# Osteoarthritis Double-Blind Placebo Controlled LifeWave Med Pain Relief Study

**Report on LifeWave Med pain relief 2-patch system**

| | |
|---|---|
| **Protocol number:** | **IW-MED2012-001** |
| **ANSM registration number:** | **2012-A00838-35** |
| **Investigational products:**<br>(Class I medical devices in contact with safe skin for less than 12 hours) | **1. LifeWave Med pain relief 2-patch system (IceWave)**<br>**2. Placebo 2-patch system** |
| **Forms:** | **Non-transdermal patches** |
| **Application:** | **Cutaneous application on both acupuncture points and special points to stimulate nerves** |
| **CRO:** | **DERMSCAN, PharmaScan**<br>Domaine Scientifique de la Doua – Bât. CEI 2<br>56 boulevard Niels Bohr<br>69623 VILLEURBANNE CEDEX<br>FRANCE |
| **Principal Investigator:** | **Dr Pierre Volckmann**<br>Clinique iris Marcy l'Etoile<br>271 rue des Sources - BP 22<br>69280 Marcy-l'Etoile |
| **Sponsor:** | **LIFEWAVE EUROPE**<br>Raheen Industrial Estate<br>ATHENRY, CO. GALWAY<br>IRELAND |
| **Date and report version number:** | **Final Version 1.0 of June 4, 2013** |



ISO 9001: 2008 certified, DERMSCAN is authorized as a clinical testing center by the French Ministry of Health and the ANSM and benefits from a governmental Research Tax Credit from the French Ministry of Research.

**PROTOCOL #:** IW-MED2012-001

**ANSM #:** 2012-A00838-35

**TITLE OF THE PROTOCOL:**

**Osteoarthritis Double-Blind Placebo Controlled LifeWave Med Pain Relief Study**

## SPONSOR SIGNATURES IN ACCORDANCE WITH THE REPORT

### SPONSOR

**Colman DILLON**
*General Manager*

Date _____ Signature _____

## CRO AND COORDINATING INVESTIGATOR SIGNATURES IN ACCORDANCE WITH THE REPORT

**Dr Pierre VOLCKMANN**
*Principal Investigator*

Dr Pierre VOLCKMANN
Directeur Médical
Médecine Physique et Réadaptation
N°69 11 3856 4 - FINESS 69 0803044
I.R.I.S.
BP 22 - 69230 SAINT MARCY L'ETOILE

June 4, 2013

Date _____ Signature _____

**Audrey NATALIZIO**
*Project manager*

June 4, 2013

Date _____ Signature _____

**Cédric JUNG**
*Biostatistician*

June 4, 2013

Date _____ Signature _____

## 2 SYNOPSIS

| | |
|---|---|
| **ANSM registration #:** | 2012-A00838-35 |
| **Study number:** | IW-MED2012-001 |
| **Protocol Title:** | **Osteoarthritis Double-Blind Placebo Controlled LifeWave Med Pain Relief Study** |
| **Sponsor:** | **LIFEWAVE EUROPE** |
| **Objectives:** | Main Objective:<br>The objective of this study was to evaluate, compared to placebo, patients with nociceptive pain experienced the reduction in pain within minutes of application of active LifeWave Med pain relief 2-patch system patches. |
| **Design:** | This was a multicentric, double-blind, placebo controlled study, in two parallel groups:<br>- LifeWave Med pain relief 2-patch system (IceWave)<br>- Placebo of 2-patch system |
| **Sample Size:** | Analyzed sample size: 100 subjects divided in two groups of 50 (one group with the active patches and the other group with placebo patches). |
| **Number of centers:** | 5 centers |
| **Inclusion criteria:** | a. Male or females<br>b. 30-70 years of age<br>c. Nociceptive pain<br>d. Absence of cognitive impairment<br>e. Absence of cutaneous pathology<br>f. Absence of hypoesthesia<br>g. Subjects must have a baseline EVA scale score of 50 mm or greater to be included (scale between 0 and 100 mm)<br>h. Subject, psychologically able to understand the study related information and to give a written informed consent.<br>i. Subject having given freely and expressly her informed consent.<br>j. Subject able to comply with protocol requirements, as defined in the protocol.<br>**k.** Subject affiliated to a health social security system. |
| **Exclusion criteria:** | a. Women who are pregnant or nursing a child (negative urinary pregnancy test at the inclusion for women able to procreate)<br>b. Allergy or sensitivity to medical adhesives<br>c. Any individual who does not meet the inclusion criteria<br>d. Subject who had been deprived of their freedom by administrative or legal decision or who is under guardianship.<br>**e.** Subject in an emergency situation. |
| **Investigational product :**<br>**Name / code:**<br>**Galenic form:** | LifeWave Med pain relief 2-patch system (IceWave)<br>Non- transdermal 2-patch system (Class I medical device) |
| **Placebo**<br>**Name / code:**<br>***Galenic form:*** | Placebo of 2-patch system<br>Non- transdermal 2-patch system (Class I medical device) |

| | |
|---|---|
| **Dosage:**<br>**Duration:**<br>**Administration route:** | NA<br>One application during one hour<br>Cutaneous application on acupuncture points (non-transdermal patches) |
| **Safety Parameters:** | Analysis of adverse events and adverse reactions. |
| **Efficacy Parameters:** | Subjective evaluation of pain with a 0-100 mm Scale EVA |
| **Study Procedures:** | Screening visit<br>+<br>Pain evaluation before patches application and 5 minutes, 15 minutes and 1 hour after patches application. |
| **Statistics:** | **Main objective analysis**<br><br>First line analysis:<br><br>To test whether the difference between both groups (product *vs* placebo for the 2-patch system) is at least greater than 15 millimeter, a one-tailed t-test (against value 15) for unpaired data was applied on each change from baseline $(ti\text{-}t0)_{with}$ i= t1h.<br><br>Second line analysis:<br><br>To test whether the difference between both groups (product *vs* placebo for the 2-patch system) is at least greater than 15 millimeter, a one-tailed t-test (against value 15) for unpaired data was applied on each change from baseline $(ti\text{-}t0)_{with}$ i= 5, 15 min<br><br>Comparison between both groups (product *vs* placebo for the 2-patch system).<br><br>• For each comparison on measurement of pain reduction using scale EVA, an ANOVA model for repeated measures was fitted to the raw data.<br><br>• A chi-squared test was used to compare at t5min, t15min and t1 hour, on the proportion of volunteers with a decrease of pain (evaluated with scale EVA) from baseline (t0). |
| **Study Duration:** | Beginning of study: December 2012<br>End of study: April 2013<br>Global duration of the study: 6 months<br>Study duration by subject: approximately 2 hours |

| | |
|---|---|
| **Results- Conclusion** | 5 minutes after patch application, IceWave patches induced a slight pain reduction, but which was equivalent to the one observed with placebo patches (about 10 mm decrease on the 0-100 mm EVA scale). 15 minutes and one hour after patch application, the pain continued to decrease with the active patches, whereas it stayed stable with the placebo patches. From 15 minutes of application, the difference between active and placebo patches was statistically significant. One hour after application, the difference of pain improvement between both products was the highest (41% of difference between both products, so about 28 mm on the EVA scale). Indeed, the active patches induced a 65% pain decrease (about 41 mm on the 0-100 mm EVA scale) *versus* only 23% of pain decrease with the placebo patches (about 13 mm on the 0-100 mm EVA scale). The primary end point has then been reached (difference of pain reduction of at least 15mm between active and placebo patches at t1hour) and the effect of active patches versus the placebo ones can be considered as clinically relevant. One hour after patch application, 94% of the subjects felt a pain improvement with the active patches, *versus* only 48% of the subjects with the placebo patches.<br><br>Moreover, the patches were very well tolerated as no adverse reaction was observed during one hour of contact with the skin.<br><br>The IceWave patches are non-transdermal patches that do not put any chemicals or drugs into the body. These patches are a new method of improving pain control by stimulating specific points on the body with a combination of pressure and infrared energy. This approach of pain control would allow avoiding the long term toxic effects of currently available pain medications. The safety and efficacy results obtained in this study show that IceWave patches could be a very interesting approach to pain control, without any secondary effects, allowing immediate and durable pain improvement. |
| **Date and report version number:** | Final Version 1.0 of June 4, 2013 |

## 3 TABLE OF CONTENTS

## LIST OF TABLES



## LIST OF FIGURES



## LIST OF GRAPHS

# 4 LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

| | |
|---|---|
| AE | Adverse Event |
| ANSM | Agence Nationale de Sécurité du Médicament et des produits de santé |
| CA | Competent Authority |
| C.N.I.L | Commission Nationale de l'Informatique et des Libertés |
| CRF | Case Report Form |
| CRA | Contract Research Associate |
| C.R.O | Contract Research Organization |
| C.S.P | Code de la Santé Publique |
| EC | Ethics Committee |
| EVA | Echelle Visuelle Analogique (Visual Analogical Scale) |
| FVFS | First Visit First Subject |
| GCP | Good Clinical Practice |
| I.C.H | International Conference on Harmonisation |
| ICF | Informed Consent Form |
| LVLS | Last Visit Last Subject |
| MD | Medical Device |
| MV | Missing Value |
| NA | Not Applicable |
| PAS | Systolic Arterial Pressure |
| PAD | Diastolic Arterial Pressure |
| SAE | Serious Adverse Event |
| SD | Standard Deviation |
| SEM | Standard Error on the Mean |

# 5 ETHICS

## 5.1 Independent Ethics Committee and Competent Authority

The protocol was reviewed and approved by an Independent Ethics Committee (Comité de Protection des Personnes [CPP]) of "Centre Léon Bérard – Sud Est IV- Lyon - France", on September 4, 2012 and was authorized by the french competent authority (ANSM) on July 27, 2012.
All modifications of the protocol asked by these authorities have obtained the agreement of the principal investigator and the sponsor before being submitted again for approbation.

## 5.2 Ethical conduct of the study

**Declaration of HELSINKI**[(1)]
The current revision of the Declaration of Helsinki is the accepted basis for clinical study ethics, and must be fully followed and respected by all engaged in research on human beings. Any exceptions must be justified and stated in the protocol. Independent insurance that subjects are protected can only be provided by an ethics committee and freely obtained informed consent.

**Good Clinical Practice**[(2)]
Good clinical practice is a standard for clinical studies, which encompasses the design, conduct, monitoring, termination, audit, analyses, reporting and documentation of the studies. It ensures the studies are ethically justified and scientifically sound, and that the clinical properties of the diagnostic/therapeutic/prophylactic product under investigation are properly documented.

**Ethics Committee and Competent Authority**[(3)]
It is the responsibility of the sponsor or its legal representative to submit a copy of the protocol and detailed patient information sheet and consent form to an ethics committee/institutional review board in order to obtain independent approval to conduct the study. Ethics committee/institutional review board approval must be obtained before the study is started. The approval of the ethics committee/institutional review board must be sent in writing, to the sponsor or its legal representative. The Ethics Committee approval letter must mention the Ethics Committee members and their function.
In parallel or after the Ethics Committee submission, the sponsor or its legal representative must address an authorization request to the French authorities.
Any clinical trial cannot been performed without having obtained the agreement of the Ethics Committee and the inherent authorization of the French authority in a regulatory delay of 60 days beginning at the reception of the file by the French authority.

**« Informatique et libertés » Law**[(4)]
The medical data collected close to the patients during the study, are saved in informatics files which are analysed for or by the sponsor in order to evaluate the benefit of the treatment.
These confidential data (each subject is assigned with an anonymous identification code) may be transmitted, if requested, to health authorities.
In accordance with the French law « informatique et libertés », the patient may have an access to his/her data and has the right to correct them close to the CRO, at any moment.

### 5.3 Subject information and consent form

It was the responsibility of the investigator(s) to obtain informed consent from each subject participating in the study, after explanation of the aims, methods, benefits and potential hazards of the study.
It was completely and unambiguously clear to each subject that she/he was free to refuse to participate in the study, or that she/he could withdraw her/his consent at any time and for any reason, without incurring any penalty or withholding of treatment on the part of the investigator.

The consent obtaining was done under such conditions that permit to the subject to consider in the best way the ratio benefits/ risks associated to his/her participation in the study.
The investigator insured that the content of the information and consent form was appropriate to the study and that the process for obtaining the consent was in conformity with the applicable regulation.

In the frame of this study, the consent has been obtained before any study-specific procedures were performed, and thus in accordance with the Helsinki declaration.
No subject could be included and/or randomized before having signed the consent form, written in an understandable language.

Each subject received oral and written information concerning the studied product(s), its nature, the duration and the conditions of the study. The consent was personally signed and dated by the subject in two exemplars and by the person in charge of the consent obtaining.
Each subject received an original of the information sheet and consent form, dated and signed. The second original of the signed and dated consent form was archived in the investigator file.

## 6 INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

The study was planned to be conducted in the following centers:

Center 1 :
CMPR Iris
271 rue des Sources - BP 22
69280 Marcy-l'Etoile/
25, rue André Lwoff
69800 Saint Priest/
63 bis rue Maryse Bastié
69008 Lyon

Center 2 :
CMPR du Bourget
7 rue Rigaud
93 350 Le Bourget

Center 3 :
CSSR Choisy
9 bis rue Ledru Rollin
94 600 Choisy-le-Roi

Center 4 :
CMPR Rosemond
61-67 avenue des Goumiers
13 008 Marseille

Center 5 :
CMPR Le Floride,
Avenue Thalassa
66421 Le Barcares

The list of the main participants in the study is presented in Appendix 16.1.4.

# 7 INTRODUCTION

## 7.1 Scientific background and rationale of the study

Pain, as defined by the International Association for the Study of Pain, is "an unpleasant sensory and emotional experience usually associated with actual or potential tissue damage, or described in terms of such damage". In 2001, the Joint Commission on Accreditation of Healthcare Organization (JCAHO) recommended pain as the fifth vital sign (in addition to patient's temperature, blood pressure, heart rate, and respiratory rate). In the medical, as well as Physical Medicine and Rehabilitation (PM&R) settings, pain is one of the most common reasons for patients seeking care. In North America, the estimated costs of chronic pain, including direct medical expenses, lost income, lost productivity, compensation payments, and legal charges, are approximately $90 billion a year [Tan, 2005].

It is clear from this brief description that pain is a significant problem worthy of study and that safe and effective treatment of pain can be beneficial for both the patient and society. Chronic musculoskeletal pain could consist of categories such as chronic low back pain, non-inflammatory arthritis (e.g., osteoarthritis), inflammatory arthritis (e.g., rheumatoid arthritis), fibromyalgia and myofacial pain syndrome. Chronic pain treatments include TENS, acupuncture, thermal therapies, lasers, and drugs such as antidepressants, NSAIDS, opioids, and other medications [Tan, 2005]. Therapies involving infrared heat, non-thermal infrared treatments with low energy lasers, acupuncture and electronic modalities, such as microcurrent devices, are all accepted treatments for musculoskeletal pain. Most people who have pain will typically choose either nonprescription analgesics or use prescribed medications for pain control. However, the long term use of nonprescription analgesic medications and prescribed anti-inflammatory drugs and narcotics will cause serious side effects in a significant number of people. The issue of long term toxic effects to all currently available pain medications makes investigation of nontoxic approaches a valuable pursuit. For medical personnel, the relief of pain is both a moral and professional responsibility. It has been shown in multiple double-blind-placebo-controlled clinical studies that LifeWave pain patches reduce pain and provide a thermoregulating effect to the body, promoting the parasympathetic nervous system activity.

The parasympathetic nervous system is one of the main divisions of the autonomic nervous system (ANS). The ANS, in turn, is the component of the nervous system that is responsible for balancing and regulating all of the internal organs and glands, which occurs unconsciously. The parasympathetic system specifically is responsible for controlling the processes of the body that occur when the body is at rest. Activating the parasympathetic nervous system has a cooling and relaxing effect which, in turn elicits the desirable physiological response helping with different physiological functions [Nazeran et al, 2005; Clark, 2005; Budzynski et al, 2008; Nazeran, 2007].

Previous studies have already shown a positive effect of IceWave patches on pain reduction using VAS. One study was conducted on 30 subjects with pain of different origins. Results of this study showed that a significant pain improvement was observed within minutes of patch application. However, this study was not placebo controlled. Another double-blind placebo-controlled clinical study on 60 subjects with knee pain was conducted with application of IceWave patches during 2 days. This study demonstrated that both active and placebo patches induced a pain improvement with an effect significantly more important with the active on the second day. However, no double-blind placebo controlled study evaluated the immediate effect of IceWave patches (in the first hour).

## 7.2 Identification and description of the experimental product(s)

The LifeWave Med pain relief 2-patch system patches are non-transdermal patches that do not put any chemicals or drugs into the body. These patches are a new method of improving pain control by stimulating either points on the skin or acupuncture points by reflecting specific wavelengths of visible and infrared light. In short, this is a new method of phototherapy.

**Acupressure Mechanism**
A textbook definition of acupuncture is the "stimulation of points and channels". The stimulation can be produced by various modalities including needling and or pressure (acupressure) (O'Connor, 1981).Evidence obtained from clinical trials in both acupuncture studies with needles and acupressure studies has determined that point location is important. For example, in studies of nausea using either needle acupuncture or acupressure of the acupoint known as Pericardium 6 (P6) have shown that stimulation of a nearby area has little effect on nausea and is primarily a placebo. Real P6 acupuncture or acupressure shows a consistent 60-70% response rate, whereas sham acupuncture or sham acupressure on a nearby area only a 25-30% response rate, consistent with it being primarily a placebo (Dundee et al., 1992; Bayreuther et al., 1994).

LifeWave Med pain relief 2-patch system patches are a safe and effective, new technology capable of gently stimulating acupuncture points without the use of needles. LifeWave Med's pain relief 2-patch system patches utilize this innovative technology to stimulate acupuncture points on the body for improving the flow of energy in the acupuncture meridians. The patches are designed to stimulate acupuncture points by several mechanisms that involve both acupressure and energetic principles. The self-adhesive patches utilize the principles of Oriental medicine and needleless acupuncture to gently stimulate points on the body that have been used to balance and improve the flow of energy in the human body for thousands of years. Because the patches are non transdermal, the use of these patches results in a natural way of improving the quality of life without any chemicals, drugs or stimulants or sedatives entering the body.

**Energetic Mechanism**
LifeWave Med pain relief 2-patch system patches reflect energy back into the body and do not have internal power sources that generate energy. The non-toxic materials in the patches act like frequency specific reflectors (narrow-band) as compared to the ceramic fibers found in infrared products, which are broadband reflectors. Placing a LifeWave patch on the skin will allow the patch to trap and passively absorb wide-band infrared energy and re-emit narrow-band infrared energy back into the body. By way of example, infrared wraps contain inorganic ceramic fibers. These inorganic fibers absorb infrared energy from the body and then re-emit the energy across a wide energy band. LifeWave patches contain materials, which mirror back the energy that the body is already emitting. The difference between the LifeWave Med pain relief 2-patch system patches and infrared products is that the LifeWave patches only mirror back a very narrow band of frequencies depending on the patch product selected. In summary, LifeWave patches are designed to deliver infrared wavelengths to enhance the electrical conductivity of the skin and are a new method of stimulating acupuncture points.

**Phototherapy**
Phototherapy is a scientifically proven light therapy that has been used for decades for benefits such as pain relief and reducing wrinkles. It refers to the stimulation of points on the skin through the use of light. The company has designed an entirely new patch technology around this method that is inexpensive and convenient to use. Our patches are composed of non-toxic organic crystals that are activated by body heat to reflect specific wavelengths of light that affect points on the body when applied to the skin.

# 8 STUDY OBJECTIVES

## 8.1 Primary objective

The objective of this study was to show that when compared to placebo, patients with nociceptive pain experienced a reduction in pain within minutes of application of active LifeWave Med pain relief 2-patch system patches.

## 8.2 Secondary objective(s)

Not applicable.

# 9 CONCEPTION OF THE STUDY

## 9.1 Methodology of the study

The study was:

- double-blind,
- randomized,
- in parallel groups,
- versus placebo
- multicentric,
- on patients with nociceptive pain.

## 9.2 Study flow chart

**Figure 1 - Study flow chart**

| Procedure | Screening/ Baseline | 5 min. post-application | 15 min. post-application | 1 hour post application |
|---|---|---|---|---|
| Informed Consent | X | | | |
| Medical examination, medical history, previous or concomitant medications | X | | | |
| Urinary pregnancy test | X | | | |
| Inclusion/Exclusion | X | | | |
| Randomization | X | | | |
| Subjective Pain Assessment | X | X | X | X |
| Safety Assessment | | | | X |
| Exit from Study | | | | X |

## 9.3 Description of the study schedule

- Patients presenting with nociceptive pain established qualification for inclusion and for establishment of the baseline pain measurement. The information was evaluated by the clinical investigators to determine the relevance and appropriateness of the participant. The study investigator obtained consent prior to participation and qualified the patient for participation based

on the patient meeting requirements of inclusion and exclusion criteria. A clinical examination was made and medical history and concomitant treatments were collected in the CRF. Qualified patients must have had pain level of at least 50 mm on a 0-100mm **Scale EVA.** For women able to procreate, urinary pregnancy test (payable by the Sponsor) must have been negative.

