Placebo (n=64)
Prior medications	Number of prior medications	n	9	2
	Number of patients with prior medications	n	6	2
	% Patients with prior medications	%	9.1	3.1
Prior and concomitant medications	Number of prior and concomitant medications	n	37	21
	Number of patients with prior and concomitant medications	n	26	16
	% Patients with prior and concomitant medications	%	39.4	25.0
Concomitant medications	Number of concomitant medications	n	20	11
	Number of patients with concomitant medications	n	11	4
	% Patients with concomitant medications	%	16.7	6.3

Source: Table 14.1. 30, Table 14.1. 31, Table 14.1. 32

11.2.3 PREVIOUS AND CONCOMITANT DISEASES

Tables 14.1.41 to 14.1.50 in Section 14.1 provide summaries of previous and concomitant diseases. The corresponding listings are provided in Listings 16.2.20 to 16.2.24 in Appendix 16.2.4.

There were slightly more patients with documented previous diseases in the Ibuprofen 200mg group compared to placebo (Ibuprofen 200 mg: n=24, placebo: n=5).

The number of concomitant diseases was similar in both treatment groups (Ibuprofen 200 mg: n=44, placebo: n=48). The most common concomitant diseases are presented by preferred terms in Table 11.2.11.

Table 11.2 - 11 Most common concomitant diseases by preferred term (FAS/PP)

		Ibuprofen 200 mg (n=66)	Placebo (n=64)
Any concomitant disease	n (%)	44 (66.6)	48 (75.0)
Seasonal allergy	n (%)	9 (13.6)	3 (4.7)
Hypercholesterolaemia	n (%)	4 (6.1)	3 (4.7)
Hypertension	n (%)	2 (3.0)	2 (3.1)
Food allergy	n (%)	3 (4.5)	0 (0.0)
Hypersensitivity	n (%)	3 (4.5)	0 (0.0)
Drug hypersensitivity	n (%)	2 (3.0)	1 (1.6)

Source: Table 14.1.45

Table 11.2.12 shows the frequency of all concomitant diseases by System Organ Classes (SOC). Immune system disorders were more often observed in the Ibuprofen group, whereas musculoskeletal and connective tissue disorders were more often observed in the placebo group.

Table 11.2 - 12 Concomitant diseases by SOC (FAS/PP)

		Ibuprofen 200 mg (n=66)	Placebo (n=64)
Immune system disorders	n (%)	20 (30.3)	5 (7.8)
Musculoskeletal and connective tissue disorders	n (%)	4 (6.1)	10 (15.6)
Metabolism and nutrition disorders	n (%)	7 (10.6)	7 (10.9)
Respiratory, thoracic and mediastinal disorders	n (%)	2 (3.0)	5 (7.8)
Infections and infestations	n (%)	2 (3.0)	4 (6.3)
Cardiac disorders	n (%)	2 (3.0)	4 (6.3)
Vascular disorders	n (%)	2 (3.0)	2 (3.1)
Surgical and medical procedures	n (%)	0 (0.0)	2 (3.1)
Injury, poisoning and procedural complications	n (%)	2 (3.0)	0 (0.0)
Hepatobiliary disorders	n (%)	2 (3.0)	0 (0.0)
Blood and lymphatic system disorders	n (%)	2 (3.0)	0 (0.0)
Nervous system disorders	n (%)	0 (0.0)	2 (3.1)
Gastrointestinal disorders	n (%)	1 (1.5)	1 (1.6)
Psychiatric disorders	n (%)	0 (0.0)	1 (1.6)
Skin and subcutaneous tissue disorders	n (%)	1 (1.5)	0 (0.0)
Renal and urinary disorders	n (%)	1 (1.5)	0 (0.0)
Endocrine disorders	n (%)	0 (0.0)	1 (1.6)

Source: Table 14.1.46

11.3 MEASUREMENTS OF TREATMENT COMPLIANCE

According to the trial protocol, compliance was checked at the day 1, 2, 3 and 5 assessments. If a patient did not comply with the treatment schedule, it was deemed a protocol deviation and was to be documented appropriately. If considered appropriate by both the Investigator and the sponsor the patient was to continue in the study. The compliance data did not reveal any significant deviations and all patients continued with the study.

Detachment of the patches was observed only in rare cases. There were no marked differences between treatments regarding the frequency of detached patches (see Table 11.3.1).

Table 11.3 - 1 Detachment of patches (FAS/PP)

Day		Ibuprofen 200 mg (n=66)	Placebo (n=64)
1	n (%)	1 (1.5)	4 (6.3)
2	n (%)	3 (4.5)	3 (4.7)
3	n (%)	2 (3.0)	2 (3.1)
5	n (%)	0 (0.0)	4 (6.3)

Source: Table 14.1.52

Table 11.3.2 below shows that the average number of the patches returned was similar in both treatment groups.

Table 11.3 - 2 Number of returned patches (FAS/PP)

	Ibuprofen 200 mg (n=66)	Placebo (n=64)
Mean	4.92	4.88
SD	0.54	0.60
Median	5.00	5.00

Source: Table 14.1.53

More information regarding detached and returned patches is provided in Tables 14.1.52 and 14.1.53 in Section 14.1. The corresponding listings are presented in Appendix 16.2.5.

11.4 EFFICACY RESULTS

11.4.1 ANALYSIS OF EFFICACY

11.4.1.1 PRIMARY VARIABLE - VAS AUC_{0-3D}

The primary efficacy variable was the area under the VAS assessment of pain on movement curve over Days 0-3, VAS AUC_{0-3d}, (Visits 1 to 4). Missing VAS assessment of pain on movement values between two time points were linearly interpolated. If last values were missing, missing data were replaced using the last-observation-carried-forward (LOCF) approach. Case-wise listings are presented in Section 16.2.6.

The VAS AUC_{0-3d} was significantly lower (less pain) for Ibuprofen 200 mg compared to placebo (ANCOVA: p=0.0011) at the two-tailed significance level of 1 %. The difference between the least square means of VAS AUC_{0-3d} (Ibuprofen 200 mg – Placebo) was -693.78 mm*h (see Table 11.4.1, Section 14.2, Table 14.2.1 and Section 16.1.9, Appendix 16.1.9.1).

Table 11.4 - 1 VAS AUC0-3d (FAS/PP)

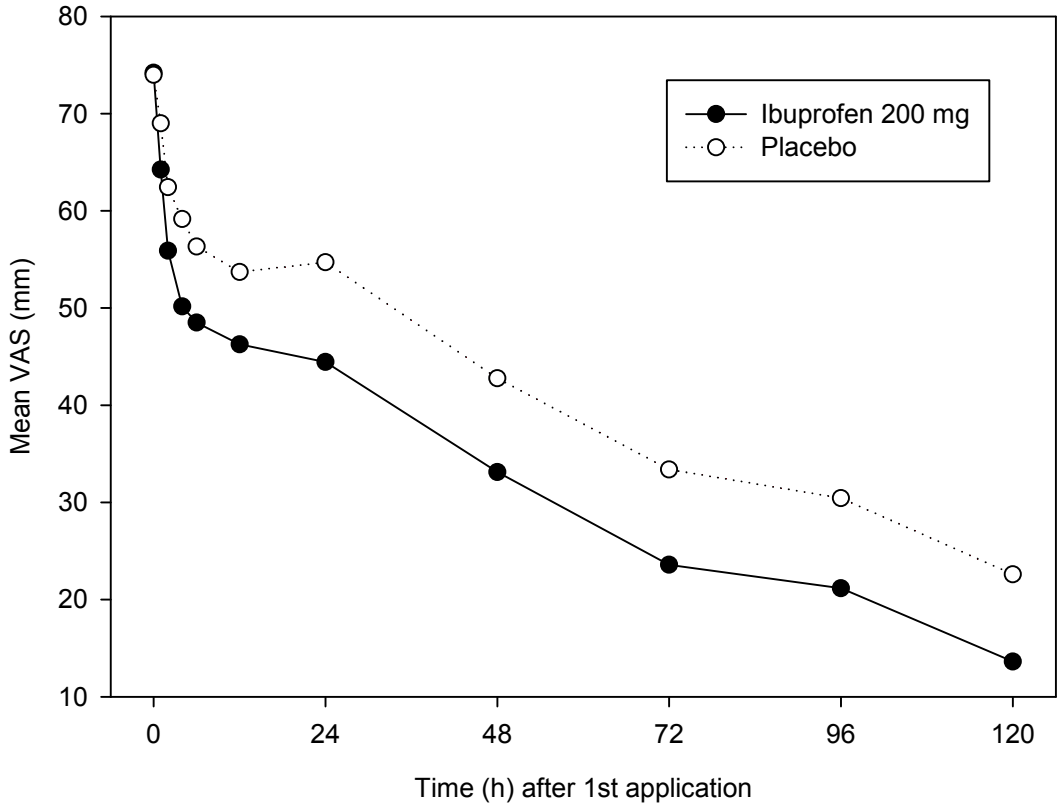
		Ibuprofen 200 mg (n=66)	**Placebo (n=64)**
Descriptive statistics			
VAS AUC_{0-3d} [mm*h]	Mean	2768.13	3430.95
	SD	1501.29	1253.14
	Median	2984.00	3537.75
ANOVA model information			
Least Square Means		2731.74	3425.52
Least Square Means Difference (Ibuprofen 200 mg – Placebo) and 99% confidence interval		-693.78 (-1237.28 to -150.27)	
p (ANCOVA*)		0.0011	

*ANCOVA – Analysis-of-covariance test with total sum of RICE duration and VAS at BL as covariates and treatment and centre as fixed effects

Source: Table 14.2.1, Appendix 16.1.9.1

The profiles of the mean of the VAS values over the study period for each treatment are presented in Figure 11.4.1. The AUC at any time point is represented as the area under the relevant curve between baseline and that time point.

Figure 11.4 - 1 Mean of VAS values over time (FAS/PP)



Missing data was replaced using the LOCF approach

Descriptive statistics of VAS $AUC_{0\text{-}3d}$ by centre are provided in Section 14.2, Table 14.2.2. As an exploratory analysis, the ANOVA model used in the primary analysis was also used with an added fixed term for the centre x treatment interaction (see Section 16.1.9, Appendix 16.1.9.2). There was significant evidence of such a quantitative interaction ($p<0.0001$).

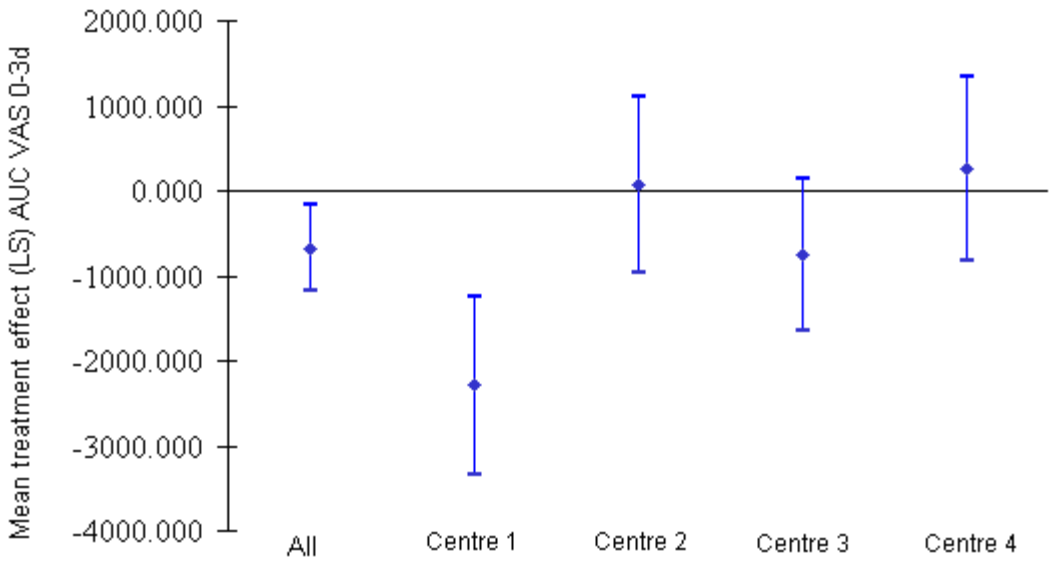
From the resulting ANOVA models the least square means for the VAS $AUC_{0\text{-}3d}$ for each treatment were obtained and are presented in Table 11.4.2 and graphically in Figure 11.4.2 below. These show significantly less pain for the Ibuprofen group compared to the placebo group at Centre 1 ($p<0.0001$) at the 1% level and Centre 3 ($p=0.0313$) at the 5% level. There was observed to be small differences between the treatments at Centres 2 and 4 which slightly favoured the placebo. Neither of these differences were statistically significant.

Table 11.4 - 2 VAS AUC0-3d by centre (FAS/PP)

	Difference in least square means	99% CI		
Centre	**(Ibuprofen 200 mg - Placebo)**	**Lower**	**Upper**	**p-value**
1	-2291.75	-3334.09	-1249.40	p<0.0001
2	62.56	-975.07	1100.19	p=0.8749
3	-743.64	-1636.79	149.52	p=0.0313
4	253.50	-829.21	1336.20	p=0.5412

Source: Appendix 16.1.9.2

Figure 11.4 - 2 Treatment effects on VAS AUC0-3d by centre (Least Square Means: Ibuprofen 200mg – Placebo) (FAS/PP)



To test for a qualitative centre x treatment interaction, a one-sided Gail-Simon test was used to test the null hypothesis that all true treatment differences in VAS $AUC_{0\text{-}3d}$ across centres favour the Ibuprofen product. There was no evidence to reject this hypothesis (p=0.7351– see Section 14.2, Table 14.2.37).

11.4.1.2 SECONDARY VARIABLES

All further exploratory statistical tests performed for secondary efficacy variables were two-tailed with a level of significance of 5 %.

11.4.1.2.1 VAS AUC

A summary of the area under the VAS curve at 12 hours, 24 hours and 5 days for each treatment are provided in Section 14.2, Tables 14.2.3, 14.2.9 and 14.2.15. The ANOVA model details are provided in Section 16.1.9, Appendices 16.1.9.3, 16.1.9.5 and 16.1.9.7.

The least square means of the VAS AUC from the ANOVA models are presented in Table 11.4.3 below for each treatment along with the differences and 95% confidence intervals for the differences at each time point.

Table 11.4 - 3 VAS AUC at each time point (FAS/PP)

	Least square means [mm*h]		Least square mean difference [mm*h]	95% CI for least square mean difference [mm*h]		
Time point	Ibuprofen 200mg	Placebo	(Ibuprofen 200 mg - Placebo)	Lower	Upper	p-value
0 – 12 hours	607.91	699.37	-91.48	-155.64	-27.31	p=0.0056
0 – 24 hours	1140.90	1345.71	-204.81	-338.00	-71.62	p=0.0029
0 – 5 days	3677.75	4877.55	-1199.80	-1904.59	-495.01	p=0.0010

Source: Appendices 16.1.9.3, 16.1.9.5 and 16.1.9.7

As well as after 3 days (primary endpoint) there was also significant evidence that the AUC for VAS was lower for the Ibuprofen group compared to placebo at after 12 hours, 24 hours and 5 days ($p<0.01$ at all time points) post baseline.

The VAS AUC is summarised by centre in Section 14.2, Tables 14.2.4, 14.2.10 and 14.2.16. An exploratory analysis for each time point was conducted such that the fitted ANOVA model also included a fixed term for the centre x treatment interaction. Details of all exploratory analysis to assess the centre x treatment interaction are provided in Section 14.2, Tables 14.2.5, 14.2.11 and 14.2.17 as well as Section 16.1.9, Appendices 16.1.9.4, 16.1.9.6 and 16.1.9.8.

There was significant evidence of such a quantitative interaction at all time points (all time points, p=0.0002). The same pattern of interaction was observed at each time point with the largest least square mean differences at centres 1 and 3 both favouring the Ibuprofen group. The treatment difference within centre 1 was statistically significant at all timepoints (p<0.0001) but at centre 3 there was only statistical significance for the treatment difference at day 5 (12 hours: p=0.1649, 24 hours: p=0.1080, 5 days: p=0.0146). Within centres 2 and 4 there was very slight treatment differences with the least square mean slightly favouring placebo.

To test for a qualitative interaction at each time point, a one-sided Gail-Simon test was used to test for a qualitative centre x treatment interaction and the null hypothesis that all true treatment differences in VAS AUC across centres favour the Ibuprofen product. There was no evidence to reject this hypothesis at all time points (p=0.7765, 12 hours; p=0.8168, 24 hours; p=0.7920, 5 days – see Section 14.2, Table 14.2.37).

11.4.1.2.2 VAS ASSESSMENT OF PAIN ON MOVEMENT

Summaries of the VAS score over the study period for each treatment are provided in Table 11.4.5 below and more descriptively in Section 14.2, Tables 14.2.6, 14.2.12. The ANOVA model details of the VAS score at 12 and 24 hours are provided in Section 16.1.9., Appendices 16.1.9.9 and 16.1.9.11.

The least square means from the ANOVA models for the VAS score at 12 and 24 hours are presented in Table 11.4.4 below for each treatment along with the differences and 95% confidence intervals for the differences at each time point.

Table 11.4 - 4 VAS score after 12 and 24 hours (FAS/PP)

	Least square means [mm]		Least square mean difference [mm]	95% CI for least square mean difference [mm]		
Time point	Ibuprofen 200mg	Placebo	(Ibuprofen 200 mg - Placebo)	Lower	Upper	p-value
12 hours	45.41	53.53	-8.12	-14.85	-1.39	p=0.0184
24 hours	43.71	54.47	-10.76	-16.90	-4.62	p=0.0007

Source: Appendices 16.1.9.9 and 16.1.9.11

There was strong statistical evidence of a lower VAS score for the Ibuprofen group compared to the placebo group after both 12 (p=0.0184) and 24 hours (p=0.0007) from baseline.

Table 11.4 - 5 VAS values at all timepoints (FAS/PP)

VAS (mm)		Ibuprofen 200 mg (n=66)	Placebo (n=64)	Mean Treatment effect
0 h	Mean SD	74.21 11.43	73.98 10.24	0.23
1 h	Mean SD	64.24 14.11	69.00 9.18	-4.76
2 h	Mean SD	55.89 18.08	62.42 12.04	-6.53
4 h	Mean SD	50.17 21.17	59.14 14.30	-8.97
6 h	Mean SD	48.50 22.73	56.33 16.65	-7.83
12 h	Mean SD	46.26 24.28	53.69 18.81	-7.43
24 h	Mean SD	44.45 23.33	54.70 17.91	-10.25
2 days	Mean SD	33.12 22.96	42.77 20.93	-9.64
3 days	Mean SD	23.58 21.64	33.38 21.39	-9.80
4 days	Mean SD	21.18 22.73	30.44 22.28	-9.26
5 days	Mean SD	13.62 18.74	22.59 19.61	-8.97

Source: Tables 14.2.43 to 14.2.53

The VAS score across all time points are summarised by centre in Section 14.2, Tables 14.2.7, 14.2.13 and 14.2.54 to 14.2.64. An exploratory analysis for the VAS score at 12 and 24 hours was conducted such that the fitted ANOVA model also included a fixed term for the centre x treatment interaction. Details of all exploratory analysis to assess the centre x treatment interaction are provided in Section 14.2, Tables 14.2.8 and 14.2.14 as well as Section 16.1.9, Appendices 16.1.9.10 and 16.1.9.12.

There was significant evidence of such a quantitative interaction at both time points (12 hours: p=0.0011, 24 hours: p=0.0009). At centre 1 there was statistically significance in terms of lower pain for the Ibuprofen group after both 12 and 24 hours (p<0.0001). At centre 3 the difference in least squares means also favoured the Ibuprofen group at both time points. Although this was not statistically significant after 12 hours (p=0.2376) there was marginal statistical evidence of a difference after 24 hours (p=0.0628). At centres 2 and 4, the difference in least square means suggests very small non-significant treatment effects favouring both Ibuprofen (Centre 4 at 24 hours) and placebo groups (Centre 2 and 4 at 12 hours and Centre 2 at 24 hours).

To test for a qualitative interaction at each time point, a one-sided Gail-Simon test was used to test for a qualitative centre x treatment interaction and the null hypothesis that all true treatment differences in the VAS score across centres favour the Ibuprofen product. There was no evidence to reject this hypothesis at all time points (p=0.7545, 12 hours; p=0.9272, 24 hours – see Section 14.2, Table 14.2.37).

11.4.1.2.3 ALGOMETRY (TENDERNESS): AUC OF INJURED SITE

Summaries of the AUC for the Algometry (tenderness) of the injured site after 3 and 5 days are provided in Section 14.2, Tables 14.2.18 and 14.2.28. The ANOVA model details are provided in Section 16.1.9., Appendices 16.1.9.13 and 16.1.9.15.

The least square means of the AUC for Algometry (tenderness) values from the ANOVA models are presented in Table 11.4.6 below for each treatment along with the differences and 95% confidence intervals for the differences at each time point.

The algometry (tenderness) was measured such that the greater the algometry value, the greater the pressure required to produce the first tenderness reaction. Therefore, greater algometry values indicate less pain at the site of interest.

Table 11.4 - 6 Algometry (tenderness): AUC for the injured site at each time point (FAS/PP)

	Least square means [N/cm²*d]		Least square mean difference [N/cm²*d]	95% CI for least square mean difference [N/cm²*d]		
Time point	**Ibuprofen 200mg**	**Placebo**	**(Ibuprofen 200 mg - Placebo)**	**Lower**	**Upper**	**p-value**
0 – 3 days	7.44	6.50	0.94	0.43	1.44	p=0.0004
0 – 5 days	14.71	12.84	1.87	0.87	2.88	p=0.0003

Source: Appendices 16.1.9.13 and 16.1.9.15

There was very strong statistical evidence of a greater AUC for the algometry score (lower pain) at the injured site for the Ibuprofen group compared to the placebo group after both 3 days (p=0.0004) and 5 days (p=0.0003) from baseline.

The AUC for the Algometry (tenderness) of the injured site at 3 and 5 days is summarised by centre in Section 14.2, Tables 14.2.19 and 14.2.29. An exploratory analysis for each time point was conducted such that the fitted ANOVA model also included a fixed term for the centre x treatment interaction. Details of all exploratory analysis to assess the centre x treatment interaction are provided in Section 14.2, Tables 14.2.20 and 14.2.30 as well as Section 16, Appendices 16.1.9.14 and 16.1.9.16.

There was significant evidence of such a quantitative interaction at both time points (3 days: p<0.0001, 5 days: p=0.0002). At centres 1 and 3 there was statistically significance in terms of greater AUC algometry values (lower pain) for the Ibuprofen group after both 3 and 5 hours (p<0.01). At centre 2 the difference in least square means suggests very small non-significant treatment effects favouring the placebo group at day 3 and the Ibuprofen group at day 5. The observed difference at centre 4 favours the placebo group at both timepoints although both are not statistically significant (day 3: p=0.1913, day 5: p=0.4932).

To test for a qualitative interaction at each time point, a one-sided Gail-Simon test was used to test for a qualitative centre x treatment interaction and the null hypothesis that all true treatment differences in the AUC for Algometry scores across centres favour the Ibuprofen product. There was no evidence to reject this hypothesis at all time points (p=0.4112, day 3; p=0.7113, day 5 – see Section 14.2, Table 14.2.37).

11.4.1.2.4 ALGOMETRY (TENDERNESS) OF THE INJURED SITE

Summaries of the algometry (tenderness) of the injured site across the study period are presented in Table 11.4.8 below and more descriptively in Section 14.2, Tables 14.2.21 and 14.2.65 to 14.2.69. The ANOVA model details of the algometry (tenderness) of the injured site are provided in Section 16.1.9, Appendix 16.1.9.17.

The least square means of the for Algometry (tenderness) from the ANOVA models are presented in Table 11.4.7 below for each treatment along with the differences and 95% confidence intervals for the differences at each time point.

The algometry (tenderness) was measured such that the greater the algometry value, the greater the pressure required to produce the first tenderness reaction. Therefore, greater algometry values indicate less pain at the site of interest.

Table 11.4 - 7 Algometry (tenderness): Injured site at 24 hours (FAS/PP)

Least square means [N/cm²]		Least square mean difference [N/cm²]	95% CI for least square mean difference [N/cm²]		
Ibuprofen 200mg	**Placebo**	**(Ibuprofen 200 mg - Placebo)**	**Lower**	**Upper**	**p-value**
2.20	1.89	0.30	0.14	0.47	p=0.0003

Source: Appendix 16.1.9.17

There was very strong statistical evidence of a greater algometry score (lower pain) at the injured site for the Ibuprofen group compared to the placebo group after 24 hours (p=0.0003).

Table 11.4 - 8 Algometry/tenderness values over time at injured site (FAS/PP)

Tenderness at injured site (N/cm²)		Ibuprofen 200 mg (n=66)	Placebo (n=64)	Mean Treatment effect
Baseline	Mean SD	1.37 0.86	1.46 0.96	-0.09
24 hours	Mean SD	2.17 0.97	1.96 1.10	0.22
Day 2	Mean SD	2.83 1.23	2.52 1.31	0.31
Day 3	Mean SD	3.30 1.26	2.95 1.37	0.35
Day 5	Mean SD	3.88 1.32	3.51 1.47	0.37

Source: Tables 14.2.65 to 14.2.69

The algometry (tenderness) of the injured site at each time point during the study is summarised by centre in Section 14.2, Tables 14.2.24 to 14.2.27. An exploratory analysis for each time point was conducted such that the fitted ANOVA model also included a fixed term for the centre x treatment interaction. Details of all exploratory analysis to assess the centre x treatment interaction are provided in Section 14.2, Table 14.2.23 as well as Section 16.1.9, Appendix 16.1.9.18.

There was significant evidence of a quantitative interaction (p=0.0016). At centres 1 and 3 there was statistically significance in terms of greater algometry values (lower pain) for the Ibuprofen group (p<0.01). At centre 2 and 4 the least square mean differences were very slight with no statistical significant differences.

To test for a qualitative interaction at each time point, a one-sided Gail-Simon test was used to test for a qualitative centre x treatment interaction and the null hypothesis that all true treatment differences in the Algometry scores at the injured site at 24 hours across centres favour the Ibuprofen product. There was no evidence to reject this hypothesis (p=0.7929 – see Section 14.2, Table 14.2.37).

11.4.1.2.5 ALGOMETRY (TENDERNESS): AUC OF RATIO (INJURED SITE /CONTRALATERAL SITE)

As well as at the injured site, an additional algometry measurement was taken at a contralateral site which was not injured. A high ratio between the two sites (injured / contralateral) indicates low pain at the injured site which is relevant to the patient's unique resistance to pain.

Summaries of the AUC for the algometry (tenderness) ratio (injured/contralateral) after 3 and 5 days are provided in Section 14.2, Tables 14.2.31 and 14.2.34. The ANOVA model details are provided in Section 16.1.9, Appendices 16.1.9.19 and 16.1.9.21.

The least square means of the AUC for the algometry (tenderness) ratio (injured/contralateral) from the ANOVA models are presented in Table 11.4.9 below for each treatment along with the differences and 95% confidence intervals for the differences at each time point.

Table 11.4 - 9 Algometry (tenderness) ratio (injured site /contralateral site) at each time point (FAS/PP)

	Least square means		Least square mean difference	95% CI for least square mean difference		
Time point	Ibuprofen 200mg	Placebo	(Ibuprofen 200 mg - Placebo)	Lower	Upper	p-value
0 – 3 days	1.58	1.35	0.23	0.11	0.35	p=0.0003
0 – 5 days	3.13	2.72	0.41	0.18	0.64	p=0.0006

Source: Appendices 16.1.9.19 and 16.1.9.21

There was very strong statistical evidence of a greater AUC for the ratio of algometry scores (injured site / collateral site) (lower pain) for the Ibuprofen group compared to the placebo group after both 3 days (p=0.0003) and 5 days (p=0.0006) from baseline.

The algometry (tenderness) ratio (injured/contralateral) at 3 and 5 days is summarised by centre in Section 14.2, Tables 14.2.32 and 14.2.35. An exploratory analysis for each time point was conducted such that the fitted ANOVA model also included a fixed term for the centre x treatment interaction. Details of all exploratory analysis to assess the centre x treatment interaction are provided in Section 14.2, Tables 14.2.33 and 14.2.36 as well as Section 16.1.9, Appendices 16.1.9.20 and 16.1.9.22.

There was significant evidence of a quantitative interaction at both 3 and 5 days ($p<0.0001$). At centres 1 and 3 there was statistically significance in terms of greater AUC for algometry ratios (lower pain) for the Ibuprofen group ($p<0.01$) after both 3 and 5 days. At centre 2 and 4 the least square mean differences favoured the placebo group very slightly with no statistical significant differences at either day.

To test for a qualitative interaction at each time point, a one-sided Gail-Simon test was used to test for a qualitative centre x treatment interaction and the null hypothesis that all true treatment differences in the Algometry ratios across centres favour the Ibuprofen product. There was no evidence to reject this hypothesis after both 3 and 5 days ($p=0.6639$, day 3; $p=0.7780$, day 5 – see Section 14.2, Table 14.2.37).

Descriptive summaries of the algometry (tenderness) ratio (injured/contralateral) over the study period are provided in Section 14.2, Tables 14.2.71 to 14.2.75.

11.4.1.2.6 TIME TO RESOLUTION OF PAIN

The time from baseline to reach the contralateral (healthy) values of algometry at the injured site was determined as the time to the resolution of pain for a patient.

The Kaplan Meier analysis of the time from baseline to reach the contralateral (healthy) values of algometry at the injured site is presented in Section 16.1.9, Appendix 16.1.9.23. The number of patients that had resolution of pain was very low and therefore the median time to resolution of pain could not be assessed for either treatment.

There was a significantly lower time to resolution of pain for the Ibuprofen group compared to the placebo group (log rank test: $p=0.0071$).

Only 23/130 (17.7%) of patients had resolution of pain during the 5 days post-baseline. Pain had resolved completely for a higher percentage of the Ibuprofen group (17/66 = 25.8%) when compared to the placebo group (6/64 = 9.4%).

For the Ibuprofen group, the numbers of days to the resolution of pain were 2 days (1 patient), 3 days (7 patients), and 5 days (9 patients) with no resolution after 5 days for 49 patients. For the placebo group, the numbers of days to the resolution of pain were 3 days (1 patient), and 5 days (5 patients) with no resolution after 5 days for 58 patients

11.4.1.2.7 USE OF RESCUE MEDICATION AND TIME OF USE OF RESCUE MEDICATION

The patients received at a package containing 20 tablets of rescue medication (Paracetamol 500 mg) at visit 1. Use of rescue medication and time of use of rescue medication were checked at days 1, 2, 3 and 5 post-baseline. The use of rescue medication is detailed in Section 14.2, Tables 14.2.38 to 14.2.40.

Table 11.4.10 summarises the use of rescue medication by visit. There were no relevant differences between the two treatment groups.

Table 11.4 - 10 Use of rescue medication by visit and over the study (FAS/PP)

	Ibuprofen 200 mg (n=66)				**Placebo (n=64)**			
	Day 1	**Day 2**	**Day 3**	**Day 5**	**Day 1**	**Day 2**	**Day 3**	**Day 5**
Used rescue medication	4 (6.1%)	3 (4.5%)	2 (3.0%)	2 (3.0%)	4 (6.3%)	3 (4.7%)	1 (1.6%)	1 (1.6%)
	At any point during study							
	6 (9.1%)				4 (6.3%)			

Source: Tables 14.2.38, 14.2.39

There was no evidence of a difference in the number of patients that used any rescue medication at any point during the study period between treatment groups (Logistic regression odds ratio=1.441, p=0.5960, see Section 16.1.9, Appendix 16.1.9.24). A slightly greater percentage of the Ibuprofen group (9.1%) took rescue medication compared to the placebo group (6.3%).

The total sum of time of use of rescue medication is summarised in Section 14.2, Table 14.2.40. The Ibuprofen group had a slightly greater mean duration of rescue medication usage by 0.09 days compared to the placebo group (Means: Ibuprofen 0.23 days, placebo 0.14 days).

For the Ibuprofen group the number of days of which rescue medication was taken were 4 days (1 patient), 3 days (1 patient), and 1 day (4 patients) with 60 patients receiving no rescue medication. For the placebo group the number of days of which rescue medication was taken were 1 day (4 patients) with 60 patients receiving no rescue medication.

The time to first intake of rescue medication was calculated. Patients who did not use rescue medication were censored at the last visit. The Kaplan Meier analysis of the time to first use of rescue medication is presented in Section 16.1.9, Appendix 16.1.9.25. The number of patients that used rescue medication was very low and therefore the median time to time to first intake of rescue medication could not be assessed for either treatment.

There was no significant difference in time to first rescue medication intake between the treatment groups (log rank test: p=0.5696).

11.4.1.2.8 GLOBAL ASSESSMENT OF TREATMENT EFFICACY

On assessment days 1, 3, and 5, the treatment efficacy of ibuprofen 200 mg and placebo were assessed globally by the patients and investigators using a 5-step score (none, poor, fair, good, excellent) in response to the questions below respectively:

To the patient: Considering all the ways your injury has affected you, how do you evaluate the effect of therapy today?

To the investigator: Considering all the ways the injury has affected your patient, how do you consider the effect of therapy today?

The global assessment of treatment efficacy by the patients is presented in Tables 11.4.11 and 11.4.12 as well as graphically in Figure 11.4.8. Details of the logistic regression models are provided in Section 16.1.9, Appendices 16.1.9.26 to 16.1.9.28.

Table 11.4 - 11 Global assessment of treatment efficacy by patient (FAS/PP)

	Ibuprofen 200 mg			Placebo (n=64)		
	Day 1 (n=65)	Day 3 (n=66)	Day 5 (n=66)	Day 1	Day 3	Day 5
excellent	12 (18.5%)	21 (31.8%)	33 (50.0%)	1 (1.6%)	11 (17.2%)	12 (18.8%)
good	17 (26.2%)	22 (33.3%)	17 (25.8%)	20 (31.3%)	15 (23.4%)	16 (25.0%)
fair	18 (27.7%)	10 (15.2%)	5 (7.6%)	13 (20.3%)	12 (18.8%)	11 (17.2%)
poor	13 (20.0%)	8 (12.1%)	6 (9.1%)	18 (28.1%)	19 (29.7%)	16 (25.0%)
none	5 (7.7%)	5 (7.6%)	5 (7.6%)	12 (18.8%)	7 (10.9%)	9 (14.1%)

Source: Table 14.2.41

Table 11.4 - 12 Results of logistic regression for global assessment of treatment efficacy by patient (FAS/PP)

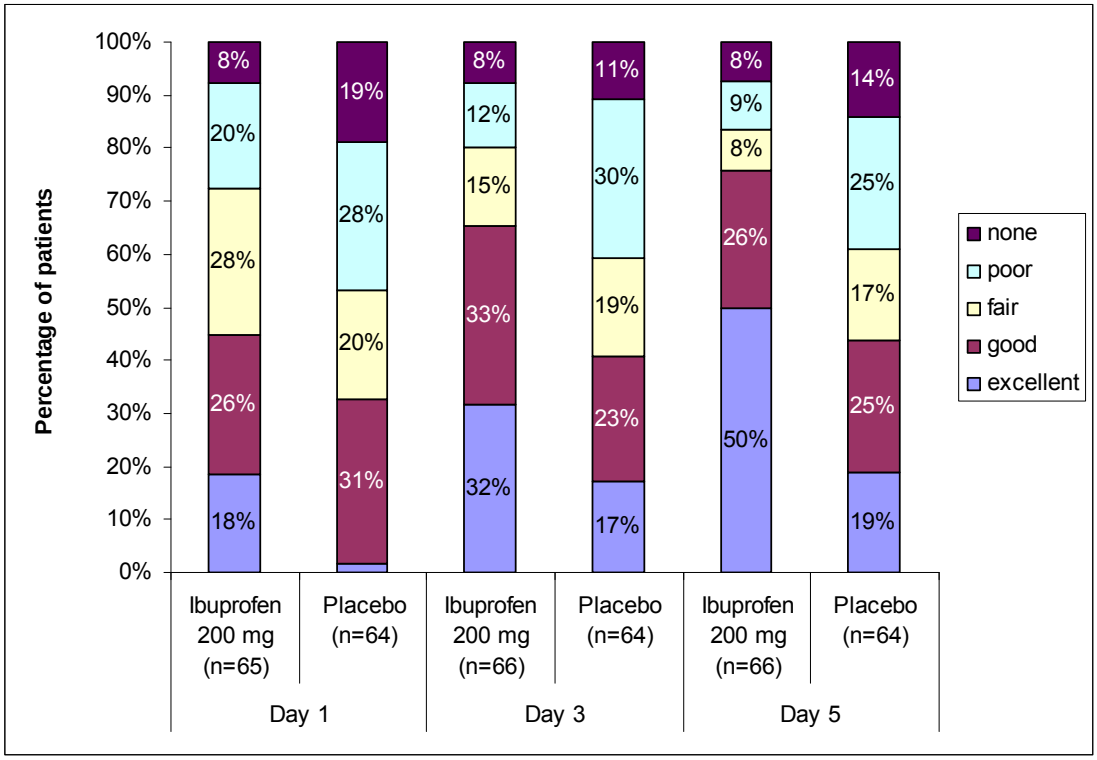
	Odds ratio (Ibuprofen 200mg : placebo)	Wald 95% CI for odds ratio		
Time point		**Lower**	**Upper**	**p-value**
Day 1	2.510	1.325	4.757	p=0.0048
Day 3	2.782	1.467	5.274	p=0.0017
Day 5	3.969	2.052	7.675	p<0.0001

Source: Appendices 16.1.9.26 to 16.1.9.28

There was significant evidence that the patients in the Ibuprofen group rated the treatment efficacy higher than those in the Placebo group at all time points ($p<0.01$ – Table 11.4.12).

At all time points there was observed to be a greater percentage of patients which assessed efficacy as at least good for the Ibuprofen group compared to the placebo group (Ibuprofen / Placebo comparisons; Day 1: 45% / 33%, Day 3: 65% / 41%, Day 5: 76% / 44%).

Figure 11.4 - 3 Global assessment of treatment efficacy by patient (FAS/PP)



An exploratory analysis using the day 5 assessments was conducted such that the fitted logistic regression model also included a fixed term for the centre x treatment interaction. Details of all exploratory analysis to assess the centre x treatment interaction are provided in Section 16.1.9, Appendix 16.1.9.29. There was significant evidence of a quantitative interaction (p=0.0077).

At day 5 the percentage of patients which assessed efficacy as at least good for each group were as follows: Ibuprofen/ Placebo comparisons; Centre 1: 71% / 20%, Centre 2: 50% / 47%, Centre 3: 90% / 25%, Centre 4: 71% / 93%.

The global assessment of treatment efficacy by the investigator is presented in Tables 11.4.13 and 11.4.14 as well as graphically in Figure 11.4.9. Details of the logistic regression models are provided in Section 16.1.9, Appendices 16.1.9.30 to 16.1.9.32.

