NOTE TO FILE n°1

Erratum in table 11 of the PIAS005-06 Addendum to the Clinical Trial Report (p20/30)

The upper limit of the 95% confidence interval in Table 11 p20/30 in the PIAS005-006 Addendum to the Clinical Trial Report is noted -6.22. This is a typo.
Based on the statistical tables (volume 2, section 5.3 p30/39), the UCL is -9.02.

This correction has been validated by Florence Masson in an email dated 22JAN2019.

On behalf of **EXPANSCIENCE:**
RCTs represented by
Karine MARI (Statistician)

08/02/2019

1 TITLE PAGE

ADDENDUM TO THE CLINICAL TRIAL REPORT

Prospective multicentric open clinical study comparing the efficacy and safety of Piascledine 300 plus standard treatment versus standard treatment only in patients with osteoarthritis of the knee

NAME OF THE PRODUCT: PIASCLEDINE® 300

INDICATION: Osteoarthritis of the Knee

DESIGN: Prospective, multicentre, open, parallel-group study

Laboratoires Expanscience
10, Avenue de l'Arche
F-92400 Courbevoie
France

TRIAL NUMBER : PIAS005/06

Phase IV

First patient enrolled on	**08/09/2008**
Last patient completed on	**02/11/2009**

Coordinator:	**Prof. Ruxandra Ionescu**

Company representatives:	**Dr. Véronique Leblanc**
	Dr. Florence Masson

Study performed in compliance with Good Clinical Practices

Date of Final Report: 06 September 2010
Date of Addendum: 27 January 2016

Volume 1

Laboratoires Expanscience
10, Avenue de l'Arche
F-92400 Courbevoie
France

Prospective multicentric open clinical study comparing the efficacy and safety of Piascledine 300 plus standard treatment versus standard treatment only in patients with osteoarthritis of the knee

Date of Final Report: 06 September 2010
Date of Addendum: 27 January 2016

SIGNATURES

Dr. Véronique Leblanc	**Medical Director** **Expanscience**
Dr. Florence Masson	**Project Manager** **Expanscience**
Ms. Karine Mari	**Responsible Statistician** **RCTs**
Mr. Alain Baleydier	**Medical Writer** **RCTs**

Justification for the Addendum to the Clinical Trial Report

An Addendum to the Clinical Trial Report for study PIAS005/06 was made to present more adequate statistical approaches to analyse primary and secondary criteria.

For the following endpoints:

- the number of patients which did not require DICLOFENAC or equivalent NSAID from the beginning of V2 in both groups (primary endpoint)
- the number of patients who did not take Paracetamol from the beginning of V2 in both groups (secondary endpoints)

the difference of proportions between both groups was computed as well as the parametric two-sided 95% confidence interval of the difference and the p-value. If the 95% lower confidence limit was strictly greater than 0% superiority of PIASCLEDINE® was concluded.

For the following secondary endpoints:

- Number of NSAID tablets
- Number of Paracetamol tablets
- Pain evaluation
- Lequesne index

an ANOVA model with repeated measures, accounting for the fixed effects of treatment, visit and treatment-visit interaction was used. Two-sided 95% confidence intervals were computed.

For the secondary endpoints regarding SF12, PCS and MCS scores were computed and analysed using an ANOVA model with repeated measures, accounting for the fixed effects of treatment, visit and treatment-visit interaction. Two-sided 95% confidence intervals were computed.

Finally, for the following secondary endpoints:

- the overall assessment of efficacy by the patient and by the investigator (efficacy)
- the overall assessment of tolerability by the patient and the investigator (safety)

the two treatment groups were compared using a χ^2 test.

2 SYNOPSIS

Name of sponsor company: Laboratoires Expanscience	Individual Study Table Referring to Part of the Dossier	*(For National Authority Use only)*
Name of Finished Product: PIASCLEDINE® 300	Volume: Page	
Name of Active Ingredient: Unsaponifiable fraction from avocado oil 100mg Unsaponifiable fraction from soy oil 200mg		
Title of study: Prospective multicentric open clinical study comparing the efficacy and safety of Piascledine 300 plus standard treatment versus standard treatment only in patients with osteoarthritis of the knee		
Investigators: See Final Clinical Trial Report		
Study centres: See Final Clinical Trial Report		
Publication (reference): See Final Clinical Trial Report		
Study period: First patient enrolled on **08 September 2008** Last patient completed on **02 November 2009**	Phase of development: Phase IV	
Objectives: To evaluate the efficacy and safety of PIASCLEDINE® 300 in the treatment of osteoarthritis of the knee, by comparing two parallel groups: PIASCLEDINE® 300 associated with Standard Treatment (PAST) versus Standard Treatment Only (STO). To evaluate the Quality of Life and the consumption of rescue medication.		
Number of patients: 300 (150 PAST; 150 STO).		
Diagnosis and main criteria for inclusion: Female or male outpatients aged 45 years or more suffering from femoro-tibial osteoarthritis of the knee, uni- or bicompartmental, uni- or bilateral and/or femoro-patellar, progressing for at least 6 months, with overall pain assessed between 25 and 50 mm on the VAS, in spite of daily intake of DICLOFENAC 75 to 150 mg/d or equivalent for at least 10 days per month, for at least 3 months prior to inclusion.		
Test product, dose and mode of administration: PIASCLEDINE® 300 mg capsules, oral, once 300 mg daily		
Duration of treatment: 180 days with 5 visits per patient (D0, D45, D90, D135, D180)		
Reference therapy, dose and mode of administration: Group 1: Standard Treatment Only (NSAIDs) = Diclofenac, Ibuprofen, Naproxen, Nimeluside, Piroxicam, in equivalent dosages (=STO) Group 2: PIASCLEDINE® 300mg once daily + Standard Treatment (=PAST)		

Name of sponsor company: Laboratoires Expanscience	Individual Study Table Referring to Part of the Dossier	*(For National Authority Use only)*
Name of Finished Product: PIASCLEDINE® 300	Volume: Page	
Name of Active Ingredient: Unsaponifiable fraction from avocado oil 100mg Unsaponifiable fraction from soy oil 200mg		

Criteria for evaluation:

Efficacy:
Number of patients who do not take NSAIDs from the beginning of V2.
Number of patients who do not take Paracetamol from the beginning of V2.
Number of rescue medication (NSAIDs and Paracetamol tablets) used between V2 and V5
Pain evaluation at each visit
Lequesne index at each visit
Quality of life measured by PCS and MCS in the SF12 scale at each visit
Overall assessment of efficacy by the investigator and the patient
Overall assessment of tolerability by the investigator and the patient

Safety:
Adverse events monitoring (See Final Clinical Trial Report)

Statistical methods:

Primary criterion:
The primary criterion (number of patients who do not take NSAIDs) was assessed on the population of randomised patients. A descriptive analysis was performed. The difference of proportions between PAST and STO for patients who did not take NSAIDs was estimated. The parametric two-sided 95% confidence interval of the difference was computed as well as the p-value. If the 95% lower confidence limit was strictly greater than 0% superiority of PIASCLEDINE® could be concluded.

Secondary criteria:
The secondary criteria were assessed on the population of randomised patients.
The number of patients who did not take Paracetamol was evaluated with the same methodology used for the primary criterion.
Pain evaluation, Lequesne index and SF12 PCS and MCS were analysed using an ANOVA model with repeated measures, accounting for the fixed effects of treatment, visit and treatment-visit interaction. Two-sided 95% confidence intervals were computed.
The overall assessment of efficacy by the patient and by the investigator and the overall assessment of tolerability by the patient and the investigator were compared between treatment groups using a χ^2 test.
The number of NSAID tablets and Paracetamol tablets used were also described using an ANOVA model with repeated measures, accounting for the fixed effects of treatment, visit and treatment-visit interaction. Two-sided 95% confidence intervals were computed.

Summary conclusions:
- Efficacy results:

For the primary efficacy criterion, the proportion of patients in the PAST group who did not take NSAIDs, starting at V2, was statistically greater than in the STO group.
For the secondary efficacy criteria:
- the proportion of patients in the PAST group who did not take Paracetamol, starting at V2, was statistically greater than in the STO group;
- patients in the PAST group took a statistically lower number of NSAIDs tablets than patients in the STO group;
- patients in the PAST group took a statistically lower number of Paracetamol tablets than patients in STO group;
- patients in the PAST group had a statistically lower pain level (VAS), starting at V2, than patients in the STO group;
- patients in the PAST group had a statistically lower Lequesne index, starting at V2, than patients in the STO group;
- patients in the PAST group had a statistically greater PCS score, starting at V2, than patients in the STO group;
- no statistical difference was observed between both treatment groups for the MCS score;
- the overall assessments of efficacy and tolerability by the investigator and by the patient were statistically better in the PAST group than in the STO group.

Regarding the rescue medications, even though the results were in favour of the PAST group, they must be taken with caution. Indeed, the results were based on a count of tablets when only an analysis based on dosage or equivalent would have been relevant.

Name of sponsor company: Laboratoires Expanscience	Individual Study Table Referring to Part of the Dossier	*(For National Authority* *Use only)*
Name of Finished Product: PIASCLEDINE® 300	Volume: Page	
Name of Active Ingredient: Unsaponifiable fraction from avocado oil 100mg Unsaponifiable fraction from soy oil 200mg		

-Safety results:

See Final Clinical Trial Report.

Three SAEs have been observed during the trial in the PAST group (one death due to a lung tumour, one cholestatic icterus, one biliary colic) without or with unlikely relation to the treatment.

In the PAST group, 29 patients (19.3%) reported 35 AEs, from which 6 have been assessed as possibly or probably related to the treatment, while 28 observations were not or unlikely related to the treatment (infections, accident etc.)

In the STO group, 9 patients (6.0%) reported 14 AEs, mostly known side effects of the NSAIDs.

Conclusion:

The addition of PIASCLEDINE® to standard treatment had a significant positive effect on the symptomatology of osteoarthritis (pain, Lequesne index), on quality of life (physical component of SF12) and on the overall assessments of efficacy and tolerability by both patients and investigators.

Date of the addendum:

27/01/2016

3 TABLE OF CONTENTS FOR THE INDIVIDUAL CLINICAL STUDY REPORT

3.1 LIST OF TABLES

3.2 LIST OF FIGURES

4 LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

AE(s)	Adverse Event(s)
ASU	Avocado/Soybean Unsaponifiables
CI	Confidence interval
CRF	Case report form
CRA	Clinical Research Assistant
CRO	Contract Research Organisation
DBP	Diastolic Blood Pressure (mm Hg)
DDD	Defined Daily Dose
EC	Ethics committee
EULAR	European League Against Rheumatism
GCP	Good Clinical Practices
IEC	Independent Ethics Committee
IRB	Institutional Review Board
MCS	Mental Component Summary
N	Number of patients
NA	Not Applicable
NS	Non Significant
NSAID	Non Steroidal Anti-Inflammatory Drugs
PCS	Physical Component Summary
PAST	PIASCLEDINE® and Standard Therapy
QL/QoL	Quality of Life
SAE(s)	Serious Adverse Event(s)
SBP	Systolic Blood Pressure (mm Hg)
SD	Standard Deviation
SOP	Standard Operative Procedure
STO	Standard Treatment Only
SYSADOA	Symptomatic Slow Acting Drugs of OsteoArthritis
WHO	World Health Organisation

Terms used in the report for the visits:

Visit 1	Day 0, Randomisation visit
Visit 2	Study day 45 $\pm$ 15
Visit 3	Study day 90 $\pm$ 15
Visit 4	Study day 135 $\pm$ 15
Visit 5	Study day 180 $\pm$ 15, End of study

5 ETHICS

No change; see Final Clinical Trial Report.

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

5.2 ETHICAL CONDUCT OF THE STUDY

5.3 PATIENT INFORMATION AND CONSENT

6 INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

No change; see Final Clinical Trial Report.

6.1 INVESTIGATORS

6.2 COMMITTEES AND TECHNICAL CENTRES

6.2.1 Committees

6.2.2 Technical centres

6.3 COORDINATOR'S SIGNATURE

7 INTRODUCTION

No change; see Final Clinical Trial Report.

7.1 SIDE EFFECTS

7.2 INVESTIGATIONAL DRUG

7.3 COMPARATIVE DRUG

8 STUDY OBJECTIVES

The objective of the study was to evaluate the efficacy and safety of PIASCLEDINE® 300 in the treatment of osteoarthritis of the knee, by comparing two parallel groups: PIASCLEDINE® 300 associated with Standard Treatment (PAST) versus Standard Treatment Only (STO).

8.1 PRIMARY OBJECTIVE

The primary objective was to evaluate the efficacy of PIASCLEDINE® 300 in the treatment of the osteoarthritis of the knee from day 45 (V2) by comparing the use of NSAIDs in both groups.

8.2 SECONDARY OBJECTIVES

The secondary objectives were to evaluate the consumption of rescue medication, the pain (VAS), the Lequesne index, the quality of life, and the overall assessment of efficacy and tolerability by the investigator and the patient in both groups.
The safety of PIASCLEDINE® was also evaluated.

9 INVESTIGATIONAL PLAN

9.1 OVERALL STUDY DESIGN AND PLAN: DESCRIPTION

No change; see Final Clinical Trial Report.

9.2 TIME SCHEDULE/STUDY DURATION

No change; see Final Clinical Trial Report.

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

No change; see Final Clinical Trial Report.

9.4 SELECTION OF STUDY POPULATION

No change; see Final Clinical Trial Report.

9.5 TREATMENTS

No change; see Final Clinical Trial Report.

9.6 ASSESSMENT OF EFFICACY, TOLERABILITY AND COMPLIANCE

9.6.1 Evaluation criteria

9.6.1.1 Primary criterion

The primary criterion for efficacy was the number of patients which did not require DICLOFENAC or equivalent NSAID from the beginning of V2 in both groups.

- Number of patients who did not take NSAIDs between V2 and V3;
- Number of patients who did not take NSAIDs between V3 and V4;
- Number of patients who did not take NSAIDs between V4 and V5.

The primary criterion was assessed on the population of randomised patients.

9.6.1.2 Secondary criteria

The secondary criteria for efficacy were:

- The number of patients who did not take Paracetamol from the beginning of V2 in both groups;
- The number of rescue medication (NSAIDs and Paracetamol tablets) used between V2 and V5;
- The pain evaluation at each visit;
- The Lequesne index at each visit;
- The quality of life measured by PCS and MCS in the SF12 scale at each visit;
- The overall assessment of efficacy by the investigator and the patient;
- The overall assessment of tolerability by the investigator and the patient.

The secondary criteria were assessed on the population of randomised patients.

9.6.2 Clinical tolerability evaluation criteria

No change; see Final Clinical Trial Report.

9.6.3 Final safety report

No change; see Final Clinical Trial Report.

9.7 DATA QUALITY ASSURANCE

No change; see Final Clinical Trial Report.

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

9.8.1 Methodology

See Final Clinical Trial.

For the addendum:
The analysis for this addendum was performed by the biostatistics Department of RCTs with SAS 9.2.

The only population described was the population of randomised patients.

9.8.2 Sample of patients

No Change. See Final Clinical Trial Report.

9.8.3 Statistical methods used

See Final Clinical Trial Report.

For the addendum:
The difference of proportions between PAST and STO for patients who did not take NSAIDs was estimated. The parametric two-sided 95% confidence interval of the difference was computed as well as the p-value.

If the 95% lower confidence limit was strictly greater than 0% superiority of PIASCLEDINE® could be concluded.

The number of patients who did not take Paracetamol was evaluated with the same methodology used for the primary criterion.

The number of NSAID tablets and Paracetamol tablets used were also described using an ANOVA model with repeated measures, accounting for the fixed effects of treatment, visit and treatment-visit interaction. Two-sided 95% confidence intervals were computed.

Pain evaluation, Lequesne index and SF12 PCS and MCS were analysed using an ANOVA model with repeated measures, accounting for the fixed effects of treatment, visit and treatment-visit interaction. Two-sided 95% confidence intervals were computed.

The overall assessment of efficacy by the patient and by the investigator and the overall assessment of tolerability by the patient and the investigator were compared between treatment groups using a χ^2 test.

9.9 CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

See Final Clinical Trial Report.

For the Addendum:

The number of days until NSAID was stopped, the number of days until NSAID was resumed, the paracetamol intake in g, as well as the NSAID intake (Diclofenac equivalent), were defined in the protocol as secondary criteria.

However, data regarding the NSAID types and the dosages for rescue medications were not collected in the CRF and required using the patients' diaries which were not available. Therefore only the number of NSAID and Paracetamol tablets taken by the patient could be analysed.

10 STUDY PATIENTS

10.1 DISPOSITION OF PATIENTS

10 centres included 300 patients between 08SEP2008 and 01JUN2009:

- 150 patients were included in the PAST group
- 150 patients were included in the STO group

On average the number of patients per centre was 30.0 (median: 31.0; minimum: 12; maximum: 60).

Among the 300 included patients, 5 did not complete the study (they did not have V5: 3 in PAST group, 2 in STO group).
Of the 295 completers, 4 patients (all PAST) did not have all intermediary visits.

For the initial presentation of disposition of patients, see Final Clinical Trial Report.

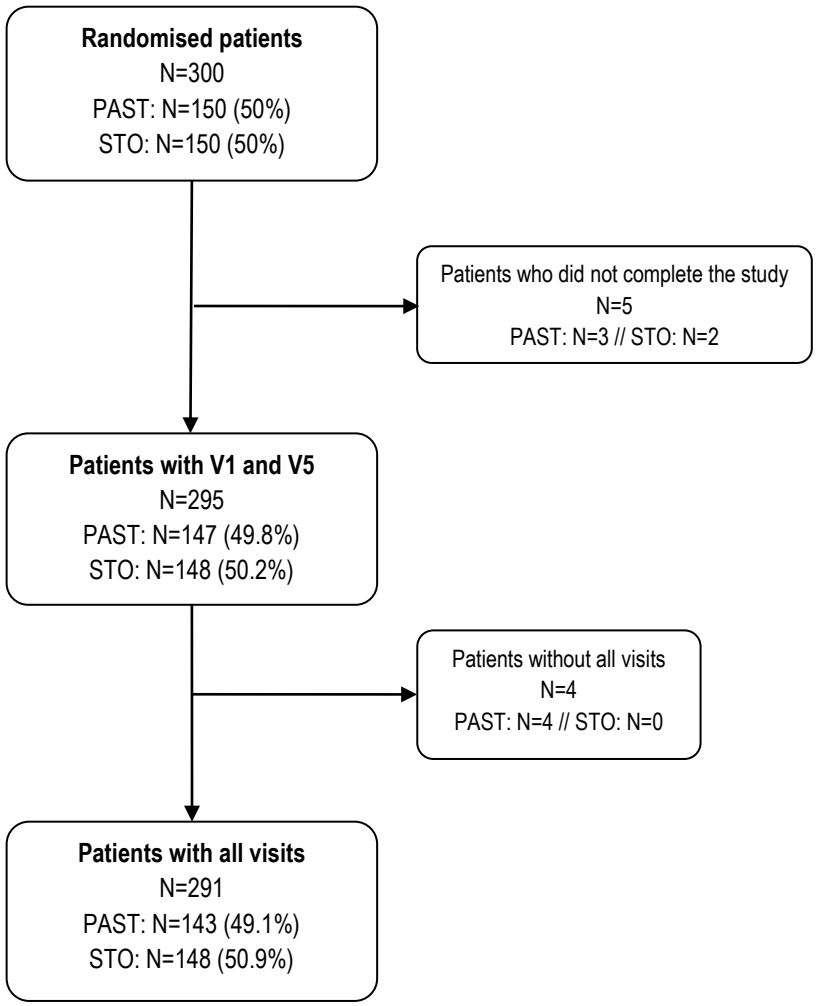
10.2 PROTOCOL DEVIATIONS

No change; see Final Clinical Trial Report.