- Once subjects were screened, enrolled, and assigned to a treatment group in a random way. They were patched with LifeWave Med pain relief 2-patch system patches or corresponding placebo patches by the Investigator. All subjects were patched by the same trained person whatever the investigation site.

- Subjects were asked to remain close-by for the evaluations. The investigator worked with the subject to determine which locations were most effective. Once the final location was located and the patches were applied, as directed by the investigator, a stop watch recorded how long it took for the subject begin to experience pain relief. The final patch location was noted on the case report form, as well as how long it took, if prior to the first post-patch evaluation.

- Assessments of pain on Scale EVA were completed at 5 minutes, 15 minutes and 1 hour **starting after application of the patches in their final location.**

### 9.3.1 Inclusion criteria

- Male or females
- 30-70 years of age
- Nociceptive pain
- Absence of cognitive impairment
- Absence of cutaneous pathology
- Absence of hypoesthesia
- Subjects must have a baseline EVA scale score of 50 mm or greater to be included (scale from 0 to 100 mm)
- Subject, psychologically able to understand the study related information and to give a written informed consent.
- Subject having given freely and expressly her informed consent.
- Subject able to comply with protocol requirements, as defined in the protocol.
- Subject affiliated to a health social security system.

### 9.3.2 Exclusion criteria

- Women who are pregnant or nursing a child (negative urinary pregnancy test at the inclusion for women able to procreate).
- Allergy or sensitivity to medical adhesives
- Any individual who does not meet the inclusion criteria
- Subject who had been deprived of their freedom by administrative or legal decision or who is under guardianship.
- Subject in an emergency situation.

### 9.3.3 Withdrawal criteria

Any deviation to the protocol that can affect:
- the primary evaluation criterion,
- the adherence of the subjects to the study schedule,
- the adherence relative to the products use,
- the inclusion / exclusion criteria,

can be considered as an exclusion criterion. Before any exclusion of the subject from the study, each case will be discussed with the sponsor who will make the final decision if the subject must be excluded from the study.

### 9.3.4 Premature study exit

#### *9.3.4.1 Criteria and modalities of premature end of treatment or subject exclusion from the study*

Subjects were free to withdraw from the study at any time if they wish so and for any reason, without having to provide any justification to the investigator.
The investigator had the right to withdraw a subject for any reason, for subject's best interests, including illness or adverse events.
The sponsor may decide to withdraw subjects for major deviation to the protocol, for administrative reasons or for any other valuable reason ethically justified.

Subjects may discontinue the study for the following reasons:

1. *Subject consent withdrawal:* subjects had the right to exit from the study at any time and for any motive, without their right to treatment being affected.
2. *Medical reasons or adverse events:* the investigator had the right to withdraw a subject in case of intercurrent illness or adverse events or if in the investigator's opinion, continuation in the study would be detrimental to the subject's well-being.
3. *Appearance of an exclusion criterion.*
4. *Failure to follow-up:* if a subject did not come to the scheduled visits, several attempts had to be done to try to contact him/her; to obtain the reasons for non-attendance.
5. *Violations and deviations from the protocol.*
6. *Administrative reasons.*

#### *9.3.4.2 Modalities and calendar of recording data*

Withdrawal due to intercurrent disease or adverse event must be fully documented in the case report form and should include any available and/or appropriate complementary information.

In all cases, the reason for withdrawal was recorded in the case report form. The subject was followed up to state the reason for withdrawal and to establish whether the reason was an adverse event. Since the moment the investigator knew the early termination or exclusion, the withdrawal of the subject was formalized by a visit. If possible, all examinations scheduled for the final study day were to be performed on all subjects who received the investigational product but do not complete the study according to protocol.
The investigator should make every effort to contact subjects who dropped-out of the study early. In the case where no visit was possible, this withdrawal should be recorded by the investigator in the case report form and the source data documentation, and, if necessary, the registered letter with acknowledgement of receipt, to the subject. All the documentation concerning that subject should be as complete as possible.

#### *9.3.4.3 Modalities for the follow-up of these subjects*

When the premature exit was due to an adverse event, the subject must be followed until the resolution or the stabilization of the symptoms.

## 9.4 Treatment(s) administered

### 9.4.1 Authorized medication(s) and treatment(s)

Any concomitant medication at inclusion of the subject into the study must be reported in the study CRF at the initial visit and was taken into consideration by the Investigator deeming study eligibility.
Any modification on these medications during the study *must* be reported in the study CRF.
Use of any concomitant medication during the study was recorded in the CRF with the following information:

- Indication for use of the treatment;
- Name of the drug, type of formulation, and unit strength;
- Dose administered;
- Duration of treatment (start and stop date).

### 9.4.2 Prohibited Treatment(s) and Medication(s)

No antalgic medication was authorized during the study duration.
More generally, subjects were not allowed, during the study, to take any medication which might interfere with the performance or interpretation of the study end point evaluations specified in this protocol, unless the subject elects to withdraw from the study.
The data from subjects who repeatedly violate these medication restrictions were excluded from efficacy analysis.

### 9.4.3 Product(s) used but not studied

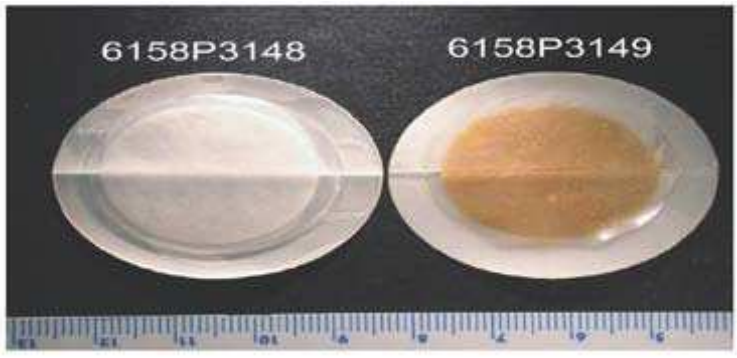
Not applicable.

## 9.5 Investigational products

### 9.5.1 Description of the investigational product(s)

#### *9.5.1.1 LifeWave Med pain relief 2-patch system (IceWave)*

Figure 1. Picture of LifeWave Med pain relief 2-patch system




Set of LifeWave Med pain relief 2-patch system consists of one white (positive polarity) and one dark (negative polarity).

LifeWave Med pain relief 2-patch system consists in two non-transdermal patches: one white (positive polarity) and one dark (negative polarity) (IceWave patches).

The LifeWave Med pain relief 2-patch system patches are disposable nontransdermal patches. The LifeWave patches contain a polyester pad, which is sealed within a polyethylene shell. The top side of

the patch is composed of water- resistant polyethylene film made by the 3M Corporation (Part No. A19-48G) that is sealed to the bottom portion that is composed of water-resistant single coated Medical-grade polyethylene tape also made by the 3M Corporation (Part No. 1525L). The bottom side of the Medical-grade polyethylene tape that attaches the IceWave patches to the body is coated with a hypoallergenic pressure sensitive Acrylate adhesive that allows the patch to adhere to the body. Because of the nature of construction none of the materials in the IceWave patches enter into the body making the LifeWave IceWave patches non-transdermal patches.

*9.5.1.2 Placebo of 2-patch system*

Both the white and dark placebo patches are constructed as follows : The top side of the patch is composed of water-resistant polyethylene film made by the 3M Corporation (Part No. A19-48G) that is sealed to the bottom portion that is composed of water-resistant single coated Medical-grade polyethylene tape also made by the 3M Corporation (Part No. 1525L). The bottom side of the Medical-grade polyethylene tape that attaches the patches to the body is coated with a hypoallergenic pressure sensitive Acrylate adhesive that allows the patch to adhere to the body. Placebo patches do not contain the polyester pad or any solution.

### 9.5.2 Dosage

Each patch system was in contact with the skin during one hour.

### 9.5.3 Instructions of use

*9.5.3.1 Administration route and recommendation(s)*

1. The LifeWave patches are removed from the package.
2. The liner is removed from the adhesive backing
3. The LifeWave patches are applied to the skin, using the medical grade adhesive side of the patch to secure patch placement. All patches were applied by the same trained person, whatever the investigation site.

**SCRIPT FOR PATCHING SUBJECTS AND DETERMINING BEST AND FINAL LOCATION:**

Tell the subject: "*This is an 'electrical method' of pain control so it can work very quickly in reducing pain if the patches are placed in a helpful location. I am going to move the patches around to different locations and I want you to tell me each time I move the patches if the pain has changed and by how much compared to before the patches were placed there*."

INVESTIGATOR: The ideal scenario is to remove the pain completely. If at any placement, the pain has completely subsided, remove the masking tape, remove the paper from the patches and affix to body. Record the EVA scale score.

You only have to <u>wait 20 seconds</u> to ask if the pain has changed, if the pain has not changed move to the next position.

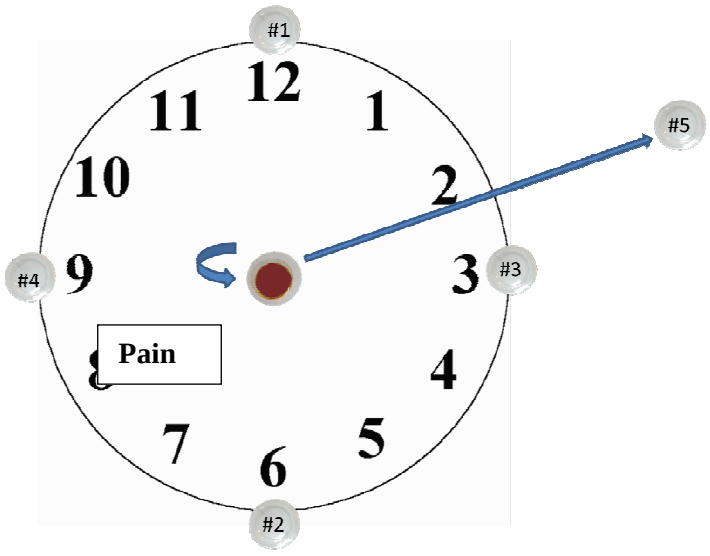
<u>The clock method</u>

First, have the person point with one finger to the location where the pain is most intense.
This will be considered the center of a clock and the dark patch will be placed on this location using a strip of medical tape to temporarily keep the dark patch in position.

1. For position #1 put the white patch, using a strip of medical tape, 2,5 to 5 cm above the dark patch at the 12 O'clock position. Ask the subject is there a decrease in pain? Investigator: Is the decrease at least 80% from baseline? If not, continue to next position. If yes, then note the

amount of decrease in pain, but continue to next position. If the pain is completely resolved take the backing off of the patches and apply the patches to the skin in the identified positions.

2. For position #2 leave the dark patch on the pain and only move the white patch using a strip of medical tape to the bottom of the clock at the 6 O'clock position. Ask the subject is there a decrease in pain? Investigator: Is the decrease at least 80% from baseline? If not, continue to next position. If yes, then note the amount of decrease in pain, but continue to next position. If the pain is completely resolved take the backing off of the patches and apply the patches to the skin in the identified positions.
3. For position #3 leave the dark patch on the pain and only move the white patch using a strip of medical tape to the right side of the clock at the 3 O'clock position. Ask the subject is there a decrease in pain? Investigator: Is the decrease at least 80% from baseline? If not, continue to next position. If yes, then note the amount of decrease in pain, but continue to next position. If the pain is completely resolved take the backing off of the patches and apply the patches to the skin in the identified positions.
4. For position #4 leave the dark patch on the pain and only move the white patch using a strip of medical tape to the left side of the clock at the 9 O'clock position. Ask the subject is there a decrease in pain? Investigator: Is the decrease at least 80% from baseline? If not, continue to next position. If yes, then note the amount of decrease in pain, but continue to next position. If the pain is completely resolved take the backing off of the patches and apply the patches to the skin in the identified positions.
5. For position #5 leave the dark patch on the pain and draw an imaginary line thru the body to the opposite side of the body and put the white patch there using a strip of medical tape. For instance if it is low back pain the line going thru the body would end up on the lower abdomen. If it is shoulder pain and the dark patch is on the back of the shoulder then only move the white patch to the front side of the shoulder. Ask the subject is there a decrease in pain? Investigator: Is the decrease at least 80% from baseline? If not, continue to next position. If yes, then note the amount of decrease in pain, but continue to next position. If the pain is completely resolved take the backing off of the patches and apply the patches to the skin in the identified positions.

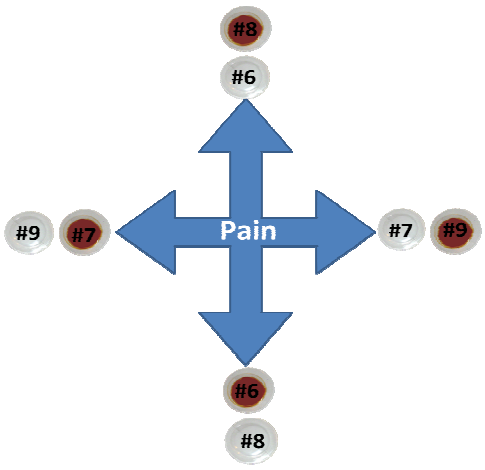



The bracketing method

6. For position #6 again have the person point with one finger to the location where the pain is most intense. Now you will try to "bracket " the pain, which for position #6 means you will put the patches above and below the pain. Place the white patch using a strip of medical tape 2.5 to 5 cm above the area of pain and the dark patch 2.5 to 5 cm below the area of pain. Ask the subject is there a decrease in pain? Investigator: Is the decrease at least 80% from baseline? If not, continue to next position. If yes, then note the amount of decrease in pain, but continue to next position. If

the pain is completely resolved take the backing off of the patches and apply the patches to the skin in the identified positions.

7. For position #7 again you will try to "bracket " the pain, which for position #7 means you will place the white patch using a strip of medical tape 2.5 to 5 cm to the right of the area of pain and the dark patch 2.5 to 5 cm to the left of the area of pain. Ask the subject is there a decrease in pain? Investigator: Is the decrease at least 80% from baseline? If not, continue to next position. If yes, then note the amount of decrease in pain, but continue to next position. If the pain is completely resolved take the backing off of the patches and apply the patches to the skin in the identified positions.
8. For position #8 again you will try to "bracket " the pain, which for position #8 means you will place the white patch using a strip of medical tape 2.5 to 5 cm below the area of pain and the dark patch 2.5 to 5 cm above the area of pain. Ask the subject is there a decrease in pain? Investigator: Is the decrease at least 80% from baseline? If not, continue to next position. If yes, then note the amount of decrease in pain, but continue to next position. If the pain is completely resolved take the backing off of the patches and apply the patches to the skin in the identified positions.
9. For position #9 again you will try to "bracket " the pain, which for position #9 means you will place the white patch using a strip of medical tape 2.5 to 5 cm to the left of the area of pain and the dark patch 2.5 to 5 cm to the right of the area of pain. Ask the subject is there a decrease in pain? Investigator: Is the decrease at least 80% from baseline? If not, continue to next position. If yes, then note the amount of decrease in pain, but continue to next position.. If the pain is completely resolved take the backing off of the patches and apply the patches to the skin in the identified positions. If the pain is not significantly reduced by at least 80% from baseline move to position #10.




Whole body method

10. For position #10 place a WHITE patch on the bottom of right foot using a strip of medical tape, and the dark patch on bottom of left foot (on the acupuncture position named Kidney 1). Ask the subject is there a decrease in pain? Investigator: Is the decrease at least 80% from baseline? If not, continue to next position. If yes, then note the amount of decrease in pain, but continue to next position. If the pain is completely resolved take the backing off of the patches and apply the patches to the skin in the identified positions. If pain has not been reduced in 20 seconds, go back to the location that felt like it had the most effect and affix there. Remove all adhesive and stick firmly to skin.

**11.** Position #11 (may not be applicable): If at any time the pain gets worse, switch the location of the patches. Move the white patch using a strip of medical tape to the location where the dark patch was placed and move the dark patch to the location where the white patch had been placed.

Then ask the subject is there any change in a decrease in pain? Investigator: Is the decrease at least 80% from baseline? If not, continue to next position. If yes, then note the amount of decrease in pain, but continue to next position. If the pain is completely resolved take the backing off of the patches and apply the patches to the skin in the identified positions.

If pain has not been reduced by at least 80% by any of the patch placements, then use the location that had the best effect as the final position. If there was no change at any patch placement use, Kidney 1 (soles of feet) as final position.

#### *9.5.3.2 Labelling*

Study articles were coded to distinguish between active and placebo, but the code was kept blind for the investigators until the code break is requested.

Example of labelling
The labelling of the products was realized by the Sponsor.

- Coordinating Investigator name: Dr. Pierre Volckmann
- Emergency phone number :
- Study number : **IW-MED2012-001**
- Product code :
- Batch number :
- Storage conditions :Store in a cool dark place away from x-ray machines and other diagnostic equipment.
- Expiration date : To use before…….
- Legal mention :For clinical trail only. To use under strict medical supervision. Keep out of reach of children

#### *9.5.3.3 Storage conditions*

Study articles were kept away from prolonged exposure to sunlight and extreme temperatures, kept out of reach of children and stored in a cool dark place away from x-ray machines and other diagnostic equipment.

#### *9.5.3.4 Dispensing and accountability of investigational product(s)*

The tested products were only be dispensed under the supervision of a physician approved for the study. The investigator was responsible for dispensing the study products to the subjects who were included in the study.

### 9.5.4 Treatments allocation – Randomisation - Blinding

Each product was allocated in a random way to each subject. The randomization list is presented in Appendix 16.1.9.

### 9.5.5 Follow-up of adherence to treatments use

The subject's participation in the study did not exceed 2 hours, so subject compliance was not expected to be an issue. Subjects were asked to remain on-site until after the one hour evaluation.

## 9.6 Evaluation variables

### 9.6.1 Evaluation criteria

#### *9.6.1.1 Main evaluation criterion*

Primary endpoint was measured by a minimum of 15 millimeter reduction on the EVA pain scale in the post-baseline pain assessments in the active patch groups when compared to the placebo treatment groups, after one hour of patches application.

#### *9.6.1.2 Secondary evaluation criteria*

Secondary endpoint was measured by

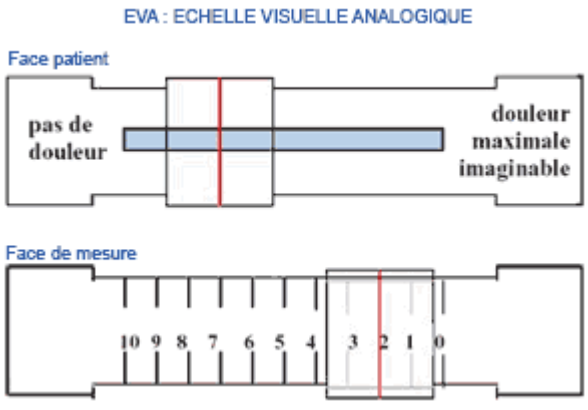
- a minimum of 15 millimeter reduction on the EVA pain scale in the post-baseline pain assessments in the active patch groups when compared to the placebo treatment groups, after 5 and 15 minutes of patches application
- a reduction in pain levels for the duration of the one-hour period.

### 9.6.2 Efficacy Evaluation

#### *9.6.2.1 Description of the efficacy parameters*

The **Scale EVA** is a commonly used pain scale in France. It consists of a 100mm horizontal line with verbal anchors indicating a continuum from "no pain" at one end to "severe pain" ("pain as bad as it could be") at the other end. The patient is asked to mark on the line the pain he or she is now experiencing (e.g., how bad is your pain?).

The **Scale EVA** is simple to use, sensitive to changes in pain intensity; also with good sensitivity to treatment effects. The **Scale EVA** gives reproducible results and it has positive association with other self-report measures. Also, it can be used to reassess pain in the same patient at different times.




#### *9.6.2.2 Method and calendar for measure, collect and analyze the efficacy parameters*

Pain evaluation with Scale EVA occured at baseline, before patches application. The Scale EVA was repeated at 5 minutes, 15 minutes and 1 hour after either the placebo or active LifeWave Med pain relief 2-patch system patches were applied.

### 9.6.3 Safety Evaluation

The subject's exposure to the study article was limited to less than two hours. A safety check, i.e., a review of whether or not one of the anticipated adverse events listed in the risk assessment has occurred, was recorded at the completion of the subject's participation. An adverse event form was completed for any reported reactions. For serious adverse events, the Principal Investigator followed-up with the subject within a week to obtain another statement and discover if symptoms worsened, reduced, or subsided. This was reported to the Sponsor within 48 if the event has become serious. Otherwise, regular reporting procedures were followed.

Safety assessment occured after the patches have been removed, at the completion of the subject's participation.