Table 11.4 - 13 Global assessment of treatment efficacy by the investigator (FAS/PP)

	Ibuprofen 200 mg			Placebo (n=64)		
	Day 1 (n=65)	Day 3 (n=66)	Day 5 (n=66)	Day 1	Day 3	Day 5
excellent	11 (16.9%)	22 (33.3%)	36 (54.5%)	0 (0.0%)	8 (12.5%)	12 (18.8%)
good	17 (26.2%)	21 (31.8%)	13 (19.7%)	16 (25.0%)	14 (21.9%)	14 (21.9%)
fair	20 (30.8%)	9 (13.6%)	6 (9.1%)	17 (26.6%)	17 (26.6%)	10 (15.6%)
poor	12 (18.5%)	9 (13.6%)	5 (7.6%)	20 (31.3%)	16 (25.0%)	20 (31.3%)
none	5 (7.7%)	5 (7.6%)	6 (9.1%)	11 (17.2%)	9 (14.1%)	8 (12.5%)

Source: Table 14.2.41

Table 11.4 - 14 Results of logistic regression for global assessment of treatment efficacy by investigator (FAS/PP)

	Odds ratio (Ibuprofen 200mg : placebo)	Wald 95% CI for odds ratio		
Time point		**Lower**	**Upper**	**p-value**
Day 1	3.071	1.604	5.879	p=0.0007
Day 3	3.645	1.899	6.993	p=0.0001
Day 5	4.654	2.375	9.122	p<0.0001

Source: Appendices 16.1.9.30 to 16.1.9.32

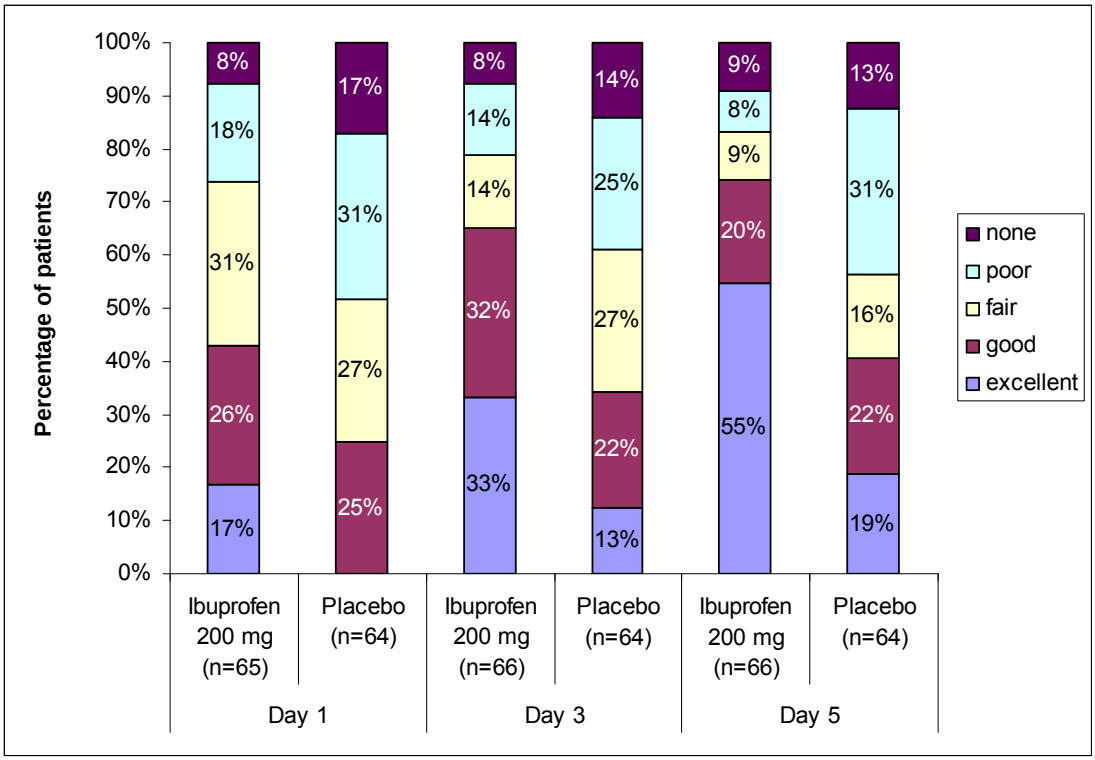
There was significant evidence that the investigators rated the treatment efficacy for Ibuprofen patients higher than for those in the Placebo group at all time points ($p<0.01$ – Table 11.4.14).

At all time points there was observed to be a greater percentage patients for which the investigator assessed efficacy as at least good for the Ibuprofen group compared to the placebo group (Ibuprofen / Placebo comparisons; Day 1: 42% / 25%, Day 3: 64% / 34%, Day 5 74% / 41%).

An exploratory analysis using the day 5 assessments was conducted such that the fitted logistic regression model also included a fixed term for the centre x treatment interaction. Details of all exploratory analysis to assess the centre x treatment interaction are provided in Section 16.1.9, Appendix 16.1.9.33. There was significant evidence of a quantitative interaction ($p=0.0081$).

At day 5 the percentage of times the investigator assessed efficacy as at least good for each patient group were as follows: Ibuprofen/ Placebo comparisons; Centre 1: 87% / 13%, Centre 2: 50% / 47%, Centre 3: 90% / 30%, Centre 4: 64% / 79% (see Section 14.2, Table 14.2.42.

Figure 11.4 - 4 Global assessment of treatment efficacy by investigator (FAS/PP)



11.4.2 ANALYTICAL ISSUES

Detailed documentation of statistical methods, as the final Statistical Analysis Plan (SAP), is presented in Appendix 16.1.9.

11.4.2.1 ADJUSTMENTS FOR COVARIATES

The quantitative efficacy variables were analysed by means of analysis-of covariance models (ANCOVA) with terms in the model for treatment group, centre and total sum of RICE duration. For endpoints relating to the VAS score, the baseline VAS score and baseline algometry of the injured site (not for the primary endpoint - VAS AUC_{0-3d}) were also included. For Algometry endpoints, only the relevant baseline measure (injured site or injured/collateral site ratio) corresponding to the endpoint being analysed was included in the model.

11.4.2.2 HANDLING OF DROPOUTS OR MISSING DATA

There were no dropouts in this clinical trial. For AUC analyses, missing values between two time points were linearly interpolated. If last values were missing, missing data were replaced using the last-observation-carried-forward (LOCF) approach. For all non-AUC analyses, missing efficacy data were replaced using the LOCF approach.

11.4.2.3 INTERIM ANALYSES AND DATA MONITORING

No interim analyses were performed and there was no data monitoring, therefore this section is not applicable.

11.4.2.4 MULTI-SITE STUDIES

Individual site results were presented by means of descriptive statistical methods for the demographical and efficacy data. Moreover, the treatment*centre interaction was assessed by means of an ANCOVA model for the primary variable and other secondary variables. Furthermore, Gail-Simon's test[38] for qualitative interaction was carried out for the primary variable and other secondary variables.

11.4.2.5 MULTIPLE COMPARISON/MULTIPLICITY

No multiple comparisons were made in the confirmatory part of the evaluation of the primary variable; therefore this section is not applicable.

11.4.2.6 USE OF AN "EFFICACY SUBSET" OF PATIENTS

No efficacy subsets of patients were created; therefore this section is not applicable.

11.4.2.7 ACTIVE-CONTROL STUDIES INTENDED TO SHOW EQUIVALENCE

This study was not designed to test equivalence, therefore this section is not applicable.

11.4.2.8 EXAMINATION OF SUBGROUPS

Centre-specific subgroup analysis was carried out.

11.4.3 TABULATION OF INDIVIDUAL RESPONSE DATA

In addition to tables giving group data for efficacy variables, relevant individual patient data, are presented in by-patient tabular listings in Appendix 16.2.6.1.

No individual response data are presented in the body of the report.

11.4.4 DRUG DOSE, DRUG CONCENTRATION AND RELATIONSHIPS TO RESPONSE

This was not a dose response study and fixed doses of study medication were used, therefore this section is not applicable.

11.4.5 DRUG-DRUG AND DRUG-DISEASE INTERACTIONS

No drug/drug or drug/disease interactions were seen in this study and so this section is not applicable.

11.4.6 BY-PATIENT DISPLAYS

Group mean data represent the principal analysis in this study and so this section is not applicable.

11.4.7 EFFICACY CONCLUSIONS

A total of 130 patients (Ibuprofen n=66; placebo n=64), 88 male (Ibuprofen n=44; placebo n=44) and 42 female (Ibuprofen n=22; placebo n=20), with a mean age of 34.09 years (Ibuprofen) and 30.08 years (placebo) with acute sports-related traumatic blunt soft tissue injury/contusion were included in the trial.

The primary objective of the study, which was to demonstrate that the Ibuprofen 200mg patch was superior to placebo in terms of the area under the VAS score curve between baseline and 3 days, was met at the two-tailed 1% level of significance (p=0.0011). The mean treatment effect was 662.82 mm*h in favour of Ibuprofen 200 mg.

Patients treated with the Ibuprofen patch were shown to have significantly lower VAS pain scores both in terms of the AUC after 12 hours, 24 hours, 3 hours and 5 hours (all $p<0.01$) and also the actual VAS scores after 12 (least square mean difference = -8.12 mm, $p=0.0184$) and 24 hours (least square mean difference = -10.76 mm, $p=0.0007$).

Superiority of the ibuprofen patch was also demonstrated across all algometry assessments (i.e. reductions in tenderness) in terms of the actual injured site AUC after 3 and 5 days as well as the scores at 24 hours ($p<0.001$). This was also seen for the ratio scores (injured/contralateral) AUC after 3 and 5 days ($p<0.001$).

Across all VAS and algometry assessments, there was a significant treatment x centre interaction present ($p<0.01$) showing evidence of differing treatment effects between centres. There was a similar trend across outcomes at all time points such that at centres 1 (always significantly) and 3 (mostly significantly) the difference favoured the Ibuprofen product. At centres 2 and 4, very small treatment effects were observed and mostly favoured the placebo group slightly with no statistical significance although it must be noted that these comparisons were not powered to do so. Gail-Simon tests were carried out to investigate qualitative centre x treatment interactions at all such endpoints in order to test the hypothesis that the treatment effect at all centres favours the Ibuprofen group and that instances where this was not observed were due to random error. This hypothesis could not be rejected, although again the study was not powered to prove this hypothesis.

The resolution of pain (algometry of injured site returns to algometry of contralateral site) was achieved for 17.7% of patients, the time taken to achieve this was proved statistically superior for the Ibuprofen patch ($p=0.0071$).

There was low usage of rescue medication (7.7% of patients) and there was no evidence of a difference between the Ibuprofen product and placebo in terms of any use over the study (9.1% Ibuprofen v 6.3% Placebo, $p=0.5960$) or time to first use ($p=0.5696$).

At all time points there was significant evidence that the patient and investigator rated the Ibuprofen patch more efficacious than placebo ($p<0.01$). The percentage of patients rating their treatment as at least good for the Ibuprofen group compared to the placebo group (Ibuprofen / Placebo) was; Day 1: 45% / 33%, Day 3: 65% / 41%, Day 5 76% / 44%). The percentage of patients for which the investigator rated the treatment as at least good for the Ibuprofen group compared to the placebo group (Ibuprofen / Placebo) was Day 1: 42% / 25%, Day 3: 64% / 34%, Day 5 74% / 41%.

A similar significant treatment x centre interaction was found ($p<0.01$) for both the patient and investigator assessments at day 5, with the same trend observed as was with the VAS and algometry outcomes with Centres 1 and 3 greatly favouring the Ibuprofen group and smaller differences noted at Centre 2 (favouring Ibuprofen) and 4 (favouring placebo).

The results confirm that the new Ibuprofen patch has a favourable impact on the outcome of patients suffering from fresh blunt injuries.

The clinically meaningful benefit was assessed by reference to the single point VAS score at 24 hours. The least square mean for this (end of first day of treatment) was 43.7mm for the Ibuprofen patch and 54.5mm for the placebo patch. This difference between products (10.8mm) was shown to be statstically significant where $p=0.0007$. In an acute pain setting (as is this clinical study) it has been shown that the minimum VAS change for a clinically significant benefit is 9mm[40]. In this study, the mean 24 hour difference noted between products was in excess of this value, it can therefore be concluded that the difference observed between the active and placebo patches is clinically relevant.

Patients treated with the new Ibuprofen patch had statistically significant and clinically relevant reductions in pain scores and a decrease in tenderness. Overall patients reached a pain-free condition significantly earlier than patients in the placebo group.

12 SAFETY EVALUATION

All patients who received at least one dose of study medication were included in the safety analysis.

12.1 EXTENT OF EXPOSURE

For each patient, the individual extent of exposure was calculated in terms of

- total duration of treatment, calculated in days as "$d_{last} – d_{first} +1$", where d_{last} and d_{first} are the dates of the last and the first application of study medication including times of application, respectively,
- study duration, calculated in days as "$d_{lastVisit} – d_{IC} +1$", where $d_{lastVisit}$ is the date of last visit documented and d_{IC} is the date of informed consent, respectively.

As shown in the Table 12.1.1, total duration of treatment and study duration was comparable between treatment groups among patients in the SAF population.

Table 12.1 - 1 Extent of exposure (SAF)

		Ibuprofen 200 mg (n=66)	Placebo (n=64)
Total duration of treatment (days)	Mean SD Median	4.99 0.05 5.00	4.98 0.14 5.00
Study duration (days)	Mean SD Median	6.00 0.00 6.00	6.00 0.00 6.00

Source: Table 14.1.20, Table 14.1.21

The individual patient listings for the extent of exposure data are presented in Appendix 16.2.5.

12.2 ADVERSE EVENTS (AES)

All adverse events for each patient, including the same event on several occasions are listed in appendix 16.2.7, giving both preferred terms according to MedDRA Version 12.1 and the original term used by the Investigator.

The tables that follow describe adverse events occurring after the initiation of treatment with study medication (Treatment-Emergent Adverse Events (TEAE)). Where appropriate, abbreviated tables are included here, with full tables included in Section 14.3.

12.2.1 BRIEF SUMMARY OF EVENTS

A total of 15 patients (Ibuprofen 200 mg: n=7 (10.6 %), Placebo: n=8 (12.5 %)) had at least one TEAE during the course of the clinical trial. Eighteen TEAEs were documented during the trial.

The System Organ Class (SOC) most frequently affected was “General disorders and administration site conditions” (Ibuprofen 200 mg: n=4, Placebo: n=5). “General disorders and administration site conditions” as well as “Infections and infestations” were more often observed in placebo group compared to Ibuprofen 200 mg.

The most frequent non-serious TEAE’s were Nasopharyngitis (Ibuprofen 200 mg: n=0, Placebo: n=2), headache (Ibuprofen 200 mg: n=1, Placebo: n=1), application site pruritus (Ibuprofen 200 mg: n=1, Placebo: n=1), application site reaction (Ibuprofen 200 mg: n=0, Placebo: n=2) and application site hypersensitivity (Ibuprofen 200 mg: n=2, Placebo: n=0).

All TEAEs in this clinical trial were non-serious and of mild severity.

Nine non-serious TEAEs were classified as drug-related (probable, possible, definite) in the treatment groups (Ibuprofen 200 mg: n=4, Placebo: n=5). Most cases were probably drug-related.

For individual patient data see the case-wise listings in Appendix 16.2.7.

12.2.2 DISPLAY OF ADVERSE EVENTS

All 130 patients enrolled who received at least one dose of the study medication were included in the safety population.

All documented adverse events (AEs) were classified into treatment-emergent AEs (TEAEs) or non-treatment-emergent AEs. All documented AEs were TEAEs with a comparable proportion of TEAEs in both treatment groups.

A total of 15 patients (Ibuprofen 200 mg: n=7 (10.6 %), Placebo: n=8 (12.5 %)) had at least one TEAE during the course of the clinical trial.

Table 12.2 - 1 Number of TEAEs (SAF)

		Ibuprofen 200 mg (n=66)	Placebo (n=64)
Number of TEAEs	n	10	8
Number of patients with TEAEs	n (%)	7 (10.6)	8 (12.5)
Total number of patients treated	n (%)	66 (100.0)	64 (100.0)

Source: Table 14.3.2

All TEAEs in this clinical trial were non-serious and of mild severity (see Table 14.3.6 in Section 14.3).

The System Organ Class (SOC) most frequently affected was “General disorders and administration site conditions”. Table 12.2.2 summarizes the TEAEs by SOC for both treatment groups.

Table 12.2 - 2 Non-serious TEAEs by SOC (SAF)

	Ibuprofen 200 mg (n=66)	Placebo (n=64)	Total (n=130)
General disorders and administration site conditions	4	5	9
Infections and infestations	0	2	2
Nervous system disorders	1	1	2
Gastrointestinal disorders	1	0	1
Cardiac disorders	1	0	1
Ear and labyrinth disorders	1	0	1
Psychiatric disorders	1	0	1
Musculoskeletal and connective tissue disorders	1	0	1
Total	10	8	18

Multiple citations possible, Source: Table 14.3.11

The most frequent non-serious TEAEs were Nasopharyngitis (Ibuprofen 200 mg: n=0, Placebo: n=2), headache (Ibuprofen 200 mg: n=1, Placebo: n=1), application site pruritus (Ibuprofen 200 mg: n=1, Placebo: n=1), application site reaction (Ibuprofen 200 mg: n=0, Placebo: n=2), and application site hypersensitivity (Ibuprofen 200 mg: n=2, Placebo: n=0).

Table 12.2.3 summarizes the TEAEs by preferred term for both treatment groups.

Table 12.2 - 3 Non-serious TEAEs by preferred term (SAF)

	Ibuprofen 200 mg (n=66)	**Placebo (n=64)**	**Total (n=130)**
Nasopharyngitis	0	2	2
Headache	1	1	2
Application site pruritus	1	1	2
Application site reaction	0	2	2
Application site hypersensitivity	2	0	2
Pain	1	0	1
Application site erythema	0	1	1
Toothache	1	0	1
Application site discomfort	0	1	1
Angina pectoris	1	0	1
Vertigo	1	0	1
Sleep disorder	1	0	1
Joint swelling	1	0	1
Total	10	8	18

Multiple citations possible, Source: Table 14.3.9

Nine non-serious TEAEs were classified as drug-related (probable, possible, definite) in the treatment groups (Ibuprofen 200 mg: n=4, Placebo: n=5, see Table 14.3.9 in Section 14.3). Most cases were probably drug-related.

TEAEs by causality are summarized in Table 12.2.4.

Table 12.2 - 4 Non-serious TEAEs by preferred term and causality (SAF)

		Ibuprofen 200 mg (n=66)	Placebo (n=64)	Total (n=66)
none	Nasopharyngitis	0	2	2
	Headache	1	1	2
	Toothache	1	-	1
probable	Application site reaction	0	2	2
	Application site hypersensitivity	2	0	2
	Joint swelling	1	0	1
unlikely	Pain	1	0	1
	Angina pectoris	1	0	1
	Vertigo	1	0	1
	Sleep disorder	1	0	1
possible	Application site pruritus	1	1	2
	Application site erythema	0	1	1
	Application site discomfort	0	1	1
Total		10	8	18

Multiple citations possible, Source: Table 14.3.13

12.2.3 ANALYSIS OF ADVERSE EVENTS

“General disorders and administration site conditions” as well as “Infections and infestations” were more often observed in the placebo group compared to the Ibuprofen 200 mg group. All TEAEs in this clinical trial were non-serious and of mild severity.

All TEAE details are presented in Section 14.3 and Appendix 16.2.7, respectively.

12.3 OTHER SERIOUS ADVERSE EVENTS (SAES) AND OTHER SIGNIFICANT ADVERSE EVENTS

There were no deaths, other serious or significant adverse events in this study.

12.3.1 LISTING OF DEATHS, OTHER SERIOUS ADVERSE EVENTS, AND OTHER SIGNIFICANT ADVERSE EVENTS

12.3.1.1 DEATHS

There were no deaths in this study.

12.3.1.2 OTHER SERIOUS ADVERSE EVENTS

There were no other serious adverse events in this study.

12.3.1.3 OTHER SIGNIFICANT ADVERSE EVENTS

There were no other significant adverse events in this study.

12.3.2 NARRATIVES OF DEATHS, OTHER SERIOUS ADVERSE EVENTS AND CERTAIN OTHER SIGNIFICANT ADVERSE EVENTS

There were no deaths, other serious or significant averse events in this study.

12.3.3 ANALYSIS AND DISCUSSION OF DEATHS, OTHER SERIOUS ADVERSE EVENTS AND OTHER SIGNIFICANT ADVERSE EVENTS

There were no deaths, other serious or significant averse events in this study.

12.4 CLINICAL LABORATORY EVALUATION

No clinical laboratory evaluations were performed in this study.

12.4.1 LISTING OF INDIVIDUAL LABORATORY MEASUREMENTS BY SUBJECT AND EACH CLINICALLY SIGNIFICANT ABNORMAL LABORATORY VALUE

Not applicable.

12.4.2 EVALUATION OF EACH LABORATORY PARAMETER

Not applicable.

12.5 VITAL SIGNS, PHYSICAL FINDINGS AND OTHER OBSERVATIONS RELATED TO SAFETY

12.5.1 VITAL SIGNS

At baseline (Visit 1) and at the end of the study (Visit 5) the following vital signs were determined: systolic blood pressure, diastolic blood pressure, heart rate, and oral temperature.

In both treatment groups there were no clinically significant mean changes from baseline in any of the vital signs.

Table 12.5.1 summarises the results for the vital signs.

Table 12.5 - 1 Vital signs and weight (Safety)

		Active patch 200 mg ibuprofen (n=66)				Placebo patch (n=64)			
		V1	V5	V5-V1	V5-V1 (%)	V1	V5	V5-V1	V5-V1 (%)
BP_s [mmHg]	Mean	126.32	125.09	-1.23	-0.62	125.69	126.89	1.20	1.74
	SD	14.57	13.36	8.88	7.19	16.79	14.09	12.44	10.44
	Median	126.00	125.00	-0.50	-0.42	127.00	126.00	2.00	1.56
BP_d [mmHg]	Mean	78.03	75.59	-2.44	-2.35	75.89	76.17	0.28	1.13
	SD	10.13	8.88	8.87	11.03	10.03	9.88	9.00	12.06
	Median	75.00	75.00	-1.50	-1.63	74.50	75.00	0.00	0.00
Heart rate [bpm]	Mean	68.82	69.21	0.39	1.16	69.06	68.97	-0.09	0.77
	SD	10.71	10.06	6.37	9.38	8.85	7.36	8.28	11.95
	Median	68.00	68.00	2.00	3.03	68.00	68.00	0.50	0.57
Temperature [°C]	Mean	36.33	36.22	-0.12	-0.31	36.28	36.32	0.04	0.12
	SD	0.49	0.41	0.39	1.08	0.52	0.41	0.44	1.24
	Median	36.50	36.30	-0.10	-0.27	36.35	36.40	0.00	0.00

$BP_{s/d}$ – systolic/diastolic blood pressure, bpm - beats per minute; Source: Table 14.3.18, Table 14.3.19, Table 14.3.20, Table 14.3.21, Table 14.3.22, Table 14.3.23

The patientwise listings of the vital signs and temperature are presented in Appendix 16.2.6.

12.5.2 PHYSICAL EXAMINATION

Physical examinations were conducted at the beginning (Visit 1) and at the end of the study (Visit 5). There were few physical findings present at baseline and no clinically relevant changes were recorded during the course of the trial (see Appendix 16.2.6).

12.5.3 ASSESSENT OF LOCAL TOLERABILITY

On assessment Days 1, 3, and 5 (Visit 2, Visit 4, and Final Visit), the local tolerance of each product was assessed by the patients and investigators using a 4-step score (poor, fair, good, excellent).

At V2, a good or excellent assessment of local tolerance was documented by 92.4% of the patients in the Ibuprofen 200 mg group and by 100.0 % in the placebo group.

At V5 92.4% of the patients in the ibuprofen group and 93.8% in the placebo group recorded a good or excellent assessment . Similar results were found for the global assessment of the tolerability by the investigators (see Table 12.5.2 and Table 12.5.3).

Table 12.5 - 2 Global assessment of local tolerability by patient (SAF)

	Ibuprofen 200 mg (n=66)			**Placebo (n=64)**		
	V2	**V4**	**V5**	**V2**	**V4**	**V5**
	n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
excellent	23 (35.4)	23 (35.4)	25 (37.9)	18 (28.1)	16 (25.0)	19 (29.7)
good	38 (58.5)	41 (63.1)	36 (54.5)	46 (71.9)	48 (75.0)	41 (64.1)
fair	4 (6.2)	0 (0.0)	5 (7.6)	0 (0.0)	0 (0.0)	3 (4.7)
poor	0 (0.0)	1 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.6)

V=Visit, Source: Table 14.3.15

Table 12.5 - 3 Global assessment of local tolerability by the investigator (FAS/PP)

	Ibuprofen 200 mg (n=66)			Placebo (n=64)		
	V2	V4	V5	V2	V4	V5
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
excellent	25 (38.5)	25 (38.5)	26 (39.4)	15 (23.4)	18 (28.1)	16 (25.0)
good	37 (56.9)	38 (58.5)	34 (51.5)	49 (76.6)	46 (71.9)	44 (68.8)
fair	3 (4.6)	1 (1.5)	6 (9.1)	0 (0.0)	0 (0.0)	3 (4.7)
poor	0 (0.0)	1 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.6)

V=Visit, Source: Table 14.3.15

Figures 12.5.1 to 12.5.6 provide a graphical display of the patients' and investigators' global assessment of tolerance by visit.

Figure 12.5 - 1 Global assessment of local tolerability by patient at V2 (SAF)

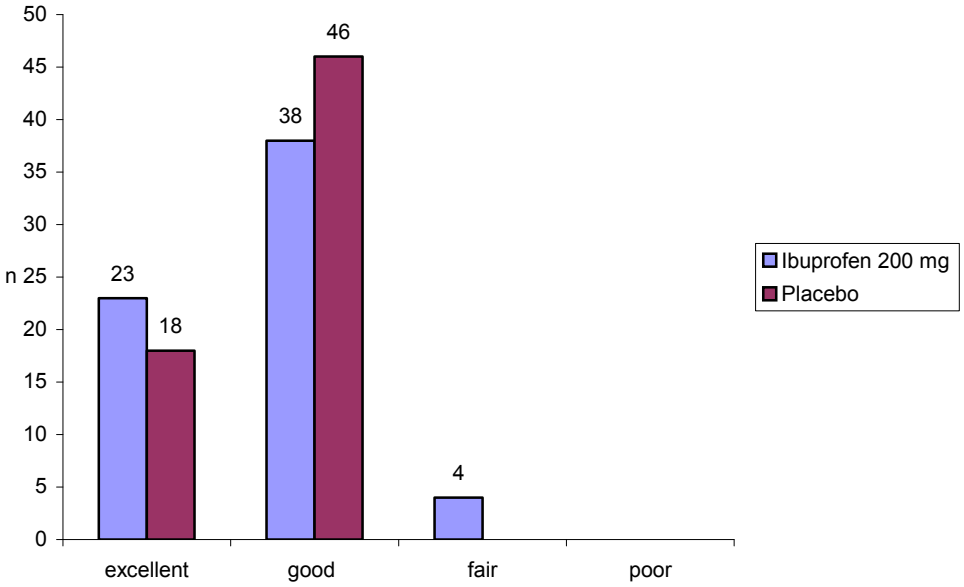


Figure 12.5 - 2 Global assessment of local tolerability by investigator at V2 (SAF)

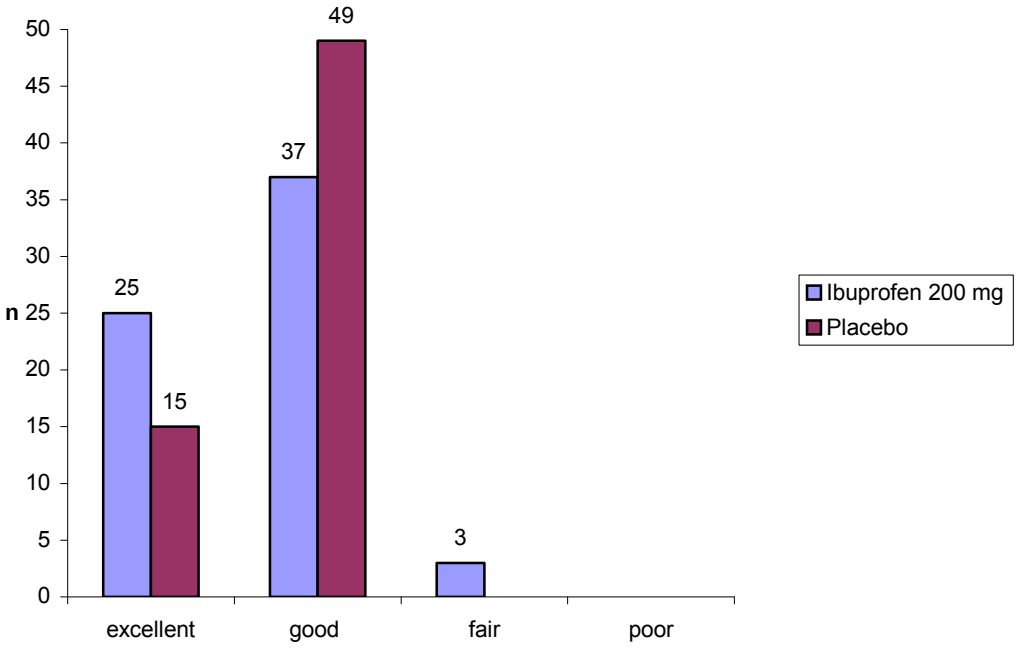


Figure 12.5 - 3 Global assessment of local tolerability by patient at V4 (SAF)

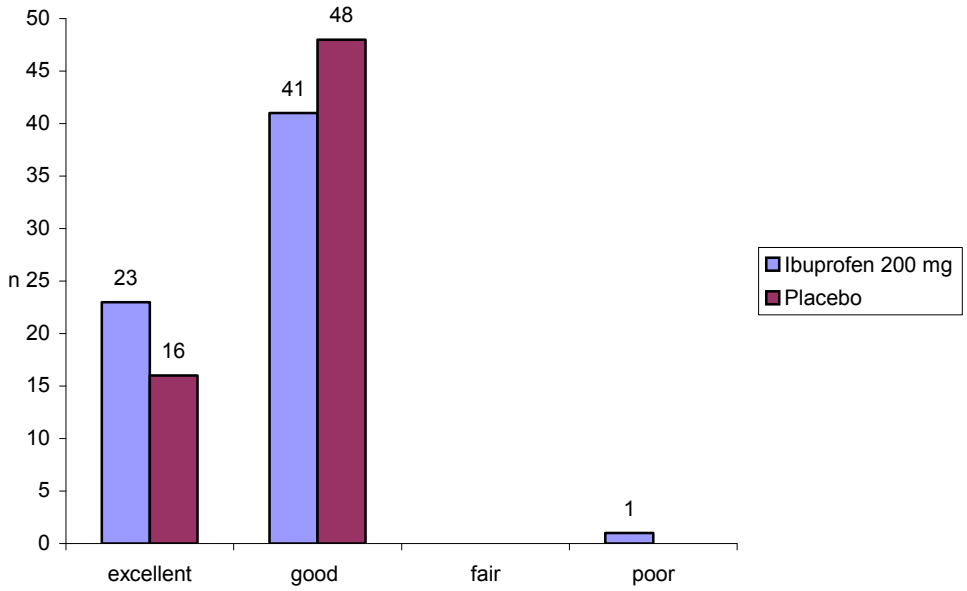


Figure 12.5 - 4 Global assessment of local tolerability by investigator at V4 (SAF)

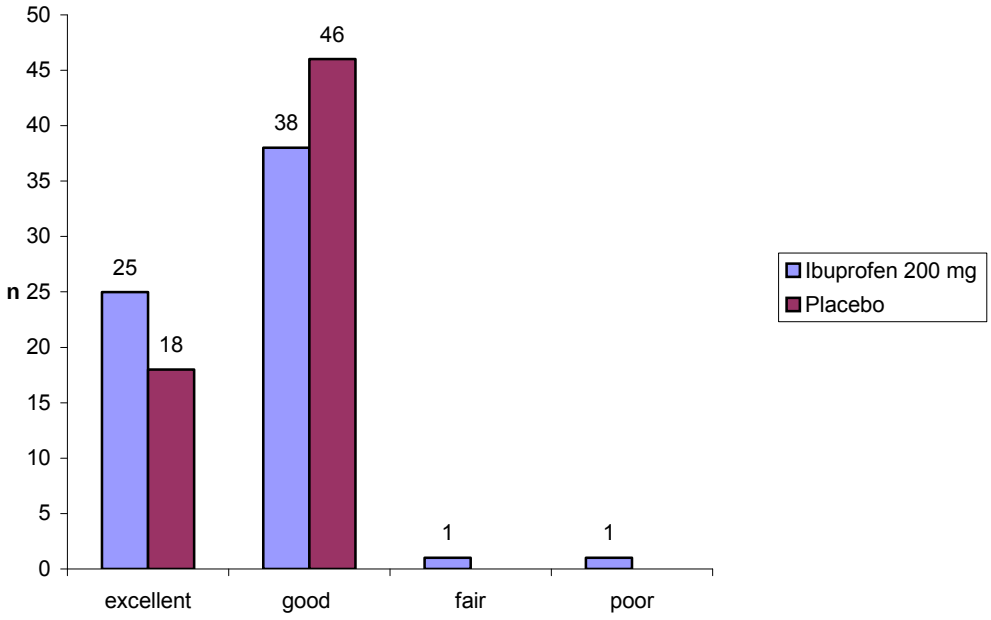


Figure 12.5 - 5 Global assessment of local tolerability by patient at V5 (SAF)

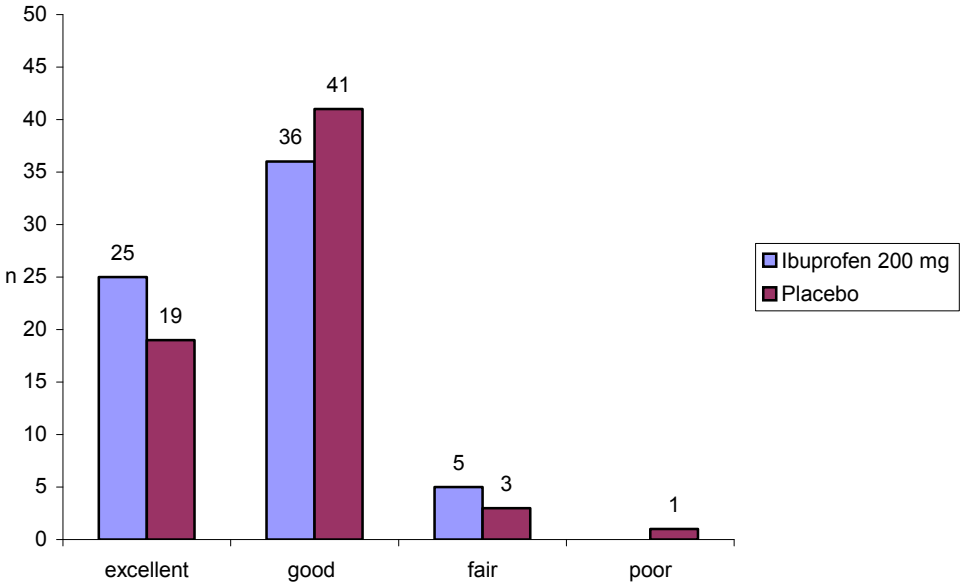
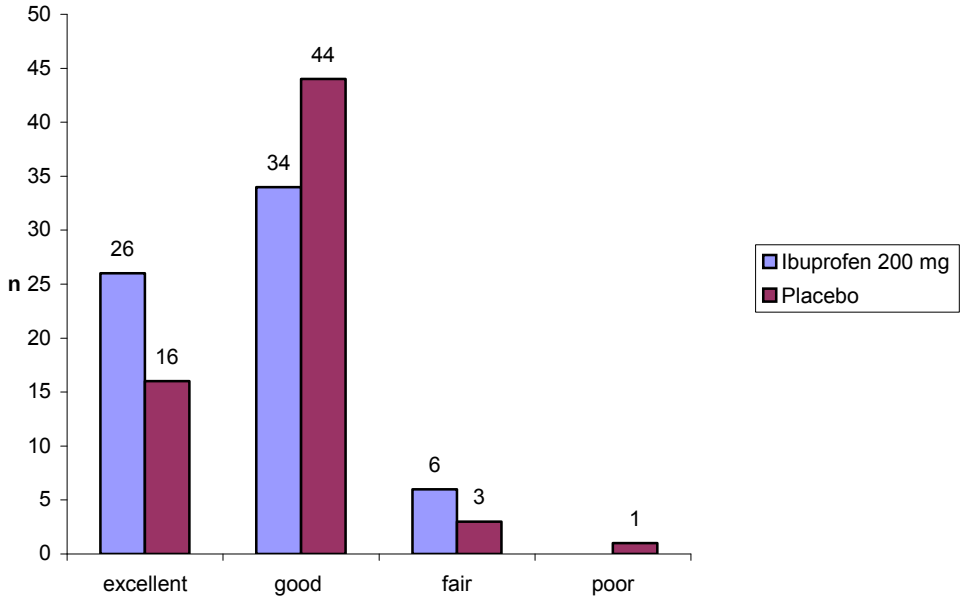


Figure 12.5 - 6 Global assessment of local tolerability by investigator at V5 (SAF)



12.6 SAFETY CONCLUSIONS

All 130 patients enrolled with acute sports-related traumatic blunt soft tissue injury/contusion who received at least one dose of the study medication were included in the safety population. All documented adverse events (AEs) were classified into treatment-emergent AEs (TEAEs) or non-treatment-emergent AEs. All documented AEs were TEAEs with a comparable proportion of TEAEs in both treatment groups.

A total of 15 patients (Ibuprofen 200 mg: n=7, Placebo: n=8) had at least one TEAE during the course of the clinical trial. The total number of TEAEs was lower in the Ibuprofen 200 mg treatment group than in the placebo group. All TEAEs in this clinical trial were non-serious and of mild severity.

The System Organ Classes most commonly affected by all non-serious TEAEs during the study were “General Disorders and Administration Site Conditions” (Ibuprofen 200 mg: n=7, Placebo: n=8) and “Infections and infestations” (Ibuprofen 200 mg: n=0, Placebo: n=2). The most frequent non-serious treatment-emergent adverse events were “Nasopharyngitis” (Ibuprofen 200 mg: n=0, Placebo: n=2), “Headache” (Ibuprofen 200 mg: n=1, Placebo: n=1), “Application site pruritus” (Ibuprofen 200 mg: n=1, Placebo: n=1), “Application site reaction” (Ibuprofen 200 mg: n=0, Placebo: n=2), and “Application site hypersensitivity” (Ibuprofen 200 mg: n=2, Placebo: n=0).

A total of nine non-serious TEAEs were classified as drug-related (probable, possible, definite) in the treatment groups (Ibuprofen 200 mg: n=4, Placebo: n=5). Most cases were probably drug-related. Due to the small number of patients and events no statistic evaluation of adverse events was performed. Other than eight adverse events relating to topical application, (Ibuprofen 200 mg: n=3, Placebo: n=5) in both treatment groups, (application site reaction, pruritus, hypersensitivity, erythema and discomfort) there was no pattern indicating any specific adverse effect related to the study drug or specifically affecting one of the study patients.

The investigation of vital signs and physical examinations did not detect any relevant safety concern. The new Ibuprofen 200 mg patch is a safe option for the treatment of acute sports-related traumatic blunt soft tissue injuries/contusions.

13 DISCUSSION AND OVERALL CONCLUSIONS

This report presents the data collected during a Phase III study to determine the ability of a new Ibuprofen patch to treat pain (tenderness) on movement (over Days 0-3) in sports-related traumatic blunt soft tissue injury/contusion, in comparison to a placebo patch.

The purpose of this study was also to assess, via VAS evaluation, pain on movement over different periods of time: 0-12 h, 0-24 h, and over Days 0-3 and over Days 0-5, AUCs over Days 0 to 3 and Days 0 to 5 using algometry, and the use of rescue medication.

A total of 130 patients (Ibuprofen n=66; placebo n=64), 88 male (Ibuprofen n=44; placebo n=44) and 42 female (Ibuprofen n=22; placebo n=20), with a mean age of 34.09 years (Ibuprofen) and 30.08 years (placebo) with acute sports-related traumatic blunt soft tissue injury/contusion were included and received five days of treatment with the Ibuprofen 200mg or placebo patch.

The VAS was used to assess pain on movement by recording, on the scale, the severity of pain at the injured site.

Pain (and therefore tenderness) at the injured site was assessed using algometry. This technique applies pressure to the site and the force required to induce pain or discomfort is recorded. The algometer has been in a number of clinical studies to assess muscle and soft tissue tenderness and sensitivity to pain[17,19,21 and 22]. An increased algometry reading relates to a decrease in pain / tenderness as the injured site is able to withstand greater applied pressure.