11 EFFICACY EVALUATION

11.1 DATA SETS ANALYSED

Figure 1. Data sets analysed



Criteria were analysed on the population of randomised patients.

11.2 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

11.2.1 Demography

11.2.1.1 Demographic data

A descriptive analysis on patients' demographic characteristics was computed, for the population of randomised patients and by treatment groups. Results of this descriptive analysis are shown in Table 1.

Table 1. Demographic data (Randomised patients)

Parameters N (%) or Mean (±sd)	PAST N=150	STO N=150	Total N=300
Sex (Female)	128 (85.3%)	128 (85.3%)	256 (85.3%)
Age (years)	61.4 (±9.0)	62.3 (±9.2)	61.8 (±9.1)
Height (cm)	163.1 (±8.6)	163.3 (±7.4)	163.2 (±8.0)
Weight (kg)	77.0 (±15.0)	78.5 (±14.4)	77.8 (±14.7)

Patients were majorly female (85.3%); on average, they were 61.8±9.1 years old and they weighed 77.8±14.7 kg.

11.2.1.2 General physical examination

A descriptive analysis on the patients' general physical examination at baseline was computed, for the population of randomised patients and by treatment groups. In a very large majority, the different systems were quoted as normal for both treatment groups. The system with the most abnormal quotations was Metabolism and Endocrine system, as shown in Table 2.

Table 2. General physical examination (Randomised patients)

Parameters N (%) or Mean (±sd)	PAST N=150	STO N=150	Total N=300
Integumentary System (**normal**)	136 (90.7%)	133 (88.7%)	269 (89.7%)
Sensory System (**normal**)	147 (98.0%)	145 (96.7%)	292 (97.3%)
Respiratory System (**normal**)	148 (98.7%)	147 (98.0%)	295 (98.3%)
Cardiovascular System (**normal**)	135 (90.0%)	134 (89.3%)	269 (89.7%)
Gastrointestinal System (**normal**)	148 (98.7%)	149 (99.3%)	297 (99.0%)
Metabolism/Endocrine System (**normal**)	96 (64.0%)	100 (66.7%)	196 (65.3%)
Nervous System (**normal**)	149 (99.3%)	150 (100.0%)	299 (99.7%)
Musculoskeletal System (**normal**)	132 (88.0%)	136 (90.7%)	268 (89.3%)
Urinary System (**normal**)	150 (100.0%)	149 (99.3%)	299 (99.7%)
Genital System (**normal or not done**)	149 (99.3%)	146 (97.3%)	295 (98.3%)

11.2.1.3 Vital signs

A descriptive analysis on patients' vital signs at baseline was computed, for the population of randomised patients and by treatment groups. Vital signs did not show any abnormalities. Results of this descriptive analysis are shown in Table 3.

Table 3. Vital signs (Randomised patients)

Parameters N (%) or Mean (±sd)	PAST N=150	STO N=150	Total N=300
Systolic Blood Pressure (mmHg)	128.6 (±12.0)	130.5 (±13.2)	129.6 (±12.6)
Diastolic Blood Pressure (mmHg)	76.5 (±7.2)	76.8 (±7.9)	76.7 (±7.5)
Heart rate (/min)	73.7 (±6.5)	73.8 (±6.7)	73.7 (±6.6)
Breath rate (/min)	16.8 (±2.8)	16.9 (±2.6)	16.8 (±2.7)

11.2.2 History and diagnosis of osteoarthritis of the knee

A descriptive analysis on patients' history of knee osteoarthritis was computed, for the population of randomised patients and by treatment groups. The results of the Kellgren-Lawrence classification of osteoarthritis of the knee are shown in Table 4: 60.0% belonged to class II of the Kellgren-Lawrence classification. For more details, see chapter 14.

Table 4. Kellgren-Lawrence classification (Randomised patients)

Parameters N (%) or Mean (±sd)		PAST N=150	STO N=150	Total N=300
Kellgren-Lawrence score	I	38 (25.3%)	28 (18.7%)	66 (22.0%)
	II	86 (57.3%)	94 (62.7%)	180 (60.0%)
	III	26 (17.3%)	28 (18.7%)	54 (18.0%)

See Final Clinical Trial Report for the initial description on history and diagnosis of osteoarthritis of the knee.

11.3 MEASUREMENTS OF TREATMENT COMPLIANCE

The assessment of compliance was performed at V2, V3, V4 and V5, for the PAST group in the population of randomised patients. Almost all patients proved an excellent compliance during the study period. Results of this descriptive analysis are shown in Table 5.

Table 5. Assessment of compliance (PAST group)

Parameters N (%) or Mean (±sd)	PAST N=150
Excellent compliance (difference ±10%) at V2	n=144 134 (95.1%)
Excellent compliance (difference ±10%) at V3	n=141 135 (95.7%)
Excellent compliance (difference ±10%) at V4	n=143 139 (97.2%)
Excellent compliance (difference ±10%) at V5	n=146 142 (97.3%)

See Final Clinical Trial Report for the initial description on measurements of treatment compliance.

11.4 EFFICACY RESULTS AND TABULATIONS OF INDIVIDUAL PATIENT DATA

11.4.1 Analysis of efficacy

11.4.1.1 Primary efficacy variable

The number of patients which did not require DICLOFENAC or equivalent NSAID from the beginning of V2 was described on the population of randomised patients and by treatment groups. The difference of proportion of:

- patients who did not take NSAIDs between V2 and V3 was estimated to be 12.8% (95%CI: [5.7%;19.9%]) in favour of PAST patients;
- patients who did not take NSAIDs between V3 and V4 was estimated to be 24.6% (95%CI: [16.4%;32.9%]) in favour of PAST patients;
- patients who did not take NSAIDs between V4 and V5 was estimated to be 27.9% (95%CI: [19.1%;36.8%]) in favour of PAST patients.

Results are presented in Table 6.

Table 6. Primary criterion: Patients who did not take NSAIDs between V2 and V3, V3 and V4, and V4 and V5 (Randomised patients)

Patients who did not take NSAIDs between V2 and V3, V3 and V4, and V4 and V5 – N (%) [95%CI]	PAST N=150	STO N=150	Difference PAST vs. STO (%)
Patients who did not take NSAIDs – between V2 and V3	25 (17.5%) [11.6%;24.7%] n=143	7 (4.7%) [1.9%;9.4%] n=150	12.8% [5.7%;19.9%] p<0.0001
Patients who did not take NSAIDs – between V3 and V4	42 (29.4%) [22.1%;37.6%] n=143	7 (4.7%) [1.9%;9.5%] n=148	24.6% [16.4%;32.9%] p<0.0001
Patients who did not take NSAIDs – between V4 and V5	52 (35.4%) [27.7%;43.7%] n=147	11 (7.4%) [3.8%;12.9%] n=148	27.9% [19.1%;36.8%] p<0.0001

The number of patients who took no NSAIDs between V2 and V5 or who took NSAIDs once, twice or three times between V2 and V5 was also described on the population of randomised patients and by treatment groups. More PAST patients did not take any NSAIDs between V2 and V5 than STO patients.

Results are shown in Table 7.

Table 7. Post-hoc analysis: Patients who took no NSAIDs between V2 and V5 (Randomised patients)

Patients and NSAIDs taken between V2 and V5 – N (%) [95%CI]	PAST N=150	STO N=150	Total N=300
	n=143	n=148	n=291
No NSAIDs taken between V2 and V5	16 (11.2%) [6.5%;17.5%]	4 (2.7%) [0.7%;6.8%]	20 (6.9%) [4.2%;10.4%]
NSAIDs taken once between V2 and V5	23 (16.1%) [10.5%;23.1%]	3 (2.0%) [0.4%;5.8%]	26 (8.9%) [5.9%;12.8%]
NSAIDs taken twice between V2 and V5	22 (15.4%) [9.9%;22.4%]	7 (4.7%) [1.9%;9.5%]	29 (10.0%) [6.8%;14.0%]
NSAIDs taken three times between V2 and V5	82 (57.3%) [48.8%;65.6%]	134 (90.5%) [84.6%;94.7%]	216 (74.2%) [68.8%;79.2%]

11.4.1.2 Secondary efficacy variables

11.4.1.2.1 Number of patients who did not take Paracetamol from the beginning of V2

The number of patients which did not take Paracetamol from the beginning of V2 groups was described on the population of randomised patients and by treatment groups. The difference of proportion of:

- patients who did not take Paracetamol between V2 and V3 was estimated to be 19.6% (95%CI: [8.4%;30.8%]) in favour of PAST patients;
- patients who did not take Paracetamol between V3 and V4 was estimated to be 22.4% (95%CI: [11.2%;33.6%]) in favour of PAST patients;
- patients who did not take Paracetamol between V4 and V5 was estimated to be 35.0% (95%CI: [24.4%;45.6%]) in favour of PAST patients.

Results are presented in Table 8.

Table 8. Secondary criterion: Patients who did not take Paracetamol between V2 and V3, V3 and V4, and V4 and V5 (Randomised patients)

Patients who did not take Paracetamol between V2 and V3, V3 and V4, and V4 and and V5 – N (%) [95%CI]	PAST N=150	STO N=150	Difference PAST vs. STO (%)
Patients who did not take Paracetamol – between V2 and V3	89 (62.2%) [53.8%;70.2%] n=143	64 (42.7%) [34.6%;51.0%] n=150	19.6% [8.4%;30.8%] p<0.0001
Patients who did not take Paracetamol – between V3 and V4	89 (62.2%) [53.8%;70.2%] n=143	59 (39.9%) [31.9%;48.2%] n=148	22.4% [11.2%;33.6%] p<0.0001
Patients who did not take Paracetamol – between V4 and V5	108 (73.5%) [65.6%;80.4%] n=143	57 (38.5%) [30.6%;46.9%] n=148	35.0% [24.4%;45.6%] p<0.0001

11.4.1.2.2 Rescue medication: number of tablets of NSAIDs and Paracetamol used

11.4.1.2.2.1 Number of NSAIDs tablets

The difference in the number of NSAIDS tablets used between PAST and STO patients was evaluated at each visit using an ANOVA model with repeated measures. Statistically significant differences were observed on the population of randomised patients between V2 and V3, V3 and V4 and V4 and V5, in favour of PAST patients: patients in PAST group took a statistically lower number of NSAIDs tablets than patients in STO group.
Results are presented in Table 9.

Table 9. Secondary criterion: Number of NSAIDs tablets

Number of NSAIDs tablets - ANOVA with repeated measures	Between V1 and V2	Between V2 and V3	Between V3 and V4	Between V4 and V5
Difference PAST vs. STO	-7.76(±1.89) [-11.46;-4.05] p<0.0001	-8.57(±1.92) [-12.34;-4.80] p<0.0001	-9.83(±1.98) [-13.71;-5.94] p<0.0001	-10.94(±2.01) [-14.89;-6.99] p<0.0001

11.4.1.2.2.2 Number of Paracetamol tablets

The difference in the number of Paracetamol tablets used between PAST and STO patients was evaluated at each visit using an ANOVA model with repeated measures. Statistically significant differences were observed on the population of randomised patients between V1 and V2, V2 and V3, V3 and V4 and V4 and V5, in favour of PAST patients: patients in PAST group took a statistically lower number of Paracetamol tablets than patients in STO group.
Results are presented in Table 10.

Table 10. Secondary criterion: Number of Paracetamol tablets

Number of Paracetamol tablets - ANOVA with repeated measures	Between V1 and V2	Between V2 and V3	Between V3 and V4	Between V4 and V5
Difference PAST vs. STO	-7.75(±2.51) [-12.69;-2.82] p=0.0021	-8.55(±2.68) [-13.81;-3.28] p=0.0015	-10.28(±2.71) [-15.60;-4.95] p=0.0002	-10.56(±2.87) [-16.20;-4.92] p=0.0003

11.4.1.2.3 Pain evaluation

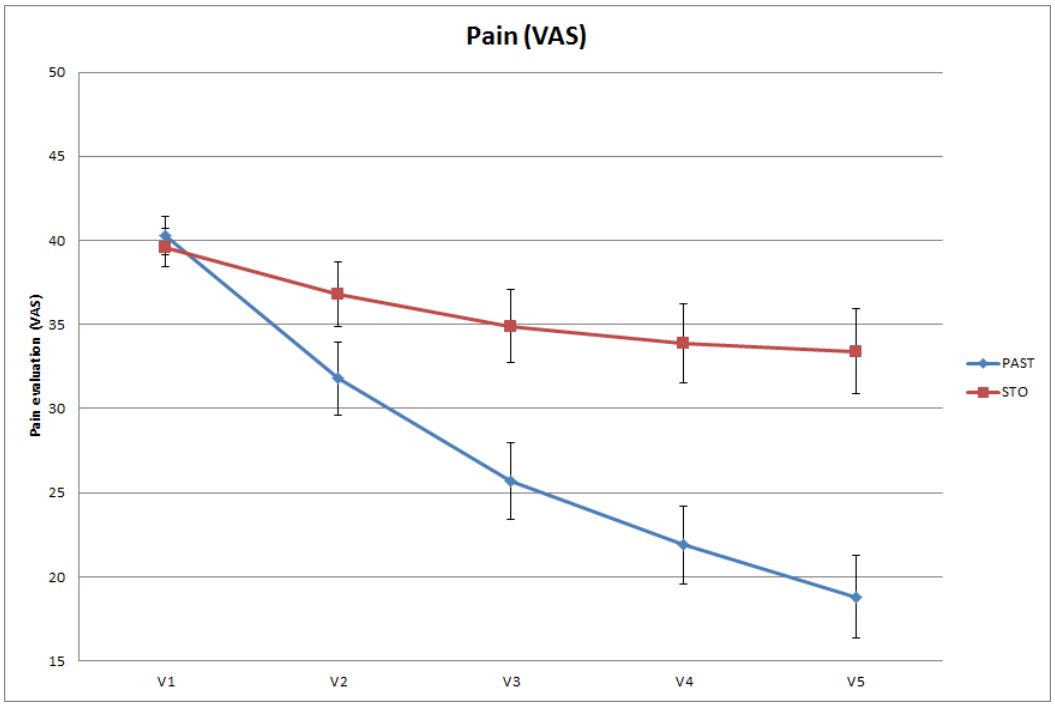
The difference in Pain between PAST and STO patients was evaluated at each visit using an ANOVA model with repeated measures. Statistically significant differences were observed on the population of randomised patients at V2, V3, V4 and V5, in favour of PAST patients: at V2, V3 and V4, patients in PAST group had a statistically lower pain than patients in STO group.

Details are presented in Table 11 and graphically in Figure 2.

Table 11. Secondary criterion: Pain at each visit (Randomised patients, N=300)

Pain at each visit - ANOVA with repeated measures	V1	V2	V3	V4	V5
Difference PAST vs. STO	0.75(±1.50) [-2.20;3.69] p=0.6193	-5.01(±1.51) [-7.96;-2.06] p=0.0009	-9.20(±1.52) [-12.18;-6.22] p<0.0001	-12.01(±1.53) [-15.00;-6.22] p<0.0001	-14.56(±1.52) [-17.53;-11.58] p<0.0001

Figure 2. Pain (VAS) evolution between V1 and V5



11.4.1.2.4 Lequesne index

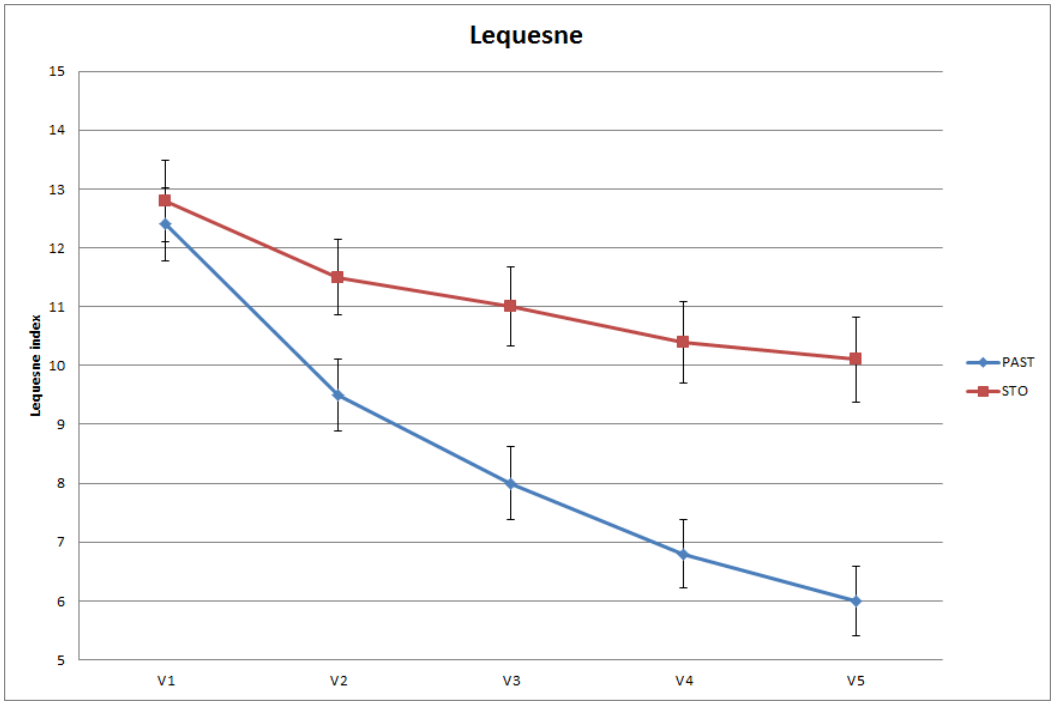
The difference in Lequesne index between PAST and STO was evaluated at each visit using an ANOVA model with repeated measures. Statistically significant differences were observed on the population of randomised patients at V2, V3, V4 and V5, in favour of PAST patients: at V2, V3 and V4, patients in PAST group had a statistically lower Lequesne index than patients in STO group.