### 9.6.4 Measures to be taken to guarantee safety in case of failure of the MD included isolated dysfunction without clinical consequence as well as bad use

Non applicable

### 9.6.5 Adverse Reactions

Expected adverse reactions are listed below.

*Redness and swelling* – The only known risks to wearing the LifeWave patches are allergic skin reactions in people who are allergic to adhesives found on medical tapes. The only contact between the patch device and the body is an adhesive layer; this is made by 3M and is hypoallergenic; 1 in 10,000 people are allergic to this adhesive
*Itching* – some itching may occur, but this is relatively rare.
*Inflammation* – no inflammation has occurred with the patch as long as it is not worn more than 24 hours at a time, and as long as the patch is placed on a different place each day.

The potential health risks from participation in this study were very minimal and are essentially limited to allergic skin rashes caused by the FDA approved medical adhesive, which is made by the 3M Company. If the adhesive used in the patches does cause significant irritation to skin at the location of application, the patches were removed and the skin area washed with soap and water and the participant discontinued their participation in the study.

## 9.7 Data Quality Assurance

### 9.7.1 Source data identification

All clinical data in the protocol and collected by the investigator were notified in the subjects Case Report Form.

### 9.7.2 Collection and data control

The case report forms were designed to identify each subject by a subject number and, where appropriate, subject's initials. One Case Report Form existed for each subject participating in the study. The case report form was completed legibly, using a black ballpoint pen. Erroneous values and/or text were not erased. Instead, the error was crossed out with a single line, the correct value/text added, and the correction signed, initialled and dated by the investigator(s).

### 9.7.3 Access right to source data

In accordance with good clinical practices and the standards of the data protection law, data obtained in the course of a biomedical research has to be treated confidentially to guarantee the subjects' privacy.

The investigator agreed that, subject to local regulations and ethical considerations, the sponsor representatives designee and/or any regulatory agency may have direct access to all study records, CRFs, corresponding subject medical records, study drug dispensing records and study drug storage area, and any other documents considered source documentation. The investigator also agreed to assist the representative, if required.

## 9.8 Data management

### 9.8.1 Data entry and treatment

Case report forms data were entered in specific data bases MS Excel.
Then a quality control of 10% of the CRF was realized by the Project Manager. The project manager or either person mandated by him ensures the coherency between captured data on computer and written data in the CRF.
When all case report forms were captured and that all check-out of data was done the database was put on read-access.

### 9.8.2 Data storage

Informatics' data sheets as well as their updates were saved according to Dermscan SOP and stayed at the disposal of anyone requiring a see them.

### 9.8.3 Blind breaking

Unblinding of the assigned treatments occured after the completion of the following steps:

1. All CRF data were entered into the computer;
2. All data clarifications, if any, were resolved;
3. Major deviations or intercurrent events, if any, were defined and identified;
4. All information necessary to analyze the data was integrated into the data base;
5. The database was formally locked.

## 9.9 Statistics

The statistical analysis was performed by the biostatistician of Dermscan.

### 9.9.1 Description of the statistical methods envisaged, and if applicable, of the interim analysis' calendar

**Data description:**

Data of pain measured with a scale EVA was summarized in tabular form with descriptive statistics (mean, median, standard deviation, standard error of the mean, minimum and maximum values, number of valid values and number of missing values) computed at each time points (t0 (baseline), t5min, t15min and t1 hour) and for the absolute changes ($\Delta_i$ = ti – t0) and the relative changes (($\Delta_{i\%}$ = (ti – t0)/t0*100) from baseline (t0) with i=5min, 15min, and 1h, for each studied group (3 and 4).

Data of proportion of volunteer with a decrease from baseline (t0) of pain were summarized in tabular form with counts and percentage at t5min, t15min and t1 hour.

**First line analysis:**

To test whether the difference between both groups at least greater than 15 millimeter, a one-tailed t-test (against value 15) was applied on each change from baseline $(ti\text{-}t0)_{with}$ i= t1h.

**Second line analysis:**

- To test whether the difference between both groups was at least greater than 15 millimeter, a one-tailed t-test (against value 15) was applied on each change from baseline $(ti\text{-}t0)_{with}$ i=5min,15min

- On the absolute change (ti-t0):

For the comparison between groups on measurement of pain reduction using scale EVA, an ANOVA model for repeated measures was fitted to the raw data with:

- within subject effect : time with 4 levels
- between subject effect : product with 2 levels

Specific contrasts of interest were constructed to assess:

- the change between each $(ti)_{with\ i=5min,\ 15min\ and\ 1h}$ from baseline (t0) within each group
- whether the difference between group 3/group 4 is significant in term of change from baseline (ti-t0)i=5min,15min or t1h.

- A chi-squared test was used to compare: at t5min, t15min and t1 hour, the proportion of volunteer with a decrease of pain (evaluated with scale EVA) from baseline (t0)

For all the analyses, assumptions underlying the model were checked. In case of strong deviation, alternative modelling approach, (*e.g.* non parametric tests) or appropriate data transformations were investigated.

### 9.9.2 Determination of sample size

The primary end point of this study was to detect a difference at least 15 mm one hour after patch application between the group “product” and the group “placebo” in term of reduction of pain.
**Review of data generated in previous studies using similar scale EVA suggest that 15 mm is a good estimation of the standard deviation for the distribution of the change assessed with scale EVA for each group of treatment** (see Khwaja SM, Minnerop M, Singer AJ. Comparison of ibuprofen, cyclobenzaprine or both in patients with acute cervical strain: a randomized controlled trial. CJEM. 2010 Jan;12(1):39-44).

The table below presents the sample size required to detect a difference of 15 mm between product and placebo groups, with a power of 95% using a one t-test at the 5% significance level.
Calculation was performed using the PROC POWER procedure (option *twosamplemeans*) of the statistical software SAS 9.2 for windows. The parameters used were:

- $\Delta$=10 or15
- SD= 15
- Power : 70 to 95% by 0.05

| Computed N Per Group | | | | |
|---|---|---|---|---|
| Index | Mean2 | Nominal Power | Actual Power | N Per Group |
| 1 | 10 | 0.70 | 0.702 | 22 |
| 2 | 10 | 0.75 | 0.751 | 25 |
| 3 | 10 | 0.80 | 0.806 | 29 |
| 4 | 10 | 0.85 | 0.859 | 34 |
| 5 | 10 | 0.95 | 0.952 | 50 |
| 6 | 15 | 0.70 | 0.732 | 11 |
| 7 | 15 | 0.75 | 0.767 | 12 |
| 8 | 15 | 0.80 | 0.824 | 14 |
| 9 | 15 | 0.85 | 0.868 | 16 |
| 10 | 15 | 0.95 | 0.955 | 23 |

Moreover, a pilot study carried out in 30 subjects has shown that application of LifeWave pain relief patches (IceWave patches) had a highly significant ($p < 0.001$) effect in attenuating the intensity and perception of severity of pain. The statistical power considering the effect size (% reduction in pain, sample number, and level of significance) from these pilot data was at least 90%. Based upon this pilot study, and the calculation of sample size above, a sample size of 75 subjects per group should be sufficient to show a difference of 15 mm between product and placebo group if this is a real difference.

### 9.9.3 Statistical significance degree

All statistical tests were assessed at $\alpha = 5\%$ level of significance in a bilateral approach, except for the comparisons with the theoretical value of 15 mm, which were made using a one-tailed t-test.

### 9.9.4 Procedure for accounting missing, unused, and spurious data

No strategy for taking in charge missing data has been defined. Data that are not valid or missing were considered and treated as missing data.

### 9.9.5 Changes in the initial statistical analysis plan

The following analysis was added:

<u>On the relative change in [(ti-t0)-t0*100]:</u>

For the comparison between groups on measurement of pain reduction using scale EVA, an ANOVA model for repeated measures was fitted to the relative change outcome with:

- within subject effect : time with 3 levels
- between subject effect : product with 2 levels

Specific contrasts of interest were constructed to assess:

- the relative change between each $(ti)_{\text{with i=5min, 15min and 1h}}$ from baseline (t0) within each group
- whether the difference between groups is significant in term of relative change from baseline [(ti-t0)-t0*100]i=5min,15min or t1h.

### 9.9.6 Choice and definition of the population to be analyzed

Only the Full Analysis Set (FAS) was considered for the statistical analysis.
FAS (Full Analysis Set): any subject included and randomized in the study with at least a basal value.
The whole randomized population was used for safety analysis.

## 9.10 Administrative Procedures

### 9.10.1 Protocol changes

**During the study, the following change to the protocol was implemented: it was decided to include all types of nociceptive pains and not only pains related to degenerative osteoarthritis as initially planned, because of recruitment issue. Moreover, all types of nociceptive pains are likely to be treated by IceWave patches and degenerative osteoarthritis origin was finally found to be too restrictive.**

### 9.10.2 Protocol deviations

All protocol deviations are listed in this clinical report in paragraph 10.2.

### 9.10.3 Archiving of study data and documents

The sponsor should archive the protocol, documentation, approvals and all other essential documents related to the study, including certificates that satisfactory audit and inspection procedures have been carried out, for 15 years. DERMSCAN will archive all documents (including ICF and CRFs) concerning the study as detailed below:

- All documents must be archived in a secure place and treated as confidential material.
- All the documents relating to this study will be archived for one year maximum at Dermscan before being sent to the society LOCARCHIVES (Parc Industriel de la Plaine de l'Ain, Allée des Cèdres, 01150 SAINT-VULBAS - FRANCE).
- Data will be archived securely as digital and paper version for 15 years from the date of dispatch of the final report's acceptance.

At the end of this period, the study archives will be destroyed only when stipulated in writing by the sponsor.

### 9.10.4 Audit and inspection

No audit and inspection occurred during the study.

### 9.10.5 Insurance

The sponsor has subscribed an insurance contract to cover the liability of the investigators, the sponsor himself and anyone involved in the study.
The copy of the insurance certificate is presented separately in the EC and CA submission file.

### 9.10.6 Publication

The sponsor reserves the right to review all the manuscript(s) and abstract(s) before their submission for publication or presentation. Publication of data will be at the discretion of the sponsor

This is not intended to restrict or hinder publication or presentation, but to allow the sponsor to protect proprietary information and to provide comments based on information that may not yet be available to the investigator(s).

# 10 STUDY SUBJECTS

## 10.1 Disposition of subjects

The table below presents a global synthesis of the recruited population in this study:

**Table 1- Number of subjects included and analysed**

| | Number (n) |
|---|---|
| **Randomised subjects** | **100** (50 active patches and 50 placebo) |
| **Subjects who ended the study normally** | 100 (50 active patches and 50 placebo) |
| **Subjects included in the data analysis** | 100 (50 active patches and 50 placebo) |

## 10.2 Protocol deviations

### 10.2.1 Number of subjects

The number of subjects included was below the planned sample size (100 subjects instead of 150 subjects) because of recruitment problems. However, according to the sample size calculation presented in paragraph 9.9.2., a sample size of 50 subjects by group (so, a total of 100 subjects) could be considered as enough to show significant differences.

### 10.2.2 Inclusion criteria

None deviation was observed.

### 10.2.3 Medical history

As explained in paragraph 9.10.1, the pain origin was not only degenerative osteoarthritis but all nociceptive pains (cf Appendix 15.2.4.1).

### 10.2.4 Prohibited treatments

No deviation.

### 10.2.5 Missing data

No missing data.

# 11 EFFICACY EVALUATION

## 11.1 Data sets analysed

All subjects randomized were analyzed.
Then, the analysis population consisted in 50 subjects for active patches and 50 subjects for placebo patches.

## 11.2 Demographic and other baseline characteristics

### 11.2.1 General characteristics of the studied population

The observations concerning all included subjects are presented in Appendix 16.2.4.1. The table below presents a synthesis of these data.

**Table 2- General characteristics of the subjects**

| Product | Number of subject analyzed | Number of subject by center | Gender | Age | Height | Weight |
|---|---|---|---|---|---|---|
| **Active patches** (RDEYH36-FR) | **50** | **Center 1 : 45**<br>**Center 2 : 0**<br>**Center 3 : 0**<br>**Center 4 : 5**<br>**Center 5 : 0** | **33 F**<br>**17 M** | **59 ± 1 years** (between 31 and 70) | **1.67 ± 0.01 m** (between 1,50 and 1,83 m) | **71 ± 2 kg** (between 43 and 118kg) |
| **Placebo patches** (RDEYH38-FR) | **50** | **Center 1 : 45**<br>**Center 2 : 0**<br>**Center 3 : 0**<br>**Center 4 : 5**<br>**Center 5 : 0** | **40 F**<br>**10 M** | **59 ± 2 years** (between 31 and 70) | **1.65 ± 0.01 m** (between 1,50 and 1,82 m) | **72 ± 2 kg** (between 46 and 120kg) |

*Legend :F : female, M : male*

**The group having received the active patches and the group having received the placebo patches were homogeneous in term of age and physical characteristics (height and weight). A little more men were included for the active patches than for the placebo patches (17 versus 10). Because of recruitment issues, the majority of the subjects were included in Center 1.**

### 11.2.2 Other baseline characteristics

*11.2.2.1 Initial clinical examinations*

The table below presents the result synthesis of the initial clinical examination (PAS, PAD and pulse rate).

**Table 3– Initial clinical examination**

| Product | PAS | PAD | Pulse rate |
|---|---|---|---|
| **Active patches** (RDEYH36-FR) | 126 ± 2 mm Hg (between 100 and 150) | 71 ± 1 mm Hg (between 60 and 80) | 71 ± 0.4 bpm/min (between 70 and 80) |
| **Placebo patches** (RDEYH38-FR) | 126 ± 2 mm Hg (between 100 and 150) | 70 ± 1 mm Hg (between 50 and 90) | 72 ± 1 bpm/min (between 60 and 90) |

All clinical examinations were judged as normal by the investigators.

*11.2.2.2 Pain origin*

The origin of the nociceptive pain treated by the patches was classified into three different categories: arthrosis (and associated pathologies), surgery and traumatology. The repartition of these three categories is summarized in the table below. The individual data are presented in Appendix 16.2.4.1.

**Table 4- Origin of pain treated by the patches**

| Product | Arthrosis | Surgery | Traumatology |
|---|---|---|---|
| **Active patches** | 32 subjects (64%) | 11 subjects (22%) | 7 subjects (14%) |
| **Placebo patches** | 22 subjects (44%) | 24 subjects (48%) | 4 subjects (8%) |

*11.2.2.3 Basal values of efficacy parameters*

Before patch application, the average pain value (evaluated on the 0-100 mm EVA scale) was 64 ± 2 mm (between 50 and 100 mm) for the "active patches group" and 59 ± 2 mm (between 50 and 90 mm) for the "placebo patches group".

*11.2.2.4 Other baseline characteristics*

The final patch location and the time necessary to obtain pain improvement if inferior to 5 minutes, are described in Appendix 16.2.4.4.

### 11.2.3 Subject Medical History and previous medications

Tables in Appendix 16.2.4.2 and 16.2.4.3 present the medical history and previous medications of all subjects at inclusion.

## 11.3 EFFICACY EVALUATION

The individual data are presented in Appendix 16.2.6. The details of the statistical analysis are presented in Appendix 16.1.11. A synthesis of the results is presented below.

### 11.3.1 Descriptive statistics

The table and graphs below show, for both products, the evolution of the average pain (in mm on the EVA scale) over time, as well as the pain reduction in mm and percentage for each product.

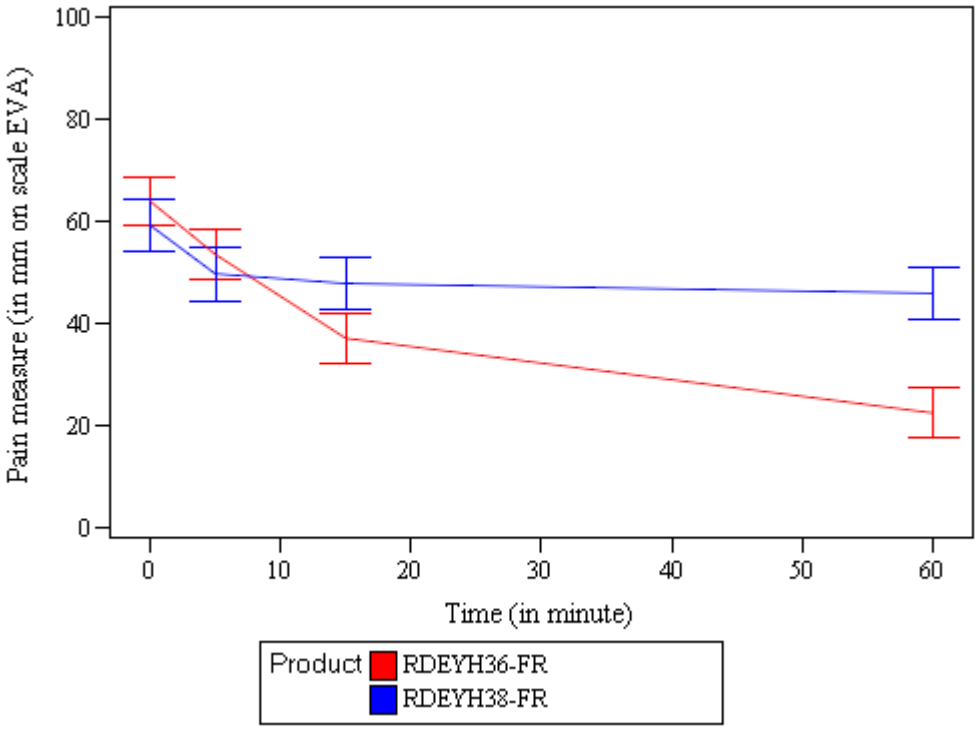
**Table 5- Pain values (in mm) over time and decrease of pain *vs* T0 (in mm and percentage)**

| Product | Time point | Pain value (in mm) Mean ± SEM | Decrease of pain *vs* T0 (in mm) Mean ± SEM | Statistical result (Ti vs T0) | Decrease of pain *vs* T0 (in %) Mean ± SEM |
|---|---|---|---|---|---|
| **Active patches** (RDEYH36-FR) | T0 | 64.0 ± 2.0 | NA | NA | NA |
| | T5min | 53.6 ± 2.6 | -10.4 ± 1.7 | **p<.0001** | -17 ± 4% |
| | T15min | 37.2 ± 2.4 | -26.8 ± 2.0 | **p<.0001** | -42 ± 4% |
| | T1h | 22.6 ± 2.7 | -41.4 ± 2.8 | **p<.0001** | -65 ± 4% |
| **Placebo patches** (RDEYH38-FR) | T0 | 59.3 ± 1.7 | NA | NA | NA |
| | T5min | 49.8 ± 2.4 | -9.5 ± 1.8 | **p<.0001** | -16 ± 4% |
| | T15min | 47.9 ± 2.8 | -11.4 ± 2.2 | **p<.0001** | -20 ± 4% |
| | T1h | 46.0 ± 3.3 | -13.3 ± 2.7 | **p<.0001** | -23 ± 4% |

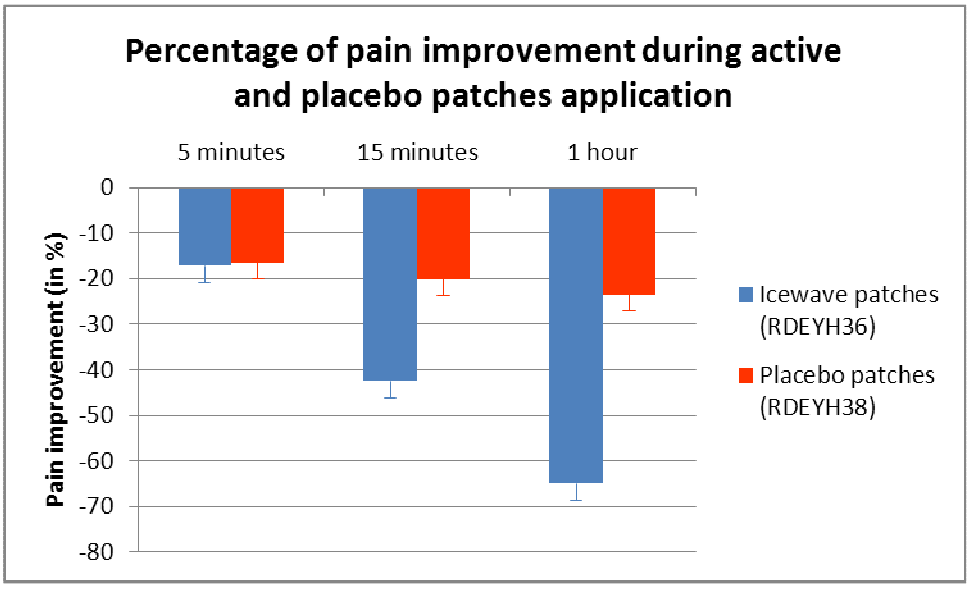
**From 5 minutes to one hour after patch application, both products (active and placebo patches) induced a significant pain improvement.**

**5 minutes after patch application, IceWave and placebo patches induced quite the same pain decrease (-10.4 ± 1.7 mm on the EVA scale for IceWave *versus* -9.5 ± 1.8 mm for placebo). However, 15 minutes and one hour after patch application, the pain reduction improved with active patches, whereas the pain reduction stayed quite stable over time with placebo patches. After one hour of patch application, the difference between active and placebo patches was the biggest: active patches induced a significant 65% pain decrease (-23 ± 3 mm on the EVA scale), whereas placebo patches induced only a 23% pain decrease (-13 ± 3 mm on the EVA scale).**

**Graph 1- Evolution of pain over time**




**Graph 2- Percentage of pain improvement**



### 11.3.2 Primary efficacy criterion

The primary efficacy criterion was to evaluate if the pain decrease in the active patch group was superior of minimum 15 millimeter on the EVA pain scale when compared to the placebo patch group, after one hour of patch application.
The statistical results are presented in the table below.