VAS $AUC_{0\text{-}3d}$ differed significantly between Ibuprofen 200 mg and placebo at a two-tailed significance level of 1%. The mean treatment effect was 662.82 mm*h in favour of the Ibuprofen 200mg patch. There was a significant difference for VAS AUC during the first 12h after treatment as well as during the first 24 h and for a period of five days. Tenderness (i.e. increases in the $AUC_{0\text{-}3d}$ and $AUC_{0\text{-}5d}$ algometry values) was also significantly improved by the Ibuprofen patch compared to placebo.

There was very little use of rescue medication during the trial and no statistically significant differences in the amount or time of use of rescue medication between groups.

After 1 day, patients documented a good or excellent assessment for 44.0 % of the patients in the ibuprofen group compared to 32.9 % in the placebo group. After 5 days 75.8 % of the patients in the ibuprofen group compared to 43.8 % in the placebo group documented a good or excellent assessment of treatment efficacy. Similar results were found for the global assessment of the efficacy by the investigators.

Topical delivery of drugs is not a new approach but is increasing in popularity. The route is effective and in some cases, for example with non-steroidal anti-inflammatory drugs (NSAIDs), there is very good evidence that the route offers improved clinical safety. In a study of an ibuprofen cream in adults with acute ankle sprains, significant reductions in pain were observed over the first 48 h of treatment and there were no drug related side effects recorded[10].

Ibuprofen is therefore considered to be a well-tolerated and safe drug whose side effect profile has been well characterised, both in the literature and through post-marketing experience.

The results of this trial confirm that the new Ibuprofen patch has a clinically relevant favourable impact on pain reduction in patients suffering from blunt injuries. Patients treated with the new Ibuprofen patch had statistically significant and clinically relevant reductions in pain scores and tenderness reaching a pain-free condition significantly earlier than patients in the placebo group.

All 130 patients enrolled who received at least one dose of the study medication were included in the safety population. All documented adverse events (AEs) were classified into treatment-emergent AEs (TEAEs) or non-treatment-emergent AEs. All documented AEs were TEAEs with a comparable proportion of TEAEs in both treatment groups.

14 TABLES, FIGURES AND GRAPHS REFERRED TO BUT NOT INCLUDED IN THE TEXT

14.1 Demographic Data

Table 14.1. 1: Patients per centre (FAS/PP)

	Treatment				All	
	Active patch 200 mg ibuprofen		Placebo patch			
	n	%	n	%	n	%
Site No.						
1	15	22.7	15	23.4	30	23.1
2	16	24.2	15	23.4	31	23.8
3	21	31.8	20	31.3	41	31.5
4	14	21.2	14	21.9	28	21.5
All	66	100.0	64	100.0	130	100.0

T_DEMOG.sas (25FEB2011)

Table 14.1. 2: Age (FAS/PP)

Age

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	34.09	30.08	32.12
SD	11.72	11.09	11.55
Min	18.00	18.00	18.00
Q1	24.00	20.50	23.00
Median	29.50	26.00	29.00

Age

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
Q3	45.00	38.50	44.00
Max	58.00	54.00	58.00

T_DEMOG.sas (07FEB2011)

Table 14.1. 3: Height (FAS/PP)

Height [cm]

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	178.47	178.78	178.62
SD	9.98	9.71	9.81
Min	152.00	159.00	152.00
Q1	171.00	172.00	172.00
Median	178.00	178.00	178.00
Q3	186.00	185.50	186.00
Max	205.00	200.00	205.00

T_DEMOG.sas (07FEB2011)

Table 14.1. 4: Weight (FAS/PP)

Weight [kg]

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	79.68	80.75	80.21
SD	14.26	17.06	15.65
Min	53.00	50.00	50.00
Q1	71.00	67.50	68.00
Median	78.00	79.00	78.00
Q3	90.00	93.50	90.00
Max	118.00	128.00	128.00

T_DEMOG.sas (07FEB2011)

Table 14.1. 5: BMI (FAS/PP)

BMI [kg/m²]

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	24.95	25.19	25.07
SD	3.49	4.57	4.04
Min	19.00	17.00	17.00
Q1	22.00	22.50	22.00
Median	24.00	24.00	24.00
Q3	27.00	27.00	27.00
Max	36.00	42.00	42.00

T_DEMOG.sas (07FEB2011)

Table 14.1. 6: Gender (FAS/PP)

	Treatment					
	Active patch 200 mg ibuprofen		Placebo patch		All	
	n	%	n	%	n	%
Sex						
male	44	66.7	44	68.8	88	67.7
female	22	33.3	20	31.3	42	32.3
All	66	100.0	64	100.0	130	100.0

T_DEMOG.sas (07FEB2011)

Table 14.1. 7: Ethnic origin (FAS/PP)

	Treatment				All	
	Active patch 200 mg ibuprofen		Placebo patch			
	n	%	n	%	n	%
Race						
Caucasian	65	98.5	64	100.0	129	99.2
Afro-Caribbean	1	1.5	.	0.0	1	0.8
All	66	100.0	64	100.0	130	100.0

T_DEMOG.sas (07FEB2011)

Table 14.1. 8: History and current use of cigarettes, alcohol and drugs (FAS/PP)

	Treatment				All	
	Active patch 200 mg ibuprofen		Placebo patch			
	n	%	n	%	n	%
Patient is smoker						
yes	18	27.3	12	18.8	30	23.1
no	48	72.7	52	81.3	100	76.9
Number of cigarettes a day						
.	48	72.7	52	81.3	100	76.9
less equal 10	10	15.2	5	7.8	15	11.5
11-30	6	9.1	6	9.4	12	9.2
more than 30	2	3.0	1	1.6	3	2.3
Patient smoked in the past						
.	16	24.2	11	17.2	27	20.8
yes	8	12.1	5	7.8	13	10.0
no	42	63.6	48	75.0	90	69.2
Patient consumed relevant amount of alc.						
no	66	100.0	64	100.0	130	100.0
Patient abused alcohol in the past year						
Yes, once in a while	41	62.1	37	57.8	78	60.0
Yes, regularly	2	3.0	2	3.1	4	3.1
No	23	34.8	25	39.1	48	36.9
Patient abused drugs in the past year						
.	.	0.0	1	1.6	1	0.8
no	66	100.0	63	98.4	129	99.2
All	66	100.0	64	100.0	130	100.0

T_DEMOG.sas (07FEB2011)

Table 14.1. 9: Age by centre (FAS/PP)

Age

	Treatment								
	Active patch 200 mg ibuprofen				Placebo patch				
	Site No.				Site No.				
	1	2	3	4	1	2	3	4	All
n	15	16	21	14	15	15	20	14	130
Mean	34.73	34.25	34.71	32.29	30.07	34.40	31.75	23.07	32.12
SD	11.92	10.95	13.33	10.84	12.14	11.71	11.64	3.56	11.55
Min	20.00	19.00	19.00	18.00	18.00	19.00	18.00	19.00	18.00
Q1	24.00	25.00	22.00	25.00	19.00	26.00	20.50	20.00	23.00
Median	29.00	30.50	31.00	29.50	26.00	31.00	31.50	23.00	29.00
Q3	44.00	44.50	45.00	41.00	39.00	44.00	44.00	25.00	44.00
Max	58.00	54.00	58.00	50.00	53.00	54.00	52.00	30.00	58.00

T_DEMOG_C.sas (21FEB2011)

Table 14.1.10: Height by centre (FAS/PP)

Height [cm]

	Treatment								
	Active patch 200 mg ibuprofen				Placebo patch				
	Site No.				Site No.				
	1	2	3	4	1	2	3	4	All
n	15	16	21	14	15	15	20	14	130
Mean	173.60	178.13	178.57	183.93	179.53	176.27	174.95	186.14	178.62
SD	9.85	9.59	10.46	7.73	10.65	8.50	8.68	7.62	9.81
Min	152.00	166.00	160.00	171.00	159.00	160.00	162.00	172.00	152.00
Q1	166.00	168.50	173.00	176.00	174.00	170.00	168.50	180.00	172.00
Median	176.00	177.00	178.00	184.50	178.00	178.00	174.00	186.50	178.00
Q3	183.00	186.50	185.00	190.00	186.00	183.00	179.00	190.00	186.00
Max	189.00	192.00	205.00	196.00	200.00	186.00	196.00	197.00	205.00

T_DEMOG_C.sas (21FEB2011)

Table 14.1.11: Weight by centre (FAS/PP)

Weight [kg]

	Treatment								
	Active patch 200 mg ibuprofen				Placebo patch				
	Site No.				Site No.				
	1	2	3	4	1	2	3	4	All
n	15	16	21	14	15	15	20	14	130
Mean	76.20	85.06	71.52	89.50	85.27	84.13	69.95	87.71	80.21
SD	9.82	17.69	11.33	9.68	21.80	17.02	13.75	6.41	15.65
Min	55.00	59.00	53.00	75.00	54.00	60.00	50.00	75.00	50.00
Q1	72.00	70.50	64.00	84.00	68.00	72.00	61.00	84.00	68.00
Median	75.00	85.50	71.00	88.00	84.00	78.00	66.00	85.50	78.00
Q3	80.00	97.00	76.00	92.00	103.00	98.00	77.50	93.00	90.00
Max	95.00	118.00	99.00	110.00	128.00	125.00	98.00	100.00	128.00

T_DEMOG_C.sas (21FEB2011)

Table 14.1.12: BMI by centre (FAS/PP)

BMI [kg/m²]

	Treatment								
	Active patch 200 mg ibuprofen				Placebo patch				
	Site No.				Site No.				
	1	2	3	4	1	2	3	4	All
n	15	16	21	14	15	15	20	14	130
Mean	25.33	26.69	22.33	26.50	26.20	27.33	22.85	25.14	25.07
SD	2.74	4.21	1.74	3.18	5.92	4.98	3.54	1.92	4.04
Min	22.00	20.00	19.00	22.00	18.00	22.00	17.00	22.00	17.00
Q1	23.00	22.00	21.00	25.00	23.00	23.00	21.00	24.00	22.00
Median	24.00	27.50	22.00	26.00	25.00	25.00	21.50	25.00	24.00
Q3	27.00	30.00	24.00	27.00	29.00	33.00	25.50	27.00	27.00
Max	31.00	32.00	25.00	36.00	42.00	38.00	31.00	28.00	42.00

T_DEMOG_C.sas (21FEB2011)

Table 14.1.13: Sex by centre (FAS/PP)

	Treatment															
	Active patch 200 mg ibuprofen Site No.								Placebo patch Site No.							
	1		2		3		4		1		2		3		4	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Sex																
male	7	46.7	12	75.0	11	52.4	14	100.0	9	60.0	12	80.0	9	45.0	14	100.0
female	8	53.3	4	25.0	10	47.6	.	0.0	6	40.0	3	20.0	11	55.0	.	0.0
All	15	100.0	16	100.0	21	100.0	14	100.0	15	100.0	15	100.0	20	100.0	14	100.0

T_DEMOG_C.sas (21FEB2011)

Table 14.1.14: Ethnic origin by centre (FAS/PP)

	Treatment							
	Active patch 200 mg ibuprofen							
	Site No.							
	1		2		3		4	
	n	%	n	%	n	%	n	%
Race								
Caucasian	14	93.3	16	100.0	21	100.0	14	100.0
Afro-Caribbean	1	6.7	.	0.0	.	0.0	.	0.0
All	15	100.0	16	100.0	21	100.0	14	100.0

	Treatment							
	Placebo patch							
	Site No.							
	1		2		3		4	
	n	%	n	%	n	%	n	%
Race	15	100.0	15	100.0	20	100.0	14	100.0

	Treatment							
	Placebo patch							
	Site No.							
	1		2		3		4	
	n	%	n	%	n	%	n	%
Caucasian								
Afro-Caribbean	.	0.0	.	0.0	.	0.0	.	0.0
All	15	100.0	15	100.0	20	100.0	14	100.0

T_DEMOG_C.sas (21FEB2011)

Table 14.1.15: History and current use of cigarettes, alcohol and drugs by centre (FAS/PP)

	Treatment															
	Active patch 200 mg ibuprofen								Placebo patch							
	Site No.								Site No.							
	1		2		3		4		1		2		3		4	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Patient is smoker																
yes	6	40.0	8	50.0	1	4.8	3	21.4	1	6.7	7	46.7	3	15.0	1	7.1
no	9	60.0	8	50.0	20	95.2	11	78.6	14	93.3	8	53.3	17	85.0	13	92.9
Number of cigarettes a day																
.	9	60.0	8	50.0	20	95.2	11	78.6	14	93.3	8	53.3	17	85.0	13	92.9
less equal 10	4	26.7	2	12.5	1	4.8	3	21.4	1	6.7	1	6.7	2	10.0	1	7.1
11-30	2	13.3	4	25.0	.	0.0	.	0.0	.	0.0	5	33.3	1	5.0	.	0.0
more than 30	.	0.0	2	12.5	.	0.0	.	0.0	.	0.0	1	6.7	.	0.0	.	0.0
Patient smoked in the past																
.	4	26.7	8	50.0	1	4.8	3	21.4	.	0.0	7	46.7	3	15.0	1	7.1
yes	5	33.3	1	6.3	2	9.5	.	0.0	3	20.0	1	6.7	1	5.0	.	0.0
no	6	40.0	7	43.8	18	85.7	11	78.6	12	80.0	7	46.7	16	80.0	13	92.9

	Treatment															
	Active patch 200 mg ibuprofen								Placebo patch							
	Site No.								Site No.							
	1		2		3		4		1		2		3		4	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Patient consumed relevant amount of alc.																
no	15	100.0	16	100.0	21	100.0	14	100.0	15	100.0	15	100.0	20	100.0	14	100.0
Patient abused alcohol in the past year																
Yes, once in a while	10	66.7	13	81.3	4	19.0	14	100.0	10	66.7	14	93.3	2	10.0	11	78.6
Yes, regularly	2	13.3	.	0.0	.	0.0	.	0.0	2	13.3	.	0.0	.	0.0	.	0.0
No	3	20.0	3	18.8	17	81.0	.	0.0	3	20.0	1	6.7	18	90.0	3	21.4
Patient abused drugs in the past year																
.	.	0.0	.	0.0	.	0.0	.	0.0	1	6.7	.	0.0	.	0.0	.	0.0
no	15	100.0	16	100.0	21	100.0	14	100.0	14	93.3	15	100.0	20	100.0	14	100.0
All	15	100.0	16	100.0	21	100.0	14	100.0	15	100.0	15	100.0	20	100.0	14	100.0

T_DEMOG_C.sas (21FEB2011)

Table 14.1. 16: Time to injury (h) (FAS/PP)

Time from injury to 1st application (h)

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	1.67	1.63	1.65
SD	0.72	0.76	0.74
Min	0.33	0.17	0.17
Q1	1.00	0.88	1.00
Median	1.75	1.61	1.67
Q3	2.17	2.25	2.25
Max	3.17	3.25	3.25

Table 14.1. 17: Time to injury (min) (FAS/PP)

Time from injury to 1st application (min)

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	100.09	98.09	99.11
SD	43.44	45.74	44.42
Min	20.00	10.00	10.00
Q1	60.00	52.50	60.00
Median	105.00	96.50	100.00
Q3	130.00	135.00	135.00
Max	190.00	195.00	195.00

Table 14.1. 18: Time to injury (h) by centre (FAS/PP)

Time from injury to 1st application (h)

	Centre								
	1		2		3		4		
	Treatment		Treatment		Treatment		Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	All
n	15	15	16	15	21	20	14	14	130
Mean	1.63	2.01	2.44	2.07	1.32	1.33	1.34	1.21	1.65
SD	0.57	0.58	0.41	0.82	0.62	0.52	0.66	0.80	0.74
Min	0.75	0.75	1.67	0.83	0.33	0.42	0.50	0.17	0.17
Q1	1.25	1.75	2.13	1.25	0.83	0.83	1.00	0.58	1.00
Median	1.58	2.25	2.54	2.25	1.25	1.33	1.08	1.21	1.67
Q3	1.92	2.50	2.75	2.75	1.92	1.71	1.83	1.63	2.25
Max	2.75	2.83	3.17	3.25	2.33	2.25	2.83	3.02	3.25

Table 14.1. 19: Time to injury (min) by centre (FAS/PP)

Time from injury to 1st application (min)

	Centre								
	1		2		3		4		
	Treatment		Treatment		Treatment		Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	All
n	15	15	16	15	21	20	14	14	130
Mean	98.00	120.33	146.56	124.00	79.29	80.00	80.43	72.36	99.11
SD	34.27	34.61	24.75	49.03	37.02	30.95	39.70	47.91	44.42
Min	45.00	45.00	100.00	50.00	20.00	25.00	30.00	10.00	10.00
Q1	75.00	105.00	127.50	75.00	50.00	50.00	60.00	35.00	60.00
Median	95.00	135.00	152.50	135.00	75.00	80.00	65.00	72.50	100.00

Time from injury to 1st application (min)

	Centre								
	1		2		3		4		
	Treatment		Treatment		Treatment		Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	All
Q3	115.00	150.00	165.00	165.00	115.00	102.50	110.00	98.00	135.00
Max	165.00	170.00	190.00	195.00	140.00	135.00	170.00	181.00	195.00

T_TIME_INJURY.sas (25FEB2011)

Table 14.1. 20: Study duration (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
Study Duration (d)	n	66	64
	Mean	6.00	6.00
	SD	0.00	0.00
	Min	6.00	6.00
	Q1	6.00	6.00
	Median	6.00	6.00
	Q3	6.00	6.00
	Max	6.00	6.00

T_TIM.sas (28FEB2011)

Table 14.1. 21: Total duration of treatment (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
Total duration of treatment (d)	n	66	64
	Mean	4.99	4.98
	SD	0.05	0.14
	Min	4.67	4.00
	Q1	4.99	4.99
	Median	5.00	5.00
	Q3	5.00	5.02
	Max	5.08	5.24

T_TIM.sas (28FEB2011)

Table 14.1. 22: Size of injury/contusion (FAS/PP)

Size of injury/contusion [cm²]

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	51.05	46.48	48.80
SD	23.43	19.58	21.66
Min	25.00	25.00	25.00
Q1	35.00	30.00	30.00
Median	45.00	40.00	40.00
Q3	60.00	57.50	60.00
Max	120.00	120.00	120.00

T_DEMOG.sas (25FEB2011)

Table 14.1. 23: Size of injury/contusion by centre (FAS/PP)

Size of injury/contusion [cm²]

	Treatment								
	Active patch 200 mg ibuprofen				Placebo patch				
	Site No.				Site No.				
	1	2	3	4	1	2	3	4	All
n	15	16	21	14	15	15	20	14	130
Mean	33.07	48.44	64.52	53.07	33.67	42.33	55.25	52.14	48.80
SD	6.08	15.02	27.11	25.19	13.37	11.00	22.74	20.45	21.66
Min	25.00	30.00	30.00	30.00	25.00	25.00	30.00	30.00	25.00
Q1	28.00	35.00	45.00	35.00	28.00	35.00	40.00	35.00	30.00
Median	30.00	45.00	60.00	49.00	30.00	40.00	50.00	47.50	40.00
Q3	36.00	57.50	80.00	60.00	36.00	55.00	67.50	60.00	60.00
Max	45.00	80.00	120.00	110.00	80.00	60.00	120.00	100.00	120.00

T_DEMOG_C.sas (25FEB2011)

Table 14.1. 24: Localisation of injury (FAS/PP)

	Treatment				All	
	Active patch 200 mg ibuprofen		Placebo patch			
	n	%	n	%	n	%
Location - category						
Feet	1	1.5	4	6.3	5	3.8
Lower leg	10	15.2	14	21.9	24	18.5
Knee	6	9.1	2	3.1	8	6.2
Upper leg	14	21.2	16	25.0	30	23.1
Hip	4	6.1	3	4.7	7	5.4
Upper back	1	1.5	.	0.0	1	0.8
Upper arm	15	22.7	12	18.8	27	20.8
Forearm	4	6.1	5	7.8	9	6.9
Chest	3	4.5	3	4.7	6	4.6
Low back	1	1.5	2	3.1	3	2.3
Shoulder	7	10.6	3	4.7	10	7.7
All	66	100.0	64	100.0	130	100.0

T_DEMOG.sas (25FEB2011)

Table 14.1. 25: Localisation of injury by centre (FAS/PP)

		Treatment			
		Active patch 200 mg ibuprofen		Placebo patch	
		n	%	n	%
Location - category	Site No.				
Feet	1	.	0.0	.	0.0
	2	.	0.0	.	0.0
	3	.	0.0	3	4.7
	4	1	1.5	1	1.6
Lower leg	1	3	4.5	3	4.7
	2	1	1.5	4	6.3
	3	6	9.1	5	7.8
	4	.	0.0	2	3.1
Knee	1	.	0.0	.	0.0
	2	.	0.0	.	0.0
	3	2	3.0	2	3.1
	4	4	6.1	.	0.0
Upper leg	1	1	1.5	1	1.6
	2	6	9.1	6	9.4
	3	3	4.5	2	3.1
	4	4	6.1	7	10.9
Hip	1	.	0.0	.	0.0
	2	.	0.0	.	0.0
	3	1	1.5	2	3.1
	4	3	4.5	1	1.6
Upper back	1	1	1.5	.	0.0
	2	.	0.0	.	0.0
	3	.	0.0	.	0.0
	4	.	0.0	.	0.0
Upper arm	1	7	10.6	6	9.4
	2	6	9.1	4	6.3

		Treatment			
		Active patch 200 mg ibuprofen		Placebo patch	
		n	%	n	%
	3	2	3.0	2	3.1
	4	.	0.0	.	0.0
Forearm	1	2	3.0	4	6.3
	2	.	0.0	.	0.0
	3	2	3.0	1	1.6
	4	.	0.0	.	0.0
Chest	1	.	0.0	.	0.0
	2	1	1.5	.	0.0
	3	1	1.5	1	1.6
	4	1	1.5	2	3.1
Low back	1	.	0.0	1	1.6
	2	.	0.0	.	0.0
	3	1	1.5	1	1.6
	4	.	0.0	.	0.0
Shoulder	1	1	1.5	.	0.0
	2	2	3.0	1	1.6
	3	3	4.5	1	1.6
	4	1	1.5	1	1.6
All		66	100.0	64	100.0

T_DEMOG_C.sas (25FEB2011)

Table 14.1. 26: Size of injury by localisation (FAS/PP)

Treatment Active patch 200 mg ibuprofen

	Size of injury/contusion [cm²]							
	n	Mean	SD	Min	Q1	Median	Q3	Max
Location - category								
Feet	1	60.00	.	60.00	60.00	60.00	60.00	60.00
Lower leg	10	48.40	18.42	28.00	36.00	42.50	65.00	80.00
Knee	6	45.00	23.24	30.00	30.00	35.00	50.00	90.00
Upper leg	14	61.57	20.36	40.00	50.00	57.50	70.00	120.00
Hip	4	60.75	29.81	30.00	39.00	56.50	82.50	100.00
Upper back	1	36.00	.	36.00	36.00	36.00	36.00	36.00
Upper arm	15	35.00	7.78	28.00	30.00	30.00	40.00	50.00
Forearm	4	36.50	8.50	25.00	30.50	38.00	42.50	45.00
Chest	3	93.33	20.82	70.00	70.00	100.00	110.00	110.00
Low back	1	90.00	.	90.00	90.00	90.00	90.00	90.00
Shoulder	7	53.29	31.05	28.00	30.00	45.00	55.00	120.00

Treatment Placebo patch

	Size of injury/contusion [cm²]							
	n	Mean	SD	Min	Q1	Median	Q3	Max
Location - category								
Feet	4	56.25	24.96	30.00	40.00	52.50	72.50	90.00
Lower leg	14	40.79	13.54	30.00	30.00	35.50	50.00	80.00
Knee	2	50.00	14.14	40.00	40.00	50.00	60.00	60.00
Upper leg	16	53.81	19.04	30.00	40.00	52.50	65.00	100.00
Hip	3	60.00	20.00	40.00	40.00	60.00	80.00	80.00
Upper arm	12	39.00	13.97	27.00	28.00	35.50	45.00	70.00
Forearm	5	31.00	8.03	25.00	27.00	28.00	30.00	45.00
Chest	3	46.67	12.58	35.00	35.00	45.00	60.00	60.00
Low back	2	75.00	63.64	30.00	30.00	75.00	120.00	120.00
Shoulder	3	41.67	20.82	25.00	25.00	35.00	65.00	65.00

T_DEMOG.sas (25FEB2011)

Table 14.1. 27: Number of prior medications (FAS/PP)

No. of prior medications	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	N	%	N	%
0	60	90.9	62	96.9
1	4	6.1	2	3.1
2	1	1.5	.	.
3	1	1.5	.	.

T_MED.sas (21FEB2011)

Table 14.1. 28: Number of prior and concomitant medications (FAS/PP)

No. of prior and concomitant medications	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	N	%	N	%
0	40	60.6	48	75.0
1	21	31.8	13	20.3
2	3	4.5	2	3.1
4	1	1.5	1	1.6
6	1	1.5	.	.

T_MED.sas (21FEB2011)

Table 14.1. 29: Number of concomitant medications (FAS/PP)

No. of concomitant medications	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	N	%	N	%
0	55	83.3	60	93.8
1	6	9.1	1	1.6
2	3	4.5	2	3.1
3	1	1.5	.	.
5	1	1.5	.	.
6	.	.	1	1.6

T_MED.sas (21FEB2011)

Table 14.1. 30: Frequency of prior medications (FAS/PP)

		Active patch 200 mg ibuprofen	Placebo patch
Number of prior medications	n	9	2
Number of patients with prior medications	n	6	2
Total number of patients treated	n	66	64
Patients with prior medications	%	9.1	3.1

T_MED.sas (21FEB2011)

Table 14.1. 31: Frequency of prior and concomitant medications (FAS/PP)

		Active patch 200 mg ibuprofen	Placebo patch
Number of 'prior and concomitant' medications	n	37	21
Number of patients with 'prior and concomitant' medications	n	26	16
Total number of patients treated	n	66	64
Patients with 'prior and concomitant' medications	%	39.4	25.0

T_MED.sas (21FEB2011)

Table 14.1. 32: Frequency of concomitant medications (FAS/PP)

		Active patch 200 mg ibuprofen	Placebo patch
Number of concomitant medications	n	20	11
Number of patients with concomitant medications	n	11	4
Total number of patients treated	n	66	64
Patients with concomitant medications	%	16.7	6.3

T_MED.sas (21FEB2011)

Table 14.1. 33: Prior and concomitant medication (FAS/PP)

	Treatment				All	
	Active patch 200 mg ibuprofen		Placebo patch			
	n	%	n	%	n	%
Med. Type						
Prior	9	13.6	2	5.9	11	11.0
Prior and concomitant	37	56.1	21	61.8	58	58.0
Concomitant	20	30.3	11	32.4	31	31.0
All	66	100.0	34	100.0	100	100.0

T_MED.sas (21FEB2011)

Multiple citations possible

Table 14.1. 34: Prior medication by ATC classification (FAS/PP)

	Treatment	
	Active patch 200 mg ibuprofen	Placebo patch
	n	n
ATC classification		
ANTIBIOTICS	1	.
BACTERIAL AND VIRAL VACCINES, COMBINED	.	1
BETA BLOCKING AGENTS, NON-SELECTIVE	1	.
MACROLIDES	2	.
Non-drug treatment (incl. RICE)	2	.
OTHER ANTIFUNGALS FOR TOPICAL USE	1	.
PROPIONIC ACID DERIVATIVES	.	1

	Treatment	
	Active patch 200 mg ibuprofen	Placebo patch
	n	n
SELECTIVE SEROTONIN (5HT1) AGONISTS	1	.
SULFUR-CONTAINING IMIDAZOLE DERIVATIVES	1	.
All	9	2

T_MED.sas (21FEB2011)

Multiple citations possible.

Table 14.1. 35: Prior and concomitant medication by ATC class (FAS/PP)

	Treatment	
	Active patch 200 mg ibuprofen n	Placebo patch n
ATC classification		
ACE INHIBITORS, PLAIN	.	1
ANGIOTENSIN II ANTAGONISTS AND DIURETICS	1	.
ANGIOTENSIN II ANTAGONISTS, PLAIN	1	.
ANTIANDROGENS AND ESTROGENS	.	1
BETA BLOCKING AGENTS, NON-SELECTIVE	1	.
BETA BLOCKING AGENTS, SELECTIVE	3	.
CORTICOSTEROIDS, POTENT (GROUP III)	.	1
DIHYDROPYRIDINE DERIVATIVES	1	.
ESTROGENS	1	1
EXPECTORANTS	.	1
GLUCOCORTICOIDS	1	.
HMG COA REDUCTASE INHIBITORS	1	.
INTRAUTERINE CONTRACEPTIVES	1	.
INTRAVAGINAL CONTRACEPTIVES	.	1
MEDICATED DRESSINGS WITH ANTIINFECTIVES	1	.
Non-drug treatment (incl. RICE)	1	.
OTHER ANTIFUNGALS FOR TOPICAL USE	.	1
OTHER ANTIPSORIATICS FOR TOPICAL USE	.	1
PENICILLINS WITH EXTENDED SPECTRUM	1	.
PREPARATIONS INHIBITING URIC ACID PRODUCTION	.	1
PROGESTOGENS	1	2
PROGESTOGENS AND ESTROGENS, FIXED COMBINATIONS	13	6
PROGESTOGENS AND ESTROGENS,SEQUENTIAL PREPARATIONS	1	3
PROPULSIVES	1	.
PROTON PUMP INHIBITORS	1	.
RENIN-INHIBITORS	.	1
SALICYLIC ACID PREPARATIONS	1	.
SELECTIVE BETA-2-ADRENORECEPTOR AGONISTS	1	.

	Treatment	
	Active patch 200 mg ibuprofen	Placebo patch
	n	n
SULFONAMIDES, PLAIN	1	.
THIAZIDES, PLAIN	1	.
THYROID THERAPY	2	.
All	37	21

T_MED.sas (21FEB2011)

Multiple citations possible.

Table 14.1. 36: Concomitant medication by ATC classification (FAS/PP)

	Treatment	
	Active patch 200 mg ibuprofen n	Placebo patch n
ATC classification		
ANILIDES	14	9
MACROLIDES	1	.
NASAL DECONGESTANTS FOR SYSTEMIC USE	1	.
Non-drug treatment (incl. RICE)	3	2
PROTON PUMP INHIBITORS	1	.
All	20	11

T_MED.sas (21FEB2011)

Multiple citations possible.

Table 14.1. 37: Number of patients with concomitant medication by ATC classification (FAS/PP)

	Number of patients who received the medication	
	Treatment	
	Active patch 200 mg ibuprofen	Placebo patch
ATC description		
ANILIDES	6	4
Non-drug treatment (incl. RICE)	2	1
MACROLIDES	1	.

	Number of patients who received the medication	
	Treatment	
	Active patch 200 mg ibuprofen	Placebo patch
NASAL DECONGESTANTS FOR SYSTEMIC USE	1	.
PROTON PUMP INHIBITORS	1	.

T_MED.sas (21FEB2011)

Table 14.1. 38: Treatment duration of prior medications (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
Treatment duration (d)	n	5	1
	Mean	6.80	1.00
	SD	8.84	.
	Min	1.00	1.00
	Q1	1.00	1.00
	Median	3.00	1.00
	Q3	7.00	1.00
	Max	22.00	1.00

T_MED.sas (21FEB2011)

Table 14.1. 39: Treatment duration of prior and concomitant medications (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
Treatment duration (d)	n	1	1
	Mean	5.00	7.00
	SD	.	.
	Min	5.00	7.00
	Q1	5.00	7.00
	Median	5.00	7.00
	Q3	5.00	7.00
	Max	5.00	7.00

T_MED.sas (21FEB2011)

Table 14.1. 40: Treatment duration of concomitant medications (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
Treatment duration (d)	n	18	11
	Mean	1.17	1.00
	SD	0.51	0.00
	Min	1.00	1.00
	Q1	1.00	1.00
	Median	1.00	1.00
	Q3	1.00	1.00
	Max	3.00	1.00

T_MED.sas (21FEB2011)

Table 14.1. 41: Previous diseases by verbatim term (FAS/PP)

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
	n	n	n
COMMON COLD	1	1	2
NEURODERMITIS	2	.	2
HYPERTONY	1	.	1
DISLOCATED HIP JOINT LEFT	.	1	1
VIRAL INFECTION RESPIRATORY SYSTEM	.	1	1
ARTHROSCOPY LEFT KNEE	1	.	1
OPERATION OF INGUINAL HERNIA RIGHT	1	.	1
RELAPSE OPERATION OF INGUINAL HERNIA RIGHT	1	.	1
BRONCHITIS	1	.	1
BURN RIGHT HAND	1	.	1
SINUSITIS	1	.	1
TINEA PEDIS	1	.	1
DISC PROLAPSE LUMBAR SPINE	1	.	1
OPERATION LUMBAR SPINE BY DISC PROLAPSE	1	.	1
VIRAL INFECTION	1	.	1
BYPASS OPERATION OF HEART	1	.	1
ALCOHOL ABUSE	1	.	1
DEPRESSION	1	.	1
BURNOUT SYNDROME	1	.	1
SKULL CONTUSION	1	.	1
HYPERTHYREOSIS	1	.	1
NEURODERMITIS-HEAD	1	.	1
PATELLAR TENDON SYNDROME DENERVATION DUE TO CHRONIC PATELLAR TENDON SYNDROME	.	1	1
ACL-REPAIR RIGHT KNEE	1	.	1
ACL-REPAIR	.	1	1
NOSE FRACTURE	1	.	1

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
	n	n	n
AFTER NOSE FRACTURE	1	.	1
All	24	5	29

T_DIS.sas (01MAR2011)

Table 14.1. 42: Previous diseases by preferred term (FAS/PP)

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
	n	n	n
Neurodermatitis	3	.	3
Inguinal hernia repair	2	.	2
Nasopharyngitis	1	1	2
Ligament operation	1	1	2
Facial bones fracture	2	.	2
Hypertension	1	.	1
Joint dislocation	.	1	1
Respiratory tract infection viral	.	1	1
Arthroscopy	1	.	1
Bronchitis	1	.	1
Thermal burn	1	.	1
Sinusitis	1	.	1
Tinea pedis	1	.	1
Intervertebral disc protrusion	1	.	1
Intervertebral disc operation	1	.	1
Viral infection	1	.	1

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
	n	n	n
Vascular graft	1	.	1
Alcohol abuse	1	.	1
Depression	1	.	1
Burnout syndrome	1	.	1
Contusion	1	.	1
Hyperthyroidism	1	.	1
Patellofemoral pain syndrome	.	1	1
All	24	5	29

T_DIS.sas (01MAR2011)

Table 14.1. 43: Previous diseases by SOC (FAS/PP)

	Treatment		
	Active patch 200 mg ibuprofen n	Placebo patch n	All n
Infections and infestations	5	2	7
Surgical and medical procedures	5	1	6
Injury, poisoning and procedural complications	4	1	5
Psychiatric disorders	3	.	3
Skin and subcutaneous tissue disorders	3	.	3
Musculoskeletal and connective tissue disorders	1	1	2
Vascular disorders	1	.	1
Investigations	1	.	1
Endocrine disorders	1	.	1
All	24	5	29

T_DIS.sas (01MAR2011)

Table 14.1. 44: Concomitant diseases by verbatim term (FAS/PP)

	Treatment		
	Placebo patch n	Active patch 200 mg ibuprofen n	All n
HYPERCHOLESTEROLEMIA	4	3	7
POLLINOSIS	2	3	5
HYPERTENSION	2	2	4
CORONARY HEART DISEASE	1	1	2
ADIPOSITY	1	1	2
COUGH	1	1	2
LUMBAR SPINE SYNDROME	.	2	2
MIGRAINE	.	2	2
DISC PROLAPSE L5/S1	1	1	2
HYPERURICEMIA	1	1	2
ATRIAL FIBRILLATION	.	2	2
ALLERGY AGAINST BIRCH	2	.	2
HYSTERECTOMY	.	1	1
LESION OF ROOT OF NOSE	1	.	1
ABSCESS BUTTOCKS	.	1	1
ASTHMA	.	1	1
DEPRESSION	.	1	1
LUMBAGO CRONIC	.	1	1
TINEA GENITAL	1	.	1
PSORIASIS VULGARIS	1	.	1
STEATOSIS HEPATIS	1	.	1
COPD	.	1	1
OSTEOCHONDROSIS CERVICAL SPINE	.	1	1
LEUKOCYTOSIS	1	.	1
LYMPHOPENIA	1	.	1
HEPATOSIS	1	.	1
GOUT	1	.	1

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
WEDGE-SHAPED DEFORMITY OF VERTEBRAL LUMBAR	.	1	1
SCOLIOSIS OF LUMBAR SPINE	.	1	1
CHONDROMALACIA LEFT KNEE	.	1	1
BRONCHITIS	.	1	1
OTITIS	1	.	1
TENDINITIS RIGHT WRIST	1	.	1
SUBAORTIC STENOSIS	1	.	1
MEDIAL MENISCUS LESION RIGHT SITE	1	.	1
PERIARTHRITIS HUMEROSCAPULARIS RIGHT	1	.	1
GASTRITIS	.	1	1
ANGINA PECT.	.	1	1
GASTROENTERITIS	.	1	1
DUPUYTRENS CONTRACTURE	1	.	1
LIPOMA RIGHT KIDNEY	1	.	1
COMMON COLD	.	1	1
ALLERGIC TO BARLEY	1	.	1
ALLERGY OF HAZELNUT AND CATS	1	.	1
ALLERGY AGAINST GRASSES	1	.	1
ESOPHAGEAL REFLUX DURING SPEED RUNNING	1	.	1
ALLERGY TO BIRCH TREE, GRASES, HAZELNUT	1	.	1
ALLERGY TO NICKEL DUST	.	1	1
FOOD INTOLERANCE AGAINST TOMATOES	.	1	1
GRAS ALLERGY	1	.	1
HAY FEVER	1	.	1
ALLERGY AGAINST GRAS	1	.	1
ALLERGY AGAINST RYE	1	.	1
ALLERGY AGAINST AMOXICILLIN	1	.	1
DUST ALLERGY	1	.	1

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
CAT ALLERGY	1	.	1
EXERCISE INDUCED ASTHMA	1	.	1
STRUMA NODOSA	.	1	1
GRASS ALLERGY	1	.	1
ALLERGY AGAINST BENZOCAIN	1	.	1
STRESS ALLERGY	1	.	1
MILK ALLERGY	1	.	1
NUT ALLERGY	1	.	1
ALLERGIC ASTHMA	.	1	1
ALLERGY AGAINST PENICILLIN	.	1	1
RHINITIS ALLERGIC	.	1	1
INTOLERANCE AGAINST UNCOOKED PEACHES, APPLES, CARROTS	.	1	1
CHRONIC INFECTION ACHILLES TENDON	.	1	1
ACL-REPAIR, AFTER	.	1	1
CHRONIC LUMBAR PAIN SPINE	.	1	1
All	48	44	92

Table 14.1. 45: Concomitant diseases by preferred term (FAS/PP)

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
Seasonal allergy	9	3	12
Hypercholesterolaemia	4	3	7
Hypertension	2	2	4
Food allergy	3	.	3
Hypersensitivity	3	.	3

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
Drug hypersensitivity	2	1	3
Asthma	.	2	2
Back pain	.	2	2
Coronary artery disease	1	1	2
Obesity	1	1	2
Cough	1	1	2
Bone pain	.	2	2
Tendonitis	1	1	2
Migraine	.	2	2
Intervertebral disc protrusion	1	1	2
Hyperuricaemia	1	1	2
Atrial fibrillation	.	2	2
Food intolerance	.	2	2
Hysterectomy	.	1	1
Face injury	1	.	1
Subcutaneous abscess	.	1	1
Depression	.	1	1
Tinea cruris	1	.	1
Psoriasis	1	.	1
Hepatic steatosis	1	.	1
Chronic obstructive pulmonary disease	.	1	1
Osteochondrosis	.	1	1
Leukocytosis	1	.	1
Lymphopenia	1	.	1
Liver disorder	1	.	1
Gout	1	.	1
Spinal deformity	.	1	1
Scoliosis	.	1	1