Details are presented in Table 12 and graphically in Figure 3.

Table 12. Secondary criterion: Lequesne index at each visit (Randomised patients, N=300)

Lequesne index at each visit - ANOVA with repeated measures	V1	V2	V3	V4	V5
Difference PAST vs. STO	-0.38(±0.46) [-1.29;0.53] p=0.4130	-1.99(±0.46) [-2.90;-1.08] p<0.0001	-2.98(±0.47) [-3.90;-2.06] p<0.0001	-3.54(±0.47) [-4.47;-2.62] p<0.0001	-4.10(±0.47) [-5.02;-3.18] p<0.0001

Figure 3. Lequesne index evolution between V1 and V5



11.4.1.2.5 Quality of life (SF12)

11.4.1.2.5.1 Physical Health score – PCS

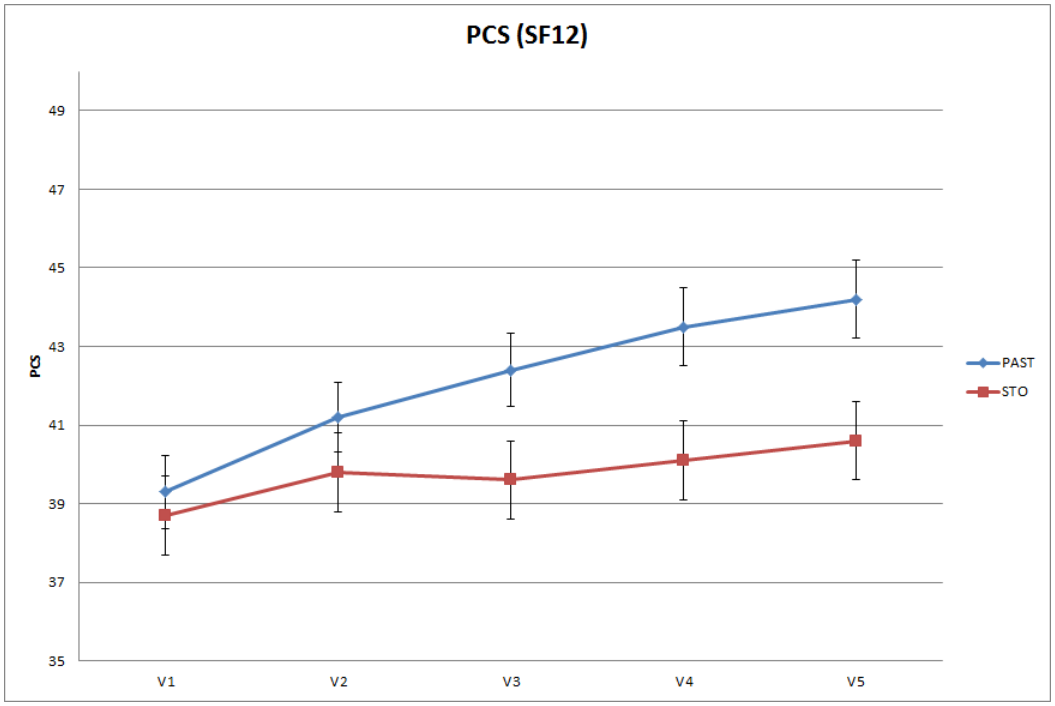
The difference in PCS between PAST and STO was evaluated at each visit using an ANOVA model with repeated measures. Statistically significant differences were observed on the population of randomised patients at V2, V3, V4 and V5, in favour of PAST patients: at V2, V3 and V4, patients in PAST group had a statistically higher QOL-PCS than patients in STO group.

Details are presented in Table 13 and graphically in Figure 4.

Table 13. Secondary criterion: PCS at each visit (Randomised patients, N=300)

PCS at each visit - ANOVA with repeated measures	V1	V2	V3	V4	V5
Difference PAST vs. STO	0.68(±0.70) [-0.70;2.06] p=0.3323	1.45(±0.70) [0.07;2.83] p=0.0395	2.77(±0.71) [1.37;4.16] p=0.0001	3.41(±0.71) [2.02;4.81] p<0.0001	3.65(±0.71) [2.26;5.04] p<0.0001

Figure 4. PCS evolution between V1 and V5



11.4.1.2.5.2 Mental Health score – MCS

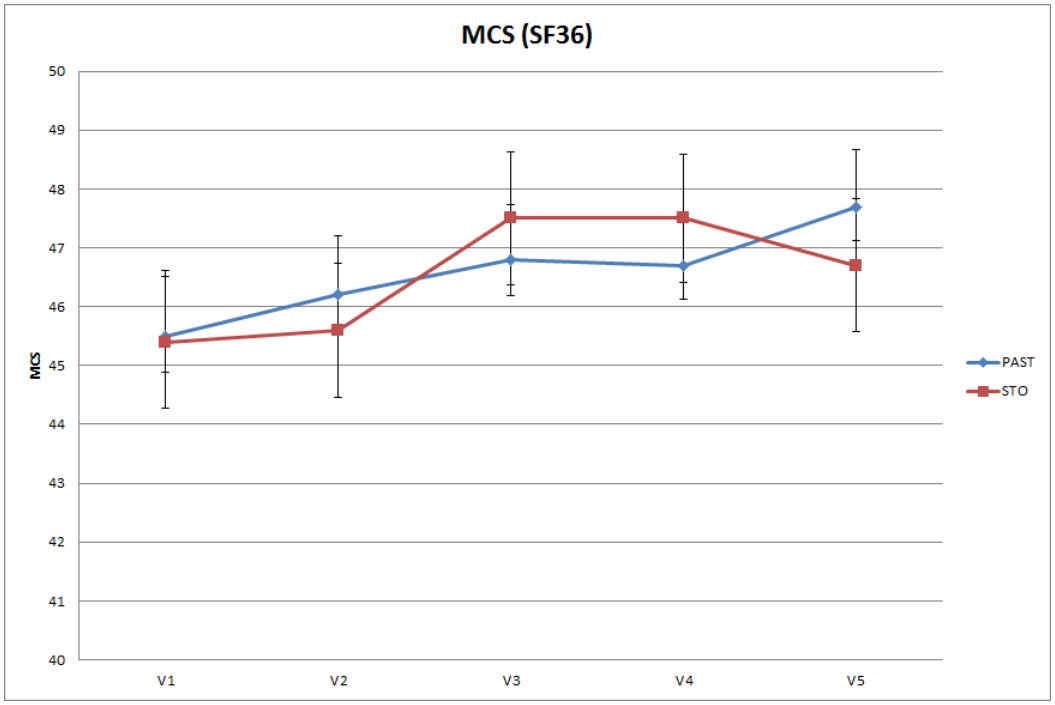
The difference in PCS between PAST and STO was evaluated at each visit using an ANOVA model with repeated measures. No statistically significant differences were observed on the population of randomised patients at V2, V3, V4 and V5, between PAST and STO groups.

Details are presented in Table 14 and graphically in Figure 5.

Table 14. Secondary criterion: MCS at each visit (Randomised patients, N=300)

MCS at each visit - ANOVA with repeated measures	V1	V2	V3	V4	V5
Difference PAST vs. STO	0.08(±0.76) [-1.41;1.57] p=0.9163	0.61(±0.76) [-0.88;2.10] p=0.4231	-0.74(±0.77) [-2.24;0.76] p=0.3348	-0.79(±0.77) [-2.30;0.72] p=0.3052	0.92(±0.77) [-0.59;2.42] P=0.2317

Figure 5. MCS evolution between V1 and V5



See Final Clinical Trial Report for the initial description on each item of the SF12 questionnaire.

11.4.1.2.6 Overall assessment of efficacy at V5

The overall assessment of efficacy at V5 by the investigator and by the patient was statistically better in PAST group than in STO group: 57.5% of investigators for patients in PAST group found that the overall efficacy at V5 was excellent compared to 12.8% of investigators for patients in STO group; and 58.2% of patients in PAST group found that the overall efficacy at V5 was excellent compared to 12.8% of patients in STO group.

Details are shown in Table 15.

Table 15. Secondary criterion: Overall assessment of efficacy at V5 (Randomised patients, N=300)

Overall assessment of efficacy at V5 N (%)			PAST N=150	STO N=150	Total N=300
Overall assessment of efficacy at V5 by the investigator			n=146	n=148	n=294
	p<0.0001	Excellent	84 (57.5%)	19 (12.8%)	103 (35.0%)
		Good	55 (37.7%)	56 (37.8%)	111 (37.8%)
		Average	4 (2.7%)	58 (39.2%)	62 (21.1%)
		Poor	3 (2.1%)	15 (10.1%)	18 (6.1%)
Overall assessment of efficacy at V5 by the patient			n=146	n=148	n=294
	p<0.0001	Excellent	85 (58.2%)	19 (12.8%)	104 (35.4%)
		Good	49 (33.6%)	55 (37.2%)	104 (35.4%)
		Average	8 (5.5%)	53 (35.8%)	61 (20.7%)
		Poor	4 (2.7%)	21 (14.2%)	25 (8.5%)

11.4.1.3 Rescue medication

No change; see Final Clinical Trial Report (section 11.4.7).

11.4.2 Statistical/analytical issues

No change; see Final Clinical Trial Report (Section 11.4.8).

11.4.3 Efficacy conclusions

For the primary efficacy criterion, the proportion of patients in the PAST group who did not take NSAIDs, starting at V2, was statistically greater than in the STO group.

For the secondary efficacy criteria:

- the proportion of patients in the PAST group who did not take Paracetamol, starting at V2, was statistically greater than in the STO group;
- patients in the PAST group took a statistically lower number of NSAIDs tablets than patients in the STO group;
- patients in the PAST group took a statistically lower number of Paracetamol tablets than patients in STO group;
- patients in the PAST group had a statistically lower pain level (VAS), starting at V2, than patients in the STO group;
- patients in the PAST group had a statistically lower Lequesne index, starting at V2, than patients in the STO group;
- patients in the PAST group had a statistically greater PCS score, starting at V2, than patients in the STO group;
- no statistical difference was observed between both treatment groups for the MCS score;
- the overall assessments of efficacy by the investigator and by the patient were statistically better in the PAST group than in the STO group.

The addition of PIASCLEDINE® to standard treatment had a significant positive effect on the symptomatology of osteoarthritis (pain, Lequesne index), quality of life (physical component of SF12) and the overall assessments of efficacy by both patients and investigators.

12 SAFETY EVALUATION

No change; see Final Clinical Trial Report.

12.1 EXTENT OF EXPOSURE

12.2 ADVERSE EVENTS (AES)

12.3 DEATHS, OTHER SERIOUS ADVERSE EVENTS, AND OTHER SIGNIFICANT ADVERSE EVENTS

12.4 CLINICAL LABORATORY EVALUATION

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

12.5.1 Vital signs

12.5.2 Physical examination

12.5.3 Concomitant treatment

12.5.4 Overall assessment of tolerability at V5

The overall assessment of tolerability at V5 by the investigator and by the patient was statistically better in PAST group than in STO group: 88.4% of investigators for patients in PAST group found that the overall tolerability at V5 was excellent compared to 26.4% of investigators for patients in STO group; and 84.9% of patients in PAST group found that the overall tolerability at V5 was excellent compared to 25.7% of patients in STO group.

Details are shown in **Erreur ! Source du renvoi introuvable.**.

Table 16. Secondary criterion: Overall assessment of tolerability at V5 (Randomised patients, N=300)

Overall assessment of tolerability at V5 N (%)			PAST N=150	STO N=150	Total N=300
Overall assessment of tolerability at V5 by the investigator			n=146	n=148	n=294
	p<0.0001	Excellent	129 (88.4%)	39 (26.4%)	168 (57.1%)
		Good	15 (10.3%)	81 (54.7%)	96 (32.7%)
		Average	0 (0.0%)	27 (18.2%)	27 (9.2%)
		Poor	2 (1.4%)	1 (0.7%)	3 (1.0%)
Overall assessment of tolerability at V5 by the patient			n=146	n=148	n=294
	p<0.0001	Excellent	124 (84.9%)	38 (25.7%)	162 (55.1%)
		Good	20 (13.7%)	80 (54.1%)	100 (34.0%)
		Average	0 (0.0%)	30 (20.3%)	30 (10.2%)
		Poor	2 (1.4%)	0 (0.0%)	2 (0.7%)

12.6 SAFETY CONCLUSIONS

See Final Clinical Trial Report.

Three SAEs have been observed during the trial in the PAST group (one death due to a lung tumour, one cholestatic icterus, one biliary colic) without or with unlikely relation to the treatment.

In the PAST group, 29 patients (19.3%) reported 35 AEs, from which 6 have been assessed as possibly or probably related to the treatment, while 28 were not or unlikely related to the treatment (infections, accident etc.).

In the STO group, 9 patients (6.0%) reported 14 AEs, mostly known side effects of NSAIDs.

The vital signs did not reveal any changes in both groups during the observation time.

The overall assessments of tolerability by the investigator and by the patient were statistically better in the PAST group than in the STO group.

Overall, safety was good in both groups.

13 DISCUSSION AND OVERALL CONCLUSIONS

Details regarding the study rationale and previous clinical study results are discussed in the Final Clinical Trial Report.

Patients taking Piascledine® did take significantly less NSAIDs and Paracetamol than patients following standard care only.
As far as patients evaluations are concerned: for pain level, severity of osteoarthritis measured by Lequesne index, quality of life measured by the Physical Composite Scale of the SF12 questionnaire and the overall assessment of efficacy, patients taking Piascledine® improved significantly more over the course of the trial than patients under standard care only. However, no statistical significance was observed between both groups for the Mental Composite Scale of the SF12 questionnaire.
As far as investigators evaluations are concerned: it was observed that the overall assessment of efficacy was significantly better for patients taking Piascledine® improved significantly more over the course of the trial than patients under standard care only

Regarding the rescue medications, even though the results were in favour of the PAST group, they must be taken with caution. Indeed, the results were based on a count of tablets when only an analysis based on dosage or equivalent would have been relevant.

Overall, safety was good in both groups. Tolerability assessments evaluated by the investigator and by the patient were significantly better for patients taking Piascledine® than for patients under standard care only.

The addition of PIASCLEDINE® to standard treatment had a significant positive effect on the symptomatology of osteoarthritis (pain, Lequesne index), quality of life (physical component of SF12) and the overall assessments of efficacy and tolerability by both patients and investigators.

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

Additional tables were produced for the Addendum: see ***VOLUME 2***.

15 REFERENCE LIST

No change; see Final Clinical Trial Report.

16 APPENDICES

See Final Clinical Trial Report Appendix 16.

17 STATISTIC TABLES

1. Disposition of Patients

1.1 First and last dates of visit for the first and last patients

		Visit date (V1)		Visit date (V5)	
Number of centers	Number of patients	First patient	Last patient	First patient	Last patient
N=10	N=300	08SEP2008	01JUN2009	15APR2008	02NOV2009

1.2 Disposition of patients per center

	Treatment group		
Centre number N (%)	PAST (N=150)	STO (N=150)	Total (N=300)
1	30 (20.0)	30 (20.0)	60 (20.0)
3	6 (4.0)	6 (4.0)	12 (4.0)
4	15 (10.0)	17 (11.3)	32 (10.7)
5	9 (6.0)	7 (4.7)	16 (5.3)
6	18 (12.0)	18 (12.0)	36 (12.0)
7	15 (10.0)	15 (10.0)	30 (10.0)
8	18 (12.0)	18 (12.0)	36 (12.0)
9	18 (12.0)	18 (12.0)	36 (12.0)
10	9 (6.0)	9 (6.0)	18 (6.0)
12	12 (8.0)	12 (8.0)	24 (8.0)

1.3 Mean, median, minimum and maximum number of patients per center

Number of patients per center			
Mean	Median	Minimum	Maximum
30.0	31.0	12	60

1.4 Flow-chart of patients

	Treatment group		
Flow-chart of patients	PAST (N=150)	STO (N=150)	Total (N=300)
Patients included in the study (patients with Visit 1) - N (%)			
Missing	0	0	0
Yes	150 (100.0%)	150 (100.0%)	300 (100.0%)
Total	150	150	300
Patients who completed the study (patients with Visit 1 and Visit 5) - N (%)			
Missing	0	0	0
No	3 (2.0%)	2 (1.3%)	5 (1.7%)
Yes	147 (98.0%)	148 (98.7%)	295 (98.3%)
Total	150	150	300
Patients with all visits - N (%)			
Missing	0	0	0
No	4 (2.7%)	0 (0.0%)	4 (1.4%)
Yes	143 (97.3%)	148 (100.0%)	291 (98.6%)
Total	147	148	295
Patients with Visit 2 - N (%)			
Missing	0		0
No	1 (25.0%)		1 (25.0%)
Yes	3 (75.0%)		3 (75.0%)
Total	4		4
Patients with Visit 3 - N (%)			
Missing	0		0
No	4 (100.0%)		4 (100.0%)
Total	4		4
Patients with Visit 4 - N (%)			
Missing	0		0
No	4 (100.0%)		4 (100.0%)
Total	4		4

2. Baseline Characteristics

2.1 Demographic Data

	Treatment group		
Demographic Data	PAST (N=150)	STO (N=150)	Total (N=300)
Sex (V1) - N (%)			
Missing	0	0	0
Male	22 (14.7%)	22 (14.7%)	44 (14.7%)
Female	128 (85.3%)	128 (85.3%)	256 (85.3%)
Total	150	150	300
Age			
Missing	0	0	0
N	150	150	300
Mean (±SD)	61.4 (±9.0)	62.3 (±9.2)	61.8 (±9.1)
Median	60.5	62.0	61.0
Q1-Q3	[54.0;68.0]	[55.0;68.0]	[55.0;68.0]
Min-Max	[46.0;86.0]	[45.0;85.0]	[45.0;86.0]
Height (V1)			
Missing	0	0	0
N	150	150	300
Mean (±SD)	163.1 (±8.6)	163.3 (±7.4)	163.2 (±8.0)
Median	162.0	163.0	162.0
Q1-Q3	[158.0;167.0]	[158.0;168.0]	[158.0;167.5]
Min-Max	[140.0;202.0]	[145.0;190.0]	[140.0;202.0]
Weight (V1)			
Missing	0	0	0
N	150	150	300
Mean (±SD)	77.0 (±15.0)	78.5 (±14.4)	77.8 (±14.7)
Median	75.0	78.0	76.5
Q1-Q3	[67.0;86.0]	[69.0;86.0]	[68.0;86.0]
Min-Max	[48.0;147.0]	[45.0;130.0]	[45.0;147.0]