**Table 6- Product comparison at t1h**

| Comparison | Time point | Difference of pain reduction between both products (in mm) Mean ± SEM | Statistical results (comparison between products) | Statistical results (comparison against value 15) | Difference of pain reduction between both products (in %) Mean ± SEM |
|---|---|---|---|---|---|
| **Active patches** (RDEYH36-FR) ***vs*** **Placebo patches** (RDEYH38-FR) | T1h-T0 | -28.1 ± 3.9 | **p<0.0001**§ | **p<0.0006°** | - 41 ± 5 % |

§: contrasts from linear model for repeated measures
°: p-value obtained from one-tailed unpaired t-test against value (-15)

**After one hour of patch application, the difference of pain reduction between both products was significantly higher than 15 mm (-28.1 ± 3.9 mm, p=0.0006). The active patches induced a pain improvement higher than the placebo patches: this difference was of 41% between both products.**

### 11.3.3 Secondary efficacy criteria

*11.3.3.1 Product comparison after 5 and 15 minutes*

**Table 7- Product comparison at t5 minutes and t15 minutes**

| Comparison | Time points | Difference of pain reduction between both products (in mm) Mean ± SEM | Statistical results (comparison between products) | Statistical results (comparison against value 15) | Difference of pain reduction between both products (in %) Mean ± SEM |
|---|---|---|---|---|---|
| **Active patches** (RDEYH36-FR) ***vs*** **Placebo patches** (RDEYH38-FR) | T5min-T0 | -0.9 ± 3.0 | p=0.7676§ | p=1.0000° | -1 ± 5 % |
| | T15min-T0 | -15.4 ± 3.0 | **p<0.0001**§ | p=0.4468° | -22 ± 5 % |

§: contrasts from linear model for repeated measures
°: p-value obtained from one-tailed unpaired t-test against value (-15)

**After 5 minutes of patch application, there was not any significant difference between active and placebo patches (p=0.7676). After 15 minutes of patch application, the difference between active and placebo patches was statistically significant (with a pain improvement higher for active patches). This difference was not different from 15 mm : -15.4 ± 3.0 mm (22 ± 5 % of difference between both products).**

*11.3.3.2 Proportion of subjects with a pain decrease*

The table below presents the proportion of subjects with a pain decrease at t5min, t15min and t1h after patch application, for each product, with the statistical comparison of both products.

**Table 8- Proportion of subjects with a pain decrease**

| Time points | Active patches (RDEYH36-FR) | Placebo patches (RDEYH38-FR) | Statistical results (comparison between products) |
|---|---|---|---|
| **T5min-T0** | 56% | 48% | 0.4233* |
| **T15min-T0** | 92% | 50% | <0.0001* |
| **T1h-T0** | 94% | 48% | <0.0001* |

*: Chi-square test

**After 5 minutes of patch application, the proportion of subjects with a pain improvement was not different between the active and placebo patches (respectively 56% and 48%, p=0.4233).**
**However, after 15 minutes and 1 hour of patch application, the proportion of subjects with a pain improvement was significantly higher with the active patches than with the placebo patches :**
- **at t15min : 92% versus 50% (p<0.0001)**
- **at t1h : 94% versus 48% (p<0.0001)**

## 12 SAFETY EVALUATION

### 12.1 Extent of Exposure

No subject stopped the patch application following intolerance reactions. All the subjects were in contact the patches during one hour.

### 12.2 Adverse events

No adverse event or adverse reaction occurred during the study.

### 12.3 Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

No death was reported. No serious adverse event was reported.

### 12.4 Clinical laboratory results

Not applicable.

### 12.5 Vital Signs, Physical Findings, and Other Observations Related to Safety

Not applicable.

### 12.6 Safety conclusions

**The patches were considered as very well tolerated as none adverse reaction was observed during one hour of application.**

## 13 DISCUSSION AND OVERALL CONCLUSION

The objective of this study was to show that, compared to placebo, patients with nociceptive pain experienced a reduction in pain within minutes of application of active LifeWave Med pain relief 2-patch system patches.
100 subjects were analyzed: 50 received the active patches and 50 subjects received the placebo patches. Assessments of pain on Scale EVA were completed before patch application and then, at 5 minutes, 15 minutes and 1 hour starting after application of the patches in their final location.
All the patches were applied in blind by the same trained person.

5 minutes after patch application, IceWave patches induced a slight pain reduction, but which was equivalent to the one observed with placebo patches (about 10 mm decrease on the 0-100 mm EVA scale). 15 minutes and one hour after patch application, the pain continued to decrease with the active patches, whereas it stayed stable with the placebo patches. From 15 minutes of application, the difference between active and placebo patches was statistically significant. One hour after application, the difference of pain improvement between both products was the highest (41% of difference between both products, so about 28 mm on the EVA scale). Indeed, the active patches induced a 65% pain decrease (about 41 mm on the 0-100 mm EVA scale) *versus* only 23% of pain decrease with the placebo patches (about 13 mm on the 0-100 mm EVA scale). The primary end point has then been reached (difference of pain reduction of at least 15mm between active and placebo patches at t1hour) and the effect of active patches versus the placebo ones can be considered as clinically relevant. One hour after patch application, 94% of the subjects felt a pain improvement with the active patches, *versus* only 48% of the subjects with the placebo patches.

Moreover, the patches were very well tolerated as no adverse reaction was observed during one hour of contact with the skin.

The IceWave patches are non-transdermal patches that do not put any chemicals or drugs into the body. These patches are a new method of improving pain control by stimulating specific points on the body with a combination of pressure and infrared energy. This approach of pain control would allow avoiding the long term toxic effects of currently available pain medications. The safety and efficacy results obtained in this study show that IceWave patches could be a very interesting approach to pain control, without any secondary effects, allowing immediate and durable pain improvement.

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

Not applicable.

## 15 REFERENCES LIST

### 15.1 Ethical aspect

1 - WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI/ Ethical Principles for Medical Research Involving Human Subjects- Helsinki Declaration (1964) and its successive updates

2 - ICH TOPIC E6/ Note for guidance on Good Clinical Practice- CPMP / ICH / 135 / 95, January 1997

3 - LOI HURIET SERUSCLAT/ CSP Titre II – Recherches Biomédicales- n°88-138 du 20 décembre 1988 modifié par la loi française 2004-806 du 9 août 2004, concernant la santé publique

4 - LOI "INFORMATIQUE ET LIBERTES"/ Loi n°78-17 du 6 janvier 1978 relative à l'informatique, aux fichiers et aux libertés mise à jour par la loi n°2004-801 du 6 août 2004 concernant la protection des personnes pour la déclaration à la CNIL.

### 15.2 Clinical study

5- SPRIET A., DUPIN-SPRIET T., SIMON P. Méthodologie des essais cliniques des médicaments Basel : Karger; 3ème ed. 1993.

### 15.3 Investigational product(s)

1- Budzynski, T et al, Heart Rate Variability Enhancement Through Nanotechnology: A Double-Blind Randomized-Control Pilot Study, Journal of Neurotherapy, Vol. 12(1), pp 45-55, 2008.

2- Clark, D et al, Summary of IceWave Clinical Research Study – Infrared Imaging, http://www.lifewave.com/research.asp.

3 - Nazeran H, Chatlapalli S, Krishnam R "Effects of Novel Nanoscale Energy Patches on Spectral and Nonlinear Dynamic Features of Heart Rate Variability Signals in Healthy Individuals during Rest and Exercise", Proceedings of the IEEE-Engineering in Medicine and Biology Society (EMBS), 27th Annual International Conference, Shanghai, China, September 1-4, 2005

4 - Nazeran H, "Heart Rate Variability Signal Parameters Quantify Skin cooling Effect of Energy Patches During Rest and Exercise in Young Healthy Individuals", Biomedical Engineering Recent Developments, Editors: Otto Wilson, Binh Tran, Jafar Vossoughi, pp 13-19, 2007.

5 - Tan J C, Practical Manual of Physical Medicine and Rehabilitation, 2nd Edition. St. Louis, Missouri: Mosby, 2005.

6 - Bayreuther J, Lewith GT, Pickering R. Acupressure for early morning sickness: a double blind, randomized controlled crossover study. Comp Ther Med 1994;2(2):70-4.

7 - Boyers D.G. Tiller W.A. Corona Discharge Photography. J of Applied Physics, 1973, 44, 3102-3112.

8 - Dundee JW, McMillan CM. P6 acupressure and postoperative vomiting. BrJAnaes 1992;68:225-6.

9 - O'Connor J, Bensky D: *Acupuncture, a comprehensive text* Chicago: Eastland Press; 1981.

# 16 APPENDICES

## 16.1 General description of the study

### 16.1.1 Protocol and amendments

Not included.

### 16.1.2 Blank Case Report Form

Not included.

### 16.1.3 List of CPP (or IRB) with the name of the president if required by the competent authority

Not included.

### 16.1.4 Blank information and consent form

Not included.

### 16.1.5 List and identification of the investigators and important personal participating in the study

| Name and address of the investigation sites | Name of the investigators of each center |
|---|---|
| **Center 1 :**<br>CMPR Iris<br>271 rue des Sources - BP 22<br>69280 Marcy-l'Etoile/<br>25, rue André Lwoff<br>69800 Saint Priest/<br>63 bis rue Maryse Bastié<br>69008 Lyon | Dr Pierre Volckmann/ Dr Didier Lechemia |
| **Center 2 :**<br>CMPR du Bourget<br>7 rue Rigaud<br>93 350 Le Bourget | Dr Emmanuel Chevrillon/ Dr Didier Lechemia |
| **Center 3 :**<br>CSSR Choisy<br>9 bis rue Ledru Rollin<br>94 600 Choisy-le-Roi | Dr Marc Pucheault/ Dr Didier Lechemia |
| **Center 4 :**<br>CMPR Rosemond<br>61-67 avenue des Goumiers<br>13 008 Marseille | Dr Patrick Rolland/ Dr Didier Lechemia |
| **Center 5 :**<br>CMPR Le Floride,<br>Avenue Thalassa<br>66421 Le Barcares | Dr Jean Raynaud/ Dr Didier Lechemia |
| **Patch application on all centers :** | Thierry Garcia |

### 16.1.6 CV of the investigator(s)

Not included.

### 16.1.7 Signatures of the principal or coordinating investigator or of the sponsor medical representative

See page 2.

### 16.1.8 Listing of subjects receiving investigational product(s) from specific batches where more than one batch was used

Not applicable.

### 16.1.9 Randomisation scheme and codes (subject identification and treatment assigned)

Legend:

RDEYH36-FR: LifeWave Med pain relief 2-patch system

RDEYH38-FR: Placebo of 2-patch system

| Investigator centre | Screening number | Randomization number | Batch number |
|---|---|---|---|
| Lyon 8 | 01-701 | 01-201 | RDEYH38-FR |
| Lyon 8 | 01-702 | 01-202 | RDEYH36-FR |
| Lyon 8 | 01-703 | 01-203 | RDEYH36-FR |
| Lyon 8 | 01-704 | 01-204 | RDEYH38-FR |
| Marcy | 01-721 | 01-221 | RDEYH36-FR |
| Marcy | 01-722 | 01-222 | RDEYH36-FR |
| Marcy | 01-723 | 01-223 | RDEYH36-FR |
| Marcy | 01-724 | 01-224 | RDEYH36-FR |
| Marcy | 01-725 | 01-225 | RDEYH38-FR |
| Marcy | 01-726 | 01-226 | RDEYH38-FR |
| Marcy | 01-727 | 01-227 | RDEYH38-FR |
| Marcy | 01-728 | 01-228 | RDEYH36-FR |
| Marcy | 01-729 | 01-229 | RDEYH36-FR |
| Marcy | 01-730 | 01-230 | RDEYH38-FR |
| Marcy | 01-731 | 01-231 | RDEYH36-FR |
| Marcy | 01-732 | 01-232 | RDEYH36-FR |
| Marcy | 01-733 | 01-233 | RDEYH38-FR |
| Marcy | 01-734 | 01-234 | RDEYH36-FR |
| Marcy | 01-735 | 01-235 | RDEYH36-FR |
| Marcy | 01-736 | 01-236 | RDEYH38-FR |
| Marcy | 01-737 | 01-237 | RDEYH38-FR |
| Marcy | 01-738 | 01-238 | RDEYH36-FR |
| Marcy | 01-739 | 01-239 | RDEYH38-FR |
| Marcy | 01-740 | 01-240 | RDEYH36-FR |
| Marcy | 01-741 | 01-241 | RDEYH38-FR |
| Marcy | 01-742 | 01-242 | RDEYH36-FR |
| Marcy | 01-743 | 01-243 | RDEYH38-FR |
| Marcy | 01-744 | 01-244 | RDEYH38-FR |
| Marcy | 01-745 | 01-245 | RDEYH36-FR |
| Marcy | 01-746 | 01-246 | RDEYH36-FR |
| Marcy | 01-747 | 01-247 | RDEYH38-FR |
| Marcy | 01-748 | 01-248 | RDEYH38-FR |
| Marcy | 01-749 | 01-249 | RDEYH36-FR |
| Marcy | 01-750 | 01-250 | RDEYH36-FR |
| Marcy | 01-751 | 01-251 | RDEYH36-FR |
| Marcy | 01-752 | 01-252 | RDEYH38-FR |
| Marcy | 01-753 | 01-253 | RDEYH38-FR |
| St Priest | 01-760 | 01-260 | RDEYH36-FR |
| St Priest | 01-761 | 01-261 | RDEYH36-FR |
| St Priest | 01-762 | 01-262 | RDEYH38-FR |
| St Priest | 01-763 | 01-263 | RDEYH38-FR |
| St Priest | 01-764 | 01-264 | RDEYH36-FR |
| St Priest | 01-765 | 01-265 | RDEYH38-FR |
| St Priest | 01-766 | 01-266 | RDEYH38-FR |
| St Priest | 01-767 | 01-267 | RDEYH38-FR |
| St Priest | 01-768 | 01-268 | RDEYH36-FR |
| St Priest | 01-769 | 01-269 | RDEYH38-FR |
| St Priest | 01-770 | 01-270 | RDEYH36-FR |
| St Priest | 01-790 | 01-290 | RDEYH38-FR |
| St Priest | 01-791 | 01-291 | RDEYH38-FR |
| St Priest | 01-792 | 01-292 | RDEYH38-FR |
| St Priest | 01-793 | 01-293 | RDEYH36-FR |
| St Priest | 01-794 | 01-294 | RDEYH36-FR |
| St Priest | 01-795 | 01-295 | RDEYH36-FR |
| St Priest | 01-796 | 01-296 | RDEYH36-FR |
| St Priest | 01-797 | 01-297 | RDEYH36-FR |
| St Priest | 01-798 | 01-298 | RDEYH36-FR |

| Investigator centre | Screening number | Randomization number | Batch number |
|---|---|---|---|
| St Priest | 01-799 | 01-299 | RDEYH36-FR |
| Lyon 8ème | 01-820 | 01-320 | RDEYH38-FR |
| Lyon 8ème | 01-821 | 01-321 | RDEYH38-FR |
| Lyon 8ème | 01-822 | 01-322 | RDEYH38-FR |
| Lyon 8ème | 01-823 | 01-323 | RDEYH36-FR |
| Lyon 8ème | 01-824 | 01-324 | RDEYH38-FR |
| Lyon 8ème | 01-825 | 01-325 | RDEYH38-FR |
| Lyon 8ème | 01-826 | 01-326 | RDEYH38-FR |
| Lyon 8ème | 01-827 | 01-327 | RDEYH38-FR |
| Lyon 8ème | 01-828 | 01-328 | RDEYH38-FR |
| Lyon 8ème | 01-829 | 01-329 | RDEYH38-FR |
| Lyon 8ème | 01-830 | 01-330 | RDEYH38-FR |
| Lyon 8ème | 01-831 | 01-331 | RDEYH36-FR |
| Lyon 8ème | 01-832 | 01-332 | RDEYH38-FR |
| Lyon 8ème | 01-833 | 01-333 | RDEYH36-FR |
| Lyon 8ème | 01-834 | 01-334 | RDEYH36-FR |
| Lyon 8ème | 01-835 | 01-335 | RDEYH36-FR |
| Marcy | 01-840 | 01-340 | RDEYH38-FR |
| Marcy | 01-841 | 01-341 | RDEYH36-FR |
| Marcy | 01-842 | 01-342 | RDEYH38-FR |
| Marcy | 01-843 | 01-343 | RDEYH36-FR |
| Marcy | 01-844 | 01-344 | RDEYH36-FR |
| Marcy | 01-845 | 01-345 | RDEYH36-FR |
| Marcy | 01-846 | 01-346 | RDEYH38-FR |
| Marcy | 01-847 | 01-347 | RDEYH36-FR |
| Marcy | 01-849 | 01-349 | RDEYH38-FR |
| Marcy | 01-850 | 01-350 | RDEYH36-FR |
| Marcy | 01-851 | 01-351 | RDEYH38-FR |
| Marcy | 01-852 | 01-352 | RDEYH38-FR |
| Marcy | 01-853 | 01-353 | RDEYH36-FR |
| Marcy | 01-854 | 01-354 | RDEYH38-FR |
| Marcy | 01-855 | 01-355 | RDEYH38-FR |
| Marcy | 01-856 | 01-356 | RDEYH36-FR |
| Marseille | 04-702 | 04-102 | RDEYH38-FR |
| Marseille | 04-703 | 04-103 | RDEYH38-FR |
| Marseille | 04-704 | 04-104 | RDEYH36-FR |
| Marseille | 04-705 | 04-105 | RDEYH38-FR |
| Marseille | 04-706 | 04-106 | RDEYH36-FR |
| Marseille | 04-707 | 04-107 | RDEYH36-FR |
| Marseille | 04-708 | 04-108 | RDEYH36-FR |
| Marseille | 04-709 | 04-109 | RDEYH38-FR |
| Marseille | 04-710 | 04-110 | RDEYH38-FR |
| Marseille | 04-711 | 04-111 | RDEYH36-FR |

### 16.1.10 Audit certificates (if available)

Not applicable.

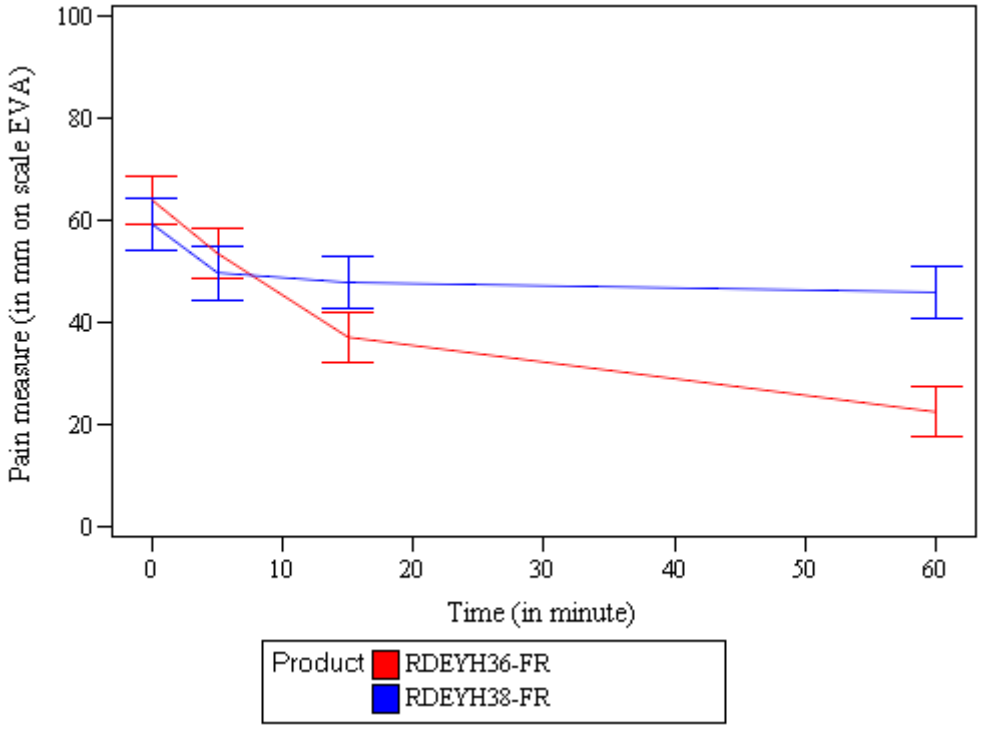
### 16.1.11 Documentation of statistical methods (statistical report)

#### *16.1.11.1 Absolute change (ti-t0)*

##### 16.1.11.1.1 Descriptive statistics

Below the graph shows the evolution of the average measure of pain (in mm, on the scale EVA) over time for both products.