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
Chondromalacia	.	1	1
Bronchitis	.	1	1
Ear infection	1	.	1
Subvalvular aortic stenosis	1	.	1
Meniscus lesion	1	.	1
Periarthritis	1	.	1
Gastritis	.	1	1
Angina pectoris	.	1	1
Gastroenteritis	.	1	1
Dupuytren's contracture	1	.	1
Renal lipomatosis	1	.	1
Nasopharyngitis	.	1	1
Gastrooesophageal reflux disease	1	.	1
Allergy to metals	.	1	1
House dust allergy	1	.	1
Allergy to animal	1	.	1
Asthma exercise induced	1	.	1
Goitre	.	1	1
Milk allergy	1	.	1
Rhinitis allergic	.	1	1
Ligament operation	.	1	1
All	48	44	92

T_DIS.sas (01MAR2011)

Table 14.1. 46: Concomitant diseases by SOC (FAS/PP)

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
Immune system disorders	20	5	25
Musculoskeletal and connective tissue disorders	4	10	14
Metabolism and nutrition disorders	7	7	14
Respiratory, thoracic and mediastinal disorders	2	5	7
Infections and infestations	2	4	6
Cardiac disorders	2	4	6
Vascular disorders	2	2	4
Surgical and medical procedures	.	2	2
Injury, poisoning and procedural complications	2	.	2
Hepatobiliary disorders	2	.	2
Blood and lymphatic system disorders	2	.	2
Nervous system disorders	.	2	2
Gastrointestinal disorders	1	1	2
Psychiatric disorders	.	1	1
Skin and subcutaneous tissue disorders	1	.	1
Renal and urinary disorders	1	.	1
Endocrine disorders	.	1	1
All	48	44	92

T_DIS.sas (01MAR2011)

Table 14.1. 47: Frequency of previous diseases (FAS/PP)

		Active patch 200 mg ibuprofen	Placebo patch
Number of Previous diseases	n	24	5
Number of patients with previous diseases	n	12	5
Total number of patients treated	n	66	64
Patients with previous diseases	%	18.2	7.8

T_DIS.sas (01MAR2011)

Table 14.1. 48: Frequency of concomitant diseases (FAS/PP)

		Active patch 200 mg ibuprofen	Placebo patch
Number of concomitant diseases	n	44	48
Number of patients with concomitant diseases	n	19	20
Total number of patients treated	n	66	64
Patients with concomitant diseases	%	28.8	31.3

T_DIS.sas (01MAR2011)

Table 14.1. 49: Number of previous diseases (FAS/PP)

No. of diseases	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	N	%	N	%
0	54	81.8	59	92.2
1	7	10.6	5	7.8
2	3	4.5	.	.
3	1	1.5	.	.
8	1	1.5	.	.
All	66	100.0	64	100.0

T_DIS.sas (01MAR2011)

Table 14.1. 50: Number of concomitant diseases (FAS/PP)

No. of diseases	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	N	%	N	%
0	47	71.2	44	68.8
1	9	13.6	6	9.4
2	4	6.1	6	9.4
3	3	4.5	5	7.8
4	.	.	2	3.1
5	1	1.5	.	.
6	1	1.5	.	.
7	1	1.5	1	1.6
All	66	100.0	64	100.0

T_DIS.sas (01MAR2011)

Table 14.1. 51: Dropouts - Study completion (SAF/FAS/PP)

	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	n	%	n	%
Completion of trial according trial protocol				
yes	66	100.0	64	100.0
Total	66	100.0	64	100.0

T_TSS.sas (17FEB2011)

Table 14.1. 52: Compliance – Patch detached (FAS/PP)

	Treatment															
	Active patch 200 mg ibuprofen Visit								Placebo patch Visit							
	2		3		4		5		2		3		4		5	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Patch became detached																
yes	1	1.5	3	4.5	2	3.0	.	0.0	4	6.3	3	4.7	2	3.1	4	6.3
no	65	98.5	63	95.5	64	97.0	66	100.0	60	93.8	61	95.3	62	96.9	60	93.8
All	66	100.0	66	100.0	66	100.0	66	100.0	64	100.0	64	100.0	64	100.0	64	100.0

T_Compliance.sas (02MAR2011)

Table 14.1. 53: Compliance – Number of used patch returned (FAS/PP)

Number of used patches returned

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	4.92	4.88	4.90
SD	0.54	0.60	0.57
Min	2.00	1.00	1.00
Q1	5.00	5.00	5.00
Median	5.00	5.00	5.00
Q3	5.00	5.00	5.00
Max	6.00	6.00	6.00

T_Compliance.sas (02MAR2011)

14.2 Efficacy Data

Table 14.2. 1: VAS AUC 0-3d (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-3d [mm*h]	n	66	64
	Mean	2768.13	3430.95
	SD	1501.29	1253.14
	Min	84.50	163.00
	Q1	1587.00	2751.50
	Median	2984.00	3537.75
	Q3	3791.50	4259.00
	Max	5488.50	6123.00

T_AUC03_VAS.sas (07FEB2011)

Table 14.2. 2: VAS AUC 0-3d by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-3d [mm*h]	n	15	15	16	15	21	20	14	14
	Mean	1268.13	3486.53	4128.66	4123.90	2498.21	3264.68	3225.25	2866.50
	SD	1538.56	1944.39	771.75	840.54	1091.69	830.99	991.09	908.50
	Min	84.50	163.00	2960.50	2764.50	1068.50	1260.00	820.00	1537.00
	Q1	140.50	1139.00	3549.00	3265.00	1607.00	2623.00	2776.50	2137.00
	Median	368.50	4183.00	3967.75	4330.50	2355.00	3516.00	3129.00	3064.00
	Q3	1705.50	4807.00	4723.75	4877.00	3127.50	3798.50	4040.50	3617.00

		Site No.							
		1 Treatment		2 Treatment		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
	Max	4545.50	6123.00	5488.50	5404.50	5430.00	4398.50	4936.00	4160.50

T_AUC03_VAS_C.sas (21FEB2011)

Table 14.2. 3: VAS AUC 0-12h (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-12h [mm*h]	n	66	64
	Mean	615.07	700.13
	SD	236.00	165.49
	Min	84.50	163.00
	Q1	456.50	642.50
	Median	663.50	716.25
	Q3	789.50	809.00
	Max	994.50	1053.00

T_AUC012h_VAS.sas (07FEB2011)

Table 14.2. 4: VAS AUC 0-12h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-12h [mm*h]	n	15	15	16	15	21	20	14	14
	Mean	370.93	694.53	756.47	734.10	624.02	703.13	701.61	665.43
	SD	255.52	256.48	193.77	198.63	136.18	63.06	186.41	104.41
	Min	84.50	163.00	316.00	256.50	401.50	597.50	238.00	493.00
	Q1	140.50	437.00	681.50	607.00	568.50	650.25	628.50	602.50
	Median	301.00	761.50	789.25	778.50	605.00	727.25	735.25	651.00
	Q3	619.50	856.00	905.50	922.00	714.00	742.25	844.00	709.00
	Max	871.50	1053.00	994.50	937.50	942.00	792.50	958.50	876.50

T_AUC012h_VAS_C.sas (21FEB2011)

Table 14.2. 5: Least square results of VAS AUC_{0-12h} by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	251.33 55.35	585.81 54.00
		Mean treatment effect (LS)	-334.48	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-458.43; -210.53 (p<0.0001)	
	2	LS Mean LS Standard error	755.21 48.68	724.93 49.82
		Mean treatment effect (LS)	30.27	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-93.15; 153.69 (p=0.6281)	
	3	LS Mean LS Standard error	678.80 40.72	753.79 41.55
		Mean treatment effect (LS)	-75.00	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-181.26; 31.27 (p=0.1649)	
	4	LS Mean LS Standard error	741.52 67.44	726.87 78.67
		Mean treatment effect (LS)	14.65	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-117.15; 146.45 (p=0.8262)	

Table 14.2. 6: VAS pain on movement at 12 h (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
VAS 12h after 1st appl. (mm)	n	66	64
	Mean	46.26	53.69
	SD	24.28	18.81
	Min	0.00	0.00
	Q1	30.00	48.00
	Median	51.50	55.50
	Q3	64.00	64.50
	Max	83.00	82.00

T_VAS_12h_24h.sas (07FEB2011)

Table 14.2. 7: VAS pain on movement at 12 h by centre (FAS/PP)

		Site No.							
		1 Treatment		2 Treatment		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS 12h after 1st appl.	n	15	15	16	15	21	20	14	14
	Mean	19.27	49.40	62.50	59.93	48.48	55.80	53.29	48.57
	SD	24.43	27.45	20.74	23.00	12.30	7.27	18.69	12.45
	Min	0.00	0.00	2.00	1.00	29.00	37.00	9.00	31.00
	Q1	0.00	16.00	59.50	54.00	40.00	52.00	42.00	33.00
	Median	6.00	55.00	67.50	58.00	47.00	58.50	58.50	50.50
	Q3	36.00	70.00	75.00	78.00	58.00	61.00	68.00	58.00
	Max	75.00	82.00	83.00	82.00	76.00	65.00	76.00	69.00

T_VAS_12h_24h_C.sas (21FEB2011)

Table 14.2. 8: : Least square results of VAS at 12 h by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	8.69 5.90	39.75 5.76
		Mean treatment effect (LS)	-31.07	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-44.29; -17.85 (p<0.0001)	
	2	LS Mean LS Standard error	61.98 5.19	59.20 5.31
		Mean treatment effect (LS)	2.78	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-10.38; 15.95 (p=0.6760)	
	3	LS Mean LS Standard error	53.12 4.34	59.91 4.43
		Mean treatment effect (LS)	-6.79	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-18.13; 4.54 (p=0.2376)	
	4	LS Mean LS Standard error	57.49 7.19	54.57 8.39
		Mean treatment effect (LS)	2.92	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-11.14; 16.97 (p=0.6817)	

Table 14.2. 9: VAS AUC 0-24 h (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-24h [mm*h]	n	66	64
	Mean	1156.86	1347.64
	SD	500.13	364.15
	Min	84.50	163.00
	Q1	822.50	1231.00
	Median	1270.75	1383.00
	Q3	1493.50	1551.00
	Max	1962.00	2103.00

T_AUC024h_VAS.sas (07FEB2011)

Table 14.2. 10: VAS AUC 0-24 h by centre (FAS/PP)

		Site No.							
		1 Treatment		2 Treatment		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-24h [mm*h]	n	15	15	16	15	21	20	14	14
	Mean	631.33	1310.53	1508.16	1472.70	1152.50	1342.88	1324.96	1260.21
	SD	559.28	603.65	346.86	355.60	306.01	170.69	360.38	208.63
	Min	84.50	163.00	730.00	628.50	707.50	984.00	400.00	956.50
	Q1	140.50	611.00	1375.50	1268.00	864.50	1235.50	1192.50	1049.00
	Median	344.50	1469.50	1546.00	1498.50	1133.00	1419.50	1377.75	1293.00
	Q3	1059.50	1723.00	1774.25	1750.00	1352.50	1464.00	1595.50	1385.00
	Max	1753.50	2103.00	1912.50	1888.50	1962.00	1566.50	1708.50	1656.50

T_AUC024h_VAS_C.sas (21FEB2011)

Table 14.2. 11: : Least square results of VAS AUC_{0-24h} by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	358.41 114.94	1062.89 112.13
		Mean treatment effect (LS)	-704.49	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-961.88; -447.09 (p<0.0001)	
	2	LS Mean LS Standard error	1512.80 101.09	1461.09 103.45
		Mean treatment effect (LS)	51.71 (p=0.6902)	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-204.57; 307.99	
	3	LS Mean LS Standard error	1283.17 84.55	1463.65 86.27
		Mean treatment effect (LS)	-180.48 (p=0.1080)	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-401.14; 40.18	
	4	LS Mean LS Standard error	1401.28 140.05	1380.24 163.37
		Mean treatment effect (LS)	21.04	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-252.64; 294.72 (p=0.8793)	

Table 14.2. 12: VAS pain on movement at 24 h (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
VAS at V2 (24h after 1st appl.) (mm)	n	66	64
	Mean	44.45	54.70
	SD	23.33	17.91
	Min	0.00	0.00
	Q1	29.00	49.00
	Median	48.00	57.50
	Q3	62.00	65.00
	Max	88.00	93.00

T_VAS_12h_24h.sas (07FEB2011)

Table 14.2. 13: VAS pain on movement at 24 h by centre (FAS/PP)

		Site No.							
		1 Treatment		2 Treatment		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS at V2 (24h after 1st appl.)	n	15	15	16	15	21	20	14	14
	Mean	22.33	52.87	62.69	63.47	42.33	52.50	50.50	50.43
	SD	29.20	31.16	10.16	8.88	16.35	10.71	15.89	11.71
	Min	0.00	0.00	44.00	50.00	17.00	23.00	18.00	28.00
	Q1	0.00	15.00	54.00	56.00	29.00	48.00	44.00	45.00
	Median	5.00	60.00	65.00	66.00	43.00	54.00	53.00	51.00
	Q3	48.00	78.00	71.50	70.00	48.00	61.00	59.00	56.00
	Max	73.00	93.00	78.00	80.00	88.00	64.00	74.00	70.00

T_VAS_12h_24h_C.sas (21FEB2011)

Table 14.2. 14: : Least square results of VAS at Hour 24 by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	8.90 5.38	40.78 5.25
		Mean treatment effect (LS)	-31.88	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-43.92; -19.84 (p<0.0001)	
	2	LS Mean LS Standard error	64.54 4.73	64.24 4.84
		Mean treatment effect (LS)	0.30	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-11.69; 12.29 (p=0.9606)	
	3	LS Mean LS Standard error	49.87 3.96	59.66 4.04
		Mean treatment effect (LS)	-9.79	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-20.11; 0.53 (p=0.0628)	
	4	LS Mean LS Standard error	51.20 6.55	52.57 7.64
		Mean treatment effect (LS)	-1.37	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-14.17; 11.43 (p=0.8326)	

Table 14.2. 15: VAS AUC 0-5 d (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-5d [mm*h]	n	66	64
	Mean	3710.86	4828.20
	SD	2379.95	2168.08
	Min	84.50	163.00
	Q1	1683.00	3026.00
	Median	3930.25	5025.00
	Q3	5109.50	6484.75
	Max	9064.50	9531.00

T_AUC05_VAS.sas (07FEB2011)

Table 14.2. 16: VAS AUC 0-5 d by centre (FAS/PP)

		Site No.							
		1 Treatment		2 Treatment		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-5d [mm*h]	n	15	15	16	15	21	20	14	14
	Mean	1680.93	5180.93	5945.16	5835.10	3029.07	4537.28	4354.96	3787.07
	SD	2324.03	3120.21	1683.82	1728.60	1806.41	1608.94	1454.76	1637.95
	Min	84.50	163.00	3694.00	3040.50	1068.50	1260.00	832.00	1628.50
	Q1	140.50	1415.00	4551.00	3960.50	1616.50	3361.00	3920.00	2285.50
	Median	368.50	6331.00	5169.25	6718.50	2465.50	4984.75	4189.50	3956.25
	Q3	2101.50	7686.00	7495.00	7313.00	4219.50	5748.75	5015.50	4992.50
	Max	6945.50	9531.00	9064.50	8044.50	8094.00	6918.50	7660.00	6272.50

T_AUC05_VAS_C.sas (21FEB2011)

Table 14.2. 17: Least square results of VAS AUC_{0-5d} by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	445.07 609.87	4052.23 594.98
		Mean treatment effect (LS)	-3607.16	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-4972.88; -2241.44 (p<0.0001)	
	2	LS Mean LS Standard error	5847.69 536.37	5655.25 548.91
		Mean treatment effect (LS)	192.44	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-1167.38; 1552.27 (p=0.7798)	
	3	LS Mean LS Standard error	3534.82 448.64	5000.04 457.76
		Mean treatment effect (LS)	-1465.22	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-2636.06; -294.37 (p=0.0146)	
	4	LS Mean LS Standard error	4928.97 743.12	4630.90 866.82
		Mean treatment effect (LS)	298.07	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-1154.08; 1750.21 (p=0.6852)	

Table 14.2. 18: AUC Tenderness of injured site 0-3d (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness of injured site 0-3d [N/cm²*d]	n	66	64
	Mean	7.34	6.68
	SD	3.03	3.46
	Min	1.80	1.50
	Q1	4.55	4.20
	Median	7.45	5.70
	Q3	9.20	8.05
	Max	13.40	16.50

T_AUC03_ALGINJ.sas (09FEB2011)

Table 14.2. 19: AUC Tenderness of injured site 0-3d by centre (FAS/PP)

		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness of injured site 0-3d [N/cm²*d]	n	15	15	16	15
	Mean	7.81	5.05	3.50	3.66
	SD	1.62	1.40	1.23	1.13
	Min	3.95	3.15	1.80	1.50
	Q1	6.85	3.80	2.55	3.10
	Median	8.30	4.65	3.70	3.50
	Q3	8.75	6.55	4.15	4.30
	Max	10.35	7.40	5.70	5.80

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness of injured site 0-3d [N/cm²*d]	n	21	20	14	14
	Mean	7.82	6.32	10.50	12.19
	SD	1.79	1.48	2.59	2.16
	Min	4.45	3.40	4.35	8.05
	Q1	6.85	5.15	9.20	10.60
	Median	8.00	6.60	11.23	12.73
	Q3	9.05	7.33	12.45	13.00
	Max	10.95	8.90	13.40	16.50

T_AUC03_ALGINJ_C.sas (21FEB2011)

Table 14.2. 20: Least square results of AUC_{0-3d} Algometry (tenderness) of injured site by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	9.34 0.38	6.55 0.37
		Mean treatment effect (LS)	2.80	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	1.85; 3.74 (p<0.0001)	
	2	LS Mean LS Standard error	5.14 0.37	5.18 0.38
		Mean treatment effect (LS)	-0.04	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-0.98; 0.91 (p=0.9408)	
	3	LS Mean LS Standard error	8.23 0.29	6.88 0.30
		Mean treatment effect (LS)	1.35	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.54; 2.168 (p=0.0013)	
	4	LS Mean LS Standard error	6.93 0.52	7.60 0.60
		Mean treatment effect (LS)	-0.67	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-1.68; 0.34 (p=0.1913)	

Table 14.2. 21: Tenderness of injured site at Day 1 (24h) (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 1 (24 h) (N/cm²)	n	66	64
	Mean	2.17	1.96
	SD	0.97	1.10
	Min	0.40	0.50
	Q1	1.30	1.10
	Median	2.10	1.75
	Q3	2.90	2.35
	Max	4.20	5.00

T_ALGINJ_24h.sas (09FEB2011)

Table 14.2. 22: Tenderness of injured site at Day 1 (24h) by centre (FAS/PP)

		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 1 (24 h)	n	15	15	16	15
	Mean	2.13	1.42	1.00	1.03
	SD	0.55	0.51	0.33	0.33
	Min	1.20	0.80	0.40	0.50
	Q1	1.70	1.00	0.80	0.80
	Median	2.00	1.30	1.00	1.00
	Q3	2.60	1.80	1.20	1.20
	Max	3.00	2.30	1.60	1.80

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 1 (24 h)	n	21	20	14	14
	Mean	2.39	1.87	3.23	3.65
	SD	0.61	0.51	0.83	0.80
	Min	1.00	1.00	1.20	2.30
	Q1	2.10	1.45	2.90	3.10
	Median	2.40	1.90	3.40	3.80
	Q3	2.80	2.25	3.60	4.10
	Max	3.50	2.90	4.20	5.00

T_ALGINJ_24h_C.sas (22FEB2011)

Table 14.2. 23: Least square results of Tenderness of injured site at Day 1 (24h) by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	2.642 0.128	1.916 0.127
		Mean treatment effect (LS)	0.726	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.403; 1.048 (p<0.0001)	
	2	LS Mean LS Standard error	1.545 0.126	1.526 0.129
		Mean treatment effect (LS)	0.019	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-0.302; 0.340 (p=0.9075)	
	3	LS Mean LS Standard error	2.523 0.099	2.057 0.102
		Mean treatment effect (LS)	0.466	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.189; 0.742 (p=0.0011)	
	4	LS Mean LS Standard error	2.043 0.176	2.128 0.205
		Mean treatment effect (LS)	-0.085	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-0.428; 0.258 (p=0.6241)	

Table 14.2. 24: Tenderness of injured site at Day 0 (Baseline) by centre (FAS/PP)

		Site No. 1 Treatment: Active patch 200 mg ibuprofen	Site No. 1 Treatment: Placebo patch	Site No. 2 Treatment: Active patch 200 mg ibuprofen	Site No. 2 Treatment: Placebo patch
Tenderness of injured site at assessment Day 0 (BL)	n	15	15	16	15
	Mean	0.85	0.87	0.81	0.87
	SD	0.27	0.22	0.28	0.31
	Min	0.50	0.50	0.40	0.30
	Q1	0.60	0.70	0.60	0.80
	Median	0.80	0.90	0.80	0.80
	Q3	1.10	1.00	1.00	1.20
	Max	1.30	1.20	1.40	1.40

		Site No. 3 Treatment: Active patch 200 mg ibuprofen	Site No. 3 Treatment: Placebo patch	Site No. 4 Treatment: Active patch 200 mg ibuprofen	Site No. 4 Treatment: Placebo patch
Tenderness of injured site at assessment Day 0 (BL)	n	21	20	14	14
	Mean	1.27	1.21	2.74	3.11
	SD	0.33	0.37	0.78	0.55
	Min	0.60	0.70	1.00	2.00
	Q1	1.00	0.95	2.30	2.70
	Median	1.20	1.10	2.85	3.00
	Q3	1.60	1.35	3.20	3.40
	Max	1.90	2.00	3.90	4.20

T_ALGINJ_24h_C.sas (22FEB2011)

Table 14.2. 25: **Tenderness of injured site at Day 2 (V3) by centre (FAS/PP)**

		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 2	n	15	15	16	15
	Mean	3.38	1.99	1.22	1.31
	SD	0.90	0.63	0.47	0.41
	Min	1.30	1.20	0.60	0.60
	Q1	2.90	1.40	0.90	1.00
	Median	3.50	2.00	1.20	1.30
	Q3	3.80	2.70	1.60	1.60
	Max	4.80	2.90	2.00	2.00

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 2	n	21	20	14	14
	Mean	3.06	2.42	3.73	4.54
	SD	0.80	0.60	0.99	0.88
	Min	1.60	1.30	1.60	3.10
	Q1	2.60	2.00	3.30	3.90
	Median	3.10	2.50	3.95	4.65
	Q3	3.50	2.90	4.10	5.20
	Max	4.70	3.50	5.40	6.50

T_ALGINJ_24h_C.sas (22FEB2011)

Table 14.2. 26: Tenderness of injured site at Day 3 (V4) by centre (FAS/PP)

		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 3	n	15	15	16	15
	Mean	3.74	2.41	1.75	1.79
	SD	0.92	0.62	0.70	0.66
	Min	1.80	1.20	1.00	0.50
	Q1	3.50	1.80	1.00	1.40
	Median	3.50	2.50	1.70	1.60
	Q3	4.60	2.90	2.40	2.20
	Max	4.90	3.40	3.00	3.00

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 3	n	21	20	14	14
	Mean	3.47	2.85	4.36	4.91
	SD	0.73	0.72	1.09	1.18
	Min	2.10	1.40	2.10	3.30
	Q1	3.00	2.25	3.90	4.00
	Median	3.30	3.05	4.45	4.55
	Q3	4.00	3.20	5.00	5.90
	Max	4.90	4.20	5.90	7.60

T_ALGINJ_24h_C.sas (22FEB2011)

Table 14.2. 27: Tenderness of injured site at Day 5 (V5) by centre (FAS/PP)

		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 5	n	15	15	16	15
	Mean	3.86	2.82	2.79	2.67
	SD	0.90	0.76	1.22	0.93
	Min	2.10	1.80	1.40	1.10
	Q1	3.50	2.50	1.60	2.00
	Median	3.70	2.60	2.80	2.40
	Q3	4.80	3.00	4.00	3.60
	Max	5.10	4.90	4.40	4.40

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 5	n	21	20	14	14
	Mean	3.77	3.18	5.32	5.64
	SD	0.71	0.64	1.30	1.40
	Min	2.40	1.70	3.20	3.90
	Q1	3.10	2.80	4.40	4.30
	Median	3.80	3.10	5.15	5.20
	Q3	4.20	3.60	6.20	6.90
	Max	5.30	4.30	8.10	8.20

T_ALGINJ_24h_C.sas (22FEB2011)

Table 14.2. 28: AUC tenderness of injured site 0-5 d (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness of injured site 0-5d [N/cm²*d]	n	66	64
	Mean	14.52	13.14
	SD	5.44	6.12
	Min	4.20	3.10
	Q1	10.50	8.60
	Median	14.45	11.98
	Q3	18.25	15.58
	Max	26.00	31.60

T_AUC05_ALGINJ.sas (07FEB2011)

Table 14.2. 29: AUC tenderness of injured site 0-5 d by centre (FAS/PP)

		Site No.			
		1 Treatment		2 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness of injured site 0-5d [N/cm²*d]	n	15	15	16	15
	Mean	15.41	10.28	8.04	8.13
	SD	3.37	2.44	3.07	2.58
	Min	7.95	6.20	4.20	3.10
	Q1	14.05	8.20	5.00	6.50
	Median	15.50	10.15	8.40	8.10
	Q3	18.25	12.35	10.25	10.10
	Max	20.35	14.40	12.70	12.80

		Site No.			
		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness of injured site 0-5d [N/cm²*d]	n	21	20	14	14
	Mean	15.06	12.34	20.18	22.74
	SD	3.13	2.75	4.72	4.26
	Min	8.95	6.50	9.65	16.05
	Q1	12.85	10.18	17.50	19.15
	Median	15.50	13.00	20.68	22.28
	Q3	17.25	14.28	23.90	26.95
	Max	21.10	17.00	26.00	31.60

T_AUC05_ALGINJ_C.sas (21FEB2011)

Table 14.2. 30: Least square results of AUC_{0-5d} tenderness of injured site by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	18.12 0.77	12.92 0.76
		Mean treatment effect (LS)	5.20	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	3.26; 7.13 (p<0.0001)	
	2	LS Mean LS Standard error	10.94 0.76	10.86 0.78
		Mean treatment effect (LS)	0.08	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-1.85; 2.01 (p=0.9321)	
	3	LS Mean LS Standard error	15.80 0.59	13.33 0.61
		Mean treatment effect (LS)	2.48	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.82; 4.14 (p=0.0038)	
	4	LS Mean LS Standard error	13.85 1.05	14.57 1.23
		Mean treatment effect (LS)	-0.72	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-2.78; 1.35 (p=0.4932)	

Table 14.2. 31: AUC tenderness ratio 0-3d (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness ratio 0-3d	n	66	64
	Mean	1.58	1.40
	SD	0.57	0.45
	Min	0.54	0.37
	Q1	1.13	1.06
	Median	1.65	1.47
	Q3	2.02	1.77
	Max	3.26	2.27

T_AUC03_RATIO.sas (07FEB2011)

Table 14.2. 32: AUC tenderness ratio 0-3d by centre (FAS/PP)

		Site No.			
		1 Treatment		2 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness ratio 0-3d	n	15	15	16	15
	Mean	1.96	1.31	0.85	0.89
	SD	0.55	0.43	0.21	0.23
	Min	0.79	0.82	0.54	0.37
	Q1	1.77	0.94	0.69	0.77
	Median	1.99	1.13	0.81	0.86
	Q3	2.12	1.57	1.03	1.05
	Max	3.26	2.11	1.19	1.40

		Site No.			
		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness ratio 0-3d	n	21	20	14	14
	Mean	1.94	1.65	1.49	1.67
	SD	0.35	0.35	0.24	0.25
	Min	0.91	1.14	1.05	1.29
	Q1	1.90	1.46	1.29	1.51
	Median	2.02	1.58	1.51	1.59
	Q3	2.21	1.92	1.62	1.88
	Max	2.30	2.27	1.90	2.12

T_AUC03_RATIO_C.sas (21FEB2011)

Table 14.2. 33: Least square results of AUC_{0-3d} algometry ratio by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	2.14 0.09	1.43 0.09
		Mean treatment effect (LS)	0.7021	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.4715; 0.9326 (p<0.0001)	
	2	LS Mean LS Standard error	1.03 0.09	1.04 0.09
		Mean treatment effect (LS)	-0.0094	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-0.2384; 0.2195 (p=0.9350)	
	3	LS Mean LS Standard error	1.87 0.07	1.58 0.07
		Mean treatment effect (LS)	0.2912	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.0943; 0.4880 (p=0.0041)	
	4	LS Mean LS Standard error	1.29 0.10	1.38 0.10
		Mean treatment effect (LS)	-0.0957	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-0.3365; 0.1450 (p=0.4326)	

Table 14.2. 34: AUC tenderness ratio 0-5 d (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness ratio 0-5d	n	66	64
	Mean	3.13	2.79
	SD	1.01	0.77
	Min	1.19	0.75
	Q1	2.39	2.27
	Median	3.26	2.75
	Q3	3.97	3.32
	Max	6.09	4.19

T_AUC05_RATIO.sas (07FEB2011)

Table 14.2. 35: AUC tenderness ratio 0-5 d by centre (FAS/PP)

		Site No.			
		1 Treatment		2 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness ratio 0-5d	n	15	15	16	15
	Mean	3.83	2.70	1.94	1.99
	SD	1.00	0.73	0.55	0.61
	Min	1.62	1.76	1.19	0.75
	Q1	3.71	2.03	1.45	1.56
	Median	3.97	2.64	1.87	1.84
	Q3	4.17	3.33	2.46	2.58
	Max	6.09	4.00	2.76	2.96

		Site No.			
		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness ratio 0-5d	n	21	20	14	14
	Mean	3.72	3.21	2.87	3.12
	SD	0.56	0.57	0.45	0.52
	Min	2.31	2.23	2.20	2.35
	Q1	3.61	2.86	2.62	2.69
	Median	3.91	3.03	2.81	3.12
	Q3	4.05	3.68	3.24	3.55
	Max	4.26	4.19	3.67	4.11

T_AUC05_RATIO_C.sas (21FEB2011)

Table 14.2. 36: Least square results of AUC_{0-5d} algometry ratio by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	4.09 0.17	2.88 0.17
		Mean treatment effect (LS)	1.2059	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.7608; 1.6510 (p<0.0001)	
	2	LS Mean LS Standard error	2.19 0.17	2.22 0.17
		Mean treatment effect (LS)	-0.02997	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-0.4720; 0.4121 (p=0.8934)	
	3	LS Mean LS Standard error	3.62 0.14	3.10 0.14
		Mean treatment effect (LS)	0.5215	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.1414; 0.9015 (p=0.0076)	
	4	LS Mean LS Standard error	2.58 0.18	2.70 0.20
		Mean treatment effect (LS)	-0.1202	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-0.5851; 0.3446 (p=0.6095)	

Table 14.2. 37: Gail Simon tests for centre x treatment interaction (FAS/PP)

Endpoint	Centre	LS mean diff	Alpha	DF	Upper CI	stderr	D^2 / s^2	Test statistic	pvalue
VAS AUC 0-3 days	1	-2291.75	0.01	120	-1249.40	398.23	0.00	0.40	0.7351
	2	62.56	0.01	120	1100.19	396.43	0.02		
	3	-743.64	0.01	120	149.52	341.24	0.00		
	4	253.50	0.01	120	1336.20	413.65	0.38		
VAS AUC 0-12 hours	1	-334.48	0.05	120	-210.53	62.60	0.00	0.28	0.7765
	2	30.27	0.05	120	153.69	62.33	0.24		
	3	-75.00	0.05	120	31.27	53.67	0.00		
	4	14.65	0.05	120	146.45	66.57	0.05		
VAS AUC 0-24 hours	1	-704.49	0.05	120	-447.09	130.00	0.00	0.18	0.8168
	2	51.71	0.05	120	307.99	129.44	0.16		
	3	-180.48	0.05	120	40.18	111.45	0.00		
	4	21.04	0.05	120	294.72	138.23	0.02		
VAS AUC 0-5 days	1	-3607.16	0.05	120	-2241.44	689.78	0.00	0.24	0.7920
	2	192.44	0.05	120	1552.27	686.80	0.08		
	3	-1465.22	0.05	120	-294.37	591.35	0.00		
	4	298.07	0.05	120	1750.21	733.43	0.17		
VAS at 12 hours	1	-31.07	0.05	120	-17.85	6.68	0.00	0.34	0.7545
	2	2.78	0.05	120	15.95	6.65	0.18		
	3	-6.79	0.05	120	4.54	5.72	0.00		
	4	2.92	0.05	120	16.97	7.10	0.17		
VAS at	1	-31.88	0.05	120	-19.84	6.08	0.00	0.00	0.9272

24 hours	2	0.30	0.05	120	12.29	6.05	0.00		
	3	-9.79	0.05	120	0.53	5.21	0.00		
	4	-1.37	0.05	120	11.43	6.47	0.00		
AUC Algometry (tenderness) at injured site 0-3 days	1	2.80	0.05	120	3.74	0.48	0.00	1.73	0.4112
	2	-0.04	0.05	120	0.91	0.48	0.01		
	3	1.35	0.05	120	2.17	0.41	0.00		
	4	-0.67	0.05	120	0.34	0.51	1.73		
AUC Algometry (tenderness) at injured site 0-5 days	1	5.20	0.05	120	7.13	0.98	0.00	0.47	0.7113
	2	0.08	0.05	120	2.01	0.97	0.00		
	3	2.48	0.05	120	4.14	0.84	0.00		
	4	-0.72	0.05	120	1.35	1.04	0.47		
AUC Algometry (tenderness) at injured site at 24 hours	1	0.73	0.05	120	1.05	0.16	0.00	0.24	0.7929
	2	0.02	0.05	120	0.34	0.16	0.00		
	3	0.47	0.05	120	0.74	0.14	0.00		
	4	-0.09	0.05	120	0.26	0.17	0.24		
AUC Algometry (tenderness) ratio (injured /contralateral) 0-3 days	1	0.70	0.05	120	0.93	0.12	0.00	0.63	0.6639
	2	-0.01	0.05	120	0.22	0.12	0.01		
	3	0.29	0.05	120	0.49	0.10	0.00		
	4	-0.10	0.05	120	0.15	0.12	0.62		
AUC Algometry (tenderness) ratio (injured /contralateral) 0-5 days	1	1.21	0.05	120	1.65	0.22	0.00	0.28	0.7780
	2	-0.03	0.05	120	0.41	0.22	0.02		
	3	0.52	0.05	120	0.90	0.19	0.00		
	4	-0.12	0.05	120	0.34	0.23	0.26		

Table 14.2. 38: Use of rescue medication by visit (FAS/PP)

	Treatment															
	Active patch 200 mg ibuprofen Visit								Placebo patch Visit							
	2		3		4		5		2		3		4		5	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Patient used rescue medication																
yes	4	6.1	3	4.5	2	3.0	2	3.0	4	6.3	3	4.7	1	1.6	1	1.6
no	62	93.9	63	95.5	64	97.0	64	97.0	60	93.8	61	95.3	63	98.4	63	98.4
Total	66	100.0	66	100.0	66	100.0	66	100.0	64	100.0	64	100.0	64	100.0	64	100.0

T_RESC_MED.sas (08FEB2011, 13:53)

Table 14.2. 39: Use of rescue medication in the study period (FAS/PP)

	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	n	%	n	%
Use of rescue medication				
yes	6	9.1	4	6.3
no	60	90.9	60	93.8
Total	66	100.0	64	100.0

T_RESC_MED.sas (08FEB2011, 13:53)

Table 14.2. 40:**Total sum of time of use of rescue medication (d) (FAS/PP)**

Total sum of time of use of rescue medication (d)

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	0.23	0.14	0.18
SD	0.84	0.61	0.73
Min	0.00	0.00	0.00
Q1	0.00	0.00	0.00
Median	0.00	0.00	0.00
Q3	0.00	0.00	0.00
Max	5.00	4.00	5.00

T_RESC_MED.sas (08FEB2011, 13:53)

Table 14.2. 41: Global Assessment of treatment efficacy (FAS/PP)

	Treatment											
	Active patch 200 mg ibuprofen						Placebo patch					
	Visit						Visit					
	2		4		5		2		4		5	
	n	%	n	%	n	%	n	%	n	%	n	%
Treatment efficacy by patient's opinion												
excellent	12	18.5	21	31.8	33	50.0	1	1.6	11	17.2	12	18.8
good	17	26.2	22	33.3	17	25.8	20	31.3	15	23.4	16	25.0
fair	18	27.7	10	15.2	5	7.6	13	20.3	12	18.8	11	17.2
poor	13	20.0	8	12.1	6	9.1	18	28.1	19	29.7	16	25.0
none	5	7.7	5	7.6	5	7.6	12	18.8	7	10.9	9	14.1
Treatment efficacy by investigator's opinion												
excellent	11	16.9	22	33.3	36	54.5	.	0.0	8	12.5	12	18.8
good	17	26.2	21	31.8	13	19.7	16	25.0	14	21.9	14	21.9
fair	20	30.8	9	13.6	6	9.1	17	26.6	17	26.6	10	15.6
poor	12	18.5	9	13.6	5	7.6	20	31.3	16	25.0	20	31.3
none	5	7.7	5	7.6	6	9.1	11	17.2	9	14.1	8	12.5
Total	65	100.0	66	100.0	66	100.0	64	100.0	64	100.0	64	100.0

T_ASS_EFF.sas (14APR2011, 07:19)

Table 14.2. 42: Global Assessment of treatment efficacy by centre (FAS/PP)

		Treatment											
		Active patch 200 mg ibuprofen						Placebo patch					
		Visit						Visit					
		2		4		5		2		4		5	
		n	%	n	%	n	%	n	%	n	%	n	%
Site No.	Treatment efficacy by patient's opinion												
1	excellent	6	40.0	8	53.3	9	60.0	.	0.0	1	6.7	.	0.0
	good	4	26.7	4	26.7	4	26.7	4	26.7	2	13.3	3	20.0
	fair	3	20.0	1	6.7	.	0.0	2	13.3	4	26.7	3	20.0
	poor	2	13.3	1	6.7	1	6.7	5	33.3	6	40.0	7	46.7
	none	.	0.0	1	6.7	1	6.7	4	26.7	2	13.3	2	13.3
	Treatment efficacy by investigator's opinion												
	excellent	5	33.3	8	53.3	9	60.0	.	0.0	.	0.0	.	0.0
	good	5	33.3	4	26.7	4	26.7	3	20.0	2	13.3	2	13.3
	fair	3	20.0	1	6.7	.	0.0	3	20.0	4	26.7	3	20.0
	poor	2	13.3	2	13.3	1	6.7	4	26.7	5	33.3	8	53.3
	none	.	0.0	.	0.0	1	6.7	5	33.3	4	26.7	2	13.3
	Total	15	100.0	15	100.0	15	100.0	15	100.0	15	100.0	15	100.0
2	Treatment efficacy by patient's opinion												
	excellent	1	6.3	1	6.3	8	50.0	.	0.0	2	13.3	5	33.3
	good	2	12.5	7	43.8	.	0.0	3	20.0	4	26.7	2	13.3
	fair	5	31.3	1	6.3	1	6.3	3	20.0	1	6.7	1	6.7
	poor	4	25.0	3	18.8	3	18.8	3	20.0	4	26.7	2	13.3
	none	4	25.0	4	25.0	4	25.0	6	40.0	4	26.7	5	33.3
	Treatment efficacy by investigator's opinion												
	excellent	1	6.3	1	6.3	8	50.0	.	0.0	2	13.3	5	33.3
	good	2	12.5	7	43.8	.	0.0	2	13.3	4	26.7	2	13.3
	fair	5	31.3	.	0.0	1	6.3	4	26.7	1	6.7	.	0.0