2.2 General Physical Examination

	Treatment group		
General Physical Examination	PAST (N=150)	STO (N=150)	Total (N=300)
Integumentary System normal ? (V1) - N (%)			
Missing	0	0	0
Abnormal	14 (9.3%)	17 (11.3%)	31 (10.3%)
Normal	136 (90.7%)	133 (88.7%)	269 (89.7%)
Total	150	150	300
Sensory System normal ? (V1) - N (%)			
Missing	0	0	0
Abnormal	3 (2.0%)	5 (3.3%)	8 (2.7%)
Normal	147 (98.0%)	145 (96.7%)	292 (97.3%)
Total	150	150	300
Respiratory System normal ? (V1) - N (%)			
Missing	0	0	0
Abnormal	2 (1.3%)	3 (2.0%)	5 (1.7%)
Normal	148 (98.7%)	147 (98.0%)	295 (98.3%)
Total	150	150	300
Cardiovascular System normal ? (V1) - N (%)			
Missing	0	0	0
Abnormal	15 (10.0%)	16 (10.7%)	31 (10.3%)
Normal	135 (90.0%)	134 (89.3%)	269 (89.7%)
Total	150	150	300
Gastrointestinal System normal ? (V1) - N (%)			
Missing	0	0	0
Abnormal	2 (1.3%)	1 (0.7%)	3 (1.0%)
Normal	148 (98.7%)	149 (99.3%)	297 (99.0%)
Total	150	150	300
Metabolism/Endocrine System normal ? (V1) - N (%)			
Missing	0	0	0
Abnormal	54 (36.0%)	50 (33.3%)	104 (34.7%)
Normal	96 (64.0%)	100 (66.7%)	196 (65.3%)
Total	150	150	300
Nervous System normal ? (V1) - N (%)			
Missing	0	0	0
Abnormal	1 (0.7%)	0 (0.0%)	1 (0.3%)
Normal	149 (99.3%)	150 (100.0%)	299 (99.7%)
Total	150	150	300
Musculoskeletal System normal ? (V1) - N (%)			
Missing	0	0	0
Abnormal	18 (12.0%)	14 (9.3%)	32 (10.7%)
Normal	132 (88.0%)	136 (90.7%)	268 (89.3%)
Total	150	150	300
Urinary System normal ? (V1) - N (%)			
Missing	0	0	0
Abnormal	0 (0.0%)	1 (0.7%)	1 (0.3%)
Normal	150 (100.0%)	149 (99.3%)	299 (99.7%)
Total	150	150	300

	Treatment group		
General Physical Examination	PAST (N=150)	STO (N=150)	Total (N=300)
Genital System normal ? (V1) - N (%)			
Missing	0	0	0
Abnormal	1 (0.7%)	4 (2.7%)	5 (1.7%)
Normal	130 (86.7%)	128 (85.3%)	258 (86.0%)
ND	19 (12.7%)	18 (12.0%)	37 (12.3%)
Total	150	150	300
Other ? (V1) - N (%)			
Missing	28	27	55
0	1 (0.8%)	3 (2.4%)	4 (1.6%)
1	26 (21.3%)	24 (19.5%)	50 (20.4%)
NA	1 (0.8%)	2 (1.6%)	3 (1.2%)
ND	94 (77.0%)	94 (76.4%)	188 (76.7%)
Total	122	123	245

2.3 Vital Signs

	Treatment group		
Vital Signs	PAST (N=150)	STO (N=150)	Total (N=300)
Systolic Blood Pressure (V1)			
Missing	0	0	0
N	150	150	300
Mean (±SD)	128.6 (±12.0)	130.5 (±13.2)	129.6 (±12.6)
Median	130.0	130.0	130.0
Q1-Q3	[120.0;135.0]	[120.0;140.0]	[120.0;140.0]
Min-Max	[100.0;180.0]	[100.0;180.0]	[100.0;180.0]
Diastolic Blood Pressure (V1)			
Missing	0	0	0
N	150	150	300
Mean (±SD)	76.5 (±7.2)	76.8 (±7.9)	76.7 (±7.5)
Median	80.0	80.0	80.0
Q1-Q3	[70.0;80.0]	[70.0;80.0]	[70.0;80.0]
Min-Max	[60.0;95.0]	[60.0;120.0]	[60.0;120.0]
Heart rate (V1)			
Missing	0	0	0
N	150	150	300
Mean (±SD)	73.7 (±6.5)	73.8 (±6.7)	73.7 (±6.6)
Median	74.0	72.5	73.5
Q1-Q3	[70.0;78.0]	[70.0;80.0]	[70.0;79.0]
Min-Max	[60.0;92.0]	[54.0;95.0]	[54.0;95.0]
Breath rate (V1)			
Missing	0	0	0
N	150	150	300
Mean (±SD)	16.8 (±2.8)	16.9 (±2.6)	16.8 (±2.7)
Median	16.5	17.0	17.0
Q1-Q3	[15.0;18.0]	[15.0;18.0]	[15.0;18.0]
Min-Max	[12.0;26.0]	[12.0;28.0]	[12.0;28.0]

2.4 History and Diagnosis of Osteoarthritis of the Knee

	Treatment group					
History and Diagnosis of Osteoarthritis of the Knee	PAST (N=150)		STO (N=150)		Total (N=300)	
Which knee has been X-rayed? (V1) - N (%)						
Missing	0		0		0	
Left	19	(12.7%)	25	(16.7%)	44	(14.7%)
Left Right	94	(62.7%)	101	(67.3%)	195	(65.0%)
Right	37	(24.7%)	24	(16.0%)	61	(20.3%)
Total	150		150		300	
Which kind of frontal picture has been taken? (V1) - N (%)						
Missing	0		0		0	
Extension	145	(96.7%)	146	(97.3%)	291	(97.0%)
Extension,flexion	1	(0.7%)	0	(0.0%)	1	(0.3%)
Flexion	1	(0.7%)	4	(2.7%)	5	(1.7%)
Flexion,Extension	3	(2.0%)	0	(0.0%)	3	(1.0%)
Total	150		150		300	
Kellgren-Lawrence score (V1) - N (%)						
Missing	0		0		0	
1	38	(25.3%)	28	(18.7%)	66	(22.0%)
2	86	(57.3%)	94	(62.7%)	180	(60.0%)
3	26	(17.3%)	28	(18.7%)	54	(18.0%)
Total	150		150		300	
Are there other known and radiologically confirmed osteoarthritic localisations? (V1) - N (%)						
Missing	0		0		0	
No	119	(79.3%)	117	(78.0%)	236	(78.7%)
Yes	31	(20.7%)	33	(22.0%)	64	(21.3%)
Total	150		150		300	
If yes, describe (V1) - N (%)						
Missing	0		0		0	
calcanean spur left right	1	(3.2%)	0	(0.0%)	1	(1.6%)
calcanean spur right left platypodia	1	(3.2%)	0	(0.0%)	1	(1.6%)
cervical spondilosis	0	(0.0%)	2	(6.1%)	2	(3.1%)
cervical spondylosis	1	(3.2%)	1	(3.0%)	2	(3.1%)
cervical toracal lumbar	1	(3.2%)	0	(0.0%)	1	(1.6%)
columna vertebral	1	(3.2%)	3	(9.1%)	4	(6.3%)
columna vertebralis	1	(3.2%)	1	(3.0%)	2	(3.1%)
columne vertebrae	1	(3.2%)	0	(0.0%)	1	(1.6%)
coxarthrosis incip. 17/12/03	1	(3.2%)	0	(0.0%)	1	(1.6%)
coxarthrosis l.dx.	0	(0.0%)	1	(3.0%)	1	(1.6%)
coxarthrosis l.sin. Left side	1	(3.2%)	0	(0.0%)	1	(1.6%)
deforming vertebrae	0	(0.0%)	1	(3.0%)	1	(1.6%)
dip joints of hands	0	(0.0%)	1	(3.0%)	1	(1.6%)
dip of hands	0	(0.0%)	1	(3.0%)	1	(1.6%)
discopathy v4-v5	1	(3.2%)	0	(0.0%)	1	(1.6%)
distal interphalangeal joints of hands both cmc and acromioclavicular joints	1	(3.2%)	0	(0.0%)	1	(1.6%)
distal phalangs	1	(3.2%)	0	(0.0%)	1	(1.6%)

	Treatment group					
History and Diagnosis of Osteoarthritis of the Knee	PAST (N=150)		STO (N=150)		Total (N=300)	
incipient arthrotic changes on the coxal 2000	1	(3.2%)	0	(0.0%)	1	(1.6%)
incipient coxarthrosis l.dx.1998	1	(3.2%)	0	(0.0%)	1	(1.6%)
ip joints of hands	1	(3.2%)	0	(0.0%)	1	(1.6%)
joint of palms	0	(0.0%)	1	(3.0%)	1	(1.6%)
left hip	1	(3.2%)	0	(0.0%)	1	(1.6%)
lombar column's spondylopathy	1	(3.2%)	0	(0.0%)	1	(1.6%)
lumbar	1	(3.2%)	0	(0.0%)	1	(1.6%)
lumbar column spondilopathy	1	(3.2%)	0	(0.0%)	1	(1.6%)
lumbar osteoarthritis left hip osteoarthritis	0	(0.0%)	1	(3.0%)	1	(1.6%)
lumbar spine	1	(3.2%)	0	(0.0%)	1	(1.6%)
lumbar spondilosis	0	(0.0%)	5	(15.2%)	5	(7.8%)
lumbar spondylosis	0	(0.0%)	1	(3.0%)	1	(1.6%)
lumbar vertebral column's osteoarthritis	0	(0.0%)	1	(3.0%)	1	(1.6%)
lumbar vertebral spondylosis	0	(0.0%)	1	(3.0%)	1	(1.6%)
osteoarthritis of columna vertebralis	1	(3.2%)	2	(6.1%)	3	(4.7%)
osteoarthritis of columne vertebralis	0	(0.0%)	1	(3.0%)	1	(1.6%)
osteoarthritis of the coxae (2007) l.dx.	0	(0.0%)	1	(3.0%)	1	(1.6%)
osteoarthritis of the coxal I.dx.	0	(0.0%)	1	(3.0%)	1	(1.6%)
osteoarthritis of the hands	1	(3.2%)	0	(0.0%)	1	(1.6%)
osteoarthritis of the hands 2002 comp.	1	(3.2%)	0	(0.0%)	1	(1.6%)
osteoarthritis of the hands 2003	1	(3.2%)	0	(0.0%)	1	(1.6%)
osteoarthritis of the hands 2005	0	(0.0%)	1	(3.0%)	1	(1.6%)
osteoarthrosis cervical vertebrae	0	(0.0%)	1	(3.0%)	1	(1.6%)
spondylarthrosis def. lis chron. spondylolistesis	1	(3.2%)	0	(0.0%)	1	(1.6%)
spondylarthrosis def.LS-VAS	0	(0.0%)	1	(3.0%)	1	(1.6%)
spondylarthrosis et spondylosis of the cervical column (vertebrogenes)	0	(0.0%)	1	(3.0%)	1	(1.6%)
spondyloarthritis	1	(3.2%)	0	(0.0%)	1	(1.6%)
spondylosis deformans	1	(3.2%)	0	(0.0%)	1	(1.6%)
spondylosis platypodia	1	(3.2%)	0	(0.0%)	1	(1.6%)
thoracal lumbar	0	(0.0%)	1	(3.0%)	1	(1.6%)
vertebral column	1	(3.2%)	0	(0.0%)	1	(1.6%)
vertebral column's osteoarthritis cervical thoracil lumbar	1	(3.2%)	0	(0.0%)	1	(1.6%)
vertebral osteoarthropathy	0	(0.0%)	1	(3.0%)	1	(1.6%)
vertebral osteoarthrosis column	0	(0.0%)	1	(3.0%)	1	(1.6%)
wrist joint left	1	(3.2%)	0	(0.0%)	1	(1.6%)
Total	31		33		64	

2.5 NSAID treatments listed at V1

Treatment group	Centre number	Pat. Nr.	NSAID treatment number	Name of Treament (generic name) (V1)	Dosage and units (V1)
PAST	7	4	1	diclofenac	100mg
PAST	7	4	2	paracetamolum	500mg
PAST	7	5	1	diclofenacum	100mg
PAST	7	6	1	etoricoxibum	90mg
PAST	7	7	1	nimesulidum	10mg
PAST	7	11	1	meloxicanum	7,5mg qd
PAST	7	12	1	meloxicanum	7,5mg qd
PAST	7	15	1	meloxicamum	7,5mg qd
PAST	7	16	1	diclofenacum	100mg qd
PAST	7	18	1	piroxicamum	20mg
PAST	7	18	2	diclofenacum	100mg
PAST	7	19	1	diclofenacum	100mg qd
PAST	7	20	1	etoricoxibum	60mg qd
PAST	7	23	1	ketoprofenum	200mg qd
PAST	7	26	1	ketoprofenum	150mg bid
PAST	7	27	1	diclofenacum	100mg qd
PAST	7	30	1	piroxicamum	20mg qd
PAST	8	32	1	etoricoxibum	90mg qd 14days/month
PAST	8	32	2	ibuprofenum	200mg qd 7days/month
PAST	8	35	1	ibuprofenum	200mg qd 15days/month
PAST	8	35	2	piroxicamum	20mg qd 10days/month
PAST	8	36	1	ketoprofenum	100mg tid 10days/month
PAST	8	36	2	piroxicamum	20mg qd 10days/month
PAST	8	37	1	diclofenacum	50mg bid 15days/month
PAST	8	37	2	piroxicamum	20mg qd 10days/month
PAST	8	40	1	nimesulidum	100mg bid 10days/month
PAST	8	40	2	piroxicamum	20mg qd 10days/month
PAST	8	41	1	nimesulidum	100mg bid 10days/month
PAST	8	43	1	nimesulidum	100mg bid 10days/month
PAST	8	43	2	diclofenacum	50mg bid 10days/month
PAST	8	45	1	nimesulidum	100mg bid 15days/month
PAST	8	48	1	meloxicamum	15mg qd 15days/month
PAST	8	48	2	nimesulidum	100mg bid 10days/month
PAST	8	52	1	nimesulidum	100mg bid 15days/month
PAST	8	52	2	meloxicamum	7,5mg qd 10days/month
PAST	8	53	1	nimesulidum	100mg bid 15days/month
PAST	8	54	1	diclofenacum	150mg qd 15days/month
PAST	8	55	1	piroxicamum	20mg qd 10days/month
PAST	8	55	2	ketoprofenum	100mg tid 10days/month
PAST	8	59	1	piroxicamum	20mg qd 10days/month
PAST	8	59	2	diclofenacum	50mg bid 15days/month
PAST	8	60	1	ibuprofenum	200mg qd 15days/month
PAST	8	60	2	diclofenacum	50mg bid 15days/month
PAST	8	64	1	piroxicamum	20mg qd 10days/month
PAST	8	64	2	diclofenacum	50mg bid 10days/month

Treatment group	Centre number	Pat. Nr.	NSAID treatment number	Name of Treament (generic name) (V1)	Dosage and units (V1)
PAST	8	65	1	meloxicamum	15mg qd 10days/month
PAST	8	65	2	nimesulidum	100mg bid 10days/month
PAST	8	66	1	diclofenacum	50mg bid 10days/month
PAST	8	66	2	piroxicamum	20mg 10days/month
PAST	9	67	1	diclofenac	100mg
PAST	9	68	1	diclofenac	100mg od
PAST	9	69	1	diclofenac	100mg od
PAST	9	74	1	nimesulid	100mg bid
PAST	9	74	2	diclofenac	100mg od
PAST	9	75	1	diclofenac	50mg tid
PAST	9	78	1	diclofenacum	100mg od
PAST	9	79	1	diclofenacum	100mg
PAST	9	81	1	ketoprofenum	100mg bid
PAST	9	85	1	diclofenacum	100mg od
PAST	9	86	1	diclofenac	100mg od
PAST	9	86	2	ketoprofen	100mg bid
PAST	9	90	1	diclofenac	50mg bid
PAST	9	92	1	ibuprofen	200mg od
PAST	9	93	1	diclofenac	50mg od
PAST	9	96	1	diclofenac	50mg od
PAST	9	100	1	diclofenac	100mg
PAST	9	101	1	diclofenac	100mg
PAST	9	102	1	diclofenac	100mg
PAST	1	105	1	nimesulide	100mg
PAST	1	105	2	dexketoprofen	25mg
PAST	1	106	1	dexketoprofen	25mg
PAST	1	107	1	nimesulide	100mg
PAST	1	109	1	nimesulide	100mg
PAST	1	110	1	meloxicam	15mg
PAST	1	110	2	paracetamol	500mg
PAST	1	114	1	meloxicam	15mg
PAST	1	116	1	nimesulide	100mg
PAST	1	117	1	diclofenac	2x50mg
PAST	1	118	1	meloxicam	15mg
PAST	1	121	1	diclofenac	100mg x1tb
PAST	1	122	1	diclofenac	75mg x1tb
PAST	1	126	1	meloxicam	15mg tbl
PAST	1	129	1	nimesulide	100mg
PAST	1	130	1	diclofenac	75mg x1tb
PAST	1	130	2	acetylsalicylic acid	500mg x1tbl
PAST	1	132	1	dexketoprofen	25mg 2x1
PAST	1	133	1	piroxicam	20mg
PAST	1	136	1	diclofenac	75mg x1tb
PAST	1	138	1	nimesulide	100mg x1tb
PAST	1	140	1	nimesulide	100mg
PAST	1	143	1	meloxicam	15mg x1tbl
PAST	1	144	1	nimesulide	100mg