**Evolution of pain over time**



Below, the table shows the descriptive statistics for the pain reduction (in mm) assessed with scale EVA at each time point $(ti)_{i=0, 5min, 15min and 1h}$ and for each changes $(ti-t0)_{i=5min, 15min and 1h}$, for product "RDEYH36-FR" and product "RDEYH38-FR".

**Evolution of pain over time**

| Product | Variable | Mean | Std Dev | SEM | Median | Minimum | Maximum |
|---|---|---|---|---|---|---|---|
| RDEYH36-FR | Pain_T0 | 64.0 | 13.9 | 2.0 | 60.0 | 50.0 | 100.0 |
| | Pain_T5min | 53.6 | 18.5 | 2.6 | 55.0 | 20.0 | 100.0 |
| | Pain_T15min | 37.2 | 16.7 | 2.4 | 40.0 | 0.0 | 80.0 |
| | Pain_T1h | 22.6 | 19.2 | 2.7 | 20.0 | 0.0 | 80.0 |
| | Pain_T5min_T0 | -10.4 | 12.1 | 1.7 | -10.0 | -50.0 | 0.0 |
| | Pain_T15min_T0 | -26.8 | 14.1 | 2.0 | -30.0 | -60.0 | 0.0 |
| | Pain_T1h_T0 | -41.4 | 19.9 | 2.8 | -40.0 | -85.0 | 0.0 |
| RDEYH38-FR | Pain_T0 | 59.3 | 11.9 | 1.7 | 52.5 | 50.0 | 90.0 |
| | Pain_T5min | 49.8 | 16.8 | 2.4 | 50.0 | 10.0 | 90.0 |
| | Pain_T15min | 47.9 | 20.1 | 2.8 | 50.0 | 0.0 | 100.0 |
| | Pain_T1h | 46.0 | 23.3 | 3.3 | 50.0 | 0.0 | 100.0 |
| | Pain_T5min_T0 | -9.5 | 12.4 | 1.8 | 0.0 | -40.0 | 0.0 |
| | Pain_T15min_T0 | -11.4 | 15.7 | 2.2 | -5.0 | -50.0 | 10.0 |
| | Pain_T1h_T0 | -13.3 | 19.3 | 2.7 | 0.0 | -60.0 | 10.0 |

*16.1.11.2 Product difference on $(ti-t0)_{i=5min, 15min and 1h}$ against value 15*

Below, the table summarizes the comparison between the products difference against value 15 for each change (Ti-T0).

**Difference between products against value 15**

| Comparison | change | Mean | SEM | p-value |
|---|---|---|---|---|
| **RDEYH36-FR** | T5im-T0 | -9.4467 | 3.3043 | 0.9525 |
| **versus** | T15min-T0 | -14.2733 | 3.3923 | 0.5847 |
| **RDEYH38-FR** | T1h-T0 | -21.5333 | 3.4139 | **0.0288°** |

°: p-value obtained from one-tailed unpaired t-test against value (-15)

**At t1h from baseline (T0), the data showed that the difference between both products (-21.53±21) in terms of reduction of pain was significantly higher than 15 (p=0.0288) There was a higher improvement in terms of reduction of pain under product "RDEYH36-FR" than under "RDEYH38-FR".**

*16.1.11.3 Change from baseline within each product group*

Below, the table presents the comparison between each time point $(ti)_{i=5min, 15min and 1h}$ and baseline, on the estimated means, for each product.

**Absolute change of pain**

| Product | Change | Estimate* | SEM* | DF | t Value | p-value§\| |
|---|---|---|---|---|---|---|
| **RDEYH36-FR** | **t5min - t0** | -10.4000 | 2.1515 | 294 | -4.83 | **<.0001** |
| | **t15min - t0** | -26.8000 | 2.1515 | 294 | -12.46 | **<.0001** |
| | **t1h - t0** | -41.4000 | 2.1515 | 294 | -19.24 | **<.0001** |
| **RDEYH38-FR** | **t5min - t0** | -9.5000 | 2.1515 | 294 | -4.42 | **<.0001** |
| | **t15min - t0** | -11.4000 | 2.1515 | 294 | -5.30 | **<.0001** |
| | **t1h - t0** | -13.3000 | 2.1515 | 294 | -6.18 | **<.0001** |

§: contrasts from linear model for repeated measures
*: estimated from LS-Means

**Whatever the product, the data showed a significant decrease in pain score (p<0.0001) on t5min, t15min and t1h in comparison with baseline (t0).**

#### 16.1.11.3.1 Comparison between products

Below, the table summarizes the comparison between the products, on the estimated means, in terms of absolute change from baseline (ti-t0).

**Comparison of products on absolute change**

| Comparison | Change | Estimate* | SEM* | DF | t Value | Pr > \|t\| |
|---|---|---|---|---|---|---|
| **RDEYH36-FR vs RDEYH38-FR** | T5min-t0 | -0.9000 | 3.0426 | 294 | -0.30 | 0.7676 |
| | T15min-t0 | -15.4000 | 3.0426 | 294 | -5.06 | **<.0001** |
| | T1h-t0 | -28.1000 | 3.0426 | 294 | -9.24 | **<.0001** |

§: contrasts from linear model for repeated measures
*: estimated from LS-Means

**The data showed a significant higher improvement of the pain with product "RDEYH36-FR" than with product "RDEYH38-FR" at t15min (-15.4±3, p<0.0001) and t1h (-28±3, p<0.0001).**

### 16.1.11.3.2 Proportion of subjects with a decrease of pain

Below, the table presents the proportion of subjects with a decrease of pain (on the scale EVA), at t5min, t5h and t1h from baseline (t0) under product.

**Proportion of subjects with a decrease of pain**

| Variation | Decrease | | RDEYH36-FR | RDEYH38-FR |
|---|---|---|---|---|
| **T5min-T0** | **Yes** | N<br>% | 28<br>56.00 | 24<br>48.00 |
| | **No** | N<br>% | 22<br>44.00 | 26<br>52.00 |
| **p-value** | | | 0.4233 | |
| | | | | |
| **T15min-T0** | **Yes** | N<br>% | 46<br>92.00 | 25<br>50.00 |
| | **No** | N<br>% | 4<br>8.00 | 25<br>50.00 |
| **p-value** | | | **<.0001** | |
| | | | | |
| **T1h-T0** | **Yes** | N<br>% | 47<br>94.00 | 24<br>48.00 |
| | **No** | N<br>% | 3<br>6.00 | 26<br>52.00 |
| **p-value** | | | **<.0001** | |

*: Chi-square test

**The data showed a significant more important proportion of subjects with a decrease of pain with product "RDEYH36-FR" than with product "RDEYH38-FR":**

- **At t15min, 46% versus 25% (p<0.0001)**
- **At t1h, 47% versus 24% (p<0.0001).**

### *16.1.11.4 Relative change (in percent)*

#### 16.1.11.4.1 Change from baseline for within each group

Below, the table shows the descriptive statistics for the relative reduction of pain (in %) assessed with scale EVA at each time point (i)$_{i=5min,\ 15min\ and\ 1h}$, for product "RDEYH36-FR" and product "RDEYH38-FR".

**Relative change of pain (in %)**

| Product | Relative change (in %) | Estimate* | SEM* | DF | t Value | p-value§\| |
|---|---|---|---|---|---|---|
| RDEYH36-FR | **(T5min - T0)/T0*100** | -17.1452 | 3.6599 | 196 | -4.68 | **<.0001** |
| | **(T15min - T0)/T0*100** | -42.4365 | 3.6599 | 196 | -11.59 | **<.0001** |
| | **(T1h - T0)/T0*100** | -64.8730 | 3.6599 | 196 | -17.73 | **<.0001** |
| RDEYH38-FR | **(T5min - T0)/T0*100** | -16.3987 | 3.6599 | 196 | -4.48 | **<.0001** |
| | **(T15min - T0)/T0*100** | -20.0987 | 3.6599 | 196 | -5.49 | **<.0001** |
| | **(T1h - T0)/T0*100** | -23.4448 | 3.6599 | 196 | -6.41 | **<.0001** |

§: contrasts from linear model for repeated measures
*: estimated from LS-Means

**Whatever the product, the data showed a significant decrease (p<0.0001) at t5min, t15min and t1h in comparison with baseline (t0), in terms of relative change from baseline (in %).**
**At t1h, the percentage of pain decrease observed was:**
- **-65% for product "RDEYH36-FR"**
- **-23% for product "RDEYH38-FR"**

#### 16.1.11.4.2 Comparison between products

Below, the table summarizes the comparison between the products, on the estimated means, in terms of relative change from baseline (in %).

**Comparison of products on relative change (in %)**

| Comparison | | Estimate* | SEM* | DF | t Value | Pr > \|t\| |
|---|---|---|---|---|---|---|
| **RDEYH36-FR** | **(T5min - T0)/T0*100** | -0.7465 | 5.1759 | 196 | -0.14 | 0.8855 |
| **vs** | **(T15min - T0)/T0*100** | -22.3378 | 5.1759 | 196 | -4.32 | **<.0001** |
| **RDEYH38-FR** | **(T1h - T0)/T0*100** | -41.4282 | 5.1759 | 196 | -8.00 | **<.0001** |

§: contrasts from linear model for repeated measures
*: estimated from LS-Means

**The data analysis showed a significant higher pain reduction from baseline (t0) with product "RDEYH36-FR" than with product "RDEYH38-FR" 15 minutes (-22%±5, p<0.0001) and 1 hour (-41%±5, p<0.0001) after the patch application.**

### 16.1.12 Documentation of inter-laboratory standardisation methods and quality assurance procedures if used

Not applicable.

### 16.1.13 Publications based on the study

Not applicable.

## 16.2 Subject data listings

### 16.2.1 Discontinued subjects

See paragraph 10.1 of the report.

### 16.2.2 Protocol deviations

See paragraph 10.2 of the report.

### 16.2.3 Patients excluded from the efficacy analysis

See paragraph 10.2 of the report.

### 16.2.4 Demographic data

*16.2.4.1 General subject characteristics*

# LifeWave Med pain relief 2-patch system

| Investigator centre | Screening number | Randomization number | Product | Subject initials | Age | Height (in m) | Weight (in kg) | PAS (in mm Hg) | PAD (in mm Hg) | Pulse rate (in bpm/min) | Sex | Origin of the pain treated by the patches |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lyon 8 | 01-702 | 01-202 | RDEYH36-FR | FP | 63 | 1,60 | 59 | 130 | 70 | 70 | F | surgery |
| Lyon 8 | 01-703 | 01-203 | RDEYH36-FR | BA | 67 | 1,79 | 118 | 120 | 80 | 70 | M | surgery |
| Marcy | 01-721 | 01-221 | RDEYH36-FR | LC | 65 | 1,72 | 78 | 130 | 70 | 75 | M | arthrosis |
| Marcy | 01-722 | 01-222 | RDEYH36-FR | CM | 39 | 1,72 | 65 | 110 | 60 | 70 | F | arthrosis |
| Marcy | 01-723 | 01-223 | RDEYH36-FR | RM | 53 | 1,78 | 103 | 150 | 80 | 75 | M | arthrosis |
| Marcy | 01-724 | 01-224 | RDEYH36-FR | MM | 65 | 1,67 | 64 | 120 | 70 | 70 | F | arthrosis |
| Marcy | 01-728 | 01-228 | RDEYH36-FR | DP | 54 | 1,68 | 71 | 100 | 70 | 70 | F | arthrosis |
| Marcy | 01-729 | 01-229 | RDEYH36-FR | BM | 61 | 1,63 | 53,5 | 130 | 70 | 70 | F | arthrosis |
| Marcy | 01-731 | 01-231 | RDEYH36-FR | MG | 63 | 1,72 | 72,5 | 120 | 80 | 70 | M | surgery |
| Marcy | 01-732 | 01-232 | RDEYH36-FR | FJ | 60 | 1,68 | 67 | 120 | 70 | 70 | M | traumatology |
| Marcy | 01-734 | 01-234 | RDEYH36-FR | VM | 55 | 1,63 | 78 | 130 | 80 | 70 | F | surgery |
| Marcy | 01-735 | 01-235 | RDEYH36-FR | GJ | 67 | 1,65 | 83 | 130 | 70 | 70 | M | arthrosis |
| Marcy | 01-738 | 01-238 | RDEYH36-FR | GP | 61 | 1,83 | 93 | 130 | 70 | 80 | M | arthrosis |
| Marcy | 01-740 | 01-240 | RDEYH36-FR | BM | 52 | 1,68 | 82 | 110 | 60 | 70 | M | traumatology |
| Marcy | 01-742 | 01-242 | RDEYH36-FR | PP | 65 | 1,65 | 47 | 120 | 70 | 70 | F | arthrosis |
| Marcy | 01-745 | 01-245 | RDEYH36-FR | GR | 67 | 1,75 | 82 | 130 | 70 | 70 | M | arthrosis |
| Marcy | 01-746 | 01-246 | RDEYH36-FR | GM | 68 | 1,50 | 48 | 130 | 80 | 75 | F | arthrosis |
| Marcy | 01-749 | 01-249 | RDEYH36-FR | LA | 62 | 1,66 | 55 | 120 | 70 | 70 | F | arthrosis |
| Marcy | 01-750 | 01-250 | RDEYH36-FR | FC | 52 | 1,67 | 49 | 120 | 80 | 70 | F | traumatology |
| Marcy | 01-751 | 01-251 | RDEYH36-FR | LE | 65 | 1,67 | 70 | 140 | 70 | 70 | F | arthrosis |
| St Priest | 01-760 | 01-260 | RDEYH36-FR | FE | 70 | 1,64 | 79 | 140 | 70 | 70 | F | traumatology |
| St Priest | 01-761 | 01-261 | RDEYH36-FR | VP | 70 | 1,80 | 92 | 130 | 70 | 75 | M | surgery |
| St Priest | 01-764 | 01-264 | RDEYH36-FR | MS | 59 | 1,60 | 88 | 125 | 70 | 75 | F | surgery |
| St Priest | 01-768 | 01-268 | RDEYH36-FR | RE | 45 | 1,65 | 66 | 110 | 60 | 70 | F | arthrosis |
| St Priest | 01-770 | 01-270 | RDEYH36-FR | VF | 50 | 1,63 | 61 | 130 | 80 | 70 | F | arthrosis |
| St Priest | 01-793 | 01-293 | RDEYH36-FR | MS | 32 | 1,70 | 72 | 110 | 60 | 70 | F | traumatology |
| St Priest | 01-794 | 01-294 | RDEYH36-FR | RP | 60 | 1,56 | 100 | 125 | 70 | 70 | F | surgery |
| St Priest | 01-795 | 01-295 | RDEYH36-FR | CM | 64 | 1,70 | 60 | 110 | 60 | 70 | F | arthrosis |
| St Priest | 01-796 | 01-296 | RDEYH36-FR | VN | 52 | 1,60 | 58 | 120 | 70 | 70 | F | arthrosis |
| St Priest | 01-797 | 01-297 | RDEYH36-FR | BC | 54 | 1,65 | 61 | 120 | 70 | 70 | F | arthrosis |
| St Priest | 01-798 | 01-298 | RDEYH36-FR | MJ | 65 | 1,55 | 43 | 150 | 80 | 75 | F | arthrosis |
| St Priest | 01-799 | 01-299 | RDEYH36-FR | CJ | 70 | 1,60 | 49 | 120 | 70 | 70 | F | arthrosis |
| Lyon 8ème | 01-823 | 01-323 | RDEYH36-FR | NM | 64 | 1,58 | 58,5 | 130 | 80 | 70 | F | arthrosis |
| Lyon 8ème | 01-831 | 01-331 | RDEYH36-FR | GY | 70 | 1,62 | 65 | 130 | 70 | 70 | F | arthrosis |
| Lyon 8ème | 01-833 | 01-333 | RDEYH36-FR | BS | 64 | 1,64 | 54 | 130 | 70 | 70 | F | arthrosis |
| Lyon 8ème | 01-834 | 01-334 | RDEYH36-FR | TJ | 68 | 1,82 | 86 | 130 | 80 | 70 | M | arthrosis |
| Lyon 8ème | 01-835 | 01-335 | RDEYH36-FR | JJ | 67 | 1,59 | 70 | 130 | 80 | 70 | F | arthrosis |
| Marcy | 01-841 | 01-341 | RDEYH36-FR | BV | 31 | 1,74 | 59 | 110 | 60 | 70 | F | traumatology |
| Marcy | 01-843 | 01-343 | RDEYH36-FR | GJ | 70 | 1,64 | 98 | 150 | 80 | 80 | F | arthrosis |
| Marcy | 01-844 | 01-344 | RDEYH36-FR | MD | 41 | 1,74 | 68 | 110 | 60 | 70 | M | arthrosis |
| Marcy | 01-845 | 01-345 | RDEYH36-FR | GC | 57 | 1,67 | 50 | 120 | 60 | 70 | F | arthrosis |
| Marcy | 01-847 | 01-347 | RDEYH36-FR | DB | 64 | 1,67 | 72 | 130 | 60 | 70 | M | arthrosis |
| Marcy | 01-850 | 01-350 | RDEYH36-FR | GP | 70 | 1,75 | 77 | 140 | 70 | 70 | M | surgery |
| Marcy | 01-853 | 01-353 | RDEYH36-FR | YC | 47 | 1,68 | 66 | 125 | 70 | 70 | F | surgery |
| Marcy | 01-856 | 01-356 | RDEYH36-FR | VC | 48 | 1,62 | 50 | 120 | 70 | 70 | F | arthrosis |
| Marseille | 04-704 | 04-104 | RDEYH36-FR | BP | 54 | 1,70 | 75 | 130 | 75 | 75 | M | surgery |
| Marseille | 04-706 | 04-106 | RDEYH36-FR | SJ | 62 | 1,57 | 79,5 | 120 | 70 | 70 | F | arthrosis |
| Marseille | 04-707 | 04-107 | RDEYH36-FR | GJ | 68 | 1,66 | 75 | 140 | 80 | 75 | M | traumatology |
| Marseille | 04-708 | 04-108 | RDEYH36-FR | DB | 69 | 1,62 | 90 | 130 | 80 | 75 | F | arthrosis |
| Marseille | 04-711 | 04-111 | RDEYH36-FR | NJ | 46 | 1,66 | 65 | 140 | 70 | 70 | M | surgery |
| | | | | **Mean** | **59** | **1,67** | **71** | **126** | **71** | **71** | | |
| | | | | Median | 63 | 1,66 | 69 | 130 | 70 | 70 | | |
| | | | | Minimum | 31 | 1,50 | 43 | 100 | 60 | 70 | | |
| | | | | Maximum | 70 | 1,83 | 118 | 150 | 80 | 80 | | |
| | | | | SEM | 1 | 0,01 | 2 | 2 | 1 | 0,4 | | |
| | | | | 95% CI | 3 | 0,02 | 5 | 3 | 2 | 1 | | |

| Sex | | Origin of the pain treated by the patches | |
|---|---|---|---|
| F | 33 | **arthrosis** | 32 |
| M | 17 | **surgery** | 11 |
| | | **traumatology** | 7 |