		Treatment											
		Active patch 200 mg ibuprofen						Placebo patch					
		Visit						Visit					
		2		4		5		2		4		5	
		n	%	n	%	n	%	n	%	n	%	n	%
	poor	4	25.0	4	25.0	3	18.8	3	20.0	3	20.0	2	13.3
	none	4	25.0	4	25.0	4	25.0	6	40.0	5	33.3	6	40.0
	Total	16	100.0	16	100.0	16	100.0	15	100.0	15	100.0	15	100.0
3	Treatment efficacy by patient's opinion												
	excellent	5	25.0	12	57.1	14	66.7	.	0.0	5	25.0	5	25.0
	good	7	35.0	5	23.8	5	23.8	4	20.0	.	0.0	.	0.0
	fair	5	25.0	.	0.0	.	0.0	5	25.0	5	25.0	6	30.0
	poor	2	10.0	4	19.0	2	9.5	9	45.0	9	45.0	7	35.0
	none	1	5.0	.	0.0	.	0.0	2	10.0	1	5.0	2	10.0
	Treatment efficacy by investigator's opinion												
	excellent	5	25.0	13	61.9	17	81.0	.	0.0	4	20.0	5	25.0
	good	9	45.0	4	19.0	2	9.5	5	25.0	1	5.0	1	5.0
	fair	3	15.0	1	4.8	.	0.0	5	25.0	7	35.0	4	20.0
	poor	3	15.0	2	9.5	1	4.8	10	50.0	8	40.0	10	50.0
	none	.	0.0	1	4.8	1	4.8	.	0.0	.	0.0	.	0.0
	Total	20	100.0	21	100.0	21	100.0	20	100.0	20	100.0	20	100.0
4	Treatment efficacy by patient's opinion												
	excellent	.	0.0	.	0.0	2	14.3	1	7.1	3	21.4	2	14.3
	good	4	28.6	6	42.9	8	57.1	9	64.3	9	64.3	11	78.6
	fair	5	35.7	8	57.1	4	28.6	3	21.4	2	14.3	1	7.1
	poor	5	35.7	.	0.0	.	0.0	1	7.1	.	0.0	.	0.0
	none	.	0.0	.	0.0	.	0.0	.	0.0	.	0.0	.	0.0
	Treatment efficacy by investigator's opinion												
	excellent	.	0.0	.	0.0	2	14.3	.	0.0	2	14.3	2	14.3
	good	1	7.1	6	42.9	7	50.0	6	42.9	7	50.0	9	64.3

	Treatment											
	Active patch 200 mg ibuprofen						Placebo patch					
	Visit						Visit					
	2		4		5		2		4		5	
	n	%	n	%	n	%	n	%	n	%	n	%
fair	9	64.3	7	50.0	5	35.7	5	35.7	5	35.7	3	21.4
poor	3	21.4	1	7.1	.	0.0	3	21.4	.	0.0	.	0.0
none	1	7.1	.	0.0	.	0.0	.	0.0	.	0.0	.	0.0
Total	14	100.0	14	100.0	14	100.0	14	100.0	14	100.0	14	100.0

T_ASS_EFF.sas (14APR2011, 07:19)

Table 14.2. 43: VAS at baseline (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS at BL	n	66	64	130
	Mean	74.21	73.98	74.10
	SD	11.43	10.24	10.82
	Min	54.00	55.00	54.00
	Q1	67.00	66.50	67.00
	Median	73.50	73.50	73.50
	Q3	81.00	80.00	81.00
	Max	97.00	97.00	97.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 44: VAS at 1 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS 1h after 1st appl.	n	66	64	130
	Mean	64.24	69.00	66.58
	SD	14.11	9.18	12.13
	Min	25.00	41.00	25.00
	Q1	56.00	64.00	61.00
	Median	64.50	69.00	67.00
	Q3	73.00	75.00	74.00
	Max	91.00	91.00	91.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 45: VAS at 2 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS 2h after 1st appl.	n	66	64	130
	Mean	55.89	62.42	59.11
	SD	18.08	12.04	15.69
	Min	5.00	18.00	5.00
	Q1	48.00	57.50	53.00
	Median	59.00	62.50	62.00
	Q3	70.00	70.00	70.00
	Max	85.00	91.00	91.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 46: VAS at 4 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS 4h after 1st appl.	n	66	64	130
	Mean	50.17	59.14	54.58
	SD	21.17	14.30	18.60
	Min	3.00	7.00	3.00
	Q1	36.00	52.00	48.00
	Median	53.00	59.00	58.00
	Q3	66.00	68.50	68.00
	Max	85.00	90.00	90.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 47: VAS at 6 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS 6h after 1st appl.	n	66	64	130
	Mean	48.50	56.33	52.35
	SD	22.73	16.65	20.27
	Min	0.00	2.00	0.00
	Q1	36.00	52.00	45.00
	Median	52.00	59.00	56.50
	Q3	65.00	66.50	66.00
	Max	83.00	90.00	90.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 48: VAS at 12 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS 12h after 1st appl.	n	66	64	130
	Mean	46.26	53.69	49.92
	SD	24.28	18.81	21.99
	Min	0.00	0.00	0.00
	Q1	30.00	48.00	38.00
	Median	51.50	55.50	55.00
	Q3	64.00	64.50	64.00
	Max	83.00	82.00	83.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 49: VAS at 24 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS at V2 (24h after 1st appl.)	n	66	64	130
	Mean	44.45	54.70	49.50
	SD	23.33	17.91	21.39
	Min	0.00	0.00	0.00
	Q1	29.00	49.00	41.00
	Median	48.00	57.50	52.00
	Q3	62.00	65.00	63.00
	Max	88.00	93.00	93.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 50: VAS at 48 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS at V3 (48h after 1st appl.)	n	66	64	130
	Mean	33.12	42.77	37.87
	SD	22.96	20.93	22.43
	Min	0.00	0.00	0.00
	Q1	10.00	32.50	16.00
	Median	36.50	45.50	44.00
	Q3	50.00	59.00	53.00
	Max	74.00	80.00	80.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 51: VAS at 72 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS at V4 (72h after 1st appl.)	n	66	64	130
	Mean	23.58	33.38	28.40
	SD	21.64	21.39	21.99
	Min	0.00	0.00	0.00
	Q1	0.00	17.00	5.00
	Median	25.00	32.00	30.00
	Q3	39.00	50.00	46.00
	Max	78.00	82.00	82.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 52: VAS at 96 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS 96h after 1st appl.	n	66	64	130
	Mean	21.18	30.44	25.74
	SD	22.73	22.28	22.90
	Min	0.00	0.00	0.00
	Q1	0.00	7.50	3.00
	Median	15.00	30.50	21.50
	Q3	38.00	52.50	46.00
	Max	85.00	71.00	85.00

Missing data was replaced using the LOCF approach, T_VAS.sas (14APR2011)

Table 14.2. 53: VAS at 120 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS at V5 (120h after 1st appl.)	n	66	64	130
	Mean	13.62	22.59	18.04
	SD	18.74	19.61	19.63
	Min	0.00	0.00	0.00
	Q1	0.00	4.00	0.00
	Median	4.00	18.00	12.00
	Q3	19.00	39.00	30.00
	Max	65.00	69.00	69.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 54: VAS at baseline by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS at BL	n	15	15	16	15	21	20	14	14
	Mean	88.07	86.73	73.19	73.60	66.86	67.50	71.57	70.00
	SD	7.18	7.86	10.19	8.12	8.88	6.06	6.25	6.87
	Min	76.00	74.00	57.00	59.00	54.00	55.00	62.00	60.00
	Q1	81.00	81.00	64.00	66.00	60.00	64.50	67.00	65.00
	Median	90.00	87.00	74.50	75.00	67.00	67.50	72.00	70.00
	Q3	95.00	95.00	80.50	78.00	72.00	71.00	76.00	74.00
	Max	97.00	97.00	90.00	85.00	89.00	79.00	82.00	88.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 55: VAS at 1 h by centre (FAS/PP)

		Site No.							
		1 Treatment		2 Treatment		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS 1h after 1st appl.	n	15	15	16	15	21	20	14	14
	Mean	62.20	75.73	67.69	70.67	62.43	66.25	65.21	63.93
	SD	23.24	8.81	9.57	10.34	10.13	5.13	11.18	8.71
	Min	25.00	62.00	55.00	41.00	44.00	54.00	41.00	44.00
	Q1	41.00	70.00	58.50	66.00	56.00	64.00	61.00	60.00
	Median	65.00	76.00	68.50	74.00	62.00	65.00	65.50	65.50
	Q3	86.00	84.00	72.50	76.00	67.00	69.50	73.00	69.00
	Max	91.00	91.00	86.00	81.00	88.00	78.00	83.00	77.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 56: VAS at 2 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS 2h after 1st appl.	n	15	15	16	15	21	20	14	14
	Mean	41.13	63.40	63.88	64.47	54.81	61.55	64.21	60.43
	SD	24.66	17.00	11.59	14.91	11.71	5.67	14.43	9.65
	Min	5.00	18.00	40.00	21.00	34.00	52.00	26.00	42.00
	Q1	15.00	60.00	55.50	58.00	48.00	57.00	58.00	53.00
	Median	41.00	67.00	64.50	70.00	54.00	62.00	68.50	60.50
	Q3	62.00	74.00	71.00	75.00	62.00	64.00	73.00	69.00
	Max	78.00	91.00	85.00	79.00	81.00	76.00	80.00	79.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 57: VAS at 4 h by centre (FAS/PP)

		Site No.							
		1 Treatment		2 Treatment		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS 4h after 1st appl.	n	15	15	16	15	21	20	14	14
	Mean	29.27	60.73	59.69	59.60	51.33	58.10	59.93	58.43
	SD	23.99	23.20	17.89	15.84	12.26	5.95	17.34	9.21
	Min	3.00	7.00	25.00	22.00	29.00	45.00	18.00	42.00
	Q1	7.00	50.00	49.50	48.00	47.00	54.00	52.00	53.00
	Median	28.00	68.00	62.00	64.00	49.00	59.00	62.00	58.50
	Q3	57.00	75.00	72.50	73.00	59.00	64.00	70.00	59.00
	Max	74.00	90.00	85.00	80.00	78.00	65.00	83.00	79.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 58: VAS at 6 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS 6h after 1st appl.	n	15	15	16	15	21	20	14	14
	Mean	23.27	53.27	62.38	57.73	50.38	57.75	56.86	56.07
	SD	23.08	24.73	19.74	21.55	12.07	5.67	16.80	11.01
	Min	0.00	7.00	16.00	2.00	29.00	45.00	18.00	37.00
	Q1	3.00	30.00	57.00	48.00	45.00	53.50	50.00	50.00
	Median	14.00	61.00	67.00	60.00	49.00	59.00	57.50	55.00
	Q3	38.00	70.00	75.00	77.00	58.00	61.50	69.00	59.00
	Max	64.00	90.00	82.00	79.00	76.00	66.00	83.00	79.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 59: VAS at 12 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS 12h after 1st appl.	n	15	15	16	15	21	20	14	14
	Mean	19.27	49.40	62.50	59.93	48.48	55.80	53.29	48.57
	SD	24.43	27.45	20.74	23.00	12.30	7.27	18.69	12.45
	Min	0.00	0.00	2.00	1.00	29.00	37.00	9.00	31.00
	Q1	0.00	16.00	59.50	54.00	40.00	52.00	42.00	33.00
	Median	6.00	55.00	67.50	58.00	47.00	58.50	58.50	50.50
	Q3	36.00	70.00	75.00	78.00	58.00	61.00	68.00	58.00
	Max	75.00	82.00	83.00	82.00	76.00	65.00	76.00	69.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 60: VAS at 24 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS at V2 (24h after 1st appl.)	n	15	15	16	15	21	20	14	14
	Mean	22.33	52.87	62.69	63.47	42.33	52.50	50.50	50.43
	SD	29.20	31.16	10.16	8.88	16.35	10.71	15.89	11.71
	Min	0.00	0.00	44.00	50.00	17.00	23.00	18.00	28.00
	Q1	0.00	15.00	54.00	56.00	29.00	48.00	44.00	45.00
	Median	5.00	60.00	65.00	66.00	43.00	54.00	53.00	51.00
	Q3	48.00	78.00	71.50	70.00	48.00	61.00	59.00	56.00
	Max	73.00	93.00	78.00	80.00	88.00	64.00	74.00	70.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 61: VAS at 48 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS at V3 (48h after 1st appl.)	n	15	15	16	15	21	20	14	14
	Mean	12.40	45.33	54.56	56.40	27.52	38.85	39.21	31.00
	SD	22.48	28.38	10.09	11.70	18.73	15.50	16.81	19.03
	Min	0.00	0.00	43.00	39.00	0.00	0.00	8.00	1.00
	Q1	0.00	12.00	45.50	47.00	13.00	28.00	31.00	15.00
	Median	1.00	49.00	52.00	61.00	27.00	45.00	39.50	35.50
	Q3	10.00	67.00	62.50	65.00	42.00	48.50	51.00	45.00
	Max	69.00	80.00	74.00	75.00	73.00	57.00	70.00	62.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 62: VAS at 72 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS at V4 (72h after 1st appl.)	n	15	15	16	15	21	20	14	14
	Mean	5.93	37.80	46.56	44.67	14.76	29.95	29.43	21.43
	SD	13.07	28.23	14.38	15.98	17.33	17.80	16.88	16.72
	Min	0.00	0.00	26.00	21.00	0.00	0.00	1.00	1.00
	Q1	0.00	7.00	35.50	31.00	0.00	17.50	17.00	4.00
	Median	0.00	43.00	46.50	46.00	7.00	31.50	27.00	20.00
	Q3	3.00	61.00	56.00	62.00	29.00	45.00	41.00	34.00
	Max	42.00	82.00	78.00	66.00	55.00	58.00	66.00	49.00

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Table 14.2. 63: VAS at 96 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS 96h after 1st appl.	n	15	15	16	15	21	20	14	14
	Mean	11.53	37.87	39.19	36.07	10.62	27.45	26.79	20.71
	SD	21.41	27.16	25.91	21.34	15.71	20.23	14.68	17.51
	Min	0.00	0.00	1.00	1.00	0.00	0.00	0.00	0.00
	Q1	0.00	4.00	20.00	13.00	0.00	14.50	15.00	5.00
	Median	0.00	48.00	38.00	43.00	1.00	24.50	24.50	16.00
	Q3	11.00	57.00	58.00	53.00	18.00	36.50	39.00	34.00
	Max	66.00	70.00	85.00	59.00	57.00	71.00	48.00	57.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 64: VAS at 120 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS at V5 (120h after 1st appl.)	n	15	15	16	15	21	20	14	14
	Mean	5.93	27.67	27.06	26.33	8.24	21.20	14.57	15.14
	SD	14.84	25.00	22.92	20.79	14.23	15.33	16.23	16.52
	Min	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	Q1	0.00	2.00	6.50	6.00	0.00	10.00	4.00	0.00
	Median	0.00	28.00	25.00	37.00	0.00	20.50	11.50	10.00
	Q3	1.00	54.00	47.50	46.00	16.00	28.50	18.00	22.00
	Max	48.00	69.00	60.00	49.00	53.00	50.00	65.00	45.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 65: Tenderness at injured site at baseline (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness of injured site at assessment Day 0 (BL)	n	66	64	130
	Mean	1.37	1.46	1.42
	SD	0.86	0.96	0.91
	Min	0.40	0.30	0.30
	Q1	0.80	0.80	0.80
	Median	1.10	1.10	1.10
	Q3	1.70	1.80	1.70
	Max	3.90	4.20	4.20

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 66: Tenderness at injured site at Day 1 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness of injured site at assessment Day 1	n	66	64	130
	Mean	2.17	1.96	2.07
	SD	0.97	1.10	1.04
	Min	0.40	0.50	0.40
	Q1	1.30	1.10	1.20
	Median	2.10	1.75	1.95
	Q3	2.90	2.35	2.80
	Max	4.20	5.00	5.00

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 67: Tenderness at injured site at Day 2 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness of injured site at assessment Day 2	n	66	64	130
	Mean	2.83	2.52	2.68
	SD	1.23	1.31	1.28
	Min	0.60	0.60	0.60
	Q1	1.70	1.50	1.60
	Median	3.05	2.15	2.65
	Q3	3.70	3.10	3.60
	Max	5.40	6.50	6.50

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 68: Tenderness at injured site at Day 3 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness of injured site at assessment Day 3	n	66	64	130
	Mean	3.30	2.95	3.13
	SD	1.26	1.37	1.32
	Min	1.00	0.50	0.50
	Q1	2.40	2.00	2.20
	Median	3.35	2.80	3.05
	Q3	4.20	3.65	4.00
	Max	5.90	7.60	7.60

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 69: Tenderness at injured site at Day 5 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness of injured site at assessment Day 5	n	66	64	130
	Mean	3.88	3.51	3.70
	SD	1.32	1.47	1.41
	Min	1.40	1.10	1.10
	Q1	3.20	2.60	2.80
	Median	3.90	3.10	3.60
	Q3	4.60	4.15	4.40
	Max	8.10	8.20	8.20

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 70: Tenderness at contralateral site at baseline (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness of contralateral site at assessment Day 0 (BL)	n	66	64	130
	Mean	4.73	4.70	4.71
	SD	1.47	1.66	1.56
	Min	2.80	2.60	2.60
	Q1	3.80	3.50	3.60
	Median	4.20	4.10	4.20
	Q3	5.00	5.35	5.10
	Max	8.70	9.00	9.00

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 71: Tenderness ratio at baseline (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness ratio at assessment Day 0 (BL)	n	66	64	130
	Mean	0.28	0.29	0.28
	SD	0.10	0.11	0.10
	Min	0.12	0.08	0.08
	Q1	0.20	0.21	0.21
	Median	0.27	0.27	0.27
	Q3	0.34	0.39	0.37
	Max	0.47	0.49	0.49

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 72: Tenderness ratio at Day 1 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness ratio at assessment Day 1	n	66	64	130
	Mean	0.46	0.41	0.44
	SD	0.18	0.15	0.17
	Min	0.14	0.12	0.12
	Q1	0.29	0.27	0.28
	Median	0.48	0.42	0.44
	Q3	0.62	0.51	0.56
	Max	0.86	0.74	0.86

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 73: Tenderness ratio at Day 2 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness ratio at assessment Day 2	n	66	64	130
	Mean	0.62	0.53	0.58
	SD	0.30	0.19	0.26
	Min	0.16	0.15	0.15
	Q1	0.42	0.38	0.38
	Median	0.60	0.53	0.55
	Q3	0.83	0.67	0.76
	Max	2.09	0.88	2.09

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 74: Tenderness ratio at Day 3 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness ratio at assessment Day 3	n	66	64	130
	Mean	0.72	0.63	0.68
	SD	0.26	0.20	0.24
	Min	0.24	0.13	0.13
	Q1	0.52	0.49	0.49
	Median	0.74	0.64	0.65
	Q3	0.95	0.74	0.90
	Max	1.57	1.04	1.57

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 75: Tenderness ratio at Day 5 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness ratio at assessment Day 5	n	66	64	130
	Mean	0.83	0.76	0.79
	SD	0.20	0.24	0.22
	Min	0.33	0.25	0.25
	Q1	0.69	0.60	0.63
	Median	0.90	0.78	0.83
	Q3	0.98	0.88	0.96
	Max	1.26	1.96	1.96

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 76: Tenderness ratio by centre (FAS/PP)

		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 0 (BL)	n	15	15	16	15
	Mean	0.20	0.22	0.20	0.21
	SD	0.06	0.07	0.04	0.06
	Min	0.14	0.12	0.13	0.08
	Q1	0.15	0.16	0.17	0.17
	Median	0.18	0.23	0.21	0.22
	Q3	0.25	0.29	0.22	0.25
	Max	0.32	0.33	0.28	0.30

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 0 (BL)	n	21	20	14	14
	Mean	0.32	0.32	0.38	0.42
	SD	0.08	0.09	0.06	0.04
	Min	0.12	0.18	0.25	0.37
	Q1	0.27	0.25	0.33	0.39
	Median	0.32	0.32	0.40	0.43
	Q3	0.37	0.40	0.43	0.45
	Max	0.44	0.46	0.47	0.49

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		Site No.			
		1 Treatment		2 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 1	n	15	15	16	15
	Mean	0.51	0.37	0.24	0.25
	SD	0.16	0.16	0.05	0.07
	Min	0.23	0.21	0.14	0.12
	Q1	0.40	0.24	0.20	0.22
	Median	0.53	0.32	0.26	0.24
	Q3	0.62	0.51	0.28	0.28
	Max	0.86	0.67	0.32	0.43

		Site No.			
		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 1	n	21	20	14	14
	Mean	0.60	0.49	0.46	0.49
	SD	0.13	0.13	0.07	0.07
	Min	0.19	0.30	0.29	0.36
	Q1	0.54	0.38	0.42	0.46
	Median	0.65	0.49	0.47	0.50
	Q3	0.69	0.56	0.51	0.54
	Max	0.74	0.74	0.58	0.63

		Site No.			
		1 Treatment		2 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 2	n	15	15	16	15
	Mean	0.87	0.51	0.29	0.31
	SD	0.39	0.18	0.09	0.08
	Min	0.26	0.30	0.16	0.15
	Q1	0.74	0.36	0.24	0.25
	Median	0.85	0.49	0.27	0.33
	Q3	0.97	0.63	0.38	0.38
	Max	2.09	0.87	0.43	0.48

		Site No.			
		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 2	n	21	20	14	14
	Mean	0.75	0.63	0.53	0.63
	SD	0.15	0.14	0.10	0.12
	Min	0.35	0.40	0.41	0.45
	Q1	0.72	0.54	0.44	0.54
	Median	0.80	0.62	0.51	0.61
	Q3	0.83	0.70	0.60	0.71
	Max	0.94	0.88	0.76	0.83

		Site No.			
		1 Treatment		2 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 3	n	15	15	16	15
	Mean	0.94	0.61	0.42	0.44
	SD	0.27	0.19	0.13	0.16
	Min	0.38	0.32	0.24	0.13
	Q1	0.95	0.45	0.32	0.33
	Median	0.98	0.62	0.38	0.42
	Q3	1.03	0.76	0.55	0.58
	Max	1.57	0.94	0.65	0.70

		Site No.			
		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 3	n	21	20	14	14
	Mean	0.86	0.74	0.63	0.68
	SD	0.12	0.14	0.14	0.18
	Min	0.57	0.48	0.43	0.48
	Q1	0.79	0.65	0.52	0.54
	Median	0.90	0.70	0.61	0.63
	Q3	0.95	0.83	0.68	0.74
	Max	1.00	0.98	0.92	1.04

		Site No.			
		1 Treatment		2 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 5	n	15	15	16	15
	Mean	0.93	0.78	0.67	0.66
	SD	0.21	0.36	0.23	0.26
	Min	0.44	0.44	0.33	0.25
	Q1	0.94	0.58	0.45	0.45
	Median	0.98	0.71	0.68	0.55
	Q3	1.02	0.88	0.89	0.88
	Max	1.26	1.96	0.91	1.12

		Site No.			
		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 5	n	21	20	14	14
	Mean	0.92	0.82	0.75	0.76
	SD	0.10	0.12	0.12	0.17
	Min	0.62	0.59	0.55	0.52
	Q1	0.90	0.75	0.66	0.62
	Median	0.97	0.82	0.75	0.76
	Q3	0.98	0.89	0.83	0.95
	Max	1.03	1.03	1.01	1.01

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 14.3. 1: Frequency of TEAEs (SAF)

	Treatment		
	Active patch 200 mg ibuprofen n	Placebo patch n	All n
TEAE			
yes	10	8	18
All	10	8	18

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Table 14.3. 2: Overview of TEAEs (SAF)

		Active patch 200 mg ibuprofen	Placebo patch
Number of TEAEs	n	10	8
Number of patients with TEAEs	n	7	8
Total number of patients treated	n	66	64
Patients with TEAEs	%	10.6	12.5

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Table 14.3. 3: Overview of drug-related TEAEs (SAF)

		Active patch 200 mg ibuprofen	Placebo patch
Number of drug-related TEAEs	n	4	5
Number of patients with drug-related TEAEs	n	3	5
Total number of patients treated	n	66	64
Patients with drug-related TEAEs	%	4.5	7.8

Drug-related: possible, probable, definite

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Table 14.3. 4: Number of TEAEs (SAF)

	Treatment				All	
	Active patch 200 mg ibuprofen		Placebo patch			
	n	%	n	%	n	%
Number of TEAEs						
0	59	89.4	56	87.5	115	88.5
1	5	7.6	8	12.5	13	10.0
2	1	1.5	.	.	1	0.8
3	1	1.5	.	.	1	0.8
All	66	100.0	64	100.0	130	100.0

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Table 14.3. 5: Number of drug-related TEAEs (SAF)

Drug related: possible, probable, definite

	Treatment				All	
	Active patch 200 mg ibuprofen		Placebo patch			
	n	%	n	%	n	%
Number of drug-related TEAEs						
0	63	95.5	59	92.2	122	93.8
1	2	3.0	5	7.8	7	5.4
2	1	1.5	.	.	1	0.8
All	66	100.0	64	100.0	130	100.0

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Table 14.3. 6: TEAE characteristics (SAF)

	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	n	%	n	%
Severity				
mild	10	100.0	8	100.0
Action taken				
none	5	50.0	8	100.0
symptomatic therapy	3	30.0	.	.
Other action	2	20.0	.	.
other action				
	8	80.0	7	87.5
NA	.	.	1	12.5
PATCH REMOVED	2	20.0	.	.
Subject has experienced this AE before				
yes	1	10.0	1	12.5
no	9	90.0	7	87.5
Outcome of AE				
Resolved	10	100.0	8	100.0
Relationship to study drug				
probable	3	30.0	2	25.0
possible	1	10.0	3	37.5
unlikely	4	40.0	.	.
none	2	20.0	3	37.5
Serious Adverse Event				
no	10	100.0	8	100.0
Total	10	100.0	8	100.0

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Table 14.3. 7: TEAEs by preferred term and corresponding SOC (SAF)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
		n	n	n
MedDRA Body System	MedDRA Preferred Term			
General disorders and administration site conditions	Application site pruritus	1	1	2
	Application site reaction	.	2	2
	Application site hypersensitivity	2	.	2
	Pain	1	.	1
	Application site erythema	.	1	1
	Application site discomfort	.	1	1
Infections and infestations	Nasopharyngitis	.	2	2
Nervous system disorders	Headache	1	1	2
Gastrointestinal disorders	Toothache	1	.	1
Cardiac disorders	Angina pectoris	1	.	1
Ear and labyrinth disorders	Vertigo	1	.	1
Psychiatric disorders	Sleep disorder	1	.	1
Musculoskeletal and connective tissue disorders	Joint swelling	1	.	1
All		10	8	18

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Table 14.3. 8: Drug-related TEAEs by preferred term and corresponding SOC (SAF)

Drug-related: possible, probable, definite

		Treatment		
		Placebo patch n	Active patch 200 mg ibuprofen n	All n
MedDRA Body System	MedDRA Preferred Term			
General disorders and administration site conditions	Application site pruritus	1	1	2
	Application site reaction	2	.	2
	Application site hypersensitivity	.	2	2
	Application site erythema	1	.	1
	Application site discomfort	1	.	1
Musculoskeletal and connective tissue disorders	Joint swelling	.	1	1
All		5	4	9

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Table 14.3. 9: TEAE by preferred term (SAF)

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
	n	n	n
MedDRA Preferred Term			
Nasopharyngitis	.	2	2
Headache	1	1	2
Application site pruritus	1	1	2
Application site reaction	.	2	2
Application site hypersensitivity	2	.	2
Pain	1	.	1
Application site erythema	.	1	1
Toothache	1	.	1
Application site discomfort	.	1	1
Angina pectoris	1	.	1
Vertigo	1	.	1
Sleep disorder	1	.	1
Joint swelling	1	.	1
All	10	8	18

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Table 14.3. 10: Drug-related TEAE by preferred term (SAF)

Drug-related: possible, probable, definite

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
MedDRA Preferred Term			
Application site pruritus	1	1	2
Application site reaction	2	.	2
Application site hypersensitivity	.	2	2
Application site erythema	1	.	1
Application site discomfort	1	.	1
Joint swelling	.	1	1
All	5	4	9

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Table 14.3. 11: TEAE by SOC (SAF)

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
	n	n	n
MedDRA Body System			
General disorders and administration site conditions	4	5	9
Infections and infestations	.	2	2
Nervous system disorders	1	1	2
Gastrointestinal disorders	1	.	1
Cardiac disorders	1	.	1
Ear and labyrinth disorders	1	.	1
Psychiatric disorders	1	.	1
Musculoskeletal and connective tissue disorders	1	.	1
All	10	8	18

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Table 14.3. 12: Drug-related TEAE by SOC (SAF)

Drug-related: possible, probable, definite

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
MedDRA Body System			
General disorders and administration site conditions	5	3	8
Musculoskeletal and connective tissue disorders	.	1	1
All	5	4	9

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Table 14.3. 13: TEAE by preferred term and causality (SAF)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
		n	n	n
Relationship to study drug	MedDRA Preferred Term			
none	Nasopharyngitis	.	2	2
	Headache	1	1	2
	Toothache	1	.	1
probable	Application site reaction	.	2	2
	Application site hypersensitivity	2	.	2
	Joint swelling	1	.	1
unlikely	Pain	1	.	1
	Angina pectoris	1	.	1
	Vertigo	1	.	1
	Sleep disorder	1	.	1
possible	Application site pruritus	1	1	2
	Application site erythema	.	1	1
	Application site discomfort	.	1	1
All		10	8	18

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Table 14.3. 14: TEAE by SOC and causality (SAF)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
		n	n	n
Relationship to study drug	MedDRA Body System			
none	Infections and infestations	.	2	2
	Nervous system disorders	1	1	2
	Gastrointestinal disorders	1	.	1
probable	General disorders and administration site conditions	2	2	4
	Musculoskeletal and connective tissue disorders	1	.	1
unlikely	General disorders and administration site conditions	1	.	1
	Cardiac disorders	1	.	1
	Ear and labyrinth disorders	1	.	1
	Psychiatric disorders	1	.	1
possible	General disorders and administration site conditions	1	3	4
All		10	8	18

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Multiple citations possible

Table 14.3. 15: Global Assessment of local tolerability (SAF)

	Treatment											
	Active patch 200 mg ibuprofen						Placebo patch					
	Visit						Visit					
	2		4		5		2		4		5	
	n	%	n	%	n	%	n	%	n	%	n	%
Local tolerability by patient's opinion												
poor	.	0.0	1	1.5	.	0.0	.	0.0	.	0.0	1	1.6
fair	4	6.2	.	0.0	5	7.6	.	0.0	.	0.0	3	4.7
good	38	58.5	41	63.1	36	54.5	46	71.9	48	75.0	41	64.1
excellent	23	35.4	23	35.4	25	37.9	18	28.1	16	25.0	19	29.7
Local tolerability by investigator's opinion												
poor	.	0.0	1	1.5	.	0.0	.	0.0	.	0.0	1	1.6
fair	3	4.6	1	1.5	6	9.1	.	0.0	.	0.0	3	4.7
good	37	56.9	38	58.5	34	51.5	49	76.6	46	71.9	44	68.8
excellent	25	38.5	25	38.5	26	39.4	15	23.4	18	28.1	16	25.0
Total	65	100.0	65	100.0	66	100.0	64	100.0	64	100.0	64	100.0

T_ASS_TOL.sas (14APR2011, 07:19)

Table 14.3. 16: Physical examination (SAF)

	Treatment							
	Active patch 200 mg ibuprofen				Placebo patch			
	Visit				Visit			
	1		5		1		5	
	n	%	n	%	n	%	n	%
General condition								
Normal	66	100.0	66	100.0	64	100.0	64	100.0
Dermatologie								
Normal	65	98.5	66	100.0	63	98.4	63	98.4
Pathological finding	1	1.5	.	0.0	1	1.6	1	1.6
Eyes, Ears, Nose, Throat								
Normal	63	95.5	64	97.0	62	96.9	63	98.4
Pathological finding	3	4.5	2	3.0	2	3.1	1	1.6
Neck								
Normal	66	100.0	66	100.0	64	100.0	64	100.0
Thyroid								
Normal	64	97.0	65	98.5	64	100.0	64	100.0
Pathological finding	2	3.0	1	1.5	.	0.0	.	0.0
Heart								
Normal	66	100.0	66	100.0	64	100.0	64	100.0
Lung, Respiratory system								
Normal	65	98.5	66	100.0	64	100.0	64	100.0
Pathological finding	1	1.5	.	0.0	.	0.0	.	0.0
Abdomen								
Normal	65	98.5	66	100.0	64	100.0	64	100.0
Pathological finding	1	1.5	.	0.0	.	0.0	.	0.0
Kidneys								
Normal	66	100.0	66	100.0	64	100.0	64	100.0
Skeletal system, Extremities								
Normal	63	95.5	63	95.5	59	92.2	61	95.3
Pathological finding	3	4.5	3	4.5	5	7.8	3	4.7

	Treatment							
	Active patch 200 mg ibuprofen				Placebo patch			
	Visit				Visit			
	1		5		1		5	
	n	%	n	%	n	%	n	%
Lymphatic system								
Normal	66	100.0	66	100.0	64	100.0	64	100.0
CNS, Neurological conditions								
Normal	66	100.0	66	100.0	64	100.0	64	100.0
Psychiatric CNS								
Normal	66	100.0	66	100.0	64	100.0	64	100.0
Others 1								
.	60	90.9	62	93.9	59	92.2	58	90.6
Normal	6	9.1	4	6.1	5	7.8	6	9.4
Others 2								
.	65	98.5	66	100.0	64	100.0	61	95.3
Normal	1	1.5	.	0.0	.	0.0	3	4.7
Total	66	100.0	66	100.0	64	100.0	64	100.0

T_PhyEX.sas (17FEB2011)

Table 14.3. 17: Arm used for measurement of Heart rate, blood pressure (SAF)

	Treatment							
	Active patch 200 mg ibuprofen				Placebo patch			
	Visit				Visit			
	1		5		1		5	
	n	%	n	%	n	%	n	%
Arm for measurement of Heart rate								
.	1	1.5	.	0.0	.	0.0	.	0.0
Right arm	34	51.5	33	50.0	33	51.6	32	50.0
Left arm	31	47.0	33	50.0	31	48.4	32	50.0
Arm for measurement of blood pressure								
Right arm	34	51.5	33	50.0	33	51.6	32	50.0
Left arm	32	48.5	33	50.0	31	48.4	32	50.0
Total	66	100.0	66	100.0	64	100.0	64	100.0

T_VitalSigns.sas (17FEB2011)

Table 14.3. 18: Heart rate, blood pressure (SAF)

		Treatment			
		Active patch 200 mg ibuprofen Visit		Placebo patch Visit	
		1	5	1	5
Puls [bpm]	n	66	66	64	64
	Mean	68.82	69.21	69.06	68.97
	SD	10.71	10.06	8.85	7.36
	Min	52.00	52.00	52.00	56.00
	Q1	60.00	60.00	64.00	64.00
	Median	68.00	68.00	68.00	68.00
	Q3	76.00	76.00	72.50	74.00
	Max	100.00	93.00	103.00	88.00
Blood pressure systolic [mmHg]	n	66	66	64	64
	Mean	126.32	125.09	125.69	126.89
	SD	14.57	13.36	16.79	14.09
	Min	90.00	90.00	100.00	100.00
	Q1	119.00	116.00	115.00	120.00
	Median	126.00	125.00	127.00	126.00
	Q3	135.00	133.00	134.00	130.50
	Max	169.00	170.00	210.00	197.00
Blood pressure diastolic [mmHg]	n	66	66	64	64
	Mean	78.03	75.59	75.89	76.17
	SD	10.13	8.88	10.03	9.88
	Min	60.00	60.00	60.00	60.00
	Q1	70.00	70.00	70.00	70.00
	Median	75.00	75.00	74.50	75.00
	Q3	87.00	80.00	81.00	80.00
	Max	106.00	104.00	116.00	119.00

T_VitalSigns.sas (17FEB2011)

Table 14.3. 19: Temperature (SAF)

		Treatment			
		Active patch 200 mg ibuprofen		Placebo patch	
		Visit		Visit	
		1	5	1	5
Oral temperature [°C]	n	66	66	64	64
	Mean	36.33	36.22	36.28	36.32
	SD	0.49	0.41	0.52	0.41
	Min	34.90	35.30	34.20	35.00
	Q1	36.00	35.90	36.00	36.00
	Median	36.50	36.30	36.35	36.40
	Q3	36.70	36.50	36.60	36.60
	Max	37.10	37.20	37.00	36.90

T_VitalSigns.sas (17FEB2011)

Table 14.3. 20: Absolute Heart rate, blood pressure changes (SAF)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
		Visit	Visit
		V5-V1	V5-V1
Puls [bpm]	n	66	64
	Mean	0.39	-0.09
	SD	6.37	8.28
	Min	-15.00	-24.00
	Q1	-4.00	-4.00
	Median	2.00	0.50
	Q3	4.00	4.00
	Max	12.00	16.00
Blood pressure systolic [mmHg]	n	66	64
	Mean	-1.23	1.20
	SD	8.88	12.44
	Min	-23.00	-30.00
	Q1	-8.00	-5.50
	Median	-0.50	2.00
	Q3	5.00	10.00
	Max	25.00	30.00
Blood pressure diastolic [mmHg]	n	66	64
	Mean	-2.44	0.28
	SD	8.87	9.00
	Min	-35.00	-25.00
	Q1	-5.00	-3.00
	Median	-1.50	0.00
	Q3	2.00	5.00
	Max	15.00	20.00

T_VitalSigns.sas (17FEB2011)

Table 14.3. 21: Relative Heart rate, blood pressure changes (SAF)

		Treatment	
		Active patch 200 mg ibuprofen Visit	Placebo patch Visit
		V5-V1 (%)	V5-V1 (%)
Puls [bpm]	n	66	64
	Mean	1.16	0.77
	SD	9.38	11.95
	Min	-17.65	-27.27
	Q1	-6.25	-5.68
	Median	3.03	0.57
	Q3	6.25	6.07
	Max	21.43	30.77
Blood pressure systolic [mmHg]	n	66	64
	Mean	-0.62	1.74
	SD	7.19	10.44
	Min	-17.04	-23.08
	Q1	-5.67	-4.21
	Median	-0.42	1.56
	Q3	4.00	8.01
	Max	23.81	30.00
Blood pressure diastolic [mmHg]	n	66	64
	Mean	-2.35	1.13
	SD	11.03	12.06
	Min	-36.84	-29.41
	Q1	-6.67	-3.75
	Median	-1.63	0.00
	Q3	2.82	7.85
	Max	25.00	33.33

T_VitalSigns.sas (17FEB2011)

able 14.3. 22: Absolute Temperature change (SAF)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
		Visit	Visit
		V5-V1	V5-V1
Oral temperature [°C]	n	66	64
	Mean	-0.12	0.04
	SD	0.39	0.44
	Min	-1.10	-0.90
	Q1	-0.20	-0.20
	Median	-0.10	0.00
	Q3	0.10	0.20
	Max	0.90	2.10

T_VitalSigns.sas (17FEB2011)

Table 14.3. 23: Relative Temperature change (SAF)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
		Visit	Visit
		V5-V1 (%)	V5-V1 (%)
Oral temperature [°C]	n	66	64
	Mean	-0.31	0.12
	SD	1.08	1.24
	Min	-3.00	-2.43

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
		Visit	Visit
		V5-V1 (%)	V5-V1 (%)
	Q1	-0.56	-0.54
	Median	-0.27	0.00
	Q3	0.28	0.55
	Max	2.58	6.14

T_VitalSigns.sas (17FEB2011)

14.3.2 Listings of Deaths, other Serious and Significant Adverse Events

Not applicable.