Treatment group	Centre number	Pat. Nr.	NSAID treatment number	Name of Treament (generic name) (V1)	Dosage and units (V1)
PAST	1	145	1	nimesulide	100mg
PAST	1	146	1	meloxicam	15mg
PAST	1	149	1	nimesulide	100mg
PAST	1	152	1	nimesulide	100mg
PAST	1	155	1	meloxicam	15mg
PAST	1	155	2	meloxicam	15mg
PAST	1	156	1	meloxicam	15mg x1tb
PAST	1	157	1	diclofenac	150mg x1tb
PAST	1	159	1	nimesulide	100mg
PAST	1	160	1	nimesulide	100mg
PAST	3	163	1	diclofenac	75mg 1tab
PAST	3	167	1	nimesulide	100mg 1x
PAST	3	168	1	febrofen ketoprofen	200mg
PAST	3	171	1	diclofenac	100mg
PAST	3	172	1	diclofenac	100mg
PAST	3	173	1	ketonal (ketoprofen)	150mg 1x1tbl
PAST	4	176	1	meloxicam	15mg
PAST	4	176	2	ketoprofen	200mg
PAST	4	178	1	ketoprofen	100mg
PAST	4	178	2	diclofenac	150mg
PAST	4	180	1	ketoprofen	200mg
PAST	4	180	2	meloxicam	15mg
PAST	4	184	1	ketoprofen	150mg
PAST	4	184	2	nimesulid	200mg
PAST	4	185	1	meloxicam	15mg
PAST	4	186	1	ketoprofen	200mg
PAST	4	186	2	diclofenac	100mg
PAST	4	187	1	diclofenac	100mg
PAST	4	187	2	diclofenac	100mg
PAST	4	187	3	diclofenac	100mg
PAST	4	188	1	ketoprofen	100mg
PAST	4	188	2	meloxicam	15mg
PAST	4	189	1	celecoxyb	200mg
PAST	4	189	2	celecoxyb	100mg
PAST	4	195	1	acemetacin	90mg
PAST	4	197	1	celecoxyb	100mg
PAST	4	198	1	meloxicam	15mg
PAST	4	201	1	celecoxyb	200mg
PAST	4	201	2	celecoxyb	200mg
PAST	4	201	3	celecoxyb	200mg
PAST	4	202	1	ketoprofenum	100mg
PAST	4	202	2	nimesulid	15mg
PAST	4	203	1	nimesulid	100mg
PAST	5	204	1	diclac diclofenac	75mg
PAST	5	204	2	butapirazol	
PAST	5	206	1	ibuprofen	200mg
PAST	5	206	2	diclofenac	100mg

Treatment group	Centre number	Pat. Nr.	NSAID treatment number	Name of Treament (generic name) (V1)	Dosage and units (V1)
PAST	5	207	1	nimesulide	100mg
PAST	5	207	2	diclofenac	150mg
PAST	5	207	3	paracetamol	500mg
PAST	5	211	1	nimesulide	100mg
PAST	5	212	1	diclofenac	100mg
PAST	5	215	1	diclofenac	150mg
PAST	5	216	1	nimesulid	100mg
PAST	5	218	1	ketoprofen	100mg
PAST	5	219	1	nimesulid	100mg bid
PAST	6	223	1	meloxicam	15mg qd
PAST	6	223	2	meloxicam	15mg qd
PAST	6	223	3	meloxicam	15mg qd
PAST	6	224	1	piroxicam	20mg qd
PAST	6	225	1	nimesulide	200mg bid
PAST	6	225	2	meloxicam	15mg qd
PAST	6	225	3	aceclofenac	100mg bid
PAST	6	226	1	celecoxib	200mg bid
PAST	6	226	2	celecoxib	200mg bid
PAST	6	226	3	celecoxib	200mg bid
PAST	6	229	1	diclofenac	150mg qd
PAST	6	229	2	piroxicam	20mg qd
PAST	6	229	3	piroxicam	20mg qd
PAST	6	231	1	ketoprofen	200mg bid
PAST	6	231	2	ketoprofen	200mg qd
PAST	6	231	3	piroxicam	20mg qd
PAST	6	232	1	piroxicam	20mg qd
PAST	6	232	2	piroxicam	20mg qd
PAST	6	232	3	piroxicam	20mg qd
PAST	6	233	1	diclofenac	50mg bid
PAST	6	233	2	piroxicam	20mg qd
PAST	6	233	3	meloxicam	15mg qd
PAST	10	237	1	diclofenac	50mg (2)
PAST	10	238	1	voltaren sr	75mg
PAST	10	240	1	ibuprofen	400mg 3-4x1
PAST	10	244	1	ibalgin	400mg (3)
PAST	10	245	1	voltaren r	50mg (2)
PAST	10	245	2	ibalgin	400mg (3)
PAST	10	246	1	ibuprofen	400mg (3)
PAST	10	252	1	ibuprofen	400mg 3x
PAST	10	253	1	veral diclofenac	50mg (3)
PAST	10	254	1	diclofenac	50mg (3)
PAST	12	256	1	meloxicam	15mg
PAST	12	257	1	diclofenac	75mg
PAST	12	260	1	aceclofenac	200mg
PAST	12	261	1	piroxicamum	20mg
PAST	12	262	1	flugalin	50mg
PAST	12	263	1	piroxicamum	20mg

Treatment group	Centre number	Pat. Nr.	NSAID treatment number	Name of Treament (generic name) (V1)	Dosage and units (V1)
PAST	12	263	2	aceclofenacum	100mg
PAST	12	267	1	celecoxib	200mg
PAST	12	269	1	meloxicam	15mg
PAST	12	271	1	aceclofenac	200mg
PAST	12	273	1	ibalgin ibuprofen	400mg
PAST	12	274	1	diclofenac	150mg
PAST	12	277	1	meloxicam	15mg
PAST	6	279	1	ibuprofen	400mg/prn
PAST	6	279	2	aceclofenac	200mg/prn
PAST	6	280	1	ketoprofen	200mg qd
PAST	6	280	2	ketoprofen	200mg qd
PAST	6	280	3	diclofenac	50mg bid
PAST	6	284	1	piroxicam	20mg qd
PAST	6	284	2	aceclofenac	100mg bid
PAST	6	284	3	meloxicam	15mg qd
PAST	6	284	4	diclofenac	50mg qd
PAST	6	285	1	diclofenac	50mg bid
PAST	6	285	2	diclofenac	75mg qd
PAST	6	287	1	diclofenac	100mg qd
PAST	6	287	2	diclofenac	100mg qd
PAST	6	287	3	diclofenac	100mg qd
PAST	6	287	4	aceclofenac	100mg bid
PAST	6	288	1	diclofenac	100mg/day
PAST	6	291	1	piroxicamum	20mg
PAST	6	292	1	piroxicam	20mg qd
PAST	6	296	1	diclofenacum	100mg/day
PAST	6	296	2	diclofenacum	100mg/day
PAST	6	296	3	diclofenacum	100mg/day
PAST	6	297	1	nimesulide	100mg bid/day
PAST	6	297	2	nimesulide	100mg bid/day
PAST	6	297	3	nimesulide	100mg bid/day
STO	7	1	1	nimesulidum	200mg
STO	7	1	2	diclofenac	100mg
STO	7	1	3	diclofenac	100mg
STO	7	2	1	etoricoxibum	60mg qd
STO	7	2	2	ketoprofen	200mg qd
STO	7	3	1	indometacinum	150mg qd
STO	7	8	1	piroxicamum	20mg
STO	7	9	1	meloxicamum	15mg
STO	7	10	1	naproxenum	220mg bid
STO	7	13	1	mydocalm	150mg
STO	7	13	2	movalis	7,5mg
STO	7	13	3	paracetamol	1,5g
STO	7	14	1	ibuprofenum	1200mg qd
STO	7	17	1	piroxicamum	20mg qd
STO	7	21	1	ketoprofenum	150mg qd
STO	7	22	1	ketoprofenum	150mg qd

Treatment group	Centre number	Pat. Nr.	NSAID treatment number	Name of Treament (generic name) (V1)	Dosage and units (V1)
STO	7	24	1	etoricoxibum	60mg qd
STO	7	25	1	piroxicamum	20mg qd
STO	7	28	1	nimesulidum	100mg qd
STO	7	29	1	etoricoxibum	90mg qd
STO	8	31	1	etoricoxibum	120mg qd 10 days/month
STO	8	31	2	piroxicamum	20mg qd 10days/month
STO	8	33	1	piroxicamum	20mg qd 15days/month
STO	8	33	2	nimesulidum	100mg bid 15days/month
STO	8	34	1	nimesulidum	100mg bid 10days/month
STO	8	34	2	tenoxicamum	20mg qd 10days/month
STO	8	38	1	etoricoxibum	90mg qd 10days/month
STO	8	38	2	ibuprofenum	200mg qd 15days/month
STO	8	39	1	ibuprofenum	200mg qd 15days/month
STO	8	42	1	piroxicamum	20mg qd 15days/month
STO	8	44	1	piroxicamum	20mg qd 10days/month
STO	8	44	2	nimesulidum	100mg bid 10days/month
STO	8	46	1	piroxicamum	20mg qd 15days/month
STO	8	47	1	etoricoxibum	120mg qd 10days/month
STO	8	47	2	meloxicamum	7,5mg qd 10days/month
STO	8	49	1	nimesulidum	100mg bid 15days/month
STO	8	50	1	piroxicamum	20mg qd 15days/month
STO	8	50	2	meloxicamum	7,5mg qd 10days/month
STO	8	51	1	piroxicamum	20mg qd 15days/month
STO	8	51	2	meloxicamum	7,5mg qd 10days/month
STO	8	56	1	meloxicamum	15mg qd 17days/month
STO	8	56	2	nimesulidum	100mg bid 15days/month
STO	8	57	1	etoricoxibum	90mg qd 10days/month
STO	8	57	2	piroxicamum	20mg qd 15days/month
STO	8	58	1	meloxicamum	7,5mg bid 10days/month
STO	8	58	2	diclofenacum	50mg bid 15days/month
STO	8	61	1	piroxicamum	20mg qd 15days/month
STO	8	61	2	meloxicamum	7,5mg qd 10days/month
STO	8	62	1	diclofenacum	50mg bid 15days/month
STO	8	62	2	nimesulidum	100mg bid 10days/month
STO	8	63	1	nimesulidum	100mg bid 10days/month
STO	8	63	2	diclofenacum	50mg bid 10days/month
STO	9	70	1	meloxicam	7,5mg bid
STO	9	71	1	diclofenac	100mg od
STO	9	72	1	diclofenac	50mg bid
STO	9	73	1	meloxicam	7,5mg bid
STO	9	73	2	diclofenac	100mg od
STO	9	76	1	diclofenac	50mg od
STO	9	77	1	diclofenac	50mg
STO	9	80	1	diclofenac	100mg
STO	9	82	1	diclofenacum	100mg
STO	9	84	1	diclofenac	100mg od
STO	9	88	1	diclofenac	50mg bid

Treatment group	Centre number	Pat. Nr.	NSAID treatment number	Name of Treament (generic name) (V1)	Dosage and units (V1)
STO	9	88	2	diclofenac	100mg od
STO	9	89	1	diclofenac	100mg od
STO	9	91	1	ketoprofen	100mg od
STO	9	94	1	diclofenac	75mg od
STO	9	95	1	diclofenac	100mg
STO	9	97	1	diclofenac	100mg od
STO	9	98	1	diclofenac	100mg od
STO	9	99	1	diclofenac	50mg bid
STO	1	103	1	diclofenac	75mg
STO	1	104	1	diclofenac	100mg
STO	1	108	1	nimesulide	100mg
STO	1	111	1	indometacin	2x25mg
STO	1	112	1	diclofenac	75mg
STO	1	113	1	piroxicam	20mg
STO	1	113	2	nimesulide	100mg
STO	1	115	1	nimesulide	100mg
STO	1	119	1	meloxicam	7,5mg
STO	1	120	1	diclofenac	75mg amp
STO	1	120	2	diclofenac	75mg tbl
STO	1	123	1	meloxicam	7,5mg x1tb
STO	1	124	1	diclofenac	100mg x1tb
STO	1	125	1	indometacin	25mg 3x1tbl
STO	1	127	1	nimesulide	100mg
STO	1	128	1	meloxicam	15mg
STO	1	131	1	profenid	50mg
STO	1	134	1	nimesulide	100mg
STO	1	135	1	nimesulide	100mg
STO	1	137	1	coxib	60mg tbl
STO	1	139	1	meloxicam	15mg tbl
STO	1	141	1	nimesulide	100mg
STO	1	142	1	diclofenac	75mg
STO	1	147	1	nimesulide	100mg
STO	1	148	1	nimesulide	100mg
STO	1	150	1	indometacin	25mg 3x1
STO	1	151	1	nimesulide	100mg
STO	1	153	1	meloxicam	15mg
STO	1	154	1	nimesulide	100mg tbl
STO	1	158	1	nimesulide	100mg
STO	1	161	1	nimesulide	100mg
STO	1	162	1	nimesulide	100mg
STO	3	164	1	dicloberl retard	100mg
STO	3	165	1	dicloberl	100mg 2x1tb
STO	3	166	1	diclofenac	75mg 1tab
STO	3	169	1	diclofenac	75mg 1x
STO	3	170	1	ketoprofen	100mg
STO	3	174	1	acemetacin	90mg
STO	4	175	1	nimesulid	100mg

Treatment group	Centre number	Pat. Nr.	NSAID treatment number	Name of Treament (generic name) (V1)	Dosage and units (V1)
STO	4	177	1	ketoprofen	200mg
STO	4	177	2	nimesulid	200mg
STO	4	177	3	ketoprofen	200mg
STO	4	179	1	nimesulid	100mg 2x
STO	4	179	2	nimesulid	100mg 2x
STO	4	179	3	nimesulid	100mg 2x
STO	4	181	1	nimesulid	200mg
STO	4	181	2	nimesulid	200mg
STO	4	182	1	ketoprofen	150mg
STO	4	182	2	ketoprofen	150mg
STO	4	183	1	ketoprofen	200mg
STO	4	183	2	diclofenac	100mg
STO	4	183	3	nimesulid	200mg
STO	4	190	1	diclofenac	100mg
STO	4	191	1	meloxicam	15mg
STO	4	192	1	meloxicam	15mg
STO	4	193	1	diclofenac	100mg
STO	4	193	2	meloxicam	15mg
STO	4	193	3	diclofenac	100mg
STO	4	194	1	meloxicam	15mg
STO	4	196	1	celecoxyb	100mg
STO	4	196	2	nimesulid	100mg
STO	4	199	1	ketoprofenum	200mg
STO	4	199	2	meloxicam	15mg
STO	4	199	3	meloxicam	15mg
STO	4	200	1	ketoprofenum	100mg
STO	4	200	2	nimesulide	100mg
STO	4	200	3	nimesulide	100mg
STO	5	205	1	ketonal forte	100mg
STO	5	205	2	nimesil nimesulid	100mg
STO	5	208	1	ketoprofen	100mg bid
STO	5	208	2	nimesulidum	100mg
STO	5	208	3	ketoprofen	100mg qd
STO	5	209	1	movalis meloxicam	7,5mg bid
STO	5	210	1	nimesulide	100mg
STO	5	213	1	nimesulid	200mg
STO	5	213	2	diclofenac	100mg
STO	5	214	1	diclofenac	150mg
STO	5	217	1	diclofenac	100mg
STO	6	220	1	ketoprofen	200mg qd
STO	6	220	2	meloxicam	15mg qd
STO	6	220	3	meloxicam	15mg qd
STO	6	221	1	diclofenac	150mg qd
STO	6	221	2	ketoprofen	200mg bid
STO	6	221	3	nimesulide	200mg bid
STO	6	222	1	meloxicam	15mg qd
STO	6	222	2	aceclofenac	100mg bid

Treatment group	Centre number	Pat. Nr.	NSAID treatment number	Name of Treament (generic name) (V1)	Dosage and units (V1)
STO	6	222	3	meloxicam	15mg qd
STO	6	227	1	ketoprofen	200mg qd
STO	6	227	2	diclofenac	150mg qd
STO	6	227	3	piroxicam	20mg qd
STO	6	227	4	meloxicam	15mg qd
STO	6	228	1	piroxicam	20mg qd
STO	6	228	2	piroxicam	20mg qd
STO	6	228	3	piroxicam	20mg qd
STO	6	230	1	piroxicam	20mg qd
STO	6	230	2	ketoprofen	200mg qd
STO	6	234	1	diclofenac	100mg/day
STO	6	235	1	piroxicam	20mg qd
STO	6	235	2	diclofenac	50mg bid
STO	6	236	1	diclofenac	50mg bid
STO	6	236	2	diclofenac	50mg tid
STO	6	236	3	diclofenac	50mg qd
STO	10	239	1	diclofenac	75mg (2)
STO	10	241	1	diclofenac	100mg (1)
STO	10	241	2	ibuprofen	400mg (3)
STO	10	242	1	diclofenac	50mg
STO	10	243	1	diclofenac	75mg (2)
STO	10	247	1	diclofenac	50mg 2x
STO	10	249	1	movalis	15mg
STO	10	250	1	diclofenac	75mg (2)
STO	10	251	1	flurbiprofen	200mg (2)
STO	10	251	2	ibalgin	400mg (3)
STO	12	255	1	diclofenac	75mg
STO	12	258	1	diclofenac	75mg
STO	12	259	1	ibuprofen	800mg
STO	12	259	2	meloxicam	15mg
STO	12	264	1	meloxicam	15mg
STO	12	265	1	piroxicamum	20mg
STO	12	266	1	ibuprofen	400mg
STO	12	268	1	meloxicam	15mg
STO	12	270	1	diclofenac	100mg
STO	12	272	1	diclofenac	150mg
STO	12	275	1	meloxicam	15mg
STO	12	276	1	diclofenac	150mg
STO	12	278	1	diclofenac	100mg
STO	6	281	1	meloxicam	15mg qd
STO	6	281	2	meloxicam	10mg qd
STO	6	281	3	meloxicam	15mg qd
STO	6	281	4	diclofenac	50mg qd
STO	6	282	1	diclofenac	50mg bid
STO	6	282	2	diclofenac	50mg bid
STO	6	282	3	diclofenac	50mg bid
STO	6	283	1	diclofenac	50mg bid

Treatment group	Centre number	Pat. Nr.	NSAID treatment number	Name of Treament (generic name) (V1)	Dosage and units (V1)
STO	6	283	2	diclofenac	50mg qd
STO	6	286	1	diclofenac	100mg qd
STO	6	286	2	nimesulide	100mg bid
STO	6	289	1	piroxicam	20mg
STO	6	290	1	diclofenac	50mg bid
STO	6	293	1	diclofenac	100mg/day as need
STO	6	294	1	diclofenacum	100mg/day
STO	6	294	2	diclofenacum	100mg/day
STO	6	294	3	diclofenacum	100mg/day
STO	6	295	1	ketoprofenum	200mg/day
STO	6	295	2	ketoprofenum	200mg/day
STO	6	295	3	ketoprofenum	200mg/day
STO	4	298	1	meloxicam	15mg
STO	4	298	2	ketoprofenum	200mg
STO	4	298	3	nimesulid	200mg
STO	4	299	1	ketoprofenum	200mg
STO	4	299	2	ketoprofenum	200mg
STO	4	299	3	ketoprofenum	150mg
STO	4	299	4	ketoprofenum	150mg
STO	4	300	1	nimesulide	200mg
STO	4	300	2	nimesulide	200mg