## Placebo of 2-patch system

| Investigator centre | Screening number | Randomization number | Product | Subject initials | Age | Height (in m) | Weight (in kg) | PAS (in mm Hg) | PAD (in mm Hg) | Pulse rate (in bpm/min) | Sex | Origin of the pain treated by the patches |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lyon 8 | 01-701 | 01-201 | RDEYH38-FR | TJ | 67 | 1,63 | 74 | 130 | 50 | 70 | F | surgery |
| Lyon 8 | 01-704 | 01-204 | RDEYH38-FR | BS | 58 | 1,60 | 68 | 120 | 70 | 70 | F | surgery |
| Marcy | 01-725 | 01-225 | RDEYH38-FR | TE | 65 | 1,60 | 55 | 140 | 70 | 70 | F | arthrosis |
| Marcy | 01-726 | 01-226 | RDEYH38-FR | CH | 69 | 1,60 | 55 | 140 | 70 | 75 | F | arthrosis |
| Marcy | 01-727 | 01-227 | RDEYH38-FR | SM | 68 | 1,63 | 60 | 140 | 70 | 75 | F | arthrosis |
| Marcy | 01-730 | 01-230 | RDEYH38-FR | VM | 45 | 1,58 | 79 | 140 | 70 | 75 | F | arthrosis |
| Marcy | 01-733 | 01-233 | RDEYH38-FR | TT | 35 | 1,72 | 69 | 120 | 70 | 70 | F | surgery |
| Marcy | 01-736 | 01-236 | RDEYH38-FR | GL | 67 | 1,59 | 73 | 140 | 90 | 80 | F | surgery |
| Marcy | 01-737 | 01-237 | RDEYH38-FR | CA | 66 | 1,65 | 100 | 130 | 80 | 80 | F | surgery |
| Marcy | 01-739 | 01-239 | RDEYH38-FR | BN | 65 | 1,76 | 84 | 120 | 70 | 70 | M | surgery |
| Marcy | 01-741 | 01-241 | RDEYH38-FR | BZ | 68 | 1,58 | 84 | 140 | 80 | 75 | F | arthrosis |
| Marcy | 01-743 | 01-243 | RDEYH38-FR | DM | 61 | 1,66 | 84 | 130 | 70 | 70 | F | surgery |
| Marcy | 01-744 | 01-244 | RDEYH38-FR | GY | 69 | 1,56 | 64 | 130 | 70 | 75 | F | traumatology |
| Marcy | 01-747 | 01-247 | RDEYH38-FR | BC | 69 | 1,70 | 75 | 130 | 70 | 70 | F | arthrosis |
| Marcy | 01-748 | 01-248 | RDEYH38-FR | RM | 51 | 1,65 | 85 | 130 | 70 | 70 | F | arthrosis |
| Marcy | 01-752 | 01-252 | RDEYH38-FR | DV | 44 | 1,68 | 64 | 120 | 70 | 70 | F | arthrosis |
| Marcy | 01-753 | 01-253 | RDEYH38-FR | PC | 70 | 1,66 | 57 | 120 | 70 | 70 | F | arthrosis |
| St Priest | 01-762 | 01-262 | RDEYH38-FR | BA | 70 | 1,58 | 88 | 130 | 70 | 70 | F | arthrosis |
| St Priest | 01-763 | 01-263 | RDEYH38-FR | GB | 47 | 1,60 | 120 | 130 | 70 | 70 | F | surgery |
| St Priest | 01-765 | 01-265 | RDEYH38-FR | AM | 49 | 1,67 | 88 | 140 | 70 | 80 | M | arthrosis |
| St Priest | 01-766 | 01-266 | RDEYH38-FR | RB | 70 | 1,50 | 83 | 150 | 80 | 75 | F | arthrosis |
| St Priest | 01-767 | 01-267 | RDEYH38-FR | BJ | 43 | 1,80 | 82 | 130 | 70 | 70 | M | surgery |
| St Priest | 01-769 | 01-269 | RDEYH38-FR | GH | 64 | 1,60 | 63,5 | 150 | 80 | 90 | F | traumatology |
| St Priest | 01-790 | 01-290 | RDEYH38-FR | VJ | 70 | 1,56 | 82 | 140 | 70 | 80 | F | surgery |
| St Priest | 01-791 | 01-291 | RDEYH38-FR | CA | 69 | 1,53 | 57 | 130 | 75 | 75 | F | arthrosis |
| St Priest | 01-792 | 01-292 | RDEYH38-FR | OR | 70 | 1,54 | 62 | 130 | 70 | 70 | F | surgery |
| Lyon 8ème | 01-820 | 01-320 | RDEYH38-FR | CC | 51 | 1,69 | 58 | 120 | 70 | 70 | F | surgery |
| Lyon 8ème | 01-821 | 01-321 | RDEYH38-FR | FS | 70 | 1,60 | 65 | 120 | 70 | 75 | F | surgery |
| Lyon 8ème | 01-822 | 01-322 | RDEYH38-FR | TA | 61 | 1,62 | 57 | 140 | 80 | 75 | F | surgery |
| Lyon 8ème | 01-824 | 01-324 | RDEYH38-FR | GF | 49 | 1,70 | 69 | 100 | 60 | 70 | F | surgery |
| Lyon 8ème | 01-825 | 01-325 | RDEYH38-FR | GM | 67 | 1,53 | 46 | 120 | 70 | 70 | F | surgery |
| Lyon 8ème | 01-826 | 01-326 | RDEYH38-FR | VY | 57 | 1,55 | 58 | 110 | 70 | 70 | F | surgery |
| Lyon 8ème | 01-827 | 01-327 | RDEYH38-FR | BB | 59 | 1,75 | 105 | 140 | 80 | 70 | M | arthrosis |
| Lyon 8ème | 01-828 | 01-328 | RDEYH38-FR | BA | 52 | 1,57 | 75 | 130 | 70 | 70 | F | surgery |
| Lyon 8ème | 01-829 | 01-329 | RDEYH38-FR | GS | 64 | 1,65 | 60 | 100 | 60 | 70 | F | arthrosis |
| Lyon 8ème | 01-830 | 01-330 | RDEYH38-FR | LM | 67 | 1,74 | 65 | 120 | 70 | 70 | F | surgery |
| Lyon 8ème | 01-832 | 01-332 | RDEYH38-FR | PG | 70 | 1,61 | 57 | 110 | 60 | 70 | F | arthrosis |
| Marcy | 01-840 | 01-340 | RDEYH38-FR | MA | 69 | 1,65 | 60 | 130 | 70 | 70 | F | arthrosis |
| Marcy | 01-842 | 01-342 | RDEYH38-FR | TY | 62 | 1,56 | 72 | 110 | 60 | 70 | F | traumatology |
| Marcy | 01-846 | 01-346 | RDEYH38-FR | RC | 33 | 1,65 | 60 | 110 | 60 | 60 | F | surgery |
| Marcy | 01-849 | 01-349 | RDEYH38-FR | VP | 51 | 1,60 | 60 | 110 | 60 | 70 | F | arthrosis |
| Marcy | 01-851 | 01-351 | RDEYH38-FR | TR | 53 | 1,74 | 67 | 110 | 50 | 70 | F | arthrosis |
| Marcy | 01-852 | 01-352 | RDEYH38-FR | TG | 69 | 1,80 | 73 | 120 | 70 | 70 | M | arthrosis |
| Marcy | 01-854 | 01-354 | RDEYH38-FR | SJ | 47 | 1,65 | 75 | 120 | 70 | 70 | F | arthrosis |
| Marcy | 01-855 | 01-355 | RDEYH38-FR | GG | 53 | 1,68 | 87,5 | 140 | 70 | 80 | F | surgery |
| Marseille | 04-702 | 04-102 | RDEYH38-FR | ZS | 57 | 1,77 | 98 | 120 | 70 | 70 | M | surgery |
| Marseille | 04-703 | 04-103 | RDEYH38-FR | TD | 40 | 1,82 | 72 | 120 | 75 | 75 | M | arthrosis |
| Marseille | 04-705 | 04-105 | RDEYH38-FR | SK | 31 | 1,70 | 55 | 110 | 60 | 60 | M | traumatology |
| Marseille | 04-709 | 04-109 | RDEYH38-FR | DM | 48 | 1,70 | 77 | 120 | 70 | 75 | M | surgery |
| Marseille | 04-710 | 04-110 | RDEYH38-FR | BL | 69 | 1,70 | 72 | 130 | 70 | 70 | M | surgery |
| | | | | **Mean** | **59** | **1,65** | **72** | **126** | **70** | **72** | | |
| | | | | Median | 63 | 1,65 | 71 | 130 | 70 | 70 | | |
| | | | | Minimum | 31 | 1,50 | 46 | 100 | 50 | 60 | | |
| | | | | Maximum | 70 | 1,82 | 120 | 150 | 90 | 90 | | |
| | | | | SEM | 2 | 0,01 | 2 | 2 | 1 | 1 | | |
| | | | | 95% CI | 3 | 0,02 | 4 | 3 | 2 | 1 | | |

| | | | |
|---|---|---|---|
| **F** | 40 | **arthrosis** | 22 |
| **M** | 10 | **surgery** | 24 |
| | | **traumatology** | 4 |

### *16.2.4.2 Medical history*

| Screening number | Randomisation # | Batch number | Description of the medical history | Date of beginning | Date of end or ongoing |
|---|---|---|---|---|---|
| 01-701 | 01-201 | RDEYH38-FR | RIGHT KNEE PROTHESIS | 01/10/2010 | 01/10/2010 |
| | | | LEFT KNEE PROTHESIS | 09/04/2012 | ONGOING |
| | | | HYPOTHYROIDISM | 01/01/1992 | ONGOING |
| | | | HYPERTENSION | 01/01/2002 | ONGOING |
| 01-702 | 01-202 | RDEYH36-FR | SURGERY OF RIGHT SHOULDER ROTATOR CUFF | 01/01/2002 | ONGOING |
| | | | SECOND SURGERY OF RIGHT SHOULDER ROTATOR CUFF | 03/26/2012 | ONGOING |
| | | | THIRD SURGERY OF RIGHT SHOULDER ROTATOR CUFF | 07/07/2012 | ONGOING |
| 01-703 | 01-203 | RDEYH36-FR | SURGERY OF RIGHT HUMERAL FRACTURE (HALF-PROTHESIS) | 09/30/12 | ONGOING |
| 01-704 | 01-204 | RDEYH38-FR | LEFT MASTECTOMY (CANCER) | 01/01/2007 | ONGOING |
| | | | LEFT HIP PROTHESIS | 01/01/2008 | 01/01/2008 |
| | | | RIGHT HIP PROTHESIS (FALL) | 01/01/2009 | ONGOING |
| | | | RIGHT SHOULDER PAIN (POST-FALL) | 09/01/2012 | ONGOING |
| 01-721 | 01-221 | RDEYH36-FR | NUCLEOUS PULPOSUS HERNIATION L5S1 SURGERY | 01/01/1989 | 01/01/1989 |
| | | | NUCLEOUS PULPOSUS HERNIATION L4L5 SURGERY | 01/01/1989 | 01/01/1989 |
| | | | DIFFUSE POLYARTHROPATHY AND SEVERE LUMBAR SPONDYLOSIS | 01/01/2000 | ONGOING |
| | | | HYPOTHYROIDISM | 01/01/2002 | ONGOING |
| 01-722 | 01-222 | RDEYH36-FR | CERVICAL ARTHRITIS (HYPERALGESIA) | 01/01/2010 | ONGOING |
| 01-723 | 01-223 | RDEYH36-FR | CERVICAL ARTHRITIS | 01/01/2002 | ONGOING |
| | | | BILATERAL COXARTHRITIS | 01/01/2009 | ONGOING |
| | | | DISCOPATHY L4L5 AND L5S1 + LEFT NUCLEOUS PULPOSUS HERNIATION L5S1 | 01/09/2012 | ONGOING |
| 01-724 | 01-224 | RDEYH36-FR | BILATERAL SHOULDER TENDINOPATHY + LEFT SHOULDER CAPSULITIS | 06/01/2012 | ONGOING |
| 01-725 | 01-225 | RDEYH38-FR | LEFT HIP PROTHESIS | 03/12/2012 | ONGOING |
| | | | HYPOTHYROIDISM | 01/01/2011 | ONGOING |
| | | | ROTATOR CUFF TENDINOPATHY | 01/01/2012 | ONGOING |
| 01-726 | 01-226 | RDEYH38-FR | RIGHT HIP PROTHESIS | 12/03/2012 | ONGOING |
| | | | LEFT HALLUX VALGUS SUGERY | 01/01/2010 | 01/01/2010 |
| | | | LEFT GLUTEAL TENDINITIS | 12/01/2011 | ONGOING |
| 01-727 | 01-227 | RDEYH38-FR | RIGHT HIP PROTHESIS | 01/01/2008 | 01/01/2008 |
| | | | RIGHT KNEE PROTHESIS | 01/01/2009 | 01/01/2009 |
| | | | SURGERY OF RIGHT ROTATOR CUFF | 01/01/2010 | 01/01/2010 |
| | | | LEFT KNEE PROTHESIS | 01/01/2011 | 01/01/2011 |
| | | | PARKINSON'S DISEASE | 01/01/2008 | ONGOING |
| | | | POLYARTHROPATY (CERVICAL ARTHRITIS) | 01/01/2008 | ONGOING |
| 01-728 | 01-228 | RDEYH36-FR | RIGHT ANKLE ARTHRITIS | 01/01/2011 | ONGOING |
| 01-729 | 01-229 | RDEYH36-FR | LEFT HIP COXARTHRITIS | 02/01/2012 | ONGOING |
| | | | RIGHT CERVICOBRACHIAL NEURALGIA (CERVICAL ARTHRITIS) | 01/01/2010 | ONGOING |
| 01-730 | 01-230 | RDEYH38-FR | HEART TRANSPLANT | 01/01/2008 | ONGOING |
| | | | HISTERECTOMY | 01/01/2011 | 01/01/2011 |
| | | | LEFT CRURALGIA | 01/01/2011 | ONGOING |
| | | | DIABETES | 01/01/2008 | ONGOING |
| | | | HYPERCHOLESTEROLEMIA | 01/01/2008 | ONGOING |
| | | | HYPERTENSION | 01/01/2008 | ONGOING |
| 01-731 | 01-231 | RDEYH36-FR | TOTAL LEFT KNEE PROTHESIS | 01/11/2010 | 01/11/2010 |
| | | | TOTAL RIGHT KNEE PROTHESIS | 11/20/2012 | ONGOING |
| | | | LEFT CRUCIATE KNEE LIGAMENT SURGERY | 01/01/1981 | 01/01/1981 |
| 01-732 | 01-232 | RDEYH36-FR | HEAD AND FACE TRAUMA (6 SURGERIES OF RIGHT HALF FACE) SEVERE ALGIA | 08/21/03 | ONGOING |
| 01-733 | 01-233 | RDEYH38-FR | LEFT AND RIGHT HALLUX VALGUS SUGERY | 01/01/1997 | ONGOING |
| | | | LEFT CRUCIATE KNEE LIGAMENT SURGERY | 12/09/2012 | ONGOING |
| 01-734 | 01-234 | RDEYH36-FR | TOTAL RIGHT MASTECTOMY (CANCER) | 05/05/2010 | 05/05/2010 |
| | | | RIGHT BREAST RECONSTRUCTION AND LEFT BREAST REDUCTION | 12/03/2012 | ONGOING |
| 01-735 | 01-235 | RDEYH36-FR | RIGHT GONARTHROSIS (HYPERALGIC) | 01/01/2005 | ONGOING |
| 01-736 | 01-236 | RDEYH38-FR | TOTAL RIGHT HIP PROTHESIS | 12/03/2012 | ONGOING |
| | | | HYPERTENSION | 01/01/2003 | ONGOING |

| Screening number | Randomisation # | Batch number | Description of the medical history | Date of beginning | Date of end or ongoing |
|---|---|---|---|---|---|
| 01-737 | 01-237 | RDEYH38-FR | LEFT KNEE PROTHESIS | 01/01/2008 | 01/01/2008 |
| | | | RIGHT KNEE PROTHESIS | 12/03/2012 | ONGOING |
| | | | RHIZOMELIC POLYARTHRITIS | 01/05/2012 | ONGOING |
| 01-738 | 01-238 | RDEYH36-FR | RIGHT GONARTHROSIS (HYPERALGIC) | 01/02/2011 | ONGOING |
| | | | LEFT LUMBAR PAIN + LEFT SCIATICA | 01/01/2012 | ONGOING |
| 01-739 | 01-239 | RDEYH38-FR | LEFT KNEE PROTHESIS | 12/03/2012 | ONGOING |
| 01-740 | 01-240 | RDEYH36-FR | ACUTE LUMBAR PAIN (CAR ACCIDENT ON 2006) | 01/01/2012 | ONGOING |
| | | | CAR ACCIDENT (2006): PELVIS FRACTURE + SPLENECTOMY + LUMBAR AND THORACIC TRAUMA | 01/01/2006 | ONGOING |
| 01-741 | 01-241 | RDEYH38-FR | FRACTURE OF LEFT FEMORAL NECK | 11/21/2012 | ONGOING |
| | | | TUMORECTOMY OF LEFT BREAST | 01/01/2011 | 01/01/2011 |
| | | | RIGHT SHOULDER ARTHRITIS | 09/01/2012 | ONGOING |
| 01-742 | 01-242 | RDEYH36-FR | SEVERE ARTHRITIS LUMBAR (HYPERALGESIA) | 11/15/2012 | ONGOING |
| 01-743 | 01-243 | RDEYH38-FR | LEFT ANKLE PROTHESIS | 09/18/2012 | ONGOING |
| | | | RIGHT KNEE PROTHESIS | 01/22/2013 | |
| 01-744 | 01-244 | RDEYH38-FR | PAIN LUMBAR (FRACTURE OF L2) | 03/27/2012 | ONGOING |
| | | | HIATUS HERNIA | 07/01/2010 | 07/01/2010 |
| | | | HYPERTENSION | 01/01/2003 | ONGOING |
| 01-745 | 01-245 | RDEYH36-FR | RIGHT GONARTHROSIS (HYPERALGIC MENISCECTOMY) | 01/01/1993 | ONGOING |
| 01-746 | 01-246 | RDEYH36-FR | ATHRITIS AND RIGHT ELBOW TENDINOPATHY | 12/01/2012 | ONGOING |
| | | | HYPERTENSION | 01/01/2008 | |
| 01-747 | 01-247 | RDEYH38-FR | SEVERE CERVICAL ARTHRITIS | 01/01/2013 | ONGOING |
| | | | LEFT KNEE PROTHESIS | 10/01/2006 | 10/01/2006 |
| | | | HYPERTENSION | 01/01/2002 | ONGOING |
| | | | HYPERCHOLESTEROLEMIA | 01/01/2002 | |
| 01-748 | 01-248 | RDEYH38-FR | BILATERAL TIBIAL OSTEOTOMY | 01/01/1983 | 01/01/1983 |
| | | | BILATERAL HALLUX VALGUS SURGERY | 01/01/2004 | 01/01/2004 |
| | | | BILATERAL GONARTHROSIS | 01/01/2006 | ONGOING |
| 01-749 | 01-249 | RDEYH36-FR | RIGHT HIP TENDINITIS | 09/01/2012 | ONGOING |
| 01-750 | 01-250 | RDEYH36-FR | CERVICAL ARTHRISIS + CERVICOBRACHIAL NEURALGIA | 01/01/2013 | ONGOING |
| 01-751 | 01-251 | RDEYH36-FR | RIGHT SHOULDER ARTHRITIS | 01/01/2010 | ONGOING |
| | | | BILATERAL GONARTHROSIS | 01/01/2010 | ONGOING |
| | | | OSTEOPOROSIS | 01/01/2010 | ONGOING |
| 01-752 | 01-252 | RDEYH38-FR | BACK ARTHRITIS | 01/01/2012 | ONGOING |
| 01-753 | 01-253 | RDEYH38-FR | POLYARTHROPATY | 01/01/1983 | ONGOING |
| 01-760 | 01-260 | RDEYH36-FR | LEFT KNEE PROTHESIS | 12/04/2012 | ONGOING |
| | | | RIGHT KNEE PROTHESIS (1st) | 01/01/2011 | |
| | | | RIGHT KNEE PROTHESIS (2nde) | 02/01/2012 | |
| 01-761 | 01-261 | RDEYH36-FR | LEFT KNEE PROTHESIS | 02/20/2013 | ONGOING |
| | | | PROSTATIC RESECTION | 01/01/2009 | 01/01/2009 |
| | | | DIABETES | 01/01/2001 | ONGOING |
| 01-762 | 01-262 | RDEYH38-FR | RIGHT ANKLE FRACTURE : OSTEOSYNTHESIS | 12/24/2012 | ONGOING |
| | | | SEVERE CERVICAL ARTHRITIS | 01/01/2000 | |
| | | | BILATERAL PAINFUL SHOULDER (PERIARTHRITIS) | 02/01/2013 | |
| | | | RIGHT KNEE GONARTHROSIS | 01/01/2011 | |
| 01-763 | 01-263 | RDEYH38-FR | NARROW LUMBAR CANAL OPERATION + NUCLEUS PULPOSUS HERNIATION L4L5-L5S1 SURGERY | 12/19/2007 | 12/19/2007 |
| | | | RETURN OF NARROW LUMBAR CANAL OPERATION + NUCLEUS PULPOSUS HERNIATION L4L5-L5S1 ARTHRODESIS | 12/20/2012 | ONGOING |
| 01-764 | 01-264 | RDEYH36-FR | LUMBAR SPINE OSTEOSYNTHESIS + NARROW VERTEBRAL CANAL | 02/12/2013 | ONGOING |
| | | | DIABETES | 01/01/1999 | |
| | | | HYPERCHOLESTEROLEMIA | | |
| 01-765 | 01-265 | RDEYH38-FR | CERVICAL ARTHRITIS | 01/01/2013 | ONGOING |
| 01-766 | 01-266 | RDEYH38-FR | RIGHT KNEE PROTHESIS | 12/07/2012 | ONGOING |
| | | | DIABETES | 01/01/2005 | |
| 01-767 | 01-267 | RDEYH38-FR | RIGHT PATELLA FRACTURE AND CRUCIATE KNEE LIGAMENTS SURGERY | 01/25/2013 | ONGOING |