14.3.3 Narratives of Deaths, other Serious and certain other Significant Adverse Events

Not applicable.

14.3.4 Clinically Significant Abnormal Laboratory Value Listing (each patient)

Not applicable.

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14 TABLES, FIGURES AND GRAPHS REFERRED TO BUT NOT INCLUDED IN THE TEXT

14.1 Demographic Data

Table 14.1. 54: Patients per centre (FAS/PP)

	Treatment				All	
	Active patch 200 mg ibuprofen		Placebo patch			
	n	%	n	%	n	%
Site No.						
1	15	22.7	15	23.4	30	23.1
2	16	24.2	15	23.4	31	23.8
3	21	31.8	20	31.3	41	31.5
4	14	21.2	14	21.9	28	21.5
All	66	100.0	64	100.0	130	100.0

T_DEMOG.sas (25FEB2011)

Table 14.1. 55: Age (FAS/PP)

Age

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	34.09	30.08	32.12
SD	11.72	11.09	11.55
Min	18.00	18.00	18.00
Q1	24.00	20.50	23.00
Median	29.50	26.00	29.00

Age

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
Q3	45.00	38.50	44.00
Max	58.00	54.00	58.00

T_DEMOG.sas (07FEB2011)

Table 14.1. 56: Height (FAS/PP)

Height [cm]

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	178.47	178.78	178.62
SD	9.98	9.71	9.81
Min	152.00	159.00	152.00
Q1	171.00	172.00	172.00
Median	178.00	178.00	178.00
Q3	186.00	185.50	186.00
Max	205.00	200.00	205.00

T_DEMOG.sas (07FEB2011)

Table 14.1. 57: Weight (FAS/PP)

Weight [kg]

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	79.68	80.75	80.21
SD	14.26	17.06	15.65
Min	53.00	50.00	50.00
Q1	71.00	67.50	68.00
Median	78.00	79.00	78.00
Q3	90.00	93.50	90.00
Max	118.00	128.00	128.00

T_DEMOG.sas (07FEB2011)

Table 14.1. 58: BMI (FAS/PP)

BMI [kg/m²]

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	24.95	25.19	25.07
SD	3.49	4.57	4.04
Min	19.00	17.00	17.00
Q1	22.00	22.50	22.00
Median	24.00	24.00	24.00
Q3	27.00	27.00	27.00
Max	36.00	42.00	42.00

T_DEMOG.sas (07FEB2011)

Table 14.1. 59: Gender (FAS/PP)

	Treatment					
	Active patch 200 mg ibuprofen		Placebo patch		All	
	n	%	n	%	n	%
Sex						
male	44	66.7	44	68.8	88	67.7
female	22	33.3	20	31.3	42	32.3
All	66	100.0	64	100.0	130	100.0

T_DEMOG.sas (07FEB2011)

Table 14.1. 60: Ethnic origin (FAS/PP)

	Treatment				All	
	Active patch 200 mg ibuprofen		Placebo patch			
	n	%	n	%	n	%
Race						
Caucasian	65	98.5	64	100.0	129	99.2
Afro-Caribbean	1	1.5	.	0.0	1	0.8
All	66	100.0	64	100.0	130	100.0

T_DEMOG.sas (07FEB2011)

Table 14.1. 61: History and current use of cigarettes, alcohol and drugs (FAS/PP)

	Treatment				All	
	Active patch 200 mg ibuprofen		Placebo patch			
	n	%	n	%	n	%
Patient is smoker						
yes	18	27.3	12	18.8	30	23.1
no	48	72.7	52	81.3	100	76.9
Number of cigarettes a day						
.	48	72.7	52	81.3	100	76.9
less equal 10	10	15.2	5	7.8	15	11.5
11-30	6	9.1	6	9.4	12	9.2
more than 30	2	3.0	1	1.6	3	2.3
Patient smoked in the past						
.	16	24.2	11	17.2	27	20.8
yes	8	12.1	5	7.8	13	10.0
no	42	63.6	48	75.0	90	69.2
Patient consumed relevant amount of alc.						
no	66	100.0	64	100.0	130	100.0
Patient abused alcohol in the past year						
Yes, once in a while	41	62.1	37	57.8	78	60.0
Yes, regularly	2	3.0	2	3.1	4	3.1
No	23	34.8	25	39.1	48	36.9
Patient abused drugs in the past year						
.	.	0.0	1	1.6	1	0.8
no	66	100.0	63	98.4	129	99.2
All	66	100.0	64	100.0	130	100.0

T_DEMOG.sas (07FEB2011)

Table 14.1. 62: Age by centre (FAS/PP)

Age

	Treatment								
	Active patch 200 mg ibuprofen				Placebo patch				
	Site No.				Site No.				
	1	2	3	4	1	2	3	4	All
n	15	16	21	14	15	15	20	14	130
Mean	34.73	34.25	34.71	32.29	30.07	34.40	31.75	23.07	32.12
SD	11.92	10.95	13.33	10.84	12.14	11.71	11.64	3.56	11.55
Min	20.00	19.00	19.00	18.00	18.00	19.00	18.00	19.00	18.00
Q1	24.00	25.00	22.00	25.00	19.00	26.00	20.50	20.00	23.00
Median	29.00	30.50	31.00	29.50	26.00	31.00	31.50	23.00	29.00
Q3	44.00	44.50	45.00	41.00	39.00	44.00	44.00	25.00	44.00
Max	58.00	54.00	58.00	50.00	53.00	54.00	52.00	30.00	58.00

T_DEMOG_C.sas (21FEB2011)

Table 14.1.63: Height by centre (FAS/PP)

Height [cm]

	Treatment								
	Active patch 200 mg ibuprofen				Placebo patch				
	Site No.				Site No.				
	1	2	3	4	1	2	3	4	All
n	15	16	21	14	15	15	20	14	130
Mean	173.60	178.13	178.57	183.93	179.53	176.27	174.95	186.14	178.62
SD	9.85	9.59	10.46	7.73	10.65	8.50	8.68	7.62	9.81
Min	152.00	166.00	160.00	171.00	159.00	160.00	162.00	172.00	152.00
Q1	166.00	168.50	173.00	176.00	174.00	170.00	168.50	180.00	172.00
Median	176.00	177.00	178.00	184.50	178.00	178.00	174.00	186.50	178.00
Q3	183.00	186.50	185.00	190.00	186.00	183.00	179.00	190.00	186.00
Max	189.00	192.00	205.00	196.00	200.00	186.00	196.00	197.00	205.00

T_DEMOG_C.sas (21FEB2011)

Table 14.1.64: Weight by centre (FAS/PP)

Weight [kg]

	Treatment								
	Active patch 200 mg ibuprofen				Placebo patch				
	Site No.				Site No.				
	1	2	3	4	1	2	3	4	All
n	15	16	21	14	15	15	20	14	130
Mean	76.20	85.06	71.52	89.50	85.27	84.13	69.95	87.71	80.21
SD	9.82	17.69	11.33	9.68	21.80	17.02	13.75	6.41	15.65
Min	55.00	59.00	53.00	75.00	54.00	60.00	50.00	75.00	50.00
Q1	72.00	70.50	64.00	84.00	68.00	72.00	61.00	84.00	68.00
Median	75.00	85.50	71.00	88.00	84.00	78.00	66.00	85.50	78.00
Q3	80.00	97.00	76.00	92.00	103.00	98.00	77.50	93.00	90.00
Max	95.00	118.00	99.00	110.00	128.00	125.00	98.00	100.00	128.00

T_DEMOG_C.sas (21FEB2011)

Table 14.1.65: BMI by centre (FAS/PP)

BMI [kg/m²]

	Treatment								
	Active patch 200 mg ibuprofen				Placebo patch				
	Site No.				Site No.				
	1	2	3	4	1	2	3	4	All
n	15	16	21	14	15	15	20	14	130
Mean	25.33	26.69	22.33	26.50	26.20	27.33	22.85	25.14	25.07
SD	2.74	4.21	1.74	3.18	5.92	4.98	3.54	1.92	4.04
Min	22.00	20.00	19.00	22.00	18.00	22.00	17.00	22.00	17.00
Q1	23.00	22.00	21.00	25.00	23.00	23.00	21.00	24.00	22.00
Median	24.00	27.50	22.00	26.00	25.00	25.00	21.50	25.00	24.00
Q3	27.00	30.00	24.00	27.00	29.00	33.00	25.50	27.00	27.00

BMI [kg/m²]

	Treatment								
	Active patch 200 mg ibuprofen				Placebo patch				
	Site No.				Site No.				
	1	2	3	4	1	2	3	4	All
Max	31.00	32.00	25.00	36.00	42.00	38.00	31.00	28.00	42.00

T_DEMOG_C.sas (21FEB2011)

Table 14.1.66: Sex by centre (FAS/PP)

	Treatment															
	Active patch 200 mg ibuprofen								Placebo patch							
	Site No.								Site No.							
	1		2		3		4		1		2		3		4	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Sex																
male	7	46.7	12	75.0	11	52.4	14	100.0	9	60.0	12	80.0	9	45.0	14	100.0
female	8	53.3	4	25.0	10	47.6	.	0.0	6	40.0	3	20.0	11	55.0	.	0.0
All	15	100.0	16	100.0	21	100.0	14	100.0	15	100.0	15	100.0	20	100.0	14	100.0

T_DEMOG_C.sas (21FEB2011)

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able 14.1.67: Ethnic origin by centre (FAS/PP)

	Treatment							
	Active patch 200 mg ibuprofen							
	Site No.							
	1		2		3		4	
	n	%	n	%	n	%	n	%
Race								
Caucasian	14	93.3	16	100.0	21	100.0	14	100.0
Afro-Caribbean	1	6.7	.	0.0	.	0.0	.	0.0
All	15	100.0	16	100.0	21	100.0	14	100.0

	Treatment							
	Placebo patch							
	Site No.							
	1		2		3		4	
	n	%	n	%	n	%	n	%
Race								
Caucasian	15	100.0	15	100.0	20	100.0	14	100.0
Afro-Caribbean	.	0.0	.	0.0	.	0.0	.	0.0
All	15	100.0	15	100.0	20	100.0	14	100.0

T_DEMOG_C.sas (21FEB2011)

Table 14.1.68: History and current use of cigarettes, alcohol and drugs by centre (FAS/PP)

	Treatment															
	Active patch 200 mg ibuprofen								Placebo patch							
	Site No.								Site No.							
	1		2		3		4		1		2		3		4	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Patient is smoker																
yes	6	40.0	8	50.0	1	4.8	3	21.4	1	6.7	7	46.7	3	15.0	1	7.1
no	9	60.0	8	50.0	20	95.2	11	78.6	14	93.3	8	53.3	17	85.0	13	92.9
Number of cigarettes a day																
.	9	60.0	8	50.0	20	95.2	11	78.6	14	93.3	8	53.3	17	85.0	13	92.9
less equal 10	4	26.7	2	12.5	1	4.8	3	21.4	1	6.7	1	6.7	2	10.0	1	7.1
11-30	2	13.3	4	25.0	.	0.0	.	0.0	.	0.0	5	33.3	1	5.0	.	0.0
more than 30	.	0.0	2	12.5	.	0.0	.	0.0	.	0.0	1	6.7	.	0.0	.	0.0
Patient smoked in the past																
.	4	26.7	8	50.0	1	4.8	3	21.4	.	0.0	7	46.7	3	15.0	1	7.1
yes	5	33.3	1	6.3	2	9.5	.	0.0	3	20.0	1	6.7	1	5.0	.	0.0
no	6	40.0	7	43.8	18	85.7	11	78.6	12	80.0	7	46.7	16	80.0	13	92.9
Patient consumed relevant amount of alc.																
no	15	100.0	16	100.0	21	100.0	14	100.0	15	100.0	15	100.0	20	100.0	14	100.0
Patient abused alcohol in the past year																
Yes, once in a while	10	66.7	13	81.3	4	19.0	14	100.0	10	66.7	14	93.3	2	10.0	11	78.6
Yes, regularly	2	13.3	.	0.0	.	0.0	.	0.0	2	13.3	.	0.0	.	0.0	.	0.0
No	3	20.0	3	18.8	17	81.0	.	0.0	3	20.0	1	6.7	18	90.0	3	21.4
Patient abused drugs in the past year	.	0.0	.	0.0	.	0.0	.	0.0	1	6.7	.	0.0	.	0.0	.	0.0

	Treatment															
	Active patch 200 mg ibuprofen								Placebo patch							
	Site No.								Site No.							
	1		2		3		4		1		2		3		4	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
.																
no	15	100.0	16	100.0	21	100.0	14	100.0	14	93.3	15	100.0	20	100.0	14	100.0
All	15	100.0	16	100.0	21	100.0	14	100.0	15	100.0	15	100.0	20	100.0	14	100.0

T_DEMOG_C.sas (21FEB2011)

Table 14.1. 69: Time to injury (h) (FAS/PP)

Time from injury to 1st application (h)

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	1.67	1.63	1.65
SD	0.72	0.76	0.74
Min	0.33	0.17	0.17
Q1	1.00	0.88	1.00
Median	1.75	1.61	1.67
Q3	2.17	2.25	2.25
Max	3.17	3.25	3.25

Table 14.1. 70: Time to injury (min) (FAS/PP)

Time from injury to 1st application (min)

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	100.09	98.09	99.11
SD	43.44	45.74	44.42
Min	20.00	10.00	10.00
Q1	60.00	52.50	60.00
Median	105.00	96.50	100.00
Q3	130.00	135.00	135.00
Max	190.00	195.00	195.00

T_TIME_INJURY.sas (25FEB2011)

Table 14.1. 71: Time to injury (h) by centre (FAS/PP)

Time from injury to 1st application (h)

	Center								
	1		2		3		4		
	Treatment		Treatment		Treatment		Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	All
n	15	15	16	15	21	20	14	14	130
Mean	1.63	2.01	2.44	2.07	1.32	1.33	1.34	1.21	1.65
SD	0.57	0.58	0.41	0.82	0.62	0.52	0.66	0.80	0.74
Min	0.75	0.75	1.67	0.83	0.33	0.42	0.50	0.17	0.17
Q1	1.25	1.75	2.13	1.25	0.83	0.83	1.00	0.58	1.00
Median	1.58	2.25	2.54	2.25	1.25	1.33	1.08	1.21	1.67
Q3	1.92	2.50	2.75	2.75	1.92	1.71	1.83	1.63	2.25
Max	2.75	2.83	3.17	3.25	2.33	2.25	2.83	3.02	3.25

Table 14.1. 72: Time to injury (min) by centre (FAS/PP)

Time from injury to 1st application (min)

	Center								
	1		2		3		4		
	Treatment		Treatment		Treatment		Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	All
n	15	15	16	15	21	20	14	14	130
Mean	98.00	120.33	146.56	124.00	79.29	80.00	80.43	72.36	99.11
SD	34.27	34.61	24.75	49.03	37.02	30.95	39.70	47.91	44.42
Min	45.00	45.00	100.00	50.00	20.00	25.00	30.00	10.00	10.00
Q1	75.00	105.00	127.50	75.00	50.00	50.00	60.00	35.00	60.00

Time from injury to 1st application (min)

	Center								
	1		2		3		4		
	Treatment		Treatment		Treatment		Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	All
Median	95.00	135.00	152.50	135.00	75.00	80.00	65.00	72.50	100.00
Q3	115.00	150.00	165.00	165.00	115.00	102.50	110.00	98.00	135.00
Max	165.00	170.00	190.00	195.00	140.00	135.00	170.00	181.00	195.00

T_TIME_INJURY.sas (25FEB2011)

Table 14.1. 73: Study duration (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
Study Duration (d)	n	66	64
	Mean	6.00	6.00
	SD	0.00	0.00
	Min	6.00	6.00
	Q1	6.00	6.00
	Median	6.00	6.00
	Q3	6.00	6.00
	Max	6.00	6.00

T_TIM.sas (28FEB2011)

Table 14.1. 74: Total duration of treatment (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
Total duration of treatment (d)	n	66	64
	Mean	4.99	4.98
	SD	0.05	0.14
	Min	4.67	4.00
	Q1	4.99	4.99
	Median	5.00	5.00
	Q3	5.00	5.02
	Max	5.08	5.24

Table 14.1. 75: Size of injury/contusion (FAS/PP)

Size of injury/contusion [cm²]

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	51.05	46.48	48.80
SD	23.43	19.58	21.66
Min	25.00	25.00	25.00
Q1	35.00	30.00	30.00
Median	45.00	40.00	40.00
Q3	60.00	57.50	60.00
Max	120.00	120.00	120.00

T_DEMOG.sas (25FEB2011)

Table 14.1. 76: Size of injury/contusion by centre (FAS/PP)

Size of injury/contusion [cm²]

	Treatment								
	Active patch 200 mg ibuprofen				Placebo patch				
	Site No.				Site No.				
	1	2	3	4	1	2	3	4	All
n	15	16	21	14	15	15	20	14	130
Mean	33.07	48.44	64.52	53.07	33.67	42.33	55.25	52.14	48.80
SD	6.08	15.02	27.11	25.19	13.37	11.00	22.74	20.45	21.66
Min	25.00	30.00	30.00	30.00	25.00	25.00	30.00	30.00	25.00
Q1	28.00	35.00	45.00	35.00	28.00	35.00	40.00	35.00	30.00
Median	30.00	45.00	60.00	49.00	30.00	40.00	50.00	47.50	40.00
Q3	36.00	57.50	80.00	60.00	36.00	55.00	67.50	60.00	60.00
Max	45.00	80.00	120.00	110.00	80.00	60.00	120.00	100.00	120.00

T_DEMOG_C.sas (25FEB2011)

Table 14.1. 77: Localisation of injury (FAS/PP)

	Treatment				All	
	Active patch 200 mg ibuprofen		Placebo patch			
	n	%	n	%	n	%
Location - category						
Feet	1	1.5	4	6.3	5	3.8
Lower leg	10	15.2	14	21.9	24	18.5
Knee	6	9.1	2	3.1	8	6.2
Upper leg	14	21.2	16	25.0	30	23.1
Hip	4	6.1	3	4.7	7	5.4
Upper back	1	1.5	.	0.0	1	0.8
Upper arm	15	22.7	12	18.8	27	20.8
Forearm	4	6.1	5	7.8	9	6.9
Chest	3	4.5	3	4.7	6	4.6
Low back	1	1.5	2	3.1	3	2.3
Shoulder	7	10.6	3	4.7	10	7.7
All	66	100.0	64	100.0	130	100.0

T_DEMOG.sas (25FEB2011)

Table 14.1. 78: Localisation of injury by centre (FAS/PP)

		Treatment			
		Active patch 200 mg ibuprofen		Placebo patch	
		n	%	n	%
Location - category	Site No.				
Feet	1	.	0.0	.	0.0
	2	.	0.0	.	0.0
	3	.	0.0	3	15.0
	4	1	7.1	1	7.1
Lower leg	1	3	20.0	3	20.0
	2	1	6.3	4	26.7
	3	6	28.6	5	25.0
	4	.	0.0	2	14.3
Knee	1	.	0.0	.	0.0
	2	.	0.0	.	0.0
	3	2	9.5	2	10.0
	4	4	28.6	.	0.0
Upper leg	1	1	6.7	1	6.7
	2	6	37.5	6	40.0
	3	3	14.3	2	10.0
	4	4	28.6	7	50.0
Hip	1	.	0.0	.	0.0
	2	.	0.0	.	0.0
	3	1	4.8	2	10.0
	4	3	21.4	1	7.1
Upper back	1	1	6.7	.	0.0
	2	.	0.0	.	0.0
	3	.	0.0	.	0.0
	4	.	0.0	.	0.0
Upper arm	1	7	46.7	6	40.0
	2	6	37.5	4	26.7

		Treatment			
		Active patch 200 mg ibuprofen		Placebo patch	
		n	%	n	%
	3	2	9.5	2	10.0
	4	.	0.0	.	0.0
Forearm	1	2	13.3	4	26.7
	2	.	0.0	.	0.0
	3	2	9.5	1	5.0
	4	.	0.0	.	0.0
Chest	1	.	0.0	.	0.0
	2	1	6.3	.	0.0
	3	1	4.8	1	5.0
	4	1	7.1	2	14.3
Low back	1	.	0.0	1	6.7
	2	.	0.0	.	0.0
	3	1	4.8	1	5.0
	4	.	0.0	.	0.0
Shoulder	1	1	6.7	.	0.0
	2	2	12.5	1	6.7
	3	3	14.3	1	5.0
	4	1	7.1	1	7.1
All		66	100.0	64	100.0

Table 14.1. 79: Size of injury by localisation (FAS/PP)

Treatment Active patch 200 mg ibuprofen

	Size of injury/contusion [cm²]							
	n	Mean	SD	Min	Q1	Median	Q3	Max
Location - category								
Feet	1	60.00	.	60.00	60.00	60.00	60.00	60.00
Lower leg	10	48.40	18.42	28.00	36.00	42.50	65.00	80.00
Knee	6	45.00	23.24	30.00	30.00	35.00	50.00	90.00
Upper leg	14	61.57	20.36	40.00	50.00	57.50	70.00	120.00
Hip	4	60.75	29.81	30.00	39.00	56.50	82.50	100.00
Upper back	1	36.00	.	36.00	36.00	36.00	36.00	36.00
Upper arm	15	35.00	7.78	28.00	30.00	30.00	40.00	50.00
Forearm	4	36.50	8.50	25.00	30.50	38.00	42.50	45.00
Chest	3	93.33	20.82	70.00	70.00	100.00	110.00	110.00
Low back	1	90.00	.	90.00	90.00	90.00	90.00	90.00
Shoulder	7	53.29	31.05	28.00	30.00	45.00	55.00	120.00

Treatment Placebo patch

	Size of injury/contusion [cm²]							
	n	Mean	SD	Min	Q1	Median	Q3	Max
Location - category								
Feet	4	56.25	24.96	30.00	40.00	52.50	72.50	90.00
Lower leg	14	40.79	13.54	30.00	30.00	35.50	50.00	80.00
Knee	2	50.00	14.14	40.00	40.00	50.00	60.00	60.00
Upper leg	16	53.81	19.04	30.00	40.00	52.50	65.00	100.00
Hip	3	60.00	20.00	40.00	40.00	60.00	80.00	80.00
Upper arm	12	39.00	13.97	27.00	28.00	35.50	45.00	70.00
Forearm	5	31.00	8.03	25.00	27.00	28.00	30.00	45.00
Chest	3	46.67	12.58	35.00	35.00	45.00	60.00	60.00
Low back	2	75.00	63.64	30.00	30.00	75.00	120.00	120.00
Shoulder	3	41.67	20.82	25.00	25.00	35.00	65.00	65.00

T_DEMOG.sas (25FEB2011)

Table 14.1. 80: Number of prior medications (FAS/PP)

No. of prior medications	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	N	%	N	%
0	60	90.9	62	96.9
1	4	6.1	2	3.1
2	1	1.5	.	.
3	1	1.5	.	.

T_MED.sas (21FEB2011)

Table 14.1. 81: Number of prior and concomitant medications (FAS/PP)

No. of prior and concomitant medications	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	N	%	N	%
0	40	60.6	48	75.0
1	21	31.8	13	20.3
2	3	4.5	2	3.1
4	1	1.5	1	1.6
6	1	1.5	.	.

T_MED.sas (21FEB2011)

Table 14.1. 82: Number of concomitant medications (FAS/PP)

No. of concomitant medications	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	N	%	N	%
0	55	83.3	60	93.8
1	6	9.1	1	1.6
2	3	4.5	2	3.1
3	1	1.5	.	.
5	1	1.5	.	.
6	.	.	1	1.6

T_MED.sas (21FEB2011)

Table 14.1. 83: Frequency of prior medications (FAS/PP)

		Active patch 200 mg ibuprofen	Placebo patch
Number of prior medications	n	9	2
Number of patients with prior medications	n	6	2
Total number of patients treated	n	66	64
Patients with prior medications	%	9.1	3.1

T_MED.sas (21FEB2011)

Table 14.1. 84: Frequency of prior and concomitant medications (FAS/PP)

		Active patch 200 mg ibuprofen	Placebo patch
Number of 'prior and concomitant' medications	n	37	21
Number of patients with 'prior and concomitant' medications	n	26	16
Total number of patients treated	n	66	64
Patients with 'prior and concomitant' medications	%	39.4	25.0

T_MED.sas (21FEB2011)

Table 14.1. 85: Frequency of concomitant medications (FAS/PP)

		Active patch 200 mg ibuprofen	Placebo patch
Number of concomitant medications	n	20	11
Number of patients with concomitant medications	n	11	4
Total number of patients treated	n	66	64
Patients with concomitant medications	%	16.7	6.3

T_MED.sas (21FEB2011)

Table 14.1. 86: Prior and concomitant medication (FAS/PP)

	Treatment				All	
	Active patch 200 mg ibuprofen		Placebo patch			
	n	%	n	%	n	%
Med. Type						
Prior	9	13.6	2	5.9	11	11.0
Prior and concomitant	37	56.1	21	61.8	58	58.0
Concomitant	20	30.3	11	32.4	31	31.0
All	66	100.0	34	100.0	100	100.0

T_MED.sas (21FEB2011)

Multiple citations possible

Table 14.1. 87: Prior medication by ATC classification (FAS/PP)

	Treatment	
	Active patch 200 mg ibuprofen	Placebo patch
	n	n
ATC classification		
ANTIBIOTICS	1	.
BACTERIAL AND VIRAL VACCINES, COMBINED	.	1
BETA BLOCKING AGENTS, NON-SELECTIVE	1	.
MACROLIDES	2	.
Non-drug treatment (incl. RICE)	2	.
OTHER ANTIFUNGALS FOR TOPICAL USE	1	.
PROPIONIC ACID DERIVATIVES	.	1

	Treatment	
	Active patch 200 mg ibuprofen	Placebo patch
	n	n
SELECTIVE SEROTONIN (5HT1) AGONISTS	1	.
SULFUR-CONTAINING IMIDAZOLE DERIVATIVES	1	.
All	9	2

T_MED.sas (21FEB2011)

Multiple citations possible.

Table 14.1. 88: Prior and concomitant medication by ATC class (FAS/PP)

	Treatment	
	Active patch 200 mg ibuprofen n	Placebo patch n
ATC classification		
ACE INHIBITORS, PLAIN	.	1
ANGIOTENSIN II ANTAGONISTS AND DIURETICS	1	.
ANGIOTENSIN II ANTAGONISTS, PLAIN	1	.
ANTIANDROGENS AND ESTROGENS	.	1
BETA BLOCKING AGENTS, NON-SELECTIVE	1	.
BETA BLOCKING AGENTS, SELECTIVE	3	.
CORTICOSTEROIDS, POTENT (GROUP III)	.	1
DIHYDROPYRIDINE DERIVATIVES	1	.
ESTROGENS	1	1
EXPECTORANTS	.	1
GLUCOCORTICOIDS	1	.
HMG COA REDUCTASE INHIBITORS	1	.
INTRAUTERINE CONTRACEPTIVES	1	.
INTRAVAGINAL CONTRACEPTIVES	.	1
MEDICATED DRESSINGS WITH ANTIINFECTIVES	1	.
Non-drug treatment (incl. RICE)	1	.
OTHER ANTIFUNGALS FOR TOPICAL USE	.	1
OTHER ANTIPSORIATICS FOR TOPICAL USE	.	1
PENICILLINS WITH EXTENDED SPECTRUM	1	.
PREPARATIONS INHIBITING URIC ACID PRODUCTION	.	1
PROGESTOGENS	1	2
PROGESTOGENS AND ESTROGENS, FIXED COMBINATIONS	13	6
PROGESTOGENS AND ESTROGENS,SEQUENTIAL PREPARATIONS	1	3
PROPULSIVES	1	.
PROTON PUMP INHIBITORS	1	.
RENIN-INHIBITORS	.	1
SALICYLIC ACID PREPARATIONS	1	.
SELECTIVE BETA-2-ADRENORECEPTOR AGONISTS	1	.

	Treatment	
	Active patch 200 mg ibuprofen	Placebo patch
	n	n
SULFONAMIDES, PLAIN	1	.
THIAZIDES, PLAIN	1	.
THYROID THERAPY	2	.
All	37	21

T_MED.sas (21FEB2011)

Multiple citations possible.

Table 14.1. 89: Concomitant medication by ATC classification (FAS/PP)

	Treatment	
	Active patch 200 mg ibuprofen n	Placebo patch n
ATC classification		
ANILIDES	14	9
MACROLIDES	1	.
NASAL DECONGESTANTS FOR SYSTEMIC USE	1	.
Non-drug treatment (incl. RICE)	3	2
PROTON PUMP INHIBITORS	1	.
All	20	11

T_MED.sas (21FEB2011)

Multiple citations possible.

Table 14.1. 90: Number of patients with concomitant medication by ATC classification (FAS/PP)

	Number of patients who received the medication	
	Treatment	
	Active patch 200 mg ibuprofen	Placebo patch
ATC description		
ANILIDES	6	4
Non-drug treatment (incl. RICE)	2	1
MACROLIDES	1	.

	Number of patients who received the medication	
	Treatment	
	Active patch 200 mg ibuprofen	Placebo patch
NASAL DECONGESTANTS FOR SYSTEMIC USE	1	.
PROTON PUMP INHIBITORS	1	.

T_MED.sas (21FEB2011)

Table 14.1. 91: Treatment duration of prior medications (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
Treatment duration (d)	n	5	1
	Mean	6.80	1.00
	SD	8.84	.
	Min	1.00	1.00
	Q1	1.00	1.00
	Median	3.00	1.00
	Q3	7.00	1.00
	Max	22.00	1.00

T_MED.sas (21FEB2011)

Table 14.1. 92: Treatment duration of prior and concomitant medications (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
Treatment duration (d)	n	1	1
	Mean	5.00	7.00
	SD	.	.
	Min	5.00	7.00
	Q1	5.00	7.00
	Median	5.00	7.00
	Q3	5.00	7.00
	Max	5.00	7.00

T_MED.sas (21FEB2011)

Table 14.1. 93: Treatment duration of concomitant medications (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
Treatment duration (d)	n	18	11
	Mean	1.17	1.00
	SD	0.51	0.00
	Min	1.00	1.00
	Q1	1.00	1.00
	Median	1.00	1.00
	Q3	1.00	1.00
	Max	3.00	1.00

T_MED.sas (21FEB2011)

Table 14.1. 94: Previous diseases by verbatim term (FAS/PP)

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
	n	n	n
COMMON COLD	1	1	2
NEURODERMITIS	2	.	2
HYPERTONY	1	.	1
DISLOCATED HIP JOINT LEFT	.	1	1
VIRAL INFECTION RESPIRATORY SYSTEM	.	1	1
ARTHROSCOPY LEFT KNEE	1	.	1
OPERATION OF INGUINAL HERNIA RIGHT	1	.	1
RELAPSE OPERATION OF INGUINAL HERNIA RIGHT	1	.	1
BRONCHITIS	1	.	1
BURN RIGHT HAND	1	.	1
SINUSITIS	1	.	1
TINEA PEDIS	1	.	1
DISC PROLAPSE LUMBAR SPINE	1	.	1
OPERATION LUMBAR SPINE BY DISC PROLAPSE	1	.	1
VIRAL INFECTION	1	.	1
BYPASS OPERATION OF HEART	1	.	1
ALCOHOL ABUSE	1	.	1
DEPRESSION	1	.	1
BURNOUT SYNDROME	1	.	1
SKULL CONTUSION	1	.	1
HYPERTHYREOSIS	1	.	1
NEURODERMITIS-HEAD	1	.	1
PATELLAR TENDON SYNDROME DENERVATION DUE TO CHRONIC PATELLAR TENDON SYNDROME	.	1	1
ACL-REPAIR RIGHT KNEE	1	.	1
ACL-REPAIR	.	1	1
NOSE FRACTURE	1	.	1

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
	n	n	n
AFTER NOSE FRACTURE	1	.	1
All	24	5	29

T_DIS.sas (01MAR2011)

Table 14.1. 95: Previous diseases by preferred term (FAS/PP)

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
	n	n	n
Neurodermatitis	3	.	3
Inguinal hernia repair	2	.	2
Nasopharyngitis	1	1	2
Ligament operation	1	1	2
Facial bones fracture	2	.	2
Hypertension	1	.	1
Joint dislocation	.	1	1
Respiratory tract infection viral	.	1	1
Arthroscopy	1	.	1
Bronchitis	1	.	1
Thermal burn	1	.	1
Sinusitis	1	.	1
Tinea pedis	1	.	1
Intervertebral disc protrusion	1	.	1
Intervertebral disc operation	1	.	1
Viral infection	1	.	1
Vascular graft	1	.	1
Alcohol abuse	1	.	1
Depression	1	.	1
Burnout syndrome	1	.	1
Contusion	1	.	1
Hyperthyroidism	1	.	1
Patellofemoral pain syndrome	.	1	1
All	24	5	29

T_DIS.sas (01MAR2011)

Table 14.1. 96: Previous diseases by SOC (FAS/PP)

	Treatment		
	Active patch 200 mg ibuprofen n	Placebo patch n	All n
Infections and infestations	5	2	7
Surgical and medical procedures	5	1	6
Injury, poisoning and procedural complications	4	1	5
Psychiatric disorders	3	.	3
Skin and subcutaneous tissue disorders	3	.	3
Musculoskeletal and connective tissue disorders	1	1	2
Vascular disorders	1	.	1
Investigations	1	.	1
Endocrine disorders	1	.	1
All	24	5	29

T_DIS.sas (01MAR2011)

Table 14.1. 97: Concomitant diseases by verbatim term (FAS/PP)

	Treatment		
	Placebo patch n	Active patch 200 mg ibuprofen n	All n
HYPERCHOLESTEROLEMIA	4	3	7
POLLINOSIS	2	3	5
HYPERTENSION	2	2	4
CORONARY HEART DISEASE	1	1	2
ADIPOSITY	1	1	2
COUGH	1	1	2
LUMBAR SPINE SYNDROME	.	2	2
MIGRAINE	.	2	2
DISC PROLAPSE L5/S1	1	1	2
HYPERURICEMIA	1	1	2
ATRIAL FIBRILLATION	.	2	2
ALLERGY AGAINST BIRCH	2	.	2
HYSTERECTOMY	.	1	1
LESION OF ROOT OF NOSE	1	.	1
ABSCESS BUTTOCKS	.	1	1
ASTHMA	.	1	1
DEPRESSION	.	1	1
LUMBAGO CRONIC	.	1	1
TINEA GENITAL	1	.	1
PSORIASIS VULGARIS	1	.	1
STEATOSIS HEPATIS	1	.	1
COPD	.	1	1
OSTEOCHONDROSIS CERVICAL SPINE	.	1	1
LEUKOCYTOSIS	1	.	1
LYMPHOPENIA	1	.	1
HEPATOSIS	1	.	1
GOUT	1	.	1

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
WEDGE-SHAPED DEFORMITY OF VERTEBRAL LUMBAR	.	1	1
SCOLIOSIS OF LUMBAR SPINE	.	1	1
CHONDROMALACIA LEFT KNEE	.	1	1
BRONCHITIS	.	1	1
OTITIS	1	.	1
TENDINITIS RIGHT WRIST	1	.	1
SUBAORTIC STENOSIS	1	.	1
MEDIAL MENISCUS LESION RIGHT SITE	1	.	1
PERIARTHRITIS HUMEROSCAPULARIS RIGHT	1	.	1
GASTRITIS	.	1	1
ANGINA PECT.	.	1	1
GASTROENTERITIS	.	1	1
DUPUYTRENS CONTRACTURE	1	.	1
LIPOMA RIGHT KIDNEY	1	.	1
COMMON COLD	.	1	1
ALLERGIC TO BARLEY	1	.	1
ALLERGY OF HAZELNUT AND CATS	1	.	1
ALLERGY AGAINST GRASSES	1	.	1
ESOPHAGEAL REFLUX DURING SPEED RUNNING	1	.	1
ALLERGY TO BIRCH TREE, GRASES, HAZELNUT	1	.	1
ALLERGY TO NICKEL DUST	.	1	1
FOOD INTOLERANCE AGAINST TOMATOES	.	1	1
GRAS ALLERGY	1	.	1
HAY FEVER	1	.	1
ALLERGY AGAINST GRAS	1	.	1
ALLERGY AGAINST RYE	1	.	1
ALLERGY AGAINST AMOXICILLIN	1	.	1
DUST ALLERGY	1	.	1

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
CAT ALLERGY	1	.	1
EXERCISE INDUCED ASTHMA	1	.	1
STRUMA NODOSA	.	1	1
GRASS ALLERGY	1	.	1
ALLERGY AGAINST BENZOCAIN	1	.	1
STRESS ALLERGY	1	.	1
MILK ALLERGY	1	.	1
NUT ALLERGY	1	.	1
ALLERGIC ASTHMA	.	1	1
ALLERGY AGAINST PENICILLIN	.	1	1
RHINITIS ALLERGIC	.	1	1
INTOLERANCE AGAINST UNCOOKED PEACHES, APPLES, CARROTS	.	1	1
CHRONIC INFECTION ACHILLES TENDON	.	1	1
ACL-REPAIR, AFTER	.	1	1
CHRONIC LUMBAR PAIN SPINE	.	1	1
All	48	44	92

Table 14.1. 98: Concomitant diseases by preferred term (FAS/PP)

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
Seasonal allergy	9	3	12
Hypercholesterolaemia	4	3	7
Hypertension	2	2	4
Food allergy	3	.	3
Hypersensitivity	3	.	3

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
Drug hypersensitivity	2	1	3
Asthma	.	2	2
Back pain	.	2	2
Coronary artery disease	1	1	2
Obesity	1	1	2
Cough	1	1	2
Bone pain	.	2	2
Tendonitis	1	1	2
Migraine	.	2	2
Intervertebral disc protrusion	1	1	2
Hyperuricaemia	1	1	2
Atrial fibrillation	.	2	2
Food intolerance	.	2	2
Hysterectomy	.	1	1
Face injury	1	.	1
Subcutaneous abscess	.	1	1
Depression	.	1	1
Tinea cruris	1	.	1
Psoriasis	1	.	1
Hepatic steatosis	1	.	1
Chronic obstructive pulmonary disease	.	1	1
Osteochondrosis	.	1	1
Leukocytosis	1	.	1
Lymphopenia	1	.	1
Liver disorder	1	.	1
Gout	1	.	1
Spinal deformity	.	1	1
Scoliosis	.	1	1

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
Chondromalacia	.	1	1
Bronchitis	.	1	1
Ear infection	1	.	1
Subvalvular aortic stenosis	1	.	1
Meniscus lesion	1	.	1
Periarthritis	1	.	1
Gastritis	.	1	1
Angina pectoris	.	1	1
Gastroenteritis	.	1	1
Dupuytren's contracture	1	.	1
Renal lipomatosis	1	.	1
Nasopharyngitis	.	1	1
Gastrooesophageal reflux disease	1	.	1
Allergy to metals	.	1	1
House dust allergy	1	.	1
Allergy to animal	1	.	1
Asthma exercise induced	1	.	1
Goitre	.	1	1
Milk allergy	1	.	1
Rhinitis allergic	.	1	1
Ligament operation	.	1	1
All	48	44	92

T_DIS.sas (01MAR2011)

Table 14.1. 99: Concomitant diseases by SOC (FAS/PP)

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
Immune system disorders	20	5	25
Musculoskeletal and connective tissue disorders	4	10	14
Metabolism and nutrition disorders	7	7	14
Respiratory, thoracic and mediastinal disorders	2	5	7
Infections and infestations	2	4	6
Cardiac disorders	2	4	6
Vascular disorders	2	2	4
Surgical and medical procedures	.	2	2
Injury, poisoning and procedural complications	2	.	2
Hepatobiliary disorders	2	.	2
Blood and lymphatic system disorders	2	.	2
Nervous system disorders	.	2	2
Gastrointestinal disorders	1	1	2
Psychiatric disorders	.	1	1
Skin and subcutaneous tissue disorders	1	.	1
Renal and urinary disorders	1	.	1
Endocrine disorders	.	1	1
All	48	44	92