3. Compliance (only for patients from Group PAST)

3.1 Visit 2

	Treatment group		
Visit 2	PAST (N=150)	STO (N=150)	Total (N=300)
COMPLIANCE: (V2)			
Missing	5	150	155
N	145	0	145
Mean (±SD)	99.0 (±7.0)	NA (±NA)	99.0 (±7.0)
Median	100.0	NA	100.0
Q1-Q3	[100.0;100.0]	[NA ; NA]	[100.0;100.0]
Min-Max	[31.0;115.0]	[NA ; NA]	[31.0;115.0]
Assessment of compliance (V2) - N (%)			
Missing	6	150	156
Excellent: Difference +/- 10%	137 (95.1%)	0 (0.0%)	137 (95.1%)
Very good: Difference +/- 20%	5 (3.5%)	0 (0.0%)	5 (3.5%)
Good: Difference +/- 30%	1 (0.7%)	0 (0.0%)	1 (0.7%)
Poor: Difference equal or higher than 40%	1 (0.7%)	0 (0.0%)	1 (0.7%)
Total	144	0	144

3.2 Visit 3

	Treatment group		
Visit 3	PAST (N=150)	STO (N=150)	Total (N=300)
COMPLIANCE: (V3)			
Missing	8	150	158
N	142	0	142
Mean (±SD)	100.4 (±6.7)	NA (±NA)	100.4 (±6.7)
Median	100.0	NA	100.0
Q1-Q3	[100.0;100.0]	[NA ; NA]	[100.0;100.0]
Min-Max	[66.6;137.8]	[NA ; NA]	[66.6;137.8]
Assessment of compliance (V3) - N (%)			
Missing	9	150	159
Excellent: Difference +/- 10%	135 (95.7%)	0 (0.0%)	135 (95.7%)
Very good: Difference +/- 20%	1 (0.7%)	0 (0.0%)	1 (0.7%)
Good: Difference +/- 30%	3 (2.1%)	0 (0.0%)	3 (2.1%)
Medium: Difference +/- 40%	2 (1.4%)	0 (0.0%)	2 (1.4%)
Total	141	0	141

3.3 Visit 4

	Treatment group		
Visit 4	PAST (N=150)	STO (N=150)	Total (N=300)
COMPLIANCE: (V4)			
Missing	7	150	157
N	143	0	143
Mean (±SD)	99.8 (±4.5)	NA (±NA)	99.8 (±4.5)
Median	100.0	NA	100.0
Q1-Q3	[100.0;100.0]	[NA ; NA]	[100.0;100.0]
Min-Max	[68.0;136.0]	[NA ; NA]	[68.0;136.0]
Assessment of compliance (V4) - N (%)			
Missing	7	150	157
Excellent: Difference +/- 10%	139 (97.2%)	0 (0.0%)	139 (97.2%)
Very good: Difference +/- 20%	2 (1.4%)	0 (0.0%)	2 (1.4%)
Good: Difference +/- 30%	1 (0.7%)	0 (0.0%)	1 (0.7%)
Medium: Difference +/- 40%	1 (0.7%)	0 (0.0%)	1 (0.7%)
Total	143	0	143

3.4 Visit 5

	Treatment group		
Visit 5	PAST (N=150)	STO (N=150)	Total (N=300)
COMPLIANCE: (V5)			
Missing	4	150	154
N	146	0	146
Mean (±SD)	99.9 (±5.4)	NA (±NA)	99.9 (±5.4)
Median	100.0	NA	100.0
Q1-Q3	[100.0;100.0]	[NA ; NA]	[100.0;100.0]
Min-Max	[63.0;131.0]	[NA ; NA]	[63.0;131.0]
Assessment of compliance (V5) - N (%)			
Missing	4	150	154
Excellent: Difference +/- 10%	142 (97.3%)	0 (0.0%)	142 (97.3%)
Very good: Difference +/- 20%	1 (0.7%)	0 (0.0%)	1 (0.7%)
Medium: Difference +/- 40%	2 (1.4%)	0 (0.0%)	2 (1.4%)
Poor: Difference equal or higher than 40%	1 (0.7%)	0 (0.0%)	1 (0.7%)
Total	146	0	146

4. Primary Efficacy Criterion: number of patients which do not require NSAIDs from the beginning of the second visit V2

4.1 Patients who did not take NSAIDs between V1 and V2

Patients who did not take NSAIDs between V1 and V2	PAST (N=150)	STO (N=150)	Difference PAST vs. STO (Patients who took NSAIDs = No)
Did the patient take NSAIDs? (V2) - N (%) - [95% CI] (binomial law)			
Missing	1	0	
Yes	125 (83.89%) [76.99%;89.40%]	148 (98.67%) [95.27%;99.84%]	
No	24 (16.11%) [10.60%;23.01%]	2 (1.33%) [0.16%;4.73%]	
Total	149	150	
Difference PAST vs. STO (Patients who took NSAIDs = No)			
Estimation for the difference in proportions			14.77%
95% CI (asymptotic)			[8.59%;20.96%]
p-value			p<.0001

If the 95% LCL is strictly greater than 0%, superiority of PAST can be concluded

4.2 Patients who did not take NSAIDs between V2 and V3

Patients who did not take NSAIDs between V2 and V3	PAST (N=150)	STO (N=150)	Difference PAST vs. STO (Patients who took NSAIDs = No)
Did the patient take NSAIDs? (V3) - N (%) - [95% CI] (binomial law)			
Missing	7	0	
Yes	118 (82.52%) [75.28%;88.36%]	143 (95.33%) [90.62%;98.10%]	
No	25 (17.48%) [11.64%;24.72%]	7 (4.67%) [1.90%;9.38%]	
Total	143	150	
Difference PAST vs. STO (Patients who took NSAIDs = No)			
Estimation for the difference in proportions			12.82%
95% CI (asymptotic)			[5.73%;19.9%]
p-value			p<.0001

If the 95% LCL is strictly greater than 0%, superiority of PAST can be concluded

4.3 Patients who did not take NSAIDs between V3 and V4

Patients who did not take NSAIDs between V3 and V4	PAST (N=150)	STO (N=150)	Difference PAST vs. STO (Patients who took NSAIDs = No)
Did the patient take NSAIDs? (V4) - N (%) - [95% CI] (binomial law)			
Missing	7	2	
Yes	101 (70.63%) [62.44%;77.94%]	141 (95.27%) [90.50%;98.08%]	
No	42 (29.37%) [22.06%;37.56%]	7 (4.73%) [1.92%;9.50%]	
Total	143	148	
Difference PAST vs. STO (Patients who took NSAIDs = No)			
Estimation for the difference in proportions			24.64%
95% CI (asymptotic)			[16.43%;32.85%]
p-value			p<.0001

If the 95% LCL is strictly greater than 0%, superiority of PAST can be concluded

4.4 Patients who did not take NSAIDs between V4 and V5

Patients who did not take NSAIDs between V4 and V5	PAST (N=150)	STO (N=150)	Difference PAST vs. STO (Patients who took NSAIDs = No)
Did the patient take NSAIDs? (V5) - N (%) - [95% CI] (binomial law)			
Missing	3	2	
Yes	95 (64.63%) [56.32%;72.33%]	137 (92.57%) [87.09%;96.23%]	
No	52 (35.37%) [27.67%;43.68%]	11 (7.43%) [3.77%;12.91%]	
Total	147	148	
Difference PAST vs. STO (Patients who took NSAIDs = No)			
Estimation for the difference in proportions			27.94%
95% CI (asymptotic)			[19.13%;36.75%]
p-value			p<.0001

If the 95% LCL is strictly greater than 0%, superiority of PAST can be concluded

5. Secondary Efficacy Criteria

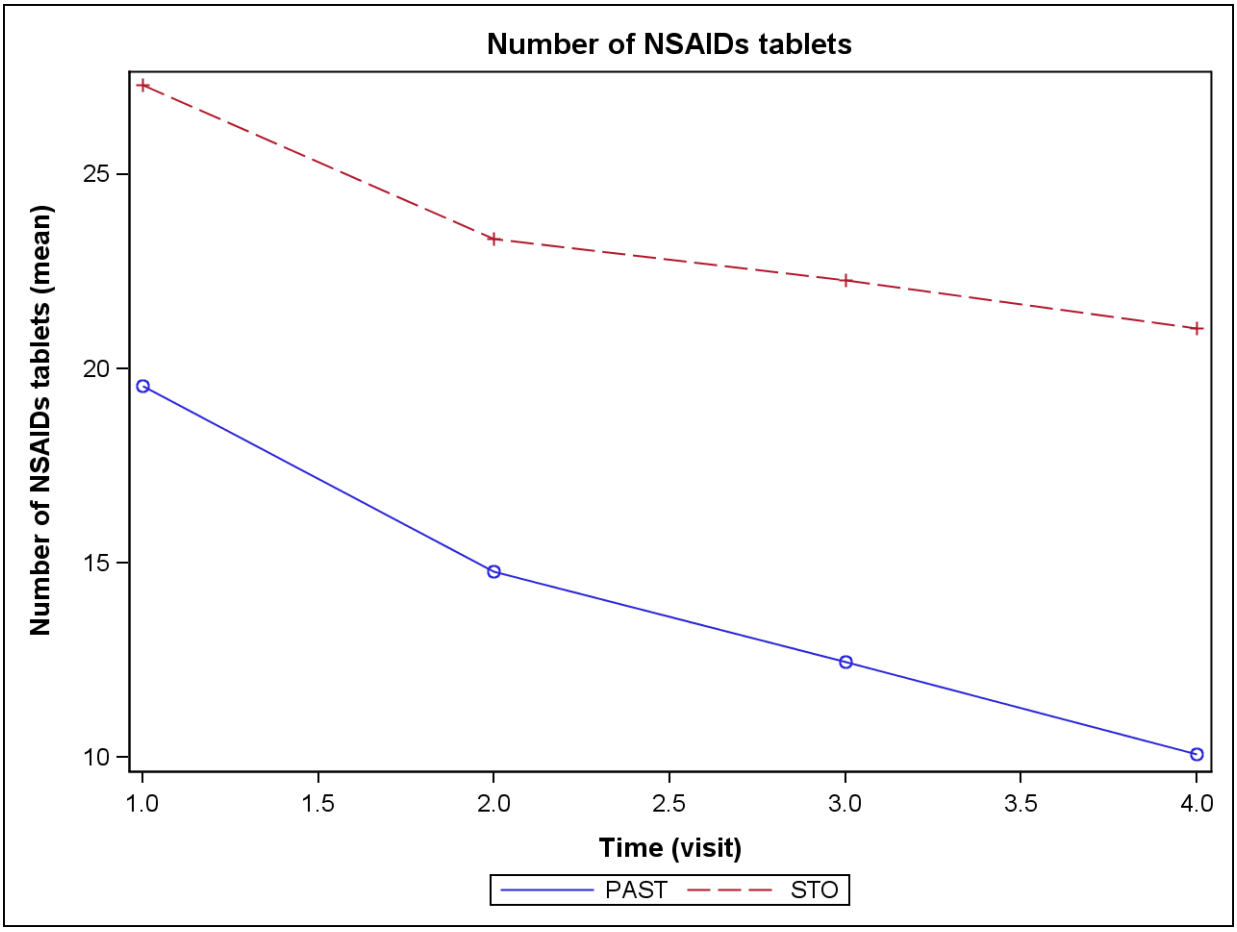
5.1 Rescue Medication: NSAIDs

5.1.1 Number of NSAIDs tablets

	Treatment group		
Number of NSAIDs tablets	PAST (N=150)	STO (N=150)	Total (N=300)
If yes, how many tablets? (count from Patient Diary) (V2)			
Missing	0	0	0
N	125	148	273
Mean (±SD)	21.7 (±17.6)	27.5 (±14.6)	24.9 (±16.3)
95% CI	[18.6;24.9]	[25.1;29.9]	[22.9;26.8]
Median	17.0	25.0	20.0
Q1-Q3	[10.0;25.0]	[18.0;35.0]	[14.0;30.0]
Min-Max	[2.0;105.0]	[5.0;91.0]	[2.0;105.0]
If yes, how many tablets? (count from Patient Diary) (V3)			
Missing	0	1	1
N	118	142	260
Mean (±SD)	16.5 (±15.2)	24.0 (±15.7)	20.6 (±15.9)
95% CI	[13.8;19.3]	[21.4;26.6]	[18.7;22.5]
Median	12.0	20.0	16.5
Q1-Q3	[8.0;20.0]	[14.0;30.0]	[10.0;26.0]
Min-Max	[1.0;93.0]	[6.0;144.0]	[1.0;144.0]
If yes, how many tablets? (count from Patient Diary) (V4)			
Missing	1	1	2
N	100	140	240
Mean (±SD)	14.9 (±14.9)	22.9 (±18.2)	19.6 (±17.3)
95% CI	[12.0;17.9]	[19.9;26.0]	[17.4;21.8]
Median	10.0	18.0	15.0
Q1-Q3	[6.0;17.5]	[12.0;28.0]	[10.0;24.0]
Min-Max	[0.0;90.0]	[4.0;138.0]	[0.0;138.0]
If yes, how many tablets? (count from Patient Diary) (V5)			
Missing	1	0	1
N	94	137	231
Mean (±SD)	12.3 (±13.4)	21.6 (±16.6)	17.9 (±16.0)
95% CI	[9.6;15.1]	[18.8;24.4]	[15.8;19.9]
Median	7.0	16.0	14.0
Q1-Q3	[5.0;16.0]	[10.0;28.0]	[8.0;22.0]
Min-Max	[1.0;92.0]	[3.0;130.0]	[1.0;130.0]

Number of NSAIDs tablets	PAST vs. STO between V1 and V2	PAST vs. STO between V2 and V3	PAST vs. STO between V3 and V4	PAST vs. STO between V4 and V5
ANOVA with repeated measures - Difference PAST vs. STO between each visit				
Mean (±SD)	-7.76(±1.89)	-8.57(±1.92)	-9.83(±1.98)	-10.94(±2.01)
95% CI	[-11.46;-4.05]	[-12.34;-4.80]	[-13.71;-5.94]	[-14.89;-6.99]
p-value	p<.0001	p<.0001	p<.0001	p<.0001

5.1.1.1 Figure: Number of NSAIDs tablets (mean values)



5.2 Rescue Medication: Paracetamol

5.2.1 Patients who did not take Paracetamol between each visit

5.2.1.1 Patients who did not take Paracetamol between V1 and V2

Patients who did not take Paracetamol between V1 and V2	PAST (N=150)	STO (N=150)	Difference PAST vs. STO (Patients who took Paracetamol = No)
Did the patient take Paracetamol (or equivalent) ? (V2) - N (%) - [95% CI] (binomial law)			
Missing	1	0	
Yes	74 (49.66%) [41.38%;57.96%]	97 (64.67%) [56.45%;72.29%]	
No	75 (50.34%) [42.04%;58.62%]	53 (35.33%) [27.71%;43.55%]	
Total	149	150	
Difference PAST vs. STO (Patients who took Paracetamol = No)			
Estimation for the difference in proportions			15%
95% CI (asymptotic)			[3.91%;26.09%]
p-value			p<.0001

If the 95% LCL is strictly greater than 0%, superiority of PAST can be concluded

5.2.1.2 Patients who did not take Paracetamol between V2 and V3

Patients who did not take Paracetamol between V2 and V3	PAST (N=150)	STO (N=150)	Difference PAST vs. STO (Patients who took Paracetamol = No)
Did the patient take Paracetamol (or equivalent) ? (V3) - N (%) - [95% CI] (binomial law)			
Missing	7	0	
Yes	54 (37.76%) [29.80%;46.25%]	86 (57.33%) [49.01%;65.36%]	
No	89 (62.24%) [53.75%;70.20%]	64 (42.67%) [34.64%;50.99%]	
Total	143	150	
Difference PAST vs. STO (Patients who took Paracetamol = No)			
Estimation for the difference in proportions			19.57%
95% CI (asymptotic)			[8.36%;30.79%]
p-value			p<.0001

If the 95% LCL is strictly greater than 0%, superiority of PAST can be concluded

5.2.1.3 Patients who did not take Paracetamol between V3 and V4

Patients who did not take Paracetamol between V3 and V4	PAST (N=150)	STO (N=150)	Difference PAST vs. STO (Patients who took Paracetamol = No)
Did the patient take Paracetamol (or equivalent) ? (V4) - N (%) - [95% CI] (binomial law)			
Missing	7	2	
Yes	54 (37.76%) [29.80%;46.25%]	89 (60.14%) [51.77%;68.08%]	
No	89 (62.24%) [53.75%;70.20%]	59 (39.86%) [31.92%;48.23%]	
Total	143	148	
Difference PAST vs. STO (Patients who took Paracetamol = No)			
Estimation for the difference in proportions			22.37%
95% CI (asymptotic)			[11.18%;33.57%]
p-value			p<.0001

If the 95% LCL is strictly greater than 0%, superiority of PAST can be concluded

5.2.1.4 Patients who did not take Paracetamol between V4 and V5

Patients who did not take Paracetamol between V4 and V5	PAST (N=150)	STO (N=150)	Difference PAST vs. STO (Patients who took Paracetamol = No)
Did the patient take Paracetamol (or equivalent) ? (V5) - N (%) - [95% CI] (binomial law)			
Missing	3	2	
Yes	39 (26.53%) [19.60%;34.44%]	91 (61.49%) [53.14%;69.36%]	
No	108 (73.47%) [65.56%;80.40%]	57 (38.51%) [30.64%;46.86%]	
Total	147	148	
Difference PAST vs. STO (Patients who took Paracetamol = No)			
Estimation for the difference in proportions			34.96%
95% CI (asymptotic)			[24.35%;45.56%]
p-value			p<.0001