| Screening number | Randomisation # | Batch number | Description of the medical history | Date of beginning | Date of end or ongoing |
|---|---|---|---|---|---|
| 01-768 | 01-268 | RDEYH36-FR | RHEUMATOID ARTHRITIS | 01/01/1998 | ONGOING |
| 01-769 | 01-269 | RDEYH38-FR | SEVERE GIBBOSITY - VERTEBRAL COMPRESSION | 01/01/2000 | ONGOING |
| 01-770 | 01-270 | RDEYH36-FR | PAINFUL SHOULDER (PERIARTHRITIS) | 11/01/2012 | ONGOING |
| | | | CHRONIC DEPRESSION | 01/01/2000 | |
| 01-790 | 01-290 | RDEYH38-FR | RIGHT KNEE PROTHESIS | 01/20/2013 | ONGOING |
| | | | LEFT KNEE PROTHESIS | 02/21/2012 | 02/21/2012 |
| | | | CATARACT OPERATION | 01/01/2012 | 01/01/2012 |
| | | | HYPERTENSION | 01/01/2000 | ONGOING |
| | | | DIABETES | 01/01/2005 | |
| | | | HYPERCHOLESTEROLEMIA | 01/01/2005 | |
| 01-791 | 01-291 | RDEYH38-FR | LEFT PAINFUL SHOULDER | 01/25/2013 | ONGOING |
| | | | HYPERTENSION | 01/01/2009 | |
| | | | HYPERCHOLESTEROLEMIA | 01/01/2004 | |
| 01-792 | 01-292 | RDEYH38-FR | NUCLEUS PULPOSUS HERNIATION L4L5 SURGERY | 02/26/2013 | ONGOING |
| | | | NUCLEUS PULPOSUS HERNIATION L5S1 SURGERY | 01/01/1998 | |
| | | | HYPOTHYROIDISM | 01/01/2000 | |
| | | | HYPERTENSION | 01/01/2000 | |
| 01-793 | 01-293 | RDEYH36-FR | MOTORBIKE ACCIDENT : RIGHT TIBIAL INTERCONDYLAR FRACTURE + RIGHT SHINBONE FRACTURE + CRUCIATE LIGAMENT RUPTURE | 06/16/2012 | ONGOING |
| 01-794 | 01-294 | RDEYH36-FR | LEFT KNEE PROTHESIS SURGERY | 10/22/2012 | ONGOING |
| | | | RIGHT KNEE PROTHESIS SURGERY | 05/05/2012 | 05/05/2012 |
| | | | DIABETES | 01/01/1998 | ONGOING |
| | | | HYPERTENSION | 01/01/1998 | ONGOING |
| 01-795 | 01-295 | RDEYH36-FR | SEVERE CERVICAL ARTHRITIS | 01/01/2010 | ONGOING |
| | | | HYPERTENSION | 01/01/2000 | |
| 01-796 | 01-296 | RDEYH36-FR | RHEUMATOID ARTHRITIS | 01/01/2009 | ONGOING |
| 01-797 | 01-297 | RDEYH36-FR | BONE MYELOMA (REMISSION) | 04/01/2012 | ONGOING |
| | | | LEFT RIBS FRACTURE | 03/19/2013 | |
| | | | DIFFUSE POLYARTHROPATHY | 01/01/2010 | |
| 01-798 | 01-298 | RDEYH36-FR | SEVERE POLYARTHROPATHY | 01/01/2000 | ONGOING |
| | | | MENINGIOMA IN D12 OPERATION | 04/01/2000 | |
| 01-799 | 01-299 | RDEYH36-FR | CERVICAL ARTHROSIS + LEFT CERVICOBRACHIAL NEURALGIA | 03/01/2013 | ONGOING |
| | | | HYPERTENSION | 01/01/2011 | |
| 01-820 | 01-320 | RDEYH38-FR | SURGERY ON RIGHT CARPAL TUNNEL (RESIDUAL PAIN) | 02/13/2007 | ONGOING |
| | | | RIGHT DUPUYTREN SURGERY (RESIDUAL PAIN) | 12/08/2009 | ONGOING |
| 01-821 | 01-321 | RDEYH38-FR | LEFT HIP PROTHESIS | 02/01/2011 | 02/01/2011 |
| | | | RIGHT HIP PROTHESIS | 02/28/2013 | ONGOING |
| | | | ANEURYSM OPERATION | 12/11/2007 | 12/11/2007 |
| 01-822 | 01-322 | RDEYH38-FR | SURGERY OF RIGHT SHOULDER ROTATOR CUFF | 01/03/2013 | ONGOING |
| 01-823 | 01-323 | RDEYH36-FR | SEVERE CERVICAL ARTHRITIS | 01/01/2000 | ONGOING |
| | | | HYPERTENSION | 01/01/2011 | |
| 01-824 | 01-324 | RDEYH38-FR | LEFT HAND TENDON RUPTURE AND FRACTURE OPERATION (AFTER-EFFECTS PAIN) | 11/07/2012 | ONGOING |
| | | | LEFT FOOT MULTIPLE FRACTURE (AFTER-EFFECTS PAIN) | 07/28/2012 | |
| 01-825 | 01-325 | RDEYH38-FR | RIGHT KNEE PROTHESIS | 03/05/2013 | ONGOING |
| | | | RIGHT LEG OSTEOTOMY | 01/01/2001 | 01/01/2001 |
| | | | LEFT HIP PROTHESIS | 01/01/2002 | 01/01/2002 |
| | | | RIGHT ANKLE PAIN (ARTHRITIS) SINCE RIGHT KNEE PTOTHESIS | 03/05/2013 | ONGOING |
| 01-826 | 01-326 | RDEYH38-FR | LEFT SHOULDER TENDON OPERATION | 01/29/2013 | ONGOING |
| | | | HYPERCHOLESTEROLEMIA | 10/01/2012 | |
| 01-827 | 01-327 | RDEYH38-FR | SURGERY OF RIGHT THIGHBONE FRACTURE | 11/10/2012 | ONGOING |
| | | | RIGHT KNEE PROTHESIS | 01/01/2010 | 01/01/2010 |
| | | | DIABETES | 01/01/1998 | ONGOING |
| | | | LUMBAGO | 11/10/2012 | ONGOING |
| 01-828 | 01-328 | RDEYH38-FR | RIGHT KNEE PROTHESIS | 03/28/2013 | ONGOING |
| | | | GASTRITIS ULCER | 04/02/2013 | |
| 01-829 | 01-329 | RDEYH38-FR | RIGHT FOOT FRACTURE | 01/16/2013 | ONGOING |
| | | | OPERATED RIGHT ELBOW FRACTURE | | |
| 01-830 | 01-330 | RDEYH38-FR | LEFT KNEE TOTAL PROTHESIS | 03/13/2013 | ONGOING |
| | | | RIGHT GONARTHROSIS | 01/01/2010 | |

| Screening number | Randomisation # | Batch number | Description of the medical history | Date of beginning | Date of end or ongoing |
|---|---|---|---|---|---|
| 01-831 | 01-331 | RDEYH36-FR | CERVICODORSAL ARTHRITIS (INVALIDATING) | 01/01/1990 | ONGOING |
| 01-832 | 01-332 | RDEYH38-FR | HAND ARTHRITIS + RIGHT THUMB ARTHRITIS | 01/01/2013 | ONGOING |
| 01-833 | 01-333 | RDEYH36-FR | RHIZOMELIC POLYARTHRITIS | 01/01/2008 | ONGOING |
| | | | LUMBAR SPONDYLOSIS | 01/01/2000 | |
| | | | HYPERTENSION | 01/01/2008 | |
| 01-834 | 01-334 | RDEYH36-FR | BILATERAL SHOULDER ARTHRITIS | 01/01/2012 | ONGOING |
| | | | HYPERTENSION | 01/01/2003 | |
| 01-835 | 01-335 | RDEYH36-FR | POLYARTHROPATHY | 01/01/2000 | ONGOING |
| 01-840 | 01-340 | RDEYH38-FR | LEFT KNEE PROTHESIS | 03/23/2013 | ONGOING |
| | | | RIGHT GONARTHROSIS | 01/01/2000 | |
| | | | L5 COLLAPSING | 11/01/2012 | |
| | | | HYPERTENSION | 01/01/2005 | |
| 01-841 | 01-341 | RDEYH36-FR | CERVICAL TRAUMA | 01/01/2013 | ONGOING |
| 01-842 | 01-342 | RDEYH38-FR | RIGHT HIP TOTAL PROTHESIS | 01/01/2006 | ONGOING |
| | | | TRAUMA WITH PROTHESIS ACETABULUM FRACTURE | 12/18/2012 | |
| | | | RIGHT BOTTOM PAIN | 12/18/2012 | |
| | | | LEFT UPPER LIMB PAIN | 12/18/2012 | |
| 01-843 | 01-343 | RDEYH36-FR | SEVERE LUMBAR ARTHRITIS | 01/01/2012 | ONGOING |
| | | | ARTHRITIS | 01/01/2000 | |
| 01-844 | 01-344 | RDEYH36-FR | NUCLEUS PULPOSUS HERNIATION L5-S1 | 01/01/2005 | ONGOING |
| | | | THREE BYPASS | 03/22/2013 | |
| 01-845 | 01-345 | RDEYH36-FR | SPLENECTOMY | 01/01/1987 | 01/01/1987 |
| | | | THYROIDECTOMY | 01/01/2007 | ONGOING |
| | | | POLYARTHROPATHY | 01/01/20110 | |
| 01-846 | 01-346 | RDEYH38-FR | RIGHT KNEE FRACTURE OSTEOSYNTHESIS | 03/12/2013 | ONGOING |
| 01-847 | 01-347 | RDEYH36-FR | LEFT CRURALGIA (PAIN) | 04/08/2013 | ONGOING |
| 01-849 | 01-349 | RDEYH38-FR | CERVICAL ARTHRITIS | 01/01/2010 | ONGOING |
| | | | HYPOTHYROIDISM | 01/01/1991 | |
| 01-850 | 01-350 | RDEYH36-FR | RIGHT KNEE TOTAL PROTHESIS | 02/22/2013 | ONGOING |
| | | | HYPERTENSION | 01/01/2010 | |
| 01-851 | 01-351 | RDEYH38-FR | CEREBROVASCULAR NEUROLOGIC DISEASE WITH UPPER LIMB PARALYSIS | 02/03/2013 | ONGOING |
| | | | LEFT SHOULDER PAIN | 03/03/2013 | |
| 01-852 | 01-352 | RDEYH38-FR | PROSTATECTOMY | 01/01/2003 | ONGOING |
| | | | LEFT HEMIPLEGIA CEREBROVASCULAR NEUROLOGIC DISEASE - LEFT SHOULDER PAIN | 11/01/2012 | |
| 01-853 | 01-353 | RDEYH36-FR | LEFT BREAST TUMORECTOMY | 02/08/2012 | ONGOING |
| | | | LEFT SHOULDER PAIN | 02/08/2012 | |
| 01-854 | 01-354 | RDEYH38-FR | LUMBAGO | 01/01/2005 | ONGOING |
| 01-855 | 01-355 | RDEYH38-FR | RIGHT HIP PROTHESIS SURGERY | 01/01/2007 | ONGOING |
| | | | LEFT HIP PROTHESIS SURGERY | 03/01/2013 | |
| | | | HYPERTENSION | 01/01/2010 | |
| 01-856 | 01-356 | RDEYH36-FR | NUCLEUS PULPOSUS HERNIATION L5-S1 | 01/01/2013 | ONGOING |
| 04-702 | 04-102 | RDEYH38-FR | LEFT KNEE PROTHESIS | 01/01/2010 | ONGOING |
| | | | RIGHT KNEE PROTHESIS | 10/22/2012 | ONGOING |
| 04-703 | 04-103 | RDEYH38-FR | FIBROMYALGIA | 01/01/2012 | ONGOING |
| | | | DIFFUSE POLYARTHROPATHY | 01/01/2002 | |
| 04-704 | 04-104 | RDEYH36-FR | NUCLEUS PULPOSUS HERNIATION L4L5 SURGERY | 11/09/2012 | 11/09/2012 |
| 04-705 | 04-105 | RDEYH38-FR | THIGH BONE FRACTURE SURGERY | 09/22/2012 | 09/22/2012 |
| | | | SCIATICA PAIN | | ONGOING |
| 04-706 | 04-106 | RDEYH36-FR | POLYARTHROPATHY | 01/01/1970 | ONGOING |
| | | | LEFT HAND ARTHRITIS | 01/01/2002 | |
| | | | NUCLEUS PULPOSUS HERNIATIONS L3L4,L5-S1 SURGERY | 11/06/2012 | 11/06/2012 |
| 04-707 | 04-107 | RDEYH36-FR | RIGHT LEG TIBIA-FIBULA SUGERY | 05/01/2012 | 05/01/2012 |
| | | | LEFT SHOULDER ROTATOR CUFF LESION | 01/01/2000 | ONGOING |
| 04-708 | 04-108 | RDEYH36-FR | NARROW LUMBAR CANAL OPERATION | 11/27/2012 | 11/27/2012 |
| | | | POLYARTHROPATHY | 01/01/1990 | ONGOING |
| 04-709 | 04-109 | RDEYH38-FR | NUCLEUS PULPOSUS HERNIATION L5-S1 SURGERY | 11/02/2012 | 11/02/2012 |
| 04-710 | 04-110 | RDEYH38-FR | LEFT HIP PROTHESIS | 09/25/2012 | 09/25/2012 |
| | | | RIGHT HIP PROTHESIS | 03/07/2003 | 03/07/2003 |
| | | | RIGHT KNEE PROTHESIS | 01/01/2008 | 01/01/2008 |
| 04-711 | 04-111 | RDEYH36-FR | NUCLEUS PULPOSUS HERNIATIONS L4L5 L5-S1 SURGERY | 11/14/2012 | 11/14/2012 |

### *16.2.4.3 Previous treatments*

| | | | Previous or concomitant treatment at the inclusion | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Screening number** | **Randomisation #** | **Batch number** | **Treatment** | **Indication** | **Posology** | **Administration route** | **Date of beginning** | **Date of end or ongoing** |
| 01-701 | 01-201 | RDEYH38-FR | VOLTARENE LP 100 | PAIN | 1/D | ORAL | 09/04/2012 | ONGOING |
| | | | LEVOTHYROX | HYPERTHYROÏDISM | | | 01/01/2012 | |
| | | | HYTACAND | HYPERTENSION | | | 01/01/2002 | |
| 01-702 | 01-202 | RDEYH36-FR | DAFALGAN CODEINE | PAIN | 6/D | ORAL | 07/07/2012 | ONGOING |
| 01-703 | 01-203 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 09/30/2012 | ONGOING |
| | | | TOPALGIC 100 mg | | | | | |
| 01-704 | 01-204 | RDEYH38-FR | TOPALGIC 100 mg | PAIN | 2/D | ORAL | 09/01/2012 | ONGOING |
| | | | MYOLASTAN | | | | | |
| 01-721 | 01-221 | RDEYH36-FR | LEVOTHYROX 75 | HYPERTHYROIDISM | 1/D | ORAL | 01/01/2002 | ONGOING |
| | | | DOLIPRANE 1000 | PAIN | 3/D | | 10/01/2012 | |
| | | | VOLTARENE LP 100 | PAIN | 1/D | | | |
| 01-722 | 01-222 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 01/01/2010 | ONGOING |
| | | | TOPALGIC | | 2/D | | 12/01/2012 | |
| | | | VOLTARENE LP 100 | | 1/D | | | |
| 01-723 | 01-223 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 09/01/2012 | ONGOING |
| | | | ART 50 | PAIN - ARTHROSIS | 2/D | | 01/01/2011 | |
| | | | CHONDROSULF | PAIN - ARTHROSIS | 3/D | | 01/01/2011 | |
| | | | TOPALGIC | PAIN | 2/D | | 09/01/2012 | |
| | | | VOLTARENE LP 100 | PAN | 2/D | | 09/01/2012 | |
| 01-724 | 01-224 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 2/D | ORAL | 06/01/2012 | ONGOING |
| | | | BIPROFENID | | 1/D | | 09/01/2012 | |
| | | | LAROXYL DROPS | | 10/D | | 10/01/2012 | |
| 01-725 | 01-225 | RDEYH38-FR | LEVOTHYROX | HYPOTHYROÏDISM | 1/D | ORAL | 01/01/2011 | ONGOING |
| 01-726 | 01-226 | RDEYH38-FR | DAFALGAN 1000 | PAIN | 1/D | ORAL | 09/01/2010 | ONGOING |
| | | | BIPROFENID | | | | 12/03/2012 | |
| 01-727 | 01-227 | RDEYH38-FR | CHONDROSULF | ARTHROSIS | 3/D | ORAL | 01/01/2008 | ONGOING |
| | | | GINKOR | VENOUS INSUFFICIENCY | 2/D | | 01/01/2000 | |
| | | | MODOPAR | PARKINSON | 5/D | | 01/01/2008 | |
| | | | REQUIP | PARKINSON | 1/D | | 01/01/2008 | |
| | | | DAFALGAN 1000 | PAIN | 3/D | | 01/01/2012 | |
| 01-728 | 01-228 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 01/01/2011 | ONGOING |
| | | | BIPROFENID | | 1/D | | 12/01/2012 | |
| 01-729 | 01-229 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 01/01/2010 | ONGOING |
| | | | VOLTARENE LP 100 | PAIN | 1/D | | 12/01/2012 | |
| | | | MYOLASTAN | MUSCLES CONTRACTION | 1/D | | 12/01/2012 | |
| 01-730 | 01-230 | RDEYH38-FR | METFORMINE 500 | DIABETES | 2/D | ORAL | 01/01/2008 | ONGOING |
| | | | JANUVIA | DIABETES | 1/D | | 01/01/2008 | |
| | | | PROGRAF | AGAINST REJECTION FOR | 5/D | | 01/01/2008 | |
| | | | MIFORTIK 360 | AGAINST REJECTION FOR | 2/D | | 01/01/2008 | |
| | | | EZETROL | HYPERCHOLESTEROLEMIA | 1/D | | 01/01/2008 | |
| | | | TAHOR 20 | HYPERCHOLESTEROLEMIA | 1/D | | 01/01/2008 | |
| | | | TAREG 80 | HYPERTENSION | 1/D | | 01/01/2008 | |
| 01-731 | 01-231 | RDEYH36-FR | TOPALGIC 100 | PAIN | 2/D | ORAL | 11/20/2012 | ONGOING |
| | | | BIPROFENID | PAIN | 1/D | | 11/20/2012 | |
| | | | MYOLASTAN | MUSCLES CONTRACTION | 1/D | | 11/20/2012 | |
| 01-732 | 01-232 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 08/21/2003 | ONGOING |
| | | | LYRICA | | 3/D | | 01/01/2012 | |
| | | | RIVOTRIL | | 1/D | | 01/01/2010 | |
| 01-733 | 01-233 | RDEYH38-FR | BIPROFENID 100 | PAIN | 2/D | ORAL | 12/09/2012 | ONGOING |
| | | | TETRAZEPAM | MUSCLES CONTRACTION | 2/D | | 12/09/2012 | |
| | | | LYRICA 25 | PAIN | 2/D | | 12/09/2012 | |
| 01-734 | 01-234 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 12/03/2012 | ONGOING |
| | | | TOPALGIC | PAIN | 2/D | | 12/03/2012 | |
| | | | TAMOXIFENE | BREAST CANCER | 1/D | | 05/05/2010 | |
| 01-735 | 01-235 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 12/01/2012 | ONGOING |
| | | | BIPROFENID LP 100 | | 1/D | | 12/01/2012 | |
| 01-736 | 01-236 | RDEYH38-FR | TOPALGIC | PAIN | 2/D | ORAL | 12/01/2012 | ONGOING |
| | | | HYPERIUM | HYPERTENSION | 1/D | | 01/01/2003 | |
| | | | COOLMETEC | HYPERTENSION | 1/D | | 01/01/2003 | |
| | | | TEMERIT | HYPERTENSION | 1/D | | 01/01/2003 | |
| 01-737 | 01-237 | RDEYH38-FR | PREDNISOLONE | POLYARTHRITIS | 1/D | ORAL | 01/05/2012 | ONGOING |
| | | | DOLIPRANE 1000 | PAIN | 3/D | | 12/03/2012 | |
| | | | TRAMADOL | PAIN | 1/D | | 12/03/2012 | |
| 01-738 | 01-238 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 01/02/2011 | ONGOING |
| | | | BIPROFENID LP 100 | | 1/D | | 01/01/2012 | |
| 01-739 | 01-239 | RDEYH38-FR | DAFALGAN 1000 | PAIN | 4/D | ORAL | 12/03/2012 | ONGOING |
| | | | BIPROFENID | | 2/D | | 12/03/2012 | |
| | | | TOPALGIC | | 2/D | | 12/03/2012 | |
| | | | ACUPAN | | 2/D | | 12/03/2012 | |
| 01-740 | 01-240 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 01/01/2012 | ONGOING |
| | | | BIPROFENID | | 2/D | | 12/01/2012 | |
| | | | TOPALGIC | | 1/D | | 12/01/2012 | 12/15/12 |