T_DIS.sas (01MAR2011)

Table 14.1. 100: Frequency of previous diseases (FAS/PP)

		Active patch 200 mg ibuprofen	Placebo patch
Number of Previous diseases	n	24	5
Number of patients with previous diseases	n	12	5
Total number of patients treated	n	66	64
Patients with previous diseases	%	18.2	7.8

T_DIS.sas (01MAR2011)

Table 14.1. 101: Frequency of concomitant diseases (FAS/PP)

		Active patch 200 mg ibuprofen	Placebo patch
Number of concomitant diseases	n	44	48
Number of patients with concomitant diseases	n	19	20
Total number of patients treated	n	66	64
Patients with concomitant diseases	%	28.8	31.3

T_DIS.sas (01MAR2011)

Table 14.1. 102: Number of previous diseases (FAS/PP)

No. of diseases	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	N	%	N	%
0	54	81.8	59	92.2
1	7	10.6	5	7.8
2	3	4.5	.	.
3	1	1.5	.	.
8	1	1.5	.	.
All	66	100.0	64	100.0

T_DIS.sas (01MAR2011)

Table 14.1. 103: Number of concomitant diseases (FAS/PP)

No. of diseases	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	N	%	N	%
0	47	71.2	44	68.8
1	9	13.6	6	9.4
2	4	6.1	6	9.4
3	3	4.5	5	7.8
4	.	.	2	3.1
5	1	1.5	.	.
6	1	1.5	.	.
7	1	1.5	1	1.6
All	66	100.0	64	100.0

T_DIS.sas (01MAR2011)

Table 14.1. 104: Dropouts - Study completion (SAF/FAS/PP)

	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	n	%	n	%
Completion of trial according trial protocol				
yes	66	100.0	64	100.0
Total	66	100.0	64	100.0

T_TSS.sas (17FEB2011)

Table 14.1. 105: Compliance – Patch detached (FAS/PP)

	Treatment															
	Active patch 200 mg ibuprofen Visit								Placebo patch Visit							
	2		3		4		5		2		3		4		5	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Patch became detached																
yes	1	1.5	3	4.5	2	3.0	.	0.0	4	6.3	3	4.7	2	3.1	4	6.3
no	65	98.5	63	95.5	64	97.0	66	100.0	60	93.8	61	95.3	62	96.9	60	93.8
All	66	100.0	66	100.0	66	100.0	66	100.0	64	100.0	64	100.0	64	100.0	64	100.0

T_Compliance.sas (02MAR2011)

Table 14.1. 106: Compliance – Number of used patch returned (FAS/PP)

Number of used patches returned

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	4.92	4.88	4.90
SD	0.54	0.60	0.57
Min	2.00	1.00	1.00
Q1	5.00	5.00	5.00
Median	5.00	5.00	5.00
Q3	5.00	5.00	5.00
Max	6.00	6.00	6.00

T_Compliance.sas (02MAR2011)

14.2 Efficacy Data

Table 14.2. 77: VAS AUC 0-3d (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-3d [mm*h]	n	66	64
	Mean	2768.13	3430.95
	SD	1501.29	1253.14
	Min	84.50	163.00
	Q1	1587.00	2751.50
	Median	2984.00	3537.75
	Q3	3791.50	4259.00
	Max	5488.50	6123.00

T_AUC03_VAS.sas (07FEB2011)

Table 14.2. 78: VAS AUC 0-3d by center (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-3d [mm*h]	n	15	15	16	15	21	20	14	14
	Mean	1268.13	3486.53	4128.66	4123.90	2498.21	3264.68	3225.25	2866.50
	SD	1538.56	1944.39	771.75	840.54	1091.69	830.99	991.09	908.50
	Min	84.50	163.00	2960.50	2764.50	1068.50	1260.00	820.00	1537.00
	Q1	140.50	1139.00	3549.00	3265.00	1607.00	2623.00	2776.50	2137.00
	Median	368.50	4183.00	3967.75	4330.50	2355.00	3516.00	3129.00	3064.00
	Q3	1705.50	4807.00	4723.75	4877.00	3127.50	3798.50	4040.50	3617.00

		Site No.							
		1 Treatment		2 Treatment		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
	Max	4545.50	6123.00	5488.50	5404.50	5430.00	4398.50	4936.00	4160.50

T_AUC03_VAS_C.sas (21FEB2011)

Table 14.2. 79: VAS AUC 0-12h (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-12h [mm*h]	n	66	64
	Mean	615.07	700.13
	SD	236.00	165.49
	Min	84.50	163.00
	Q1	456.50	642.50
	Median	663.50	716.25
	Q3	789.50	809.00
	Max	994.50	1053.00

T_AUC012h_VAS.sas (07FEB2011)

Table 14.2. 80: VAS AUC 0-12h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-12h [mm*h]	n	15	15	16	15	21	20	14	14
	Mean	370.93	694.53	756.47	734.10	624.02	703.13	701.61	665.43
	SD	255.52	256.48	193.77	198.63	136.18	63.06	186.41	104.41
	Min	84.50	163.00	316.00	256.50	401.50	597.50	238.00	493.00
	Q1	140.50	437.00	681.50	607.00	568.50	650.25	628.50	602.50
	Median	301.00	761.50	789.25	778.50	605.00	727.25	735.25	651.00
	Q3	619.50	856.00	905.50	922.00	714.00	742.25	844.00	709.00
	Max	871.50	1053.00	994.50	937.50	942.00	792.50	958.50	876.50

T_AUC012h_VAS_C.sas (21FEB2011)

Table 14.2. 81: Least square results of VAS $AUC_{0\text{-}12h}$ by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	251.33 55.35	585.81 54.00
		Mean treatment effect (LS)	-334.48	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-458.43; -210.53 (p<0.0001)	
	2	LS Mean LS Standard error	755.21 48.68	724.93 49.82
		Mean treatment effect (LS)	30.27	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-93.15; 153.69 (p=0.6281)	
	3	LS Mean LS Standard error	678.80 40.72	753.79 41.55
		Mean treatment effect (LS)	-75.00	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-181.26; 31.27 (p=0.1649)	
	4	LS Mean LS Standard error	741.52 67.44	726.87 78.67
		Mean treatment effect (LS)	14.65	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-117.15; 146.45 (p=0.8262)	

Table 14.2. 82: VAS pain on movement at 12 h (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
VAS 12h after 1st appl. (mm)	n	66	64
	Mean	46.26	53.69
	SD	24.28	18.81
	Min	0.00	0.00
	Q1	30.00	48.00
	Median	51.50	55.50
	Q3	64.00	64.50
	Max	83.00	82.00

T_VAS_12h_24h.sas (07FEB2011)

Table 14.2. 83: VAS pain on movement at 12 h by centre (FAS/PP)

		Site No.							
		1 Treatment		2 Treatment		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS 12h after 1st appl.	n	15	15	16	15	21	20	14	14
	Mean	19.27	49.40	62.50	59.93	48.48	55.80	53.29	48.57
	SD	24.43	27.45	20.74	23.00	12.30	7.27	18.69	12.45
	Min	0.00	0.00	2.00	1.00	29.00	37.00	9.00	31.00
	Q1	0.00	16.00	59.50	54.00	40.00	52.00	42.00	33.00
	Median	6.00	55.00	67.50	58.00	47.00	58.50	58.50	50.50
	Q3	36.00	70.00	75.00	78.00	58.00	61.00	68.00	58.00
	Max	75.00	82.00	83.00	82.00	76.00	65.00	76.00	69.00

T_VAS_12h_24h_C.sas (21FEB2011)

Table 14.2. 84: : Least square results of VAS at 12 h by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	8.69 5.90	39.75 5.76
		Mean treatment effect (LS)	-31.07	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-44.29; -17.85 (p<0.0001)	
	2	LS Mean LS Standard error	61.98 5.19	59.20 5.31
		Mean treatment effect (LS)	2.78	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-10.38; 15.95 (p=0.6760)	
	3	LS Mean LS Standard error	53.12 4.34	59.91 4.43
		Mean treatment effect (LS)	-6.79	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-18.13; 4.54 (p=0.2376)	
	4	LS Mean LS Standard error	57.49 7.19	54.57 8.39
		Mean treatment effect (LS)	2.92	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-11.14; 16.97 (p=0.6817)	

Table 14.2. 85: VAS AUC 0-24 h (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-24h [mm*h]	n	66	64
	Mean	1156.86	1347.64
	SD	500.13	364.15
	Min	84.50	163.00
	Q1	822.50	1231.00
	Median	1270.75	1383.00
	Q3	1493.50	1551.00
	Max	1962.00	2103.00

T_AUC024h_VAS.sas (07FEB2011)

Table 14.2. 86: VAS AUC 0-24 h by centre (FAS/PP)

		Site No.							
		1 Treatment		2 Treatment		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-24h [mm*h]	n	15	15	16	15	21	20	14	14
	Mean	631.33	1310.53	1508.16	1472.70	1152.50	1342.88	1324.96	1260.21
	SD	559.28	603.65	346.86	355.60	306.01	170.69	360.38	208.63
	Min	84.50	163.00	730.00	628.50	707.50	984.00	400.00	956.50
	Q1	140.50	611.00	1375.50	1268.00	864.50	1235.50	1192.50	1049.00
	Median	344.50	1469.50	1546.00	1498.50	1133.00	1419.50	1377.75	1293.00
	Q3	1059.50	1723.00	1774.25	1750.00	1352.50	1464.00	1595.50	1385.00
	Max	1753.50	2103.00	1912.50	1888.50	1962.00	1566.50	1708.50	1656.50

T_AUC024h_VAS_C.sas (21FEB2011)

Table 14.2. 87: : Least square results of VAS AUC_{0-24h} by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	358.41 114.94	1062.89 112.13
		Mean treatment effect (LS)	-704.49	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-961.88; -447.09 (p<0.0001)	
	2	LS Mean LS Standard error	1512.80 101.09	1461.09 103.45
		Mean treatment effect (LS)	51.71 (p=0.1660)	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-204.57; 307.99	
	3	LS Mean LS Standard error	1283.17 84.55	1463.65 86.27
		Mean treatment effect (LS)	-180.48 (p=0.1080)	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-401.14; 40.18	
	4	LS Mean LS Standard error	1401.28 140.05	1380.24 163.37
		Mean treatment effect (LS)	21.04	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-252.64; 294.72 (p=0.8793)	

Table 14.2. 88: VAS pain on movement at 24 h (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
VAS at V2 (24h after 1st appl.) (mm)	n	66	64
	Mean	44.45	54.70
	SD	23.33	17.91
	Min	0.00	0.00
	Q1	29.00	49.00
	Median	48.00	57.50
	Q3	62.00	65.00
	Max	88.00	93.00

T_VAS_12h_24h.sas (07FEB2011)

Table 14.2. 89: VAS pain on movement at 24 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS at V2 (24h after 1st appl.)	n	15	15	16	15	21	20	14	14
	Mean	22.33	52.87	62.69	63.47	42.33	52.50	50.50	50.43
	SD	29.20	31.16	10.16	8.88	16.35	10.71	15.89	11.71
	Min	0.00	0.00	44.00	50.00	17.00	23.00	18.00	28.00
	Q1	0.00	15.00	54.00	56.00	29.00	48.00	44.00	45.00
	Median	5.00	60.00	65.00	66.00	43.00	54.00	53.00	51.00
	Q3	48.00	78.00	71.50	70.00	48.00	61.00	59.00	56.00
	Max	73.00	93.00	78.00	80.00	88.00	64.00	74.00	70.00

T_VAS_12h_24h_C.sas (21FEB2011)

Table 14.2. 90: : Least square results of VAS at Hour 24 by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	8.90 5.38	40.78 5.25
		Mean treatment effect (LS)	-31.88	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-43.92; -19.84 (p<0.0001)	
	2	LS Mean LS Standard error	64.54 4.73	64.24 4.84
		Mean treatment effect (LS)	0.30	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-11.69; 12.29 (p=0.9606)	
	3	LS Mean LS Standard error	49.87 3.96	59.66 4.04
		Mean treatment effect (LS)	-9.79	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-20.11; 0.53 (p=0.0628)	
	4	LS Mean LS Standard error	51.20 6.55	52.57 7.64
		Mean treatment effect (LS)	-1.37	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-14.17; 11.43 (p=0.8326)	

Table 14.2. 91: VAS AUC 0-5 d (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-5d [mm*h]	n	66	64
	Mean	3710.86	4828.20
	SD	2379.95	2168.08
	Min	84.50	163.00
	Q1	1683.00	3026.00
	Median	3930.25	5025.00
	Q3	5109.50	6484.75
	Max	9064.50	9531.00

T_AUC05_VAS.sas (07FEB2011)

Table 14.2. 92: VAS AUC 0-5 d by centre (FAS/PP)

		Site No.							
		1 Treatment		2 Treatment		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS AUC 0-5d [mm*h]	n	15	15	16	15	21	20	14	14
	Mean	1680.93	5180.93	5945.16	5835.10	3029.07	4537.28	4354.96	3787.07
	SD	2324.03	3120.21	1683.82	1728.60	1806.41	1608.94	1454.76	1637.95
	Min	84.50	163.00	3694.00	3040.50	1068.50	1260.00	832.00	1628.50
	Q1	140.50	1415.00	4551.00	3960.50	1616.50	3361.00	3920.00	2285.50
	Median	368.50	6331.00	5169.25	6718.50	2465.50	4984.75	4189.50	3956.25
	Q3	2101.50	7686.00	7495.00	7313.00	4219.50	5748.75	5015.50	4992.50
	Max	6945.50	9531.00	9064.50	8044.50	8094.00	6918.50	7660.00	6272.50

T_AUC05_VAS_C.sas (21FEB2011)

Table 14.2. 93: Least square results of VAS AUC_{0-5d} by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	445.07 609.87	4052.23 594.98
		Mean treatment effect (LS)	-3607.16	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-4972.88; -2241.44 (p<0.0001)	
	2	LS Mean LS Standard error	5847.69 536.37	5655.25 548.91
		Mean treatment effect (LS)	192.44	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-1167.38; 1552.27 (p=0.7798)	
	3	LS Mean LS Standard error	3534.82 448.64	5000.04 457.76
		Mean treatment effect (LS)	-1465.22	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-2636.06; -294.37 (p=0.0146)	
	4	LS Mean LS Standard error	4928.97 743.12	4630.90 866.82
		Mean treatment effect (LS)	298.07	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-1154.08; 1750.21 (p=0.6852)	

Table 14.2. 94: AUC Tenderness of injured site 0-3d (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness of injured site 0-3d [N/cm²*d]	n	66	64
	Mean	7.34	6.68
	SD	3.03	3.46
	Min	1.80	1.50
	Q1	4.55	4.20
	Median	7.45	5.70
	Q3	9.20	8.05
	Max	13.40	16.50

T_AUC03_ALGINJ.sas (09FEB2011)

Table 14.2. 95: AUC Tenderness of injured site 0-3d by centre (FAS/PP)

		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness of injured site 0-3d [N/cm²*d]	n	15	15	16	15
	Mean	7.81	5.05	3.50	3.66
	SD	1.62	1.40	1.23	1.13
	Min	3.95	3.15	1.80	1.50
	Q1	6.85	3.80	2.55	3.10
	Median	8.30	4.65	3.70	3.50
	Q3	8.75	6.55	4.15	4.30

		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
	Max	10.35	7.40	5.70	5.80

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness of injured site 0-3d [N/cm²*d]	n	21	20	14	14
	Mean	7.82	6.32	10.50	12.19
	SD	1.79	1.48	2.59	2.16
	Min	4.45	3.40	4.35	8.05
	Q1	6.85	5.15	9.20	10.60
	Median	8.00	6.60	11.23	12.73
	Q3	9.05	7.33	12.45	13.00
	Max	10.95	8.90	13.40	16.50

T_AUC03_ALGINJ_C.sas (21FEB2011)

Table 14.2. 96: Least square results of AUC_{0-3d} Algometry (tenderness) of injured site by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	9.34 0.38	6.55 0.37
		Mean treatment effect (LS)	2.80	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	1.85; 3.74 (p<0.0001)	
	2	LS Mean LS Standard error	5.14 0.37	5.18 0.38
		Mean treatment effect (LS)	-0.04	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-0.98; 0.91 (p=0.9408)	
	3	LS Mean LS Standard error	8.23 0.29	6.88 0.30
		Mean treatment effect (LS)	1.35	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.54; 2.168 (p=0.0013)	
	4	LS Mean LS Standard error	6.93 0.52	7.60 0.60
		Mean treatment effect (LS)	-0.67	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-1.68; 0.34 (p=0.1913)	

Table 14.2. 97: Tenderness of injured site at Day 1 (24h) (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 1 (24 h) (N/cm²)	n	66	64
	Mean	2.17	1.96
	SD	0.97	1.10
	Min	0.40	0.50
	Q1	1.30	1.10
	Median	2.10	1.75
	Q3	2.90	2.35
	Max	4.20	5.00

T_ALGINJ_24h.sas (09FEB2011)

Table 14.2. 98: Tenderness of injured site at Day 1 (24h) by centre (FAS/PP)

		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 1 (24 h)	n	15	15	16	15
	Mean	2.13	1.42	1.00	1.03
	SD	0.55	0.51	0.33	0.33
	Min	1.20	0.80	0.40	0.50
	Q1	1.70	1.00	0.80	0.80
	Median	2.00	1.30	1.00	1.00
	Q3	2.60	1.80	1.20	1.20
	Max	3.00	2.30	1.60	1.80

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 1 (24 h)	n	21	20	14	14
	Mean	2.39	1.87	3.23	3.65
	SD	0.61	0.51	0.83	0.80
	Min	1.00	1.00	1.20	2.30
	Q1	2.10	1.45	2.90	3.10
	Median	2.40	1.90	3.40	3.80
	Q3	2.80	2.25	3.60	4.10
	Max	3.50	2.90	4.20	5.00

T_ALGINJ_24h_C.sas (22FEB2011)

Table 14.2. 99: Least square results of Tenderness of injured site at Day 1 (24h) by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	2.642 0.128	1.916 0.127
		Mean treatment effect (LS)	0.726	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.403; 1.048 (p<0.0001)	
	2	LS Mean LS Standard error	1.545 0.126	1.526 0.129
		Mean treatment effect (LS)	0.019	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-0.302; 0.340 (p=0.9075)	
	3	LS Mean LS Standard error	2.523 0.099	2.057 0.102
		Mean treatment effect (LS)	0.466	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.189; 0.742 (p=0.0011)	
	4	LS Mean LS Standard error	2.043 0.176	2.128 0.205
		Mean treatment effect (LS)	-0.085	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-0.428; 0.258 (p=0.6241)	

Table 14.2. 100: Tenderness of injured site at Day 0 (Baseline) by centre (FAS/PP)

		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 0 (BL)	n	15	15	16	15
	Mean	0.85	0.87	0.81	0.87
	SD	0.27	0.22	0.28	0.31
	Min	0.50	0.50	0.40	0.30
	Q1	0.60	0.70	0.60	0.80
	Median	0.80	0.90	0.80	0.80
	Q3	1.10	1.00	1.00	1.20
	Max	1.30	1.20	1.40	1.40

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 0 (BL)	n	21	20	14	14
	Mean	1.27	1.21	2.74	3.11
	SD	0.33	0.37	0.78	0.55
	Min	0.60	0.70	1.00	2.00
	Q1	1.00	0.95	2.30	2.70
	Median	1.20	1.10	2.85	3.00
	Q3	1.60	1.35	3.20	3.40
	Max	1.90	2.00	3.90	4.20

T_ALGINJ_24h_C.sas (22FEB2011)

Table 14.2. 101: **Tenderness of injured site at Day 2 (V3) by centre (FAS/PP)**

		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 2	n	15	15	16	15
	Mean	3.38	1.99	1.22	1.31
	SD	0.90	0.63	0.47	0.41
	Min	1.30	1.20	0.60	0.60
	Q1	2.90	1.40	0.90	1.00
	Median	3.50	2.00	1.20	1.30
	Q3	3.80	2.70	1.60	1.60
	Max	4.80	2.90	2.00	2.00

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 2	n	21	20	14	14
	Mean	3.06	2.42	3.73	4.54
	SD	0.80	0.60	0.99	0.88
	Min	1.60	1.30	1.60	3.10
	Q1	2.60	2.00	3.30	3.90
	Median	3.10	2.50	3.95	4.65
	Q3	3.50	2.90	4.10	5.20
	Max	4.70	3.50	5.40	6.50

T_ALGINJ_24h_C.sas (22FEB2011)

Table 14.2. 102: Tenderness of injured site at Day 3 (V4) by centre (FAS/PP)

		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 3	n	15	15	16	15
	Mean	3.74	2.41	1.75	1.79
	SD	0.92	0.62	0.70	0.66
	Min	1.80	1.20	1.00	0.50
	Q1	3.50	1.80	1.00	1.40
	Median	3.50	2.50	1.70	1.60
	Q3	4.60	2.90	2.40	2.20
	Max	4.90	3.40	3.00	3.00

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 3	n	21	20	14	14
	Mean	3.47	2.85	4.36	4.91
	SD	0.73	0.72	1.09	1.18
	Min	2.10	1.40	2.10	3.30
	Q1	3.00	2.25	3.90	4.00
	Median	3.30	3.05	4.45	4.55
	Q3	4.00	3.20	5.00	5.90
	Max	4.90	4.20	5.90	7.60

T_ALGINJ_24h_C.sas (22FEB2011)

Table 14.2. 103: Tenderness of injured site at Day 5 (V5) by centre (FAS/PP)

		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 5	n	15	15	16	15
	Mean	3.86	2.82	2.79	2.67
	SD	0.90	0.76	1.22	0.93
	Min	2.10	1.80	1.40	1.10
	Q1	3.50	2.50	1.60	2.00
	Median	3.70	2.60	2.80	2.40
	Q3	4.80	3.00	4.00	3.60
	Max	5.10	4.90	4.40	4.40

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness of injured site at assessment Day 5	n	21	20	14	14
	Mean	3.77	3.18	5.32	5.64
	SD	0.71	0.64	1.30	1.40
	Min	2.40	1.70	3.20	3.90
	Q1	3.10	2.80	4.40	4.30
	Median	3.80	3.10	5.15	5.20
	Q3	4.20	3.60	6.20	6.90
	Max	5.30	4.30	8.10	8.20

T_ALGINJ_24h_C.sas (22FEB2011)

Table 14.2. 104: AUC tenderness of injured site 0-5 d (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness of injured site 0-5d [N/cm²*d]	n	66	64
	Mean	14.52	13.14
	SD	5.44	6.12
	Min	4.20	3.10
	Q1	10.50	8.60
	Median	14.45	11.98
	Q3	18.25	15.58
	Max	26.00	31.60

T_AUC05_ALGINJ.sas (07FEB2011)

Table 14.2. 105: AUC tenderness of injured site 0-5 d by centre (FAS/PP)

		Site No.			
		1 Treatment		2 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness of injured site 0-5d [N/cm²*d]	n	15	15	16	15
	Mean	15.41	10.28	8.04	8.13
	SD	3.37	2.44	3.07	2.58
	Min	7.95	6.20	4.20	3.10
	Q1	14.05	8.20	5.00	6.50
	Median	15.50	10.15	8.40	8.10
	Q3	18.25	12.35	10.25	10.10
	Max	20.35	14.40	12.70	12.80

		Site No.			
		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness of injured site 0-5d [N/cm²*d]	n	21	20	14	14
	Mean	15.06	12.34	20.18	22.74
	SD	3.13	2.75	4.72	4.26
	Min	8.95	6.50	9.65	16.05
	Q1	12.85	10.18	17.50	19.15
	Median	15.50	13.00	20.68	22.28
	Q3	17.25	14.28	23.90	26.95
	Max	21.10	17.00	26.00	31.60

T_AUC05_ALGINJ_C.sas (21FEB2011)

Table 14.2. 106: Least square results of AUC_{0-5d} tenderness of injured site by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	18.12 0.77	12.92 0.76
		Mean treatment effect (LS)	5.20	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	3.26; 7.13 (p<0.0001)	
	2	LS Mean LS Standard error	10.94 0.76	10.86 0.78
		Mean treatment effect (LS)	0.08	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-1.85; 2.01 (p=0.9321)	
	3	LS Mean LS Standard error	15.80 0.59	13.33 0.61
		Mean treatment effect (LS)	2.48	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.82; 4.14 (p=0.0038)	
	4	LS Mean LS Standard error	13.85 1.05	14.57 1.23
		Mean treatment effect (LS)	-0.72	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-2.78; 1.35 (p=0.4932)	

Table 14.2. 107: AUC tenderness ratio 0-3d (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness ratio 0-3d	n	66	64
	Mean	1.58	1.40
	SD	0.57	0.45
	Min	0.54	0.37
	Q1	1.13	1.06
	Median	1.65	1.47
	Q3	2.02	1.77
	Max	3.26	2.27

T_AUC03_RATIO.sas (07FEB2011)

Table 14.2. 108: AUC tenderness ratio 0-3d by centre (FAS/PP)

		Site No.			
		1 Treatment		2 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness ratio 0-3d	n	15	15	16	15
	Mean	1.96	1.31	0.85	0.89
	SD	0.55	0.43	0.21	0.23
	Min	0.79	0.82	0.54	0.37
	Q1	1.77	0.94	0.69	0.77
	Median	1.99	1.13	0.81	0.86
	Q3	2.12	1.57	1.03	1.05
	Max	3.26	2.11	1.19	1.40

		Site No.			
		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness ratio 0-3d	n	21	20	14	14
	Mean	1.94	1.65	1.49	1.67
	SD	0.35	0.35	0.24	0.25
	Min	0.91	1.14	1.05	1.29
	Q1	1.90	1.46	1.29	1.51
	Median	2.02	1.58	1.51	1.59
	Q3	2.21	1.92	1.62	1.88
	Max	2.30	2.27	1.90	2.12

T_AUC03_RATIO_C.sas (21FEB2011)

Table 14.2. 109: Least square results of AUC_{0-3d} algometry ratio by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	2.14 0.09	1.43 0.09
		Mean treatment effect (LS)	0.7021	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.4715; 0.9326 (p<0.0001)	
	2	LS Mean LS Standard error	1.03 0.09	1.04 0.09
		Mean treatment effect (LS)	-0.0094	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-0.2384; 0.2195 (p=0.9350)	
	3	LS Mean LS Standard error	1.87 0.07	1.58 0.07
		Mean treatment effect (LS)	0.2912	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.0943; 0.4880 (p=0.0041)	
	4	LS Mean LS Standard error	1.29 0.10	1.38 0.10
		Mean treatment effect (LS)	-0.0957	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-0.3365; 0.1450 (p=0.4326)	

Table 14.2. 110: AUC tenderness ratio 0-5 d (FAS/PP)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness ratio 0-5d	n	66	64
	Mean	3.13	2.79
	SD	1.01	0.77
	Min	1.19	0.75
	Q1	2.39	2.27
	Median	3.26	2.75
	Q3	3.97	3.32
	Max	6.09	4.19

T_AUC05_RATIO.sas (07FEB2011)

Table 14.2. 111: AUC tenderness ratio 0-5 d by centre (FAS/PP)

		Site No.			
		1 Treatment		2 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness ratio 0-5d	n	15	15	16	15
	Mean	3.83	2.70	1.94	1.99
	SD	1.00	0.73	0.55	0.61
	Min	1.62	1.76	1.19	0.75
	Q1	3.71	2.03	1.45	1.56
	Median	3.97	2.64	1.87	1.84
	Q3	4.17	3.33	2.46	2.58
	Max	6.09	4.00	2.76	2.96

		Site No.			
		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
AUC Tenderness ratio 0-5d	n	21	20	14	14
	Mean	3.72	3.21	2.87	3.12
	SD	0.56	0.57	0.45	0.52
	Min	2.31	2.23	2.20	2.35
	Q1	3.61	2.86	2.62	2.69
	Median	3.91	3.03	2.81	3.12
	Q3	4.05	3.68	3.24	3.55
	Max	4.26	4.19	3.67	4.11

T_AUC05_RATIO_C.sas (21FEB2011)

Table 14.2. 112: Least square results of AUC_{0-5d} algometry ratio by centre (FAS/PP)

	Centre		Ibuprofen 200 mg (n=66)	Placebo (n=64)
	1	LS Mean LS Standard error	4.09 0.17	2.88 0.17
		Mean treatment effect (LS)	1.2059	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.7608; 1.6510 (p<0.0001)	
	2	LS Mean LS Standard error	2.19 0.17	2.22 0.17
		Mean treatment effect (LS)	-0.02997	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-0.4720; 0.4121 (p=0.8934)	
	3	LS Mean LS Standard error	3.62 0.14	3.10 0.14
		Mean treatment effect (LS)	0.5215	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	0.1414; 0.9015 (p=0.0076)	
	4	LS Mean LS Standard error	2.58 0.18	2.70 0.20
		Mean treatment effect (LS)	-0.1202	
		95 % confidence interval for the mean treatment effect (LS) (p-value)	-0.5851; 0.3446 (p=0.6095)	

Table 14.2. 113: Gail Simon tests for centre x treatment interaction (FAS/PP)

Endpoint	Centre	LS mean diff	Alpha	DF	Upper CI	stderr	D^2 / s^2	Test statistic	pvalue
VAS AUC 0-3 days	1	-2291.75	0.01	120	-1249.40	398.23	0.00	0.40	0.7351
	2	62.56	0.01	120	1100.19	396.43	0.02		
	3	-743.64	0.01	120	149.52	341.24	0.00		
	4	253.50	0.01	120	1336.20	413.65	0.38		
VAS AUC 0-12 hours	1	-334.48	0.05	120	-210.53	62.60	0.00	0.28	0.7765
	2	30.27	0.05	120	153.69	62.33	0.24		
	3	-75.00	0.05	120	31.27	53.67	0.00		
	4	14.65	0.05	120	146.45	66.57	0.05		
VAS AUC 0-24 hours	1	-704.49	0.05	120	-447.09	130.00	0.00	0.18	0.8168
	2	51.71	0.05	120	307.99	129.44	0.16		
	3	-180.48	0.05	120	40.18	111.45	0.00		
	4	21.04	0.05	120	294.72	138.23	0.02		
VAS AUC 0-5 days	1	-3607.16	0.05	120	-2241.44	689.78	0.00	0.24	0.792
	2	192.44	0.05	120	1552.27	686.80	0.08		
	3	-1465.22	0.05	120	-294.37	591.35	0.00		
	4	298.07	0.05	120	1750.21	733.43	0.17		
VAS at 12 hours	1	-31.07	0.05	120	-17.85	6.68	0.00	0.34	0.7545
	2	2.78	0.05	120	15.95	6.65	0.18		
	3	-6.79	0.05	120	4.54	5.72	0.00		
	4	2.92	0.05	120	16.97	7.10	0.17		
VAS at	1	-31.88	0.05	120	-19.84	6.08	0.00	0.00	0.9272

24 hours	2	0.30	0.05	120	12.29	6.05	0.00		
	3	-9.79	0.05	120	0.53	5.21	0.00		
	4	-1.37	0.05	120	11.43	6.47	0.00		
AUC Algometry (tenderness) at injured site 0-3 days	1	2.80	0.05	120	3.74	0.48	0.00	1.73	0.4112
	2	-0.04	0.05	120	0.91	0.48	0.01		
	3	1.35	0.05	120	2.17	0.41	0.00		
	4	-0.67	0.05	120	0.34	0.51	1.73		
AUC Algometry (tenderness) at injured site 0-5 days	1	5.20	0.05	120	7.13	0.98	0.00	0.47	0.7113
	2	0.08	0.05	120	2.01	0.97	0.00		
	3	2.48	0.05	120	4.14	0.84	0.00		
	4	-0.72	0.05	120	1.35	1.04	0.47		
AUC Algometry (tenderness) at injured site at 24 hours	1	0.73	0.05	120	1.05	0.16	0.00	0.24	0.7929
	2	0.02	0.05	120	0.34	0.16	0.00		
	3	0.47	0.05	120	0.74	0.14	0.00		
	4	-0.09	0.05	120	0.26	0.17	0.24		
AUC Algometry (tenderness) ratio (injured /contralateral) 0-3 days	1	0.70	0.05	120	0.93	0.12	0.00	0.63	0.6639
	2	-0.01	0.05	120	0.22	0.12	0.01		
	3	0.29	0.05	120	0.49	0.10	0.00		
	4	-0.10	0.05	120	0.15	0.12	0.62		
AUC Algometry (tenderness) ratio (injured /contralateral) 0-5 days	1	1.21	0.05	120	1.65	0.22	0.00	0.28	0.778
	2	-0.03	0.05	120	0.41	0.22	0.02		
	3	0.52	0.05	120	0.90	0.19	0.00		
	4	-0.12	0.05	120	0.34	0.23	0.26		

Table 14.2. 114: Use of rescue medication by visit (FAS/PP)

	Treatment															
	Active patch 200 mg ibuprofen Visit								Placebo patch Visit							
	2		3		4		5		2		3		4		5	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Patient used rescue medication																
yes	4	6.1	3	4.5	2	3.0	2	3.0	4	6.3	3	4.7	1	1.6	1	1.6
no	62	93.9	63	95.5	64	97.0	64	97.0	60	93.8	61	95.3	63	98.4	63	98.4
Total	66	100.0	66	100.0	66	100.0	66	100.0	64	100.0	64	100.0	64	100.0	64	100.0

T_RESC_MED.sas (08FEB2011, 13:53)

Table 14.2. 115: Use of rescue medication in the study period (FAS/PP)

	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	n	%	n	%
Use of rescue medication				
yes	6	9.1	4	6.3
no	60	90.9	60	93.8
Total	66	100.0	64	100.0

T_RESC_MED.sas (08FEB2011, 13:53)

Table 14.2. 116:**Total sum of time of use of rescue medication (d) (FAS/PP)**

Total sum of time of use of rescue medication (d)

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
n	66	64	130
Mean	0.23	0.14	0.18
SD	0.84	0.61	0.73
Min	0.00	0.00	0.00
Q1	0.00	0.00	0.00
Median	0.00	0.00	0.00
Q3	0.00	0.00	0.00
Max	5.00	4.00	5.00

T_RESC_MED.sas (08FEB2011, 13:53)

Table 14.2. 117: Global Assessment of treatment efficacy (FAS/PP)

	Treatment											
	Active patch 200 mg ibuprofen Visit						Placebo patch Visit					
	2		4		5		2		4		5	
	n	%	n	%	n	%	n	%	n	%	n	%
Treatment efficacy by patient's opinion												
excellent	12	18.5	21	31.8	33	50.0	1	1.6	11	17.2	12	18.8
good	17	26.2	22	33.3	17	25.8	20	31.3	15	23.4	16	25.0
fair	18	27.7	10	15.2	5	7.6	13	20.3	12	18.8	11	17.2
poor	13	20.0	8	12.1	6	9.1	18	28.1	19	29.7	16	25.0
none	5	7.7	5	7.6	5	7.6	12	18.8	7	10.9	9	14.1
Treatment efficacy by investigator's opinion												
excellent	11	16.9	22	33.3	36	54.5	.	0.0	8	12.5	12	18.8
good	17	26.2	21	31.8	13	19.7	16	25.0	14	21.9	14	21.9
fair	20	30.8	9	13.6	6	9.1	17	26.6	17	26.6	10	15.6
poor	12	18.5	9	13.6	5	7.6	20	31.3	16	25.0	20	31.3
none	5	7.7	5	7.6	6	9.1	11	17.2	9	14.1	8	12.5
Total	65	100.0	66	100.0	66	100.0	64	100.0	64	100.0	64	100.0

T_ASS_EFF.sas (14APR2011, 07:19)

Table 14.2. 118: Global Assessment of treatment efficacy by centre (FAS/PP)

		Treatment											
		Active patch 200 mg ibuprofen						Placebo patch					
		Visit						Visit					
		2		4		5		2		4		5	
		n	%	n	%	n	%	n	%	n	%	n	%
Site No.	Treatment efficacy by patient's opinion												
1	excellent	6	40.0	8	53.3	9	60.0	.	0.0	1	6.7	.	0.0
	good	4	26.7	4	26.7	4	26.7	4	26.7	2	13.3	3	20.0
	fair	3	20.0	1	6.7	.	0.0	2	13.3	4	26.7	3	20.0
	poor	2	13.3	1	6.7	1	6.7	5	33.3	6	40.0	7	46.7
	none	.	0.0	1	6.7	1	6.7	4	26.7	2	13.3	2	13.3
	Treatment efficacy by investigator's opinion												
	excellent	5	33.3	8	53.3	9	60.0	.	0.0	.	0.0	.	0.0
	good	5	33.3	4	26.7	4	26.7	3	20.0	2	13.3	2	13.3
	fair	3	20.0	1	6.7	.	0.0	3	20.0	4	26.7	3	20.0
	poor	2	13.3	2	13.3	1	6.7	4	26.7	5	33.3	8	53.3
	none	.	0.0	.	0.0	1	6.7	5	33.3	4	26.7	2	13.3
	Total	15	100.0	15	100.0	15	100.0	15	100.0	15	100.0	15	100.0
2	Treatment efficacy by patient's opinion												
	excellent	1	6.3	1	6.3	8	50.0	.	0.0	2	13.3	5	33.3
	good	2	12.5	7	43.8	.	0.0	3	20.0	4	26.7	2	13.3
	fair	5	31.3	1	6.3	1	6.3	3	20.0	1	6.7	1	6.7
	poor	4	25.0	3	18.8	3	18.8	3	20.0	4	26.7	2	13.3
	none	4	25.0	4	25.0	4	25.0	6	40.0	4	26.7	5	33.3
	Treatment efficacy by investigator's opinion												
	excellent	1	6.3	1	6.3	8	50.0	.	0.0	2	13.3	5	33.3
	good	2	12.5	7	43.8	.	0.0	2	13.3	4	26.7	2	13.3
	fair	5	31.3	.	0.0	1	6.3	4	26.7	1	6.7	.	0.0

		Treatment											
		Active patch 200 mg ibuprofen						Placebo patch					
		Visit						Visit					
		2		4		5		2		4		5	
		n	%	n	%	n	%	n	%	n	%	n	%
	poor	4	25.0	4	25.0	3	18.8	3	20.0	3	20.0	2	13.3
	none	4	25.0	4	25.0	4	25.0	6	40.0	5	33.3	6	40.0
	Total	16	100.0	16	100.0	16	100.0	15	100.0	15	100.0	15	100.0
3	Treatment efficacy by patient's opinion												
	excellent	5	25.0	12	57.1	14	66.7	.	0.0	5	25.0	5	25.0
	good	7	35.0	5	23.8	5	23.8	4	20.0	.	0.0	.	0.0
	fair	5	25.0	.	0.0	.	0.0	5	25.0	5	25.0	6	30.0
	poor	2	10.0	4	19.0	2	9.5	9	45.0	9	45.0	7	35.0
	none	1	5.0	.	0.0	.	0.0	2	10.0	1	5.0	2	10.0
	Treatment efficacy by investigator's opinion												
	excellent	5	25.0	13	61.9	17	81.0	.	0.0	4	20.0	5	25.0
	good	9	45.0	4	19.0	2	9.5	5	25.0	1	5.0	1	5.0
	fair	3	15.0	1	4.8	.	0.0	5	25.0	7	35.0	4	20.0
	poor	3	15.0	2	9.5	1	4.8	10	50.0	8	40.0	10	50.0
	none	.	0.0	1	4.8	1	4.8	.	0.0	.	0.0	.	0.0
	Total	20	100.0	21	100.0	21	100.0	20	100.0	20	100.0	20	100.0
4	Treatment efficacy by patient's opinion												
	excellent	.	0.0	.	0.0	2	14.3	1	7.1	3	21.4	2	14.3
	good	4	28.6	6	42.9	8	57.1	9	64.3	9	64.3	11	78.6
	fair	5	35.7	8	57.1	4	28.6	3	21.4	2	14.3	1	7.1
	poor	5	35.7	.	0.0	.	0.0	1	7.1	.	0.0	.	0.0
	none	.	0.0	.	0.0	.	0.0	.	0.0	.	0.0	.	0.0
	Treatment efficacy by investigator's opinion												
	excellent	.	0.0	.	0.0	2	14.3	.	0.0	2	14.3	2	14.3
	good	1	7.1	6	42.9	7	50.0	6	42.9	7	50.0	9	64.3