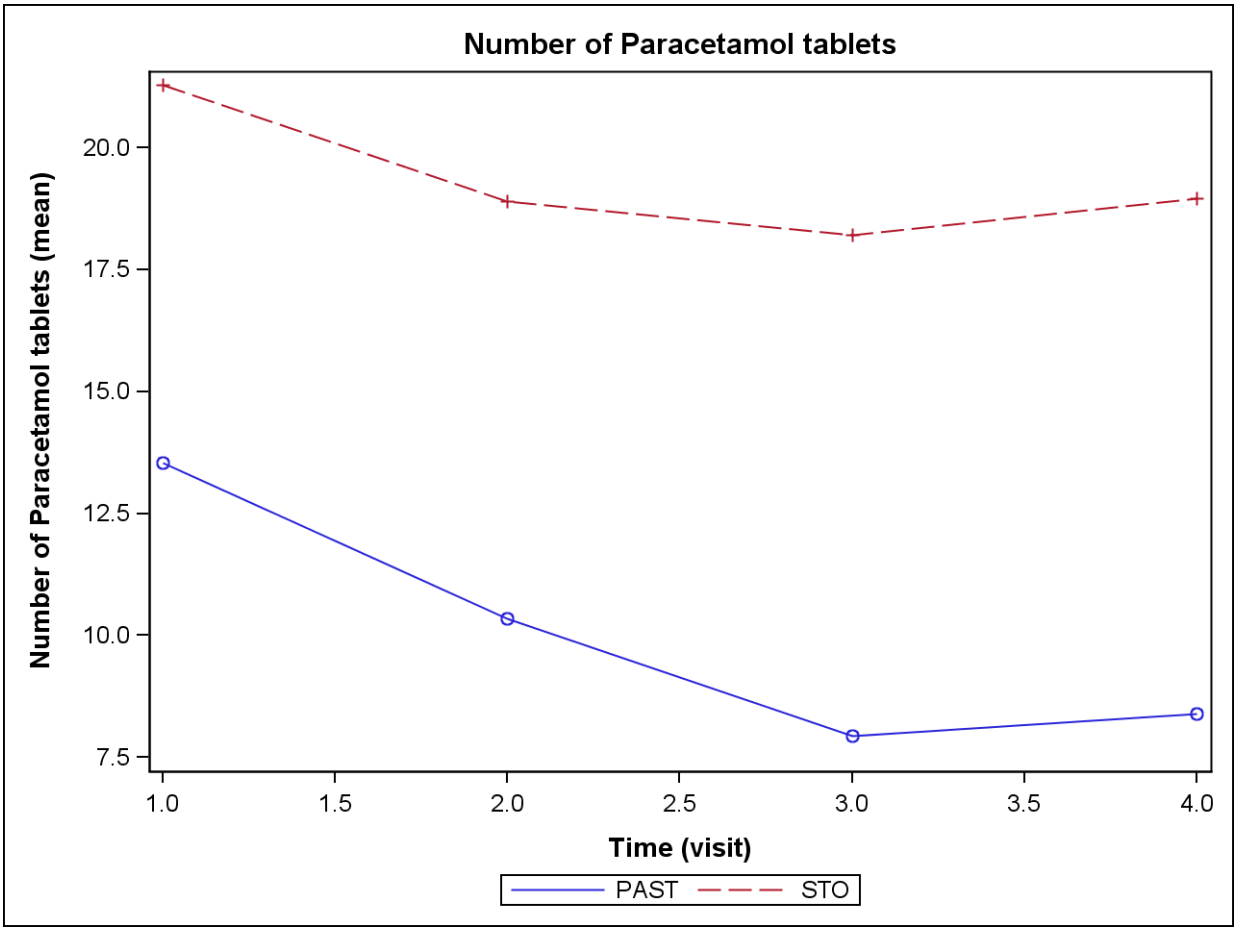
If the 95% LCL is strictly greater than 0%, superiority of PAST can be concluded

5.2.2 Number of Paracetamol tablets

	Treatment group		
Number of Paracetamol tablets	PAST (N=150)	STO (N=150)	Total (N=300)
If yes, how many tablets? (count from Patient Diary) (V2)			
Missing	0	0	0
N	74	97	171
Mean (±SD)	17.2 (±18.0)	25.5 (±20.0)	21.9 (±19.5)
95% CI	[13.0;21.4]	[21.4;29.5]	[18.9;24.8]
Median	11.5	20.0	16.0
Q1-Q3	[7.0;20.0]	[10.0;36.0]	[8.0;31.0]
Min-Max	[0.0;99.0]	[1.0;100.0]	[0.0;100.0]
If yes, how many tablets? (count from Patient Diary) (V3)			
Missing	0	0	0
N	54	86	140
Mean (±SD)	15.1 (±12.8)	23.7 (±18.0)	20.4 (±16.7)
95% CI	[11.6;18.6]	[19.9;27.6]	[17.6;23.2]
Median	12.5	19.5	15.0
Q1-Q3	[6.0;20.0]	[10.0;36.0]	[10.0;23.5]
Min-Max	[1.0;75.0]	[2.0;98.0]	[1.0;98.0]
If yes, how many tablets? (count from Patient Diary) (V4)			
Missing	0	0	0
N	54	89	143
Mean (±SD)	11.0 (±11.0)	22.5 (±20.8)	18.2 (±18.5)
95% CI	[8.0;14.0]	[18.1;26.9]	[15.1;21.2]
Median	7.0	15.0	11.0
Q1-Q3	[4.0;14.0]	[9.0;30.0]	[7.0;22.0]
Min-Max	[0.0;60.0]	[3.0;108.0]	[0.0;108.0]
If yes, how many tablets? (count from Patient Diary) (V5)			
Missing	0	0	0
N	39	91	130
Mean (±SD)	13.8 (±13.7)	21.9 (±22.7)	19.4 (±20.7)
95% CI	[9.3;18.2]	[17.1;26.6]	[15.8;23.0]
Median	8.0	14.0	12.0
Q1-Q3	[3.0;23.0]	[9.0;26.0]	[7.0;23.0]
Min-Max	[1.0;45.0]	[1.0;128.0]	[1.0;128.0]

Number of Paracetamol tablets	PAST vs. STO between V1 and V2	PAST vs. STO between V2 and V3	PAST vs. STO between V3 and V4	PAST vs. STO between V4 and V5
ANOVA with repeated measures - Difference PAST vs. STO between each visit				
Mean (±SD)	-7.75(±2.51)	-8.55(±2.68)	-10.28(±2.71)	-10.56(±2.87)
95% CI	[-12.69;-2.82]	[-13.81;-3.28]	[-15.60;-4.95]	[-16.20;-4.92]
p-value	p=0.0021	p=0.0015	p=0.0002	p=0.0003

5.2.2.1 Figure: Number of Paracetamol tablets (mean values)

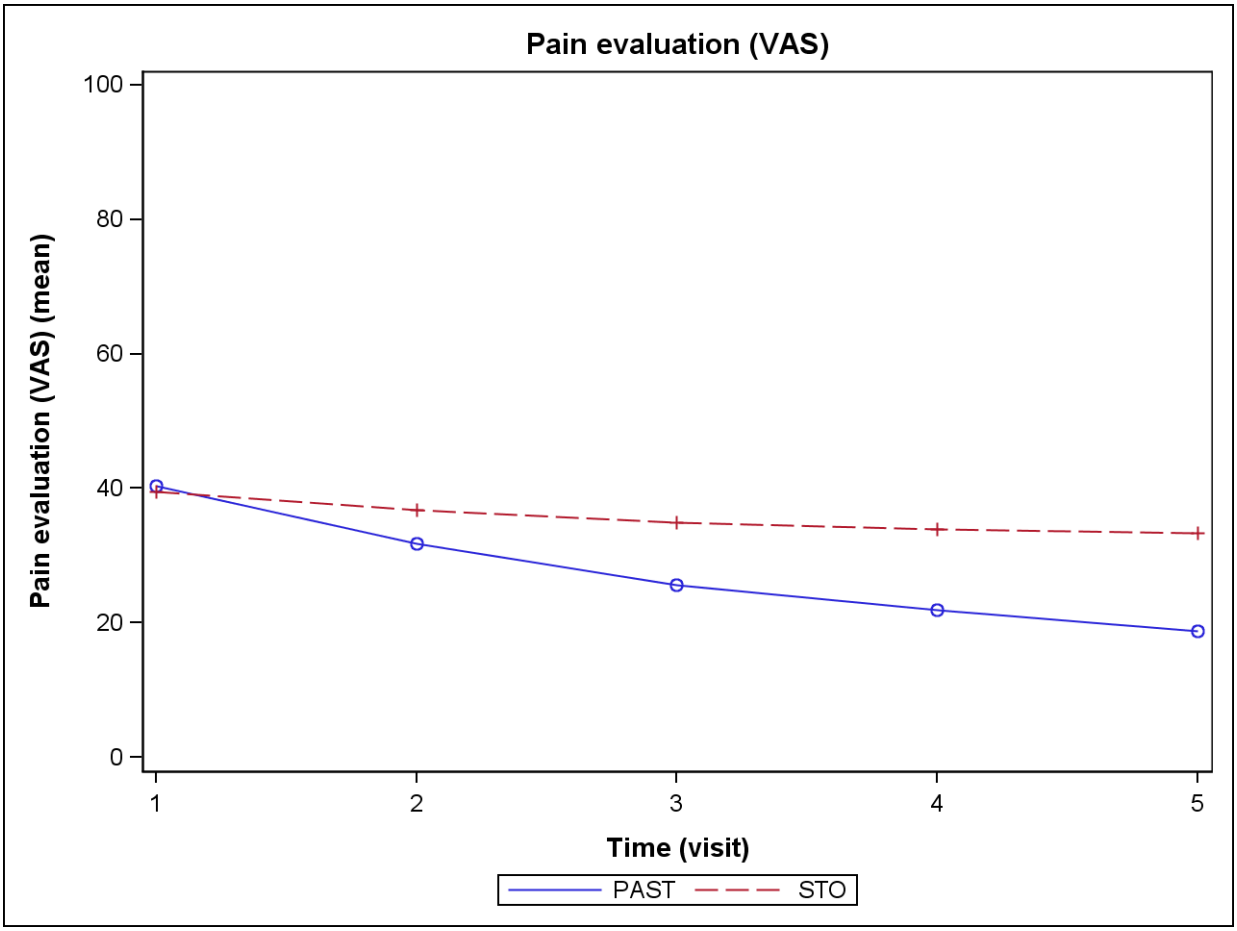


5.3 Pain evaluation (VAS)

	Treatment group		
Pain evaluation (VAS)	PAST (N=150)	STO (N=150)	Total (N=300)
VAS (V1)			
Missing	0	0	0
N	150	150	300
Mean (±SD)	40.3 (±7.0)	39.6 (±7.1)	39.9 (±7.1)
95% CI	[39.2;41.4]	[38.4;40.7]	[39.1;40.7]
Median	41.0	40.0	40.0
Q1-Q3	[34.0;47.0]	[34.0;45.0]	[34.0;47.0]
Min-Max	[25.0;50.0]	[23.0;50.0]	[23.0;50.0]
VAS (V2)			
Missing	1	0	1
N	149	150	299
Mean (±SD)	31.8 (±13.5)	36.8 (±12.0)	34.3 (±13.0)
95% CI	[29.7;34.0]	[34.9;38.8]	[32.9;35.8]
Median	31.0	38.0	35.0
Q1-Q3	[22.0;41.0]	[30.0;45.0]	[26.0;43.0]
Min-Max	[2.0;78.0]	[8.0;75.0]	[2.0;78.0]
VAS (V3)			
Missing	7	0	7
N	143	150	293
Mean (±SD)	25.7 (±13.9)	34.9 (±13.6)	30.4 (±14.5)
95% CI	[23.4;28.0]	[32.7;37.1]	[28.7;32.1]
Median	26.0	35.0	31.0
Q1-Q3	[14.0;38.0]	[27.0;45.0]	[20.0;41.0]
Min-Max	[0.0;60.0]	[6.0;83.0]	[0.0;83.0]
VAS (V4)			
Missing	7	2	9
N	143	148	291
Mean (±SD)	21.9 (±14.2)	33.9 (±14.6)	28.0 (±15.6)
95% CI	[19.5;24.2]	[31.5;36.3]	[26.2;29.8]
Median	20.0	33.5	28.0
Q1-Q3	[10.0;35.0]	[24.5;44.0]	[15.0;40.0]
Min-Max	[0.0;50.0]	[3.0;78.0]	[0.0;78.0]
VAS (V5)			
Missing	4	2	6
N	146	148	294
Mean (±SD)	18.8 (±15.2)	33.4 (±15.8)	26.1 (±17.1)
95% CI	[16.3;21.3]	[30.8;35.9]	[24.2;28.1]
Median	16.0	32.5	25.0
Q1-Q3	[5.0;31.0]	[22.0;45.0]	[12.0;40.0]
Min-Max	[0.0;52.0]	[0.0;75.0]	[0.0;75.0]

Pain evaluation (VAS)	PAST vs. STO at V1	PAST vs. STO at V2	PAST vs. STO at V3	PAST vs. STO at V4	PAST vs. STO at V5
ANOVA with repeated measures - Difference PAST vs. STO at each visit					
Mean (±SD)	0.75(±1.50)	-5.01(±1.51)	-9.20(±1.52)	-12.01(±1.53)	-14.56(±1.52)
95% CI	[-2.20;3.69]	[-7.96;-2.06]	[-12.18;-6.22]	[-15.00;-9.02]	[-17.53;-11.58]
p-value	p=0.6193	p=0.0009	p<.0001	p<.0001	p<.0001

5.3.1 Figure: Pain evaluation (VAS) (mean values)

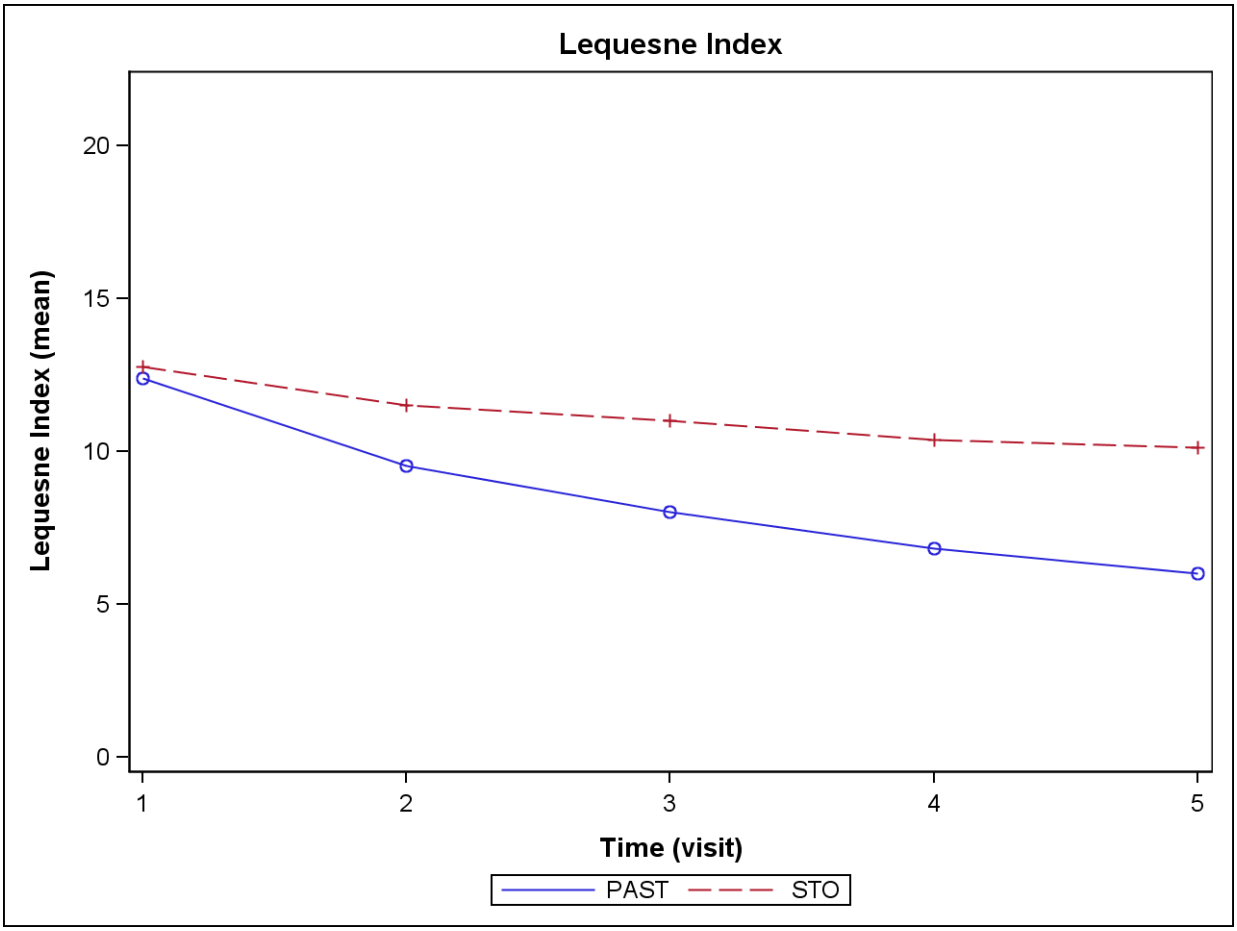


5.4 Lequesne Index

	Treatment group		
Lequesne Index	PAST (N=150)	STO (N=150)	Total (N=300)
Total index (V1)			
Missing	0	0	0
N	150	150	300
Mean (±SD)	12.4 (±3.9)	12.8 (±4.3)	12.6 (±4.1)
95% CI	[11.8;13.0]	[12.1;13.5]	[12.1;13.1]
Median	12.5	12.0	12.3
Q1-Q3	[9.5;15.5]	[9.0;17.0]	[9.5;16.0]
Min-Max	[5.0;21.0]	[5.5;22.0]	[5.0;22.0]
Total index (V2)			
Missing	1	0	1
N	149	150	299
Mean (±SD)	9.5 (±3.8)	11.5 (±4.0)	10.5 (±4.0)
95% CI	[8.9;10.1]	[10.9;12.2]	[10.1;11.0]
Median	9.0	11.5	10.0
Q1-Q3	[7.0;11.5]	[8.5;14.0]	[7.5;13.5]
Min-Max	[1.5;19.0]	[3.5;20.0]	[1.5;20.0]
Total index (V3)			
Missing	7	0	7
N	143	150	293
Mean (±SD)	8.0 (±3.8)	11.0 (±4.2)	9.6 (±4.3)
95% CI	[7.4;8.7]	[10.3;11.7]	[9.1;10.1]
Median	7.5	10.8	9.0
Q1-Q3	[5.5;10.0]	[8.0;14.0]	[6.5;13.0]
Min-Max	[0.5;19.0]	[2.0;21.5]	[0.5;21.5]
Total index (V4)			
Missing	7	2	9
N	143	148	291
Mean (±SD)	6.8 (±3.5)	10.4 (±4.3)	8.6 (±4.3)
95% CI	[6.3;7.4]	[9.7;11.1]	[8.1;9.1]
Median	6.5	10.0	8.0
Q1-Q3	[4.0;9.5]	[7.0;13.5]	[5.5;12.0]
Min-Max	[0.0;18.5]	[1.5;21.5]	[0.0;21.5]
Total index (V5)			
Missing	4	2	6
N	146	148	294
Mean (±SD)	6.0 (±3.6)	10.1 (±4.5)	8.1 (±4.6)
95% CI	[5.4;6.6]	[9.4;10.9]	[7.6;8.6]
Median	5.5	10.0	7.8
Q1-Q3	[3.0;8.0]	[7.0;13.5]	[5.0;11.0]
Min-Max	[0.0;16.5]	[0.5;21.5]	[0.0;21.5]