	Treatment											
	Active patch 200 mg ibuprofen						Placebo patch					
	Visit						Visit					
	2		4		5		2		4		5	
	n	%	n	%	n	%	n	%	n	%	n	%
fair	9	64.3	7	50.0	5	35.7	5	35.7	5	35.7	3	21.4
poor	3	21.4	1	7.1	.	0.0	3	21.4	.	0.0	.	0.0
none	1	7.1	.	0.0	.	0.0	.	0.0	.	0.0	.	0.0
Total	14	100.0	14	100.0	14	100.0	14	100.0	14	100.0	14	100.0

T_ASS_EFF.sas (14APR2011, 07:19)

Table 14.2. 119: VAS at baseline (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS at BL	n	66	64	130
	Mean	74.21	73.98	74.10
	SD	11.43	10.24	10.82
	Min	54.00	55.00	54.00
	Q1	67.00	66.50	67.00
	Median	73.50	73.50	73.50
	Q3	81.00	80.00	81.00
	Max	97.00	97.00	97.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 120: VAS at 1 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS 1h after 1st appl.	n	66	64	130
	Mean	64.24	69.00	66.58
	SD	14.11	9.18	12.13
	Min	25.00	41.00	25.00
	Q1	56.00	64.00	61.00
	Median	64.50	69.00	67.00
	Q3	73.00	75.00	74.00
	Max	91.00	91.00	91.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 121: VAS at 2 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS 2h after 1st appl.	n	66	64	130
	Mean	55.89	62.42	59.11
	SD	18.08	12.04	15.69
	Min	5.00	18.00	5.00
	Q1	48.00	57.50	53.00
	Median	59.00	62.50	62.00
	Q3	70.00	70.00	70.00
	Max	85.00	91.00	91.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 122: VAS at 4 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS 4h after 1st appl.	n	66	64	130
	Mean	50.17	59.14	54.58
	SD	21.17	14.30	18.60
	Min	3.00	7.00	3.00
	Q1	36.00	52.00	48.00
	Median	53.00	59.00	58.00
	Q3	66.00	68.50	68.00

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
	Max	85.00	90.00	90.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 123: VAS at 6 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS 6h after 1st appl.	n	66	64	130
	Mean	48.50	56.33	52.35
	SD	22.73	16.65	20.27
	Min	0.00	2.00	0.00
	Q1	36.00	52.00	45.00
	Median	52.00	59.00	56.50
	Q3	65.00	66.50	66.00
	Max	83.00	90.00	90.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 124: VAS at 12 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS 12h after 1st appl.	n	66	64	130
	Mean	46.26	53.69	49.92

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
	SD	24.28	18.81	21.99
	Min	0.00	0.00	0.00
	Q1	30.00	48.00	38.00
	Median	51.50	55.50	55.00
	Q3	64.00	64.50	64.00
	Max	83.00	82.00	83.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 125: VAS at 24 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS at V2 (24h after 1st appl.)	n	66	64	130
	Mean	44.45	54.70	49.50
	SD	23.33	17.91	21.39
	Min	0.00	0.00	0.00
	Q1	29.00	49.00	41.00
	Median	48.00	57.50	52.00
	Q3	62.00	65.00	63.00
	Max	88.00	93.00	93.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 126: VAS at 48 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS at V3 (48h after 1st appl.)	n	66	64	130
	Mean	33.12	42.77	37.87
	SD	22.96	20.93	22.43
	Min	0.00	0.00	0.00
	Q1	10.00	32.50	16.00
	Median	36.50	45.50	44.00
	Q3	50.00	59.00	53.00
	Max	74.00	80.00	80.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 127: VAS at 72 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS at V4 (72h after 1st appl.)	n	66	64	130
	Mean	23.58	33.38	28.40
	SD	21.64	21.39	21.99
	Min	0.00	0.00	0.00
	Q1	0.00	17.00	5.00
	Median	25.00	32.00	30.00
	Q3	39.00	50.00	46.00
	Max	78.00	82.00	82.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 128: VAS at 96 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS 96h after 1st appl.	n	66	64	130
	Mean	21.18	30.44	25.74
	SD	22.73	22.28	22.90
	Min	0.00	0.00	0.00
	Q1	0.00	7.50	3.00
	Median	15.00	30.50	21.50
	Q3	38.00	52.50	46.00

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
	Max	85.00	71.00	85.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 129: VAS at 120 h (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
VAS at V5 (120h after 1st appl.)	n	66	64	130
	Mean	13.62	22.59	18.04
	SD	18.74	19.61	19.63
	Min	0.00	0.00	0.00
	Q1	0.00	4.00	0.00
	Median	4.00	18.00	12.00
	Q3	19.00	39.00	30.00
	Max	65.00	69.00	69.00

Missing data was replaced using the LOCF approach

T_VAS.sas (14APR2011)

Table 14.2. 130: VAS at baseline by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS at BL	n	15	15	16	15	21	20	14	14
	Mean	88.07	86.73	73.19	73.60	66.86	67.50	71.57	70.00
	SD	7.18	7.86	10.19	8.12	8.88	6.06	6.25	6.87
	Min	76.00	74.00	57.00	59.00	54.00	55.00	62.00	60.00
	Q1	81.00	81.00	64.00	66.00	60.00	64.50	67.00	65.00
	Median	90.00	87.00	74.50	75.00	67.00	67.50	72.00	70.00
	Q3	95.00	95.00	80.50	78.00	72.00	71.00	76.00	74.00
	Max	97.00	97.00	90.00	85.00	89.00	79.00	82.00	88.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 131: VAS at 1 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS 1h after 1st	n	15	15	16	15	21	20	14	14
	Mean	62.20	75.73	67.69	70.67	62.43	66.25	65.21	63.93

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
appl.	SD	23.24	8.81	9.57	10.34	10.13	5.13	11.18	8.71
	Min	25.00	62.00	55.00	41.00	44.00	54.00	41.00	44.00
	Q1	41.00	70.00	58.50	66.00	56.00	64.00	61.00	60.00
	Median	65.00	76.00	68.50	74.00	62.00	65.00	65.50	65.50
	Q3	86.00	84.00	72.50	76.00	67.00	69.50	73.00	69.00
	Max	91.00	91.00	86.00	81.00	88.00	78.00	83.00	77.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 132: VAS at 2 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS 2h after 1st appl.	n	15	15	16	15	21	20	14	14
	Mean	41.13	63.40	63.88	64.47	54.81	61.55	64.21	60.43
	SD	24.66	17.00	11.59	14.91	11.71	5.67	14.43	9.65
	Min	5.00	18.00	40.00	21.00	34.00	52.00	26.00	42.00
	Q1	15.00	60.00	55.50	58.00	48.00	57.00	58.00	53.00
	Median	41.00	67.00	64.50	70.00	54.00	62.00	68.50	60.50
	Q3	62.00	74.00	71.00	75.00	62.00	64.00	73.00	69.00
	Max	78.00	91.00	85.00	79.00	81.00	76.00	80.00	79.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 133: VAS at 4 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS 4h after 1st appl.	n	15	15	16	15	21	20	14	14
	Mean	29.27	60.73	59.69	59.60	51.33	58.10	59.93	58.43
	SD	23.99	23.20	17.89	15.84	12.26	5.95	17.34	9.21

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
	Min	3.00	7.00	25.00	22.00	29.00	45.00	18.00	42.00
	Q1	7.00	50.00	49.50	48.00	47.00	54.00	52.00	53.00
	Median	28.00	68.00	62.00	64.00	49.00	59.00	62.00	58.50
	Q3	57.00	75.00	72.50	73.00	59.00	64.00	70.00	59.00
	Max	74.00	90.00	85.00	80.00	78.00	65.00	83.00	79.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 134: VAS at 6 h by centre (FAS/PP)

		Site No.							
		1 Treatment		2 Treatment		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS 6h after 1st appl.	n	15	15	16	15	21	20	14	14
	Mean	23.27	53.27	62.38	57.73	50.38	57.75	56.86	56.07
	SD	23.08	24.73	19.74	21.55	12.07	5.67	16.80	11.01
	Min	0.00	7.00	16.00	2.00	29.00	45.00	18.00	37.00
	Q1	3.00	30.00	57.00	48.00	45.00	53.50	50.00	50.00
	Median	14.00	61.00	67.00	60.00	49.00	59.00	57.50	55.00
	Q3	38.00	70.00	75.00	77.00	58.00	61.50	69.00	59.00
	Max	64.00	90.00	82.00	79.00	76.00	66.00	83.00	79.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 135: VAS at 12 h by centre (FAS/PP)

		Site No.							
		1 Treatment		2 Treatment		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS 12h	n	15	15	16	15	21	20	14	14

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
after 1st appl.	Mean	19.27	49.40	62.50	59.93	48.48	55.80	53.29	48.57
	SD	24.43	27.45	20.74	23.00	12.30	7.27	18.69	12.45
	Min	0.00	0.00	2.00	1.00	29.00	37.00	9.00	31.00
	Q1	0.00	16.00	59.50	54.00	40.00	52.00	42.00	33.00
	Median	6.00	55.00	67.50	58.00	47.00	58.50	58.50	50.50
	Q3	36.00	70.00	75.00	78.00	58.00	61.00	68.00	58.00
	Max	75.00	82.00	83.00	82.00	76.00	65.00	76.00	69.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 136: VAS at 24 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS at V2 (24h after 1st appl.)	n	15	15	16	15	21	20	14	14
	Mean	22.33	52.87	62.69	63.47	42.33	52.50	50.50	50.43
	SD	29.20	31.16	10.16	8.88	16.35	10.71	15.89	11.71
	Min	0.00	0.00	44.00	50.00	17.00	23.00	18.00	28.00
	Q1	0.00	15.00	54.00	56.00	29.00	48.00	44.00	45.00
	Median	5.00	60.00	65.00	66.00	43.00	54.00	53.00	51.00
	Q3	48.00	78.00	71.50	70.00	48.00	61.00	59.00	56.00
	Max	73.00	93.00	78.00	80.00	88.00	64.00	74.00	70.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 137: VAS at 48 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS at V3	n	15	15	16	15	21	20	14	14

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
(48h after 1st appl.)	Mean	12.40	45.33	54.56	56.40	27.52	38.85	39.21	31.00
	SD	22.48	28.38	10.09	11.70	18.73	15.50	16.81	19.03
	Min	0.00	0.00	43.00	39.00	0.00	0.00	8.00	1.00
	Q1	0.00	12.00	45.50	47.00	13.00	28.00	31.00	15.00
	Median	1.00	49.00	52.00	61.00	27.00	45.00	39.50	35.50
	Q3	10.00	67.00	62.50	65.00	42.00	48.50	51.00	45.00
	Max	69.00	80.00	74.00	75.00	73.00	57.00	70.00	62.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 138: VAS at 72 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS at V4 (72h after 1st appl.)	n	15	15	16	15	21	20	14	14
	Mean	5.93	37.80	46.56	44.67	14.76	29.95	29.43	21.43
	SD	13.07	28.23	14.38	15.98	17.33	17.80	16.88	16.72
	Min	0.00	0.00	26.00	21.00	0.00	0.00	1.00	1.00
	Q1	0.00	7.00	35.50	31.00	0.00	17.50	17.00	4.00
	Median	0.00	43.00	46.50	46.00	7.00	31.50	27.00	20.00
	Q3	3.00	61.00	56.00	62.00	29.00	45.00	41.00	34.00
	Max	42.00	82.00	78.00	66.00	55.00	58.00	66.00	49.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 139: VAS at 96 h by centre (FAS/PP)

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS 96h after 1st	n	15	15	16	15	21	20	14	14
	Mean	11.53	37.87	39.19	36.07	10.62	27.45	26.79	20.71

		Site No.							
		1		2		3		4	
		Treatment		Treatment		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
appl.	SD	21.41	27.16	25.91	21.34	15.71	20.23	14.68	17.51
	Min	0.00	0.00	1.00	1.00	0.00	0.00	0.00	0.00
	Q1	0.00	4.00	20.00	13.00	0.00	14.50	15.00	5.00
	Median	0.00	48.00	38.00	43.00	1.00	24.50	24.50	16.00
	Q3	11.00	57.00	58.00	53.00	18.00	36.50	39.00	34.00
	Max	66.00	70.00	85.00	59.00	57.00	71.00	48.00	57.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 140: VAS at 120 h by centre (FAS/PP)

		Site No.							
		1 Treatment		2 Treatment		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
VAS at V5 (120h after 1st appl.)	n	15	15	16	15	21	20	14	14
	Mean	5.93	27.67	27.06	26.33	8.24	21.20	14.57	15.14
	SD	14.84	25.00	22.92	20.79	14.23	15.33	16.23	16.52
	Min	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	Q1	0.00	2.00	6.50	6.00	0.00	10.00	4.00	0.00
	Median	0.00	28.00	25.00	37.00	0.00	20.50	11.50	10.00
	Q3	1.00	54.00	47.50	46.00	16.00	28.50	18.00	22.00
	Max	48.00	69.00	60.00	49.00	53.00	50.00	65.00	45.00

T_VAS_C.sas (21FEB2011)

Table 14.2. 141: Tenderness at injured site at baseline (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness of injured site at assessment Day 0 (BL)	n	66	64	130
	Mean	1.37	1.46	1.42
	SD	0.86	0.96	0.91
	Min	0.40	0.30	0.30
	Q1	0.80	0.80	0.80
	Median	1.10	1.10	1.10
	Q3	1.70	1.80	1.70
	Max	3.90	4.20	4.20

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 142: Tenderness at injured site at Day 1 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness of injured site at assessment Day 1	n	66	64	130
	Mean	2.17	1.96	2.07
	SD	0.97	1.10	1.04
	Min	0.40	0.50	0.40

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
	Q1	1.30	1.10	1.20
	Median	2.10	1.75	1.95
	Q3	2.90	2.35	2.80
	Max	4.20	5.00	5.00

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 143: Tenderness at injured site at Day 2 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness of injured site at assessment Day 2	n	66	64	130
	Mean	2.83	2.52	2.68
	SD	1.23	1.31	1.28
	Min	0.60	0.60	0.60
	Q1	1.70	1.50	1.60
	Median	3.05	2.15	2.65
	Q3	3.70	3.10	3.60
	Max	5.40	6.50	6.50

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 144: Tenderness at injured site at Day 3 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness of injured site at assessment Day 3	n	66	64	130
	Mean	3.30	2.95	3.13
	SD	1.26	1.37	1.32
	Min	1.00	0.50	0.50

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
	Q1	2.40	2.00	2.20
	Median	3.35	2.80	3.05
	Q3	4.20	3.65	4.00
	Max	5.90	7.60	7.60

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 145: Tenderness at injured site at Day 5 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness of injured site at assessment Day 5	n	66	64	130
	Mean	3.88	3.51	3.70
	SD	1.32	1.47	1.41
	Min	1.40	1.10	1.10
	Q1	3.20	2.60	2.80
	Median	3.90	3.10	3.60
	Q3	4.60	4.15	4.40
	Max	8.10	8.20	8.20

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 146: Tenderness at contralateral site at baseline (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness of contralateral site at assessment Day 0 (BL)	n	66	64	130
	Mean	4.73	4.70	4.71
	SD	1.47	1.66	1.56
	Min	2.80	2.60	2.60
	Q1	3.80	3.50	3.60
	Median	4.20	4.10	4.20

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
	Q3	5.00	5.35	5.10
	Max	8.70	9.00	9.00

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 147: Tenderness ratio at baseline (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness ratio at assessment Day 0 (BL)	n	66	64	130
	Mean	0.28	0.29	0.28
	SD	0.10	0.11	0.10
	Min	0.12	0.08	0.08
	Q1	0.20	0.21	0.21
	Median	0.27	0.27	0.27
	Q3	0.34	0.39	0.37
	Max	0.47	0.49	0.49

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 148: Tenderness ratio at Day 1 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness ratio at assessment Day 1	n	66	64	130
	Mean	0.46	0.41	0.44
	SD	0.18	0.15	0.17
	Min	0.14	0.12	0.12
	Q1	0.29	0.27	0.28

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
	Median	0.48	0.42	0.44
	Q3	0.62	0.51	0.56
	Max	0.86	0.74	0.86

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Table 14.2. 149: Tenderness ratio at Day 2 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness ratio at assessment Day 2	n	66	64	130
	Mean	0.62	0.53	0.58
	SD	0.30	0.19	0.26
	Min	0.16	0.15	0.15
	Q1	0.42	0.38	0.38
	Median	0.60	0.53	0.55
	Q3	0.83	0.67	0.76
	Max	2.09	0.88	2.09

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 150: Tenderness ratio at Day 3 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness ratio at assessment Day 3	n	66	64	130
	Mean	0.72	0.63	0.68
	SD	0.26	0.20	0.24
	Min	0.24	0.13	0.13

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
	Q1	0.52	0.49	0.49
	Median	0.74	0.64	0.65
	Q3	0.95	0.74	0.90
	Max	1.57	1.04	1.57

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 151: Tenderness ratio at Day 5 (FAS/PP)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
Tenderness ratio at assessment Day 5	n	66	64	130
	Mean	0.83	0.76	0.79
	SD	0.20	0.24	0.22
	Min	0.33	0.25	0.25
	Q1	0.69	0.60	0.63
	Median	0.90	0.78	0.83
	Q3	0.98	0.88	0.96
	Max	1.26	1.96	1.96

T_ALGOMETRY.sas (14APR2011)

Table 14.2. 152: Tenderness ratio by centre (FAS/PP)

		Site No. 1		Site No. 2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 0 (BL)	n	15	15	16	15
	Mean	0.20	0.22	0.20	0.21
	SD	0.06	0.07	0.04	0.06
	Min	0.14	0.12	0.13	0.08
	Q1	0.15	0.16	0.17	0.17
	Median	0.18	0.23	0.21	0.22
	Q3	0.25	0.29	0.22	0.25
	Max	0.32	0.33	0.28	0.30

		Site No. 3		Site No. 4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 0 (BL)	n	21	20	14	14
	Mean	0.32	0.32	0.38	0.42
	SD	0.08	0.09	0.06	0.04
	Min	0.12	0.18	0.25	0.37
	Q1	0.27	0.25	0.33	0.39
	Median	0.32	0.32	0.40	0.43

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
	Q3	0.37	0.40	0.43	0.45
	Max	0.44	0.46	0.47	0.49

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		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 1	n	15	15	16	15
	Mean	0.51	0.37	0.24	0.25
	SD	0.16	0.16	0.05	0.07
	Min	0.23	0.21	0.14	0.12
	Q1	0.40	0.24	0.20	0.22
	Median	0.53	0.32	0.26	0.24
	Q3	0.62	0.51	0.28	0.28
	Max	0.86	0.67	0.32	0.43

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
enderness ratio at assessment Day 1	n	21	20	14	14
	Mean	0.60	0.49	0.46	0.49
	SD	0.13	0.13	0.07	0.07
	Min	0.19	0.30	0.29	0.36
	Q1	0.54	0.38	0.42	0.46
	Median	0.65	0.49	0.47	0.50
	Q3	0.69	0.56	0.51	0.54
	Max	0.74	0.74	0.58	0.63

T_ALGOMETRY_C.sas (25FEB2011)

		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 2	n	15	15	16	15
	Mean	0.87	0.51	0.29	0.31
	SD	0.39	0.18	0.09	0.08
	Min	0.26	0.30	0.16	0.15
	Q1	0.74	0.36	0.24	0.25
	Median	0.85	0.49	0.27	0.33
	Q3	0.97	0.63	0.38	0.38
	Max	2.09	0.87	0.43	0.48

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 2	n	21	20	14	14
	Mean	0.75	0.63	0.53	0.63
	SD	0.15	0.14	0.10	0.12
	Min	0.35	0.40	0.41	0.45
	Q1	0.72	0.54	0.44	0.54
	Median	0.80	0.62	0.51	0.61
	Q3	0.83	0.70	0.60	0.71
	Max	0.94	0.88	0.76	0.83

T_ALGOMETRY_C.sas (25FEB2011)

		Site No.			
		1 Treatment		2 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 3	n	15	15	16	15
	Mean	0.94	0.61	0.42	0.44
	SD	0.27	0.19	0.13	0.16
	Min	0.38	0.32	0.24	0.13
	Q1	0.95	0.45	0.32	0.33
	Median	0.98	0.62	0.38	0.42
	Q3	1.03	0.76	0.55	0.58
	Max	1.57	0.94	0.65	0.70

		Site No.			
		3 Treatment		4 Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 3	n	21	20	14	14
	Mean	0.86	0.74	0.63	0.68
	SD	0.12	0.14	0.14	0.18
	Min	0.57	0.48	0.43	0.48
	Q1	0.79	0.65	0.52	0.54
	Median	0.90	0.70	0.61	0.63
	Q3	0.95	0.83	0.68	0.74

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
	Max	1.00	0.98	0.92	1.04

T_ALGOMETRY_C.sas (25FEB2011)

		Site No.			
		1		2	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 5	n	15	15	16	15
	Mean	0.93	0.78	0.67	0.66
	SD	0.21	0.36	0.23	0.26
	Min	0.44	0.44	0.33	0.25
	Q1	0.94	0.58	0.45	0.45
	Median	0.98	0.71	0.68	0.55
	Q3	1.02	0.88	0.89	0.88
	Max	1.26	1.96	0.91	1.12

		Site No.			
		3		4	
		Treatment		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch	Active patch 200 mg ibuprofen	Placebo patch
Tenderness ratio at assessment Day 5	n	21	20	14	14
	Mean	0.92	0.82	0.75	0.76
	SD	0.10	0.12	0.12	0.17
	Min	0.62	0.59	0.55	0.52
	Q1	0.90	0.75	0.66	0.62
	Median	0.97	0.82	0.75	0.76
	Q3	0.98	0.89	0.83	0.95
	Max	1.03	1.03	1.01	1.01

T_ALGOMETRY_C.sas (25FEB2011)

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 14.3. 24: Frequency of TEAEs (SAF)

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
	n	n	n
TEAE			
yes	10	8	18
All	10	8	18

T_TEAE.sas (07FEB2011, 07:38)

Multiple citations possible

Table 14.3. 25: Overview of TEAEs (SAF)

		Active patch 200 mg ibuprofen	Placebo patch
Number of TEAEs	n	10	8
Number of patients with TEAEs	n	7	8
Total number of patients treated	n	66	64

		Active patch 200 mg ibuprofen	Placebo patch
Patients with TEAEs	%	10.6	12.5

T_TEAE.sas (07FEB2011, 07:38)

Table 14.3. 26: Overview of drug-related TEAEs (SAF)

		Active patch 200 mg ibuprofen	Placebo patch
Number of drug-related TEAEs	n	4	5
Number of patients with drug-related TEAEs	n	3	5
Total number of patients treated	n	66	64
Patients with drug-related TEAEs	%	4.5	7.8

Drug-related: possible, probable, definite

T_TEAE.sas (07FEB2011, 07:38)

Table 14.3. 27: Number of TEAEs (SAF)

	Treatment					
	Active patch 200 mg ibuprofen		Placebo patch		All	
	n	%	n	%	n	%
Number of TEAEs						
0	59	89.4	56	87.5	115	88.5
1	5	7.6	8	12.5	13	10.0
2	1	1.5	.	.	1	0.8
3	1	1.5	.	.	1	0.8
All	66	100.0	64	100.0	130	100.0

T_TEAE.sas (07FEB2011, 07:38)

Table 14.3. 28: Number of drug-related TEAEs (SAF)

Drug related: possible, probable, definite

	Treatment				All	
	Active patch 200 mg ibuprofen		Placebo patch			
	n	%	n	%	n	%
Number of drug-related TEAEs						
0	63	95.5	59	92.2	122	93.8
1	2	3.0	5	7.8	7	5.4
2	1	1.5	.	.	1	0.8
All	66	100.0	64	100.0	130	100.0

T_TEAE.sas (07FEB2011, 07:38)

Table 14.3. 29: TEAE characteristics (SAF)

	Treatment			
	Active patch 200 mg ibuprofen		Placebo patch	
	n	%	n	%
Severity				
mild	10	100.0	8	100.0
Action taken				
none	5	50.0	8	100.0
symptomatic therapy	3	30.0	.	.
Other action	2	20.0	.	.
other action				
	8	80.0	7	87.5
NA	.	.	1	12.5
PATCH REMOVED	2	20.0	.	.
Subject has experienced this AE before				
yes	1	10.0	1	12.5
no	9	90.0	7	87.5
Outcome of AE				
Resolved	10	100.0	8	100.0
Relationship to study drug				
probable	3	30.0	2	25.0
possible	1	10.0	3	37.5
unlikely	4	40.0	.	.
none	2	20.0	3	37.5
Serious Adverse Event				
no	10	100.0	8	100.0
Total	10	100.0	8	100.0

T_TEAE.sas (07FEB2011, 07:38)

Multiple citations possible

Table 14.3. 30: TEAEs by preferred term and corresponding SOC (SAF)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
		n	n	n
MedDRA Body System	MedDRA Preferred Term			
General disorders and administration site conditions	Application site pruritus	1	1	2
	Application site reaction	.	2	2
	Application site hypersensitivity	2	.	2
	Pain	1	.	1
	Application site erythema	.	1	1
	Application site discomfort	.	1	1
Infections and infestations	Nasopharyngitis	.	2	2
Nervous system disorders	Headache	1	1	2
Gastrointestinal disorders	Toothache	1	.	1
Cardiac disorders	Angina pectoris	1	.	1
Ear and labyrinth disorders	Vertigo	1	.	1
Psychiatric disorders	Sleep disorder	1	.	1
Musculoskeletal and connective tissue disorders	Joint swelling	1	.	1
All		10	8	18

T_TEAE.sas (07FEB2011, 07:38)

Multiple citations possible

Table 14.3. 31: Drug-related TEAEs by preferred term and corresponding SOC (SAF)

Drug-related: possible, probable, definite

		Treatment		
		Placebo patch	Active patch 200 mg ibuprofen	All
		n	n	n
MedDRA Body System	MedDRA Preferred Term			
General disorders and administration site conditions	Application site pruritus	1	1	2
	Application site reaction	2	.	2
	Application site hypersensitivity	.	2	2
	Application site erythema	1	.	1
	Application site discomfort	1	.	1
Musculoskeletal and connective tissue disorders	Joint swelling	.	1	1
All		5	4	9

T_TEAE.sas (07FEB2011, 07:38)

Multiple citations possible

Table 14.3. 32: TEAE by preferred term (SAF)

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
	n	n	n
MedDRA Preferred Term			
Nasopharyngitis	.	2	2
Headache	1	1	2
Application site pruritus	1	1	2
Application site reaction	.	2	2
Application site hypersensitivity	2	.	2
Pain	1	.	1
Application site erythema	.	1	1
Toothache	1	.	1
Application site discomfort	.	1	1
Angina pectoris	1	.	1
Vertigo	1	.	1
Sleep disorder	1	.	1
Joint swelling	1	.	1
All	10	8	18

T_TEAE.sas (07FEB2011, 07:38)

Multiple citations possible

Table 14.3. 33: Drug-related TEAE by preferred term (SAF)

Drug-related: possible, probable, definite

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
MedDRA Preferred Term			
Application site pruritus	1	1	2
Application site reaction	2	.	2
Application site hypersensitivity	.	2	2
Application site erythema	1	.	1
Application site discomfort	1	.	1
Joint swelling	.	1	1
All	5	4	9

T_TEAE.sas (07FEB2011, 07:38)

Multiple citations possible

Table 14.3. 34: TEAE by SOC (SAF)

	Treatment		
	Active patch 200 mg ibuprofen	Placebo patch	All
	n	n	n
MedDRA Body System			
General disorders and administration site conditions	4	5	9
Infections and infestations	.	2	2
Nervous system disorders	1	1	2
Gastrointestinal disorders	1	.	1
Cardiac disorders	1	.	1
Ear and labyrinth disorders	1	.	1
Psychiatric disorders	1	.	1
Musculoskeletal and connective tissue disorders	1	.	1
All	10	8	18

T_TEAE.sas (07FEB2011, 07:38)

Multiple citations possible

Table 14.3. 35: Drug-related TEAE by SOC (SAF)

Drug-related: possible, probable, definite

	Treatment		
	Placebo patch	Active patch 200 mg ibuprofen	All
	n	n	n
MedDRA Body System	5	3	8

	Treatment		
	Placebo patch n	Active patch 200 mg ibuprofen n	All n
General disorders and administration site conditions			
Musculoskeletal and connective tissue disorders	.	1	1
All	5	4	9

T_TEAE.sas (07FEB2011, 07:38)

Multiple citations possible

Table 14.3. 36: TEAE by preferred term and causality (SAF)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
		n	n	n
Relationship to study drug	MedDRA Preferred Term			
none	Nasopharyngitis	.	2	2
	Headache	1	1	2
	Toothache	1	.	1
probable	Application site reaction	.	2	2
	Application site hypersensitivity	2	.	2
	Joint swelling	1	.	1
unlikely	Pain	1	.	1
	Angina pectoris	1	.	1
	Vertigo	1	.	1
	Sleep disorder	1	.	1
possible	Application site pruritus	1	1	2
	Application site erythema	.	1	1
	Application site discomfort	.	1	1
All		10	8	18

T_TEAE.sas (07FEB2011, 07:38)

Multiple citations possible

Table 14.3. 37: TEAE by SOC and causality (SAF)

		Treatment		
		Active patch 200 mg ibuprofen	Placebo patch	All
		n	n	n
Relationship to study drug	MedDRA Body System			
none	Infections and infestations	.	2	2
	Nervous system disorders	1	1	2
	Gastrointestinal disorders	1	.	1
probable	General disorders and administration site conditions	2	2	4
	Musculoskeletal and connective tissue disorders	1	.	1
unlikely	General disorders and administration site conditions	1	.	1
	Cardiac disorders	1	.	1
	Ear and labyrinth disorders	1	.	1
	Psychiatric disorders	1	.	1
possible	General disorders and administration site conditions	1	3	4
All		10	8	18

T_TEAE.sas (07FEB2011, 07:38)

Multiple citations possible

Table 14.3. 38: Global Assessment of local tolerability (SAF)

	Treatment											
	Active patch 200 mg ibuprofen Visit						Placebo patch Visit					
	2		4		5		2		4		5	
	n	%	n	%	n	%	n	%	n	%	n	%
Local tolerability by patient's opinion												
poor	.	0.0	1	1.5	.	0.0	.	0.0	.	0.0	1	1.6
fair	4	6.2	.	0.0	5	7.6	.	0.0	.	0.0	3	4.7
good	38	58.5	41	63.1	36	54.5	46	71.9	48	75.0	41	64.1
excellent	23	35.4	23	35.4	25	37.9	18	28.1	16	25.0	19	29.7
Local tolerability by investigator's opinion												
poor	.	0.0	1	1.5	.	0.0	.	0.0	.	0.0	1	1.6
fair	3	4.6	1	1.5	6	9.1	.	0.0	.	0.0	3	4.7
good	37	56.9	38	58.5	34	51.5	49	76.6	46	71.9	44	68.8
excellent	25	38.5	25	38.5	26	39.4	15	23.4	18	28.1	16	25.0
Total	65	100.0	65	100.0	66	100.0	64	100.0	64	100.0	64	100.0

T_ASS_TOL.sas (14APR2011, 07:19)

Table 14.3. 39: Physical examination (SAF)

	Treatment							
	Active patch 200 mg ibuprofen				Placebo patch			
	Visit				Visit			
	1		5		1		5	
	n	%	n	%	n	%	n	%
General condition								
Normal	66	100.0	66	100.0	64	100.0	64	100.0
Dermatologie								
Normal	65	98.5	66	100.0	63	98.4	63	98.4
Pathological finding	1	1.5	.	0.0	1	1.6	1	1.6
Eyes, Ears, Nose, Throat								
Normal	63	95.5	64	97.0	62	96.9	63	98.4
Pathological finding	3	4.5	2	3.0	2	3.1	1	1.6
Neck								
Normal	66	100.0	66	100.0	64	100.0	64	100.0
Thyroid								
Normal	64	97.0	65	98.5	64	100.0	64	100.0
Pathological finding	2	3.0	1	1.5	.	0.0	.	0.0
Heart								
Normal	66	100.0	66	100.0	64	100.0	64	100.0
Lung, Respiratory system								
Normal	65	98.5	66	100.0	64	100.0	64	100.0
Pathological finding	1	1.5	.	0.0	.	0.0	.	0.0
Abdomen								
Normal	65	98.5	66	100.0	64	100.0	64	100.0
Pathological finding	1	1.5	.	0.0	.	0.0	.	0.0
Kidneys								
Normal	66	100.0	66	100.0	64	100.0	64	100.0
Skeletal system, Extremities	63	95.5	63	95.5	59	92.2	61	95.3

	Treatment							
	Active patch 200 mg ibuprofen				Placebo patch			
	Visit				Visit			
	1		5		1		5	
	n	%	n	%	n	%	n	%
Normal								
Pathological finding	3	4.5	3	4.5	5	7.8	3	4.7
Lymphatic system								
Normal	66	100.0	66	100.0	64	100.0	64	100.0
CNS, Neurological conditions								
Normal	66	100.0	66	100.0	64	100.0	64	100.0
Psychiatric CNS								
Normal	66	100.0	66	100.0	64	100.0	64	100.0
Others 1								
.	60	90.9	62	93.9	59	92.2	58	90.6
Normal	6	9.1	4	6.1	5	7.8	6	9.4
Others 2								
.	65	98.5	66	100.0	64	100.0	61	95.3
Normal	1	1.5	.	0.0	.	0.0	3	4.7
Total	66	100.0	66	100.0	64	100.0	64	100.0

T_PhyEX.sas (17FEB2011)

Table 14.3. 40: Arm used for measurement of Heart rate, blood pressure (SAF)

	Treatment							
	Active patch 200 mg ibuprofen				Placebo patch			
	Visit				Visit			
	1		5		1		5	
	n	%	n	%	n	%	n	%
Arm for measurement of Heart rate								
.	1	1.5	.	0.0	.	0.0	.	0.0
Right arm	34	51.5	33	50.0	33	51.6	32	50.0
Left arm	31	47.0	33	50.0	31	48.4	32	50.0
Arm for measurement of blood pressure								
Right arm	34	51.5	33	50.0	33	51.6	32	50.0
Left arm	32	48.5	33	50.0	31	48.4	32	50.0
Total	66	100.0	66	100.0	64	100.0	64	100.0

T_VitalSigns.sas (17FEB2011)

Table 14.3. 41: Heart rate, blood pressure (SAF)

		Treatment			
		Active patch 200 mg ibuprofen		Placebo patch	
		Visit		Visit	
		1	5	1	5
Puls [bpm]	n	66	66	64	64
	Mean	68.82	69.21	69.06	68.97
	SD	10.71	10.06	8.85	7.36
	Min	52.00	52.00	52.00	56.00
	Q1	60.00	60.00	64.00	64.00
	Median	68.00	68.00	68.00	68.00
	Q3	76.00	76.00	72.50	74.00
	Max	100.00	93.00	103.00	88.00
Blood pressure systolic [mmHg]	n	66	66	64	64
	Mean	126.32	125.09	125.69	126.89
	SD	14.57	13.36	16.79	14.09
	Min	90.00	90.00	100.00	100.00
	Q1	119.00	116.00	115.00	120.00
	Median	126.00	125.00	127.00	126.00
	Q3	135.00	133.00	134.00	130.50
	Max	169.00	170.00	210.00	197.00
Blood pressure diastolic [mmHg]	n	66	66	64	64
	Mean	78.03	75.59	75.89	76.17
	SD	10.13	8.88	10.03	9.88
	Min	60.00	60.00	60.00	60.00
	Q1	70.00	70.00	70.00	70.00
	Median	75.00	75.00	74.50	75.00
	Q3	87.00	80.00	81.00	80.00
	Max	106.00	104.00	116.00	119.00

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Table 14.3. 42: Temperature (SAF)

		Treatment			
		Active patch 200 mg ibuprofen		Placebo patch	
		Visit		Visit	
		1	5	1	5
Oral temperature [°C]	n	66	66	64	64
	Mean	36.33	36.22	36.28	36.32
	SD	0.49	0.41	0.52	0.41
	Min	34.90	35.30	34.20	35.00
	Q1	36.00	35.90	36.00	36.00
	Median	36.50	36.30	36.35	36.40
	Q3	36.70	36.50	36.60	36.60
	Max	37.10	37.20	37.00	36.90

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Table 14.3. 43: Absolute Heart rate, blood pressure changes (SAF)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
		Visit V5-V1	Visit V5-V1
Puls [bpm]	n	66	64
	Mean	0.39	-0.09
	SD	6.37	8.28
	Min	-15.00	-24.00
	Q1	-4.00	-4.00
	Median	2.00	0.50
	Q3	4.00	4.00
	Max	12.00	16.00
Blood pressure systolic [mmHg]	n	66	64
	Mean	-1.23	1.20
	SD	8.88	12.44
	Min	-23.00	-30.00
	Q1	-8.00	-5.50
	Median	-0.50	2.00
	Q3	5.00	10.00
	Max	25.00	30.00
Blood pressure diastolic [mmHg]	n	66	64
	Mean	-2.44	0.28
	SD	8.87	9.00
	Min	-35.00	-25.00
	Q1	-5.00	-3.00
	Median	-1.50	0.00
	Q3	2.00	5.00

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
		Visit	Visit
		V5-V1	V5-V1
	Max	15.00	20.00

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Table 14.3. 44: Relative Heart rate, blood pressure changes (SAF)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
		Visit V5-V1 (%)	Visit V5-V1 (%)
Puls [bpm]	n	66	64
	Mean	1.16	0.77
	SD	9.38	11.95
	Min	-17.65	-27.27
	Q1	-6.25	-5.68
	Median	3.03	0.57
	Q3	6.25	6.07
	Max	21.43	30.77
Blood pressure systolic [mmHg]	n	66	64
	Mean	-0.62	1.74
	SD	7.19	10.44
	Min	-17.04	-23.08
	Q1	-5.67	-4.21
	Median	-0.42	1.56
	Q3	4.00	8.01
	Max	23.81	30.00
Blood pressure diastolic [mmHg]	n	66	64
	Mean	-2.35	1.13
	SD	11.03	12.06
	Min	-36.84	-29.41
	Q1	-6.67	-3.75
	Median	-1.63	0.00
	Q3	2.82	7.85

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
		Visit	Visit
		V5-V1 (%)	V5-V1 (%)
	Max	25.00	33.33

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Table 14.3. 45: Absolute Temperature change (SAF)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
		Visit V5-V1	Visit V5-V1
Oral temperature [°C]	n	66	64
	Mean	-0.12	0.04
	SD	0.39	0.44
	Min	-1.10	-0.90
	Q1	-0.20	-0.20
	Median	-0.10	0.00
	Q3	0.10	0.20
	Max	0.90	2.10

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Table 14.3. 46: Relative Temperature change (SAF)

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
		Visit V5-V1 (%)	Visit V5-V1 (%)
Oral temperature [°C]	n	66	64
	Mean	-0.31	0.12
	SD	1.08	1.24

		Treatment	
		Active patch 200 mg ibuprofen	Placebo patch
		Visit	Visit
		V5-V1 (%)	V5-V1 (%)
	Min	-3.00	-2.43
	Q1	-0.56	-0.54
	Median	-0.27	0.00
	Q3	0.28	0.55
	Max	2.58	6.14

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14.3.2 Listings of Deaths, other Serious and Significant Adverse Events

Not applicable.

14.3.3 Narratives of Deaths, other Serious and certain other Significant Adverse Events

Not applicable.

14.3.4 Clinically Significant Abnormal Laboratory Value Listing (each patient)

Not applicable.