Lequesne Index	PAST vs. STO at V1	PAST vs. STO at V2	PAST vs. STO at V3	PAST vs. STO at V4	PAST vs. STO at V5
ANOVA with repeated measures - Difference PAST vs. STO at each visit					
Mean (±SD)	-0.38(±0.46)	-1.99(±0.46)	-2.98(±0.47)	-3.54(±0.47)	-4.10(±0.47)
95% CI	[-1.29;0.53]	[-2.90;-1.08]	[-3.90;-2.06]	[-4.47;-2.62]	[-5.02;-3.18]
p-value	p=0.4130	p<.0001	p<.0001	p<.0001	p<.0001

5.4.1 Figure: Lequesne Index (mean values)



5.5 Overall Efficacy

5.5.1 Investigator's Assessment

Investigator's Assessment		Treatment group PAST (N=150)		Treatment group STO (N=150)		Treatment group Total (N=300)	
Investigator assessment (V5) - N (%)							
Missing		4		2		6	
Excellent	Chi-square	84	(57.5%)	19	(12.8%)	103	(35.0%)
Good	p<.0001	55	(37.7%)	56	(37.8%)	111	(37.8%)
Average		4	(2.7%)	58	(39.2%)	62	(21.1%)
Poor		3	(2.1%)	15	(10.1%)	18	(6.1%)
Total		146		148		294	

5.5.2 Patient's Assessment

Patient's Assessment		Treatment group PAST (N=150)		Treatment group STO (N=150)		Treatment group Total (N=300)	
Patient assessment (V5) - N (%)							
Missing		4		2		6	
Excellent	Chi-square	85	(58.2%)	19	(12.8%)	104	(35.4%)
Good	p<.0001	49	(33.6%)	55	(37.2%)	104	(35.4%)
Average		8	(5.5%)	53	(35.8%)	61	(20.7%)
Poor		4	(2.7%)	21	(14.2%)	25	(8.5%)
Total		146		148		294	

5.6 Overall Tolerability

5.6.1 Investigator's Assessment

Investigator's Assessment		Treatment group PAST (N=150)		STO (N=150)		Total (N=300)	
Investigator assessment (V5) - N (%)							
Missing	Chi-square	4		2		6	
Excellent	not valid	129	(88.4%)	39	(26.4%)	168	(57.1%)
Good	Fisher	15	(10.3%)	81	(54.7%)	96	(32.7%)
Average	p<.0001	0	(0.0%)	27	(18.2%)	27	(9.2%)
Poor		2	(1.4%)	1	(0.7%)	3	(1.0%)
Total		146		148		294	

5.6.2 Patient's Assessment

Patient's Assessment		Treatment group PAST (N=150)		STO (N=150)		Total (N=300)	
Patient assessment (V5) - N (%)							
Missing	Chi-square	4		2		6	
Excellent	not valid	124	(84.9%)	38	(25.7%)	162	(55.1%)
Good	Fisher	20	(13.7%)	80	(54.1%)	100	(34.0%)
Average	p<.0001	0	(0.0%)	30	(20.3%)	30	(10.2%)
Poor		2	(1.4%)	0	(0.0%)	2	(0.7%)
Total		146		148		294	

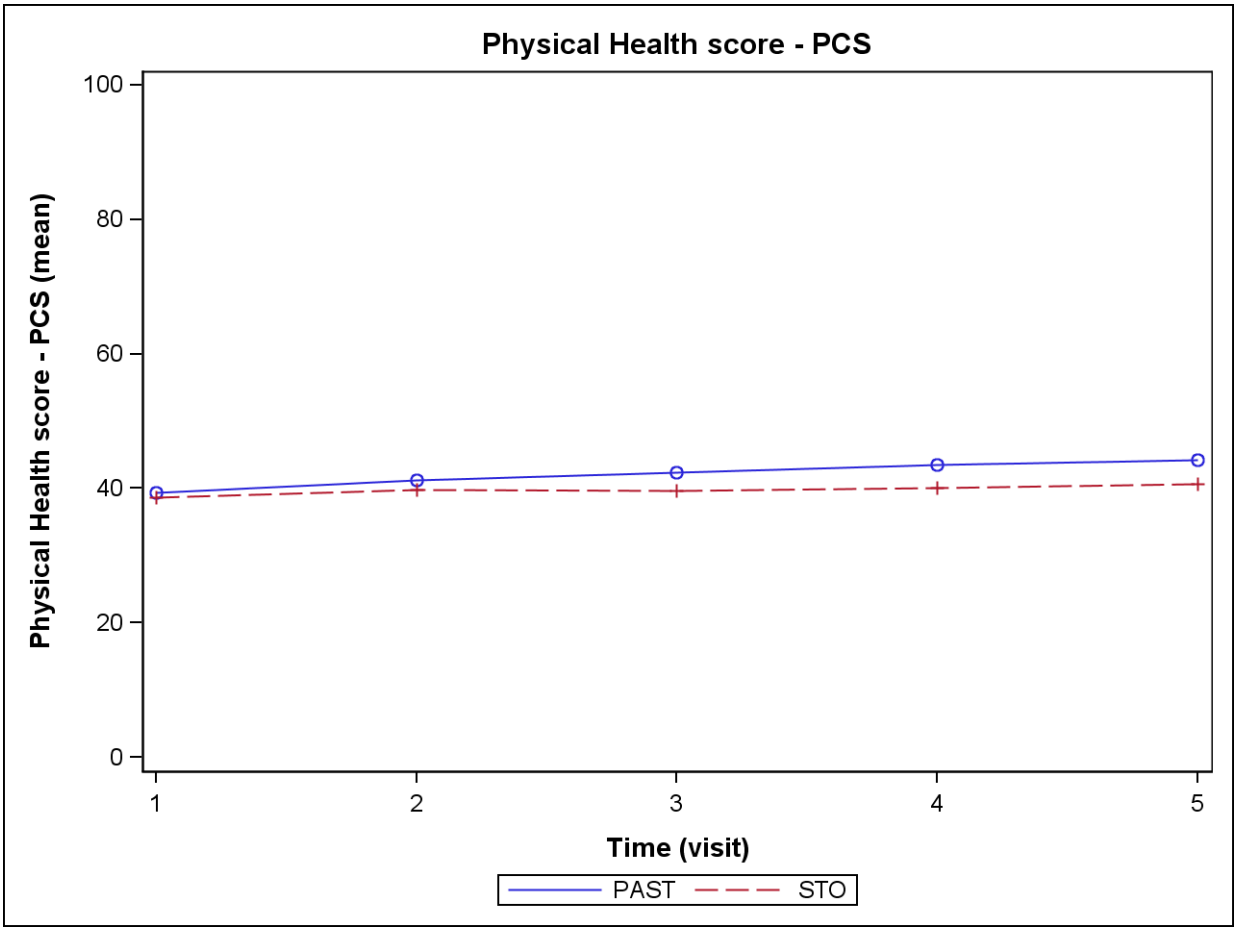
5.7 Quality-of-life SF12

5.7.1 Physical Health score - PCS

	Treatment group		
Physical Health score - PCS	PAST (N=150)	STO (N=150)	Total (N=300)
Norm-based standardization of Physical Health (PCS) V1			
Missing	0	0	0
N	150	150	300
Mean (±SD)	39.3 (±5.8)	38.7 (±6.3)	39.0 (±6.1)
95% CI	[38.4;40.3]	[37.7;39.7]	[38.3;39.7]
Median	38.6	38.5	38.5
Q1-Q3	[34.5;44.4]	[34.1;43.3]	[34.3;43.5]
Min-Max	[25.5;52.7]	[19.3;55.6]	[19.3;55.6]
Norm-based standardization of Physical Health (PCS) V2			
Missing	1	0	1
N	149	150	299
Mean (±SD)	41.2 (±5.5)	39.8 (±6.5)	40.5 (±6.1)
95% CI	[40.3;42.1]	[38.7;40.8]	[39.8;41.2]
Median	40.8	40.0	40.6
Q1-Q3	[37.9;45.1]	[36.4;43.7]	[37.1;44.6]
Min-Max	[25.6;52.6]	[18.1;56.4]	[18.1;56.4]
Norm-based standardization of Physical Health (PCS) V3			
Missing	7	0	7
N	143	150	293
Mean (±SD)	42.4 (±5.7)	39.6 (±6.5)	41.0 (±6.3)
95% CI	[41.5;43.3]	[38.6;40.7]	[40.3;41.7]
Median	42.3	40.4	41.1
Q1-Q3	[39.1;46.2]	[34.9;44.0]	[37.1;45.2]
Min-Max	[28.8;57.2]	[17.0;53.4]	[17.0;57.2]
Norm-based standardization of Physical Health (PCS) V4			
Missing	7	2	9
N	143	148	291
Mean (±SD)	43.5 (±6.1)	40.1 (±6.3)	41.8 (±6.4)
95% CI	[42.5;44.5]	[39.1;41.1]	[41.1;42.5]
Median	43.4	41.0	42.1
Q1-Q3	[40.1;48.0]	[36.4;43.8]	[38.4;46.3]
Min-Max	[28.1;63.0]	[19.3;53.2]	[19.3;63.0]
Norm-based standardization of Physical Health (PCS) V5			
Missing	4	2	6
N	146	148	294
Mean (±SD)	44.2 (±6.1)	40.6 (±5.9)	42.4 (±6.3)
95% CI	[43.2;45.2]	[39.6;41.5]	[41.7;43.1]
Median	45.0	41.3	42.8
Q1-Q3	[40.1;48.8]	[37.4;44.4]	[38.2;46.6]
Min-Max	[28.2;57.7]	[19.3;52.9]	[19.3;57.7]

Physical Health score - PCS	PAST vs. STO at V1	PAST vs. STO at V2	PAST vs. STO at V3	PAST vs. STO at V4	PAST vs. STO at V5
ANOVA with repeated measures - Difference PAST vs. STO at each visit					
Mean (±SD)	0.68(±0.70)	1.45(±0.70)	2.77(±0.71)	3.41(±0.71)	3.65(±0.71)
95% CI	[-0.70;2.06]	[0.07;2.83]	[1.37;4.16]	[2.02;4.81]	[2.26;5.04]
p-value	p=0.3323	p=0.0395	p=0.0001	p<.0001	p<.0001

5.7.1.1 Figure: Physical Health score - PCS (mean values)

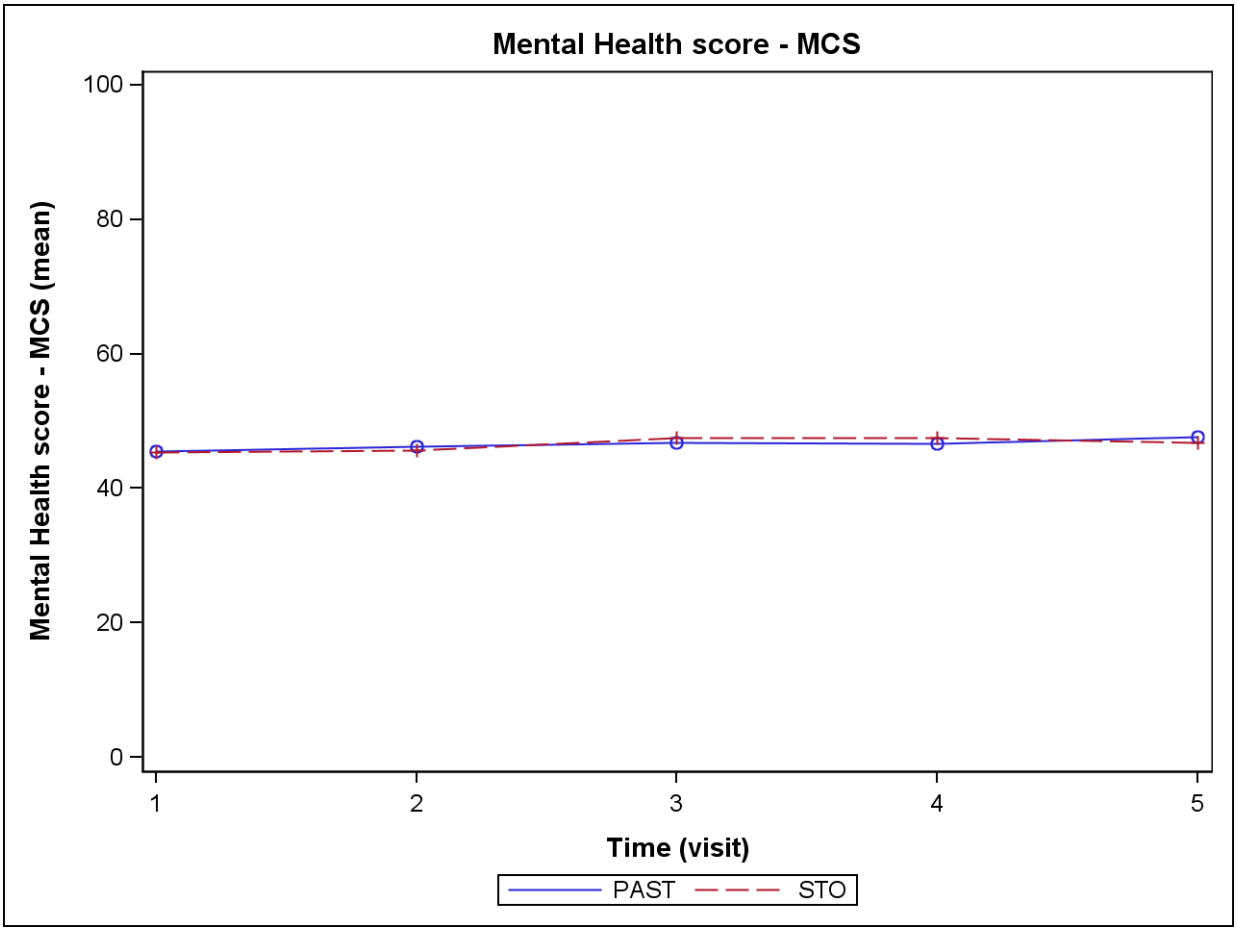


5.7.2 Mental Health score - MCS

	Treatment group		
Mental Health score - MCS	PAST (N=150)	STO (N=150)	Total (N=300)
Norm-based standardization of Mental Health (MCS) V1			
Missing	0	0	0
N	150	150	300
Mean (±SD)	45.5 (±7.0)	45.4 (±7.0)	45.5 (±7.0)
95% CI	[44.4;46.6]	[44.3;46.6]	[44.7;46.3]
Median	44.6	45.7	45.0
Q1-Q3	[40.1;51.4]	[39.9;50.7]	[40.0;51.1]
Min-Max	[26.1;61.0]	[26.3;62.2]	[26.1;62.2]
Norm-based standardization of Mental Health (MCS) V2			
Missing	1	0	1
N	149	150	299
Mean (±SD)	46.2 (±6.2)	45.6 (±7.1)	45.9 (±6.7)
95% CI	[45.2;47.2]	[44.5;46.8]	[45.2;46.7]
Median	47.5	45.7	46.5
Q1-Q3	[41.8;50.7]	[40.5;51.8]	[41.0;50.9]
Min-Max	[26.3;62.4]	[28.3;62.2]	[26.3;62.4]
Norm-based standardization of Mental Health (MCS) V3			
Missing	7	0	7
N	143	150	293
Mean (±SD)	46.8 (±5.7)	47.5 (±7.0)	47.1 (±6.4)
95% CI	[45.8;47.7]	[46.4;48.6]	[46.4;47.9]
Median	47.7	47.3	47.5
Q1-Q3	[43.8;50.6]	[43.0;52.5]	[43.4;51.2]
Min-Max	[29.6;62.1]	[26.3;64.5]	[26.3;64.5]
Norm-based standardization of Mental Health (MCS) V4			
Missing	7	2	9
N	143	148	291
Mean (±SD)	46.7 (±5.6)	47.5 (±6.7)	47.1 (±6.2)
95% CI	[45.8;47.6]	[46.4;48.6]	[46.4;47.8]
Median	47.7	47.9	47.9
Q1-Q3	[43.0;51.0]	[43.5;52.6]	[43.0;51.5]
Min-Max	[28.7;62.1]	[26.3;60.7]	[26.3;62.1]
Norm-based standardization of Mental Health (MCS) V5			
Missing	4	2	6
N	146	148	294
Mean (±SD)	47.7 (±6.0)	46.7 (±7.0)	47.2 (±6.5)
95% CI	[46.7;48.6]	[45.6;47.9]	[46.4;47.9]
Median	48.3	46.6	47.5
Q1-Q3	[43.9;52.0]	[42.0;52.1]	[42.8;52.0]
Min-Max	[19.9;66.9]	[27.1;62.0]	[19.9;66.9]

Mental Health score - MCS	PAST vs. STO at V1	PAST vs. STO at V2	PAST vs. STO at V3	PAST vs. STO at V4	PAST vs. STO at V5
ANOVA with repeated measures - Difference PAST vs. STO at each visit					
Mean (±SD)	0.08(±0.76)	0.61(±0.76)	-0.74(±0.77)	-0.79(±0.77)	0.92(±0.77)
95% CI	[-1.41;1.57]	[-0.88;2.10]	[-2.24;0.76]	[-2.30;0.72]	[-0.59;2.42]
p-value	p=0.9163	p=0.4231	p=0.3348	p=0.3052	p=0.2317

5.7.2.1 Figure: Mental Health score - MCS (mean values)



6. Post-Hoc Analysis

6.1 Patients and NSAIDs

	Treatment group		
Patients and NSAIDs	PAST (N=150)	STO (N=150)	Total (N=300)
NSAIDs taken between V2 and V5 - N (%) - [95% CI] (binomial law)			
Missing	7	2	9
No NSAIDs taken between V2 and V5	16 (11.2%) [6.5%;17.5%]	4 (2.7%) [0.7%;6.8%]	20 (6.9%) [4.2%;10.4%]
NSAIDs taken once between V2 and V5	23 (16.1%) [10.5%;23.1%]	3 (2.0%) [0.4%;5.8%]	26 (8.9%) [5.9%;12.8%]
NSAIDs taken twice between V2 and V5	22 (15.4%) [9.9%;22.4%]	7 (4.7%) [1.9%;9.5%]	29 (10.0%) [6.8%;14.0%]
NSAIDs taken three times between V2 and V5	82 (57.3%) [48.8%;65.6%]	134 (90.5%) [84.6%;94.7%]	216 (74.2%) [68.8%;79.2%]
Total	143	148	291