| | | | Previous or concomitant treatment at the inclusion | | | | | |
|---|---|---|---|---|---|---|---|---|
| Screening number | Randomisation # | Batch number | Treatment | Indication | Posology | Administration route | Date of beginning | Date of end or ongoing |
| 01-741 | 01-241 | RDEYH38-FR | DOLIPRANE | PAIN | 3/D | ORAL | 09/01/2012 | ONGOING |
| | | | TOPALGIC | | | | | |
| 01-742 | 01-242 | RDEYH36-FR | DAFALGAN CODEINE | PAIN | 2/D | ORAL | 11/15/2012 | ONGOING |
| | | | BIPROFENID | | | | | |
| 01-743 | 01-243 | RDEYH38-FR | SEROPLEX 10 | DEPRESSION | 1/D | ORAL | 01/01/2013 | ONGOING |
| | | | STABLON | | 3/D | | 01/01/2009 | |
| | | | XANAX 0,25 | ANXIETY | 3/D | | 01/01/2013 | |
| | | | STILNOX | INSOMNIA | 1/D | | | |
| | | | BIPROFENID CP 100 | PAIN | 1/D | | | |
| | | | TOPALGIC | | 2/D | | | |
| | | | DOLIPRANE 1000 | | 4/D | | | |
| 01-744 | 01-244 | RDEYH38-FR | DOLIPRANE 1000 | PAIN | 2/D | ORAL | 03/27/2012 | ONGOING |
| | | | APROVEL 75 | HYPERTENSION | 1/D | | 01/01/2003 | |
| 01-745 | 01-245 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 2/D | ORAL | 01/01/2013 | ONGOING |
| | | | IBUPROFENE | | | | 01/01/2013 | |
| 01-746 | 01-246 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 12/01/2012 | ONGOING |
| | | | IBUPROFENE | | | | 02/01/2013 | |
| | | | HYTACAND 8 | HYPERTENSION | 1/D | | 01/01/2008 | |
| 01-747 | 01-247 | RDEYH38-FR | EFFERALGAN 1000 | PAIN | 3/D | ORAL | 01/01/2013 | ONGOING |
| | | | VOLTARENE LP 100 | | 1/D | ORAL | 02/01/2013 | |
| | | | LODOZ | HYPERTENSION | 1/D | ORAL | 01/01/2002 | |
| | | | ELISOR 20 | HYPERCHOLESTEROLEMIA | 1/D | ORAL | 01/01/2002 | |
| 01-748 | 01-248 | RDEYH38-FR | PARACETAMOL 1000 | PAIN | 3/D | ORAL | 01/01/2006 | ONGOING |
| | | | IBUPROFENE | | | | 01/01/2013 | |
| 01-749 | 01-249 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 09/01/2012 | ONGOING |
| | | | APRANAX | | 1/D | | 02/01/2013 | |
| 01-750 | 01-250 | RDEYH36-FR | PARACETAMOL 1000 | PAIN | 3/D | ORAL | 01/01/2013 | ONGOING |
| 01-751 | 01-251 | RDEYH36-FR | ACTONEL | OSTEOPOROSIS | 1/D | ORAL | 01/01/2010 | ONGOING |
| | | | OROCAL D3 | | | | | |
| | | | IBUPROFENE 400 | PAIN | 3/D | | 01/01/2013 | |
| | | | EFFERALGAN 1000 | | 2/D | | | |
| 01-752 | 01-252 | RDEYH38-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 01/01/2012 | ONGOING |
| | | | IXPRIM | | 1/D | | 02/01/2013 | |
| 01-753 | 01-253 | RDEYH38-FR | EFFERALGAN 1000 | PAIN | 3/D | ORAL | 01/01/2010 | ONGOING |
| 01-760 | 01-260 | RDEYH36-FR | LAMALINE | PAIN | 3/D | ORAL | 12/04/2012 | ONGOING |
| | | | TAHOR 10 | HYPERCHOLESTEROLEMIA | 1/D | | 01/01/2010 | |
| 01-761 | 01-261 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 02/20/2013 | ONGOING |
| | | | METFORMINE 500 | DIABETES | NK | | 01/01/2001 | |
| 01-762 | 01-262 | RDEYH38-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 12/24/2012 | ONGOING |
| | | | FLECTOR TISSUGEL | | 1/D | CUTANEOUS | | |
| 01-763 | 01-263 | RDEYH38-FR | ZALDIAR | PAIN | 2/D | ORAL | 12/20/2012 | ONGOING |
| | | | DOLIPRANE 1000 | | 3/D | | 12/20/2012 | |
| | | | CELEBREX | | 2/D | | 03/01/2013 | |
| 01-764 | 01-264 | RDEYH36-FR | DOLIPRANe 1000 | PAIN | 3/D | ORAL | 12/12/2013 | ONGOING |
| | | | CRESTOR 10 | HYPERCHOLESTEROLEMIA | 1/D | | 01/01/2006 | |
| | | | METFORMINE 850 | DIABETES | 3/D | | 01/01/1999 | |
| 01-765 | 01-265 | RDEYH38-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 01/01/2013 | ONGOING |
| 01-766 | 01-266 | RDEYH38-FR | IXPRIM | PAIN | 3/D | ORAL | 03/01/2013 | ONGOING |
| | | | METFORMINE 500 | DIABETES | | | 01/01/2005 | |
| 01-767 | 01-267 | RDEYH38-FR | IXPRIM | PAIN | 3/D | ORAL | 01/25/2013 | ONGOING |
| | | | MYOLASTAN | | 2/D | | 03/01/2013 | |
| 01-768 | 01-268 | RDEYH36-FR | EFFERALGAN 1000 | PAIN | 3/D | ORAL | 01/01/2013 | ONGOING |
| 01-769 | 01-269 | RDEYH38-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 01/01/2013 | ONGOING |
| 01-770 | 01-270 | RDEYH36-FR | DAFALGAN CODEINE | PAIN | 3/D | ORAL | 01/01/2013 | ONGOING |
| | | | SEROPLEX 10 | DEPRESSION | 1/D | | 01/01/2011 | |
| | | | DEPAMIDE | | 3/D | | 11/01/2011 | |
| 01-790 | 01-290 | RDEYH38-FR | DOLIPRANE 1000 | PAIN | 4/D | ORAL | 01/20/2013 | ONGOING |
| | | | METFORMINE 850 | DIABETES | 2/D | | 01/01/2005 | |
| | | | ZOCOR 20 | HYPERCHOLESTEROLEMIA | 1/D | | 01/01/2005 | |
| | | | TENORMINE 50 | HYPERTENSION | 1/D | | 01/01/2000 | |
| 01-791 | 01-291 | RDEYH38-FR | DOLIPRANE 1000 | PAIN | 1/D | ORAL | 01/25/2013 | ONGOING |
| | | | PREVISCAN | ANTICOAGULANT | 0,75/D | | 02/25/2013 | |
| | | | TAHOR 10 | HYPERCHOLESTEROLEMIA | 1/D | | 01/01/2004 | |
| | | | ATACAND | HYPERTENSION | 1/D | | 01/01/2009 | |
| 01-792 | 01-292 | RDEYH38-FR | LAMALINE | PAIN | 3/D | ORAL | 02/26/2013 | ONGOING |
| | | | LEVOTHYROX | HYPOTHYROIDISM | NK | | 01/01/2000 | |
| | | | LOPRIL | HYPERTENSION | NK | | 01/01/2000 | |
| 01-793 | 01-293 | RDEYH36-FR | LAMALINE | PAIN | 1/D | ORAL | 06/16/2012 | ONGOING |

| | | | Previous or concomitant treatment at the inclusion | | | | | |
|---|---|---|---|---|---|---|---|---|
| Screening number | Randomisation # | Batch number | Treatment | Indication | Posology | Administration route | Date of beginning | Date of end or ongoing |
| 01-794 | 01-294 | RDEYH36-FR | TRAMADOL | PAIN | 1/D | ORAL | 10/22/2012 | ONGOING |
| | | | EFFERALGAN 500 | | 6/D | | 10/22/2012 | |
| | | | METFORMINE 500 | DIABETES | 2/D | | 01/01/1998 | |
| | | | ACEBUTOLOL | HYPERTENSION | 1/D | | 01/01/1998 | |
| | | | HYPERTEN | | 1/D | | 01/01/1998 | |
| 01-795 | 01-295 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 01/01/2013 | ONGOING |
| | | | SOTALEX | HYPERTENSION | 1/D | ORAL | 01/01/2000 | |
| 01-796 | 01-296 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 01/01/2013 | ONGOING |
| | | | ENBREL | | NK | ORAL | 01/01/2010 | |
| 01-797 | 01-297 | RDEYH36-FR | REVLIMID | MYELOMA | 1/D | ORAL | 02/01/2013 | ONGOING |
| | | | DAFALGAN CODEINE | PAIN | 3/D | | 03/19/2013 | |
| 01-798 | 01-298 | RDEYH36-FR | EFFERALGAN 1000 | PAIN | 3/D | ORAL | 01/01/2010 | ONGOING |
| 01-799 | 01-299 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 03/01/2013 | ONGOING |
| | | | IBUPROFENE | | | | | |
| | | | APROVEL 300 | HYPERTENSION | 1/D | | 01/01/2011 | |
| 01-820 | 01-320 | RDEYH38-FR | LYRICA | PAIN | 2/D | ORAL | 02/13/2007 | ONGOING |
| | | | IXPRIM | | 4/D | | | |
| | | | RIVOTRIL | | 30/D | | | |
| | | | CYMBALTA | PAIN + DEPRESSION | 1/D | | | |
| | | | LAMALINE | PAIN | 4/D | | | |
| 01-821 | 01-321 | RDEYH38-FR | AVLOCARDYL | HEART | 1/D | ORAL | 12/11/2007 | ONGOING |
| | | | ASPEGIC 100 | HEART | 1/D | | | |
| | | | IXPRIM | PAIN | 5/D | | 02/28/2013 | |
| | | | LYRICA 300 | PAIN | 1/D | | | |
| | | | TANGANIL | VERTIGO | 3/D | | | |
| | | | IMOVANE | INSOMNIA | 1/D | | | |
| | | | MENESTA 1 | STRESS | 1/D | | | |
| 01-822 | 01-322 | RDEYH38-FR | IXPRIM | PAIN | 2/D | ORAL | 01/03/2013 | ONGOING |
| | | | DOLIPRANE 1000 | | 3/D | | | |
| 01-823 | 01-323 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 03/01/2013 | ONGOING |
| | | | ASPEGIC 1000 | | 3/D | | 03/01/2013 | |
| | | | TENORETIC | HYPERTENSION | 1/D | | 01/01/2011 | |
| 01-824 | 01-324 | RDEYH38-FR | LAMALINE | PAIN | 6/D | ORAL | 07/28/2012 | ONGOING |
| | | | IMOVANE | INSOMNIA | 1/D | | | |
| | | | DEPOXAT | DEPRESSION | | | | |
| | | | MYOLASTAN | MUSCLES CONTRACTION | | | | |
| 01-825 | 01-325 | RDEYH38-FR | LAMALINE | PAIN | 3/D | ORAL | 03/05/2013 | ONGOING |
| 01-826 | 01-326 | RDEYH38-FR | LAMALINE | PAIN | 6/D | ORAL | 01/29/2013 | ONGOING |
| | | | BIPROFENID | | 1/D | | | |
| | | | DOLIPRANE 1000 | | 3/D | | | |
| | | | EZETROL | HYPERCHOLESTEROLEMIA | 1/D | | 10/01/2012 | |
| 01-827 | 01-327 | RDEYH38-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 11/10/2012 | ONGOING |
| | | | MYOLASTAN | | 1/D | | | |
| | | | TOPALGIC | | 2/D | | | |
| 01-828 | 01-328 | RDEYH38-FR | IXPRIM | PAIN | 6/D | ORAL | 04/02/2013 | ONGOING |
| | | | AMOXICILLINE | ULCER | 4/D | | | |
| | | | FLAGYL | | 2/D | | | |
| | | | ZECLAR | | 2/D | | | |
| | | | MOPRAL | | 2/D | | | |
| 01-829 | 01-329 | RDEYH38-FR | LAMALINE | PAIN | 6/D | ORAL | 01/16/2013 | ONGOING |
| | | | TETRAZEPAM | | 1/D | | | |
| 01-830 | 01-330 | RDEYH38-FR | DOLIPRANE CODEINE | PAIN | 3/D | ORAL | 03/13/2013 | ONGOING |
| | | | ACUPAN | | 1/D | | | |
| 01-831 | 01-331 | RDEYH36-FR | PARACETAMOL 1000 | PAIN | 3/D | ORAL | 01/01/2013 | ONGOING |
| 01-832 | 01-332 | RDEYH38-FR | PARACETAMOL 1000 | PAIN | 3/D | ORAL | 01/01/2012 | ONGOING |
| | | | IBUPROFENE 400 | | 2/D | | 01/01/2013 | |
| 01-833 | 01-333 | RDEYH36-FR | SOLUPRED | POLYARTHRITIS | 1/D | ORAL | 01/01/2008 | ONGOING |
| | | | OLMETEC | HYPERTENSION | | | | |
| | | | DOLIPRANE 1000 | PAIN | 3/D | | 01/01/2013 | |
| 01-834 | 01-334 | RDEYH36-FR | BIPRETERAX | HYPERTENSION | 1/D | ORAL | 01/01/2003 | ONGOING |
| | | | DOLIPRANE 1000 | PAIN | 3/D | | 01/01/2013 | |
| 01-835 | 01-335 | RDEYH36-FR | EFFERALGAN 500 | PAIN | 6/D | ORAL | 01/01/2000 | ONGOING |
| 01-840 | 01-340 | RDEYH38-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 03/28/2013 | ONGOING |
| | | | BIPRETERAX | HYPERTENSION | 1/D | | 01/01/2005 | |
| 01-841 | 01-341 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 01/01/2013 | ONGOING |
| | | | BIPROFENID | | 1/D | | 01/01/2013 | |
| 01-842 | 01-342 | RDEYH38-FR | LYRICA 50 | PAIN | 2/D | ORAL | 12/18/2012 | ONGOING |
| 01-843 | 01-343 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 2/D | ORAL | 01/01/2013 | ONGOING |
| | | | BIPROFENID | | 1/D | | 04/01/2013 | |

| | | | Previous or concomitant treatment at the inclusion | | | | | |
|---|---|---|---|---|---|---|---|---|
| Screening number | Randomisation # | Batch number | Treatment | Indication | Posology | Administration route | Date of beginning | Date of end or ongoing |
| 01-844 | 01-344 | RDEYH36-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 03/22/2013 | ONGOING |
| | | | TENORMINE 50 | ANXIETY | 1/D | | 03/22/2013 | |
| | | | ELISOR 40 | HYPERCHOLESTEROLEMIA | 1/D | | 03/22/2013 | |
| | | | KARDEGIC 75 | ANTICOAGULANT | 1/D | | 03/22/2013 | |
| 01-845 | 01-345 | RDEYH36-FR | ACUPAN | PAIN | 1/D | ORAL | 04/01/2013 | ONGOING |
| | | | LEVOTHYROX | HYPOTHYROIDISM | 1/D | | 01/01/2010 | |
| 01-846 | 01-346 | RDEYH38-FR | TOPALGIC | PAIN | 2/D | ORAL | 03/12/2013 | ONGOING |
| | | | BIPROFENID | PAIN | 2/D | | 03/12/2013 | |
| 01-847 | 01-347 | RDEYH36-FR | VOLTARENE LP | PAIN | 2/D | ORAL | 04/08/2013 | ONGOING |
| | | | DAFALGAN 1000 | PAIN | 3/D | | 04/08/2013 | |
| 01-849 | 01-349 | RDEYH38-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 01/01/2013 | ONGOING |
| | | | LEVOTHYROX | HYPOTHYROIDISM | 1/D | | 01/01/1991 | |
| 01-850 | 01-350 | RDEYH36-FR | LAMALINE | PAIN | 3/D | ORAL | 02/22/2013 | ONGOING |
| | | | COAPROVEL | HYPERTENSION | 1/D | | 01/01/2010 | |
| 01-851 | 01-351 | RDEYH38-FR | PREVISCAN | ANTICOAGULANT | 1/D | ORAL | 03/02/2013 | ONGOING |
| | | | LYRICA 25 | PAIN | 1/D | | 03/03/2013 | |
| 01-852 | 01-352 | RDEYH38-FR | DOLIPRANE 1000 | PAIN | 3/D | ORAL | 01/11/2013 | ONGOING |
| | | | KARDEGIC 75 | ANTICOAGULANT | 1/D | | 01/11/2012 | |
| 01-853 | 01-353 | RDEYH36-FR | NOLVADEX | BREAST CANCER | 1/D | ORAL | 02/08/2013 | ONGOING |
| | | | DOLIPRANE 1000 | PAIN | 1/D | | 02/08/2012 | |
| 01-854 | 01-354 | RDEYH38-FR | ADVIL 400 | PAIN | 4/D | ORAL | 01/01/2011 | ONGOING |
| 01-855 | 01-355 | RDEYH38-FR | DOLIPRANE 1000 | PAIN | 4/D | ORAL | 03/01/2013 | ONGOING |
| | | | TOPALGIC | PAIN | 1/D | | 03/01/2013 | |
| | | | NISIS 160 | HYPERTENSION | 1/D | | 01/01/2010 | |
| | | | SKENAN 30 | PAIN | 1/D | | 04/01/2013 | |
| 01-856 | 01-356 | RDEYH36-FR | IXPRIM | PAIN | 4/D | ORAL | 04/01/2013 | ONGOING |
| 04-702 | 04-102 | RDEYH38-FR | DAFALGAN 1000 | KNEE PAIN | 3/D | ORAL | 10/22/2012 | ONGOING |
| 04-703 | 04-103 | RDEYH38-FR | NEURONTIN | PAIN | 3/D | ORAL | 01/01/2012 | ONGOING |
| | | | TOPALGIC | | 3/D | | | |
| | | | MYOLASTAN | | 1/D | | | |
| | | | LAROXYL 50mg | | 1/D | | | |
| 04-704 | 04-104 | RDEYH36-FR | BIPROFENID | PAIN | 2/D | ORAL | 11/09/2012 | ONGOING |
| | | | DAFALGAN 1000 | | 3/D | | | |
| 04-705 | 04-105 | RDEYH38-FR | ACUPAN | PAIN | 2/D | ORAL | 09/22/2012 | ONGOING |
| | | | LYRICA 150 | | 1/D | | | |
| | | | VOLTARENE | | | | | |
| | | | MYOLASTAN | | | | | |
| 04-706 | 04-106 | RDEYH36-FR | ACUPAN | PAIN | 3/D | ORAL | 11/06/2012 | ONGOING |
| | | | DAFALGAN 1000 | | | | | |
| | | | TOPALGIC | | 2/D | | | |
| 04-707 | 04-107 | RDEYH36-FR | DAFALGAN 1000 | PAIN | 3/D | ORAL | 05/01/2012 | ONGOING |
| | | | HYPERIUM | HYPERTENSION | 1/D | | 01/01/2005 | |
| | | | LOXEN | HYPERTENSION | | | | |
| 04-708 | 04-108 | RDEYH36-FR | LAMALINE | PAIN | 3/D | ORAL | 11/01/2012 | ONGOING |
| | | | FORTZAAR | HYPERTENSION | 1/D | | 01/01/2010 | |
| | | | PRAVASTATINE | HYPERCHOLESTEROLEMIA | | | | |
| | | | SEROPLEX | DEPRESSION | | | 01/01/2012 | |
| 04-709 | 04-109 | RDEYH38-FR | TOPALGIC | LUMBAR PAIN | 1/D | ORAL | 11/02/2012 | ONGOING |
| | | | VOLTARENE | | 2/D | | | |
| 04-710 | 04-110 | RDEYH38-FR | DAFALGAN 1000 | PAIN | 3/D | ORAL | 01/25/2012 | ONGOING |
| | | | BIPROFENID | | 2/D | | 11/01/2012 | |
| 04-711 | 04-111 | RDEYH36-FR | DAFALGAN 1000 | LUMBAR PAIN | 3/D | ORAL | 11/14/2012 | ONGOING |
| | | | TOPALGIC | | | | | |

*16.2.4.4 Final patch location and time for pain improvement*

| Subject identification | | | Final location of the patchs | Time to obtain pain relief (if inferior to 5 minutes) |
|---|---|---|---|---|
| Screening number | Randomisation # | Initials | | |
| 01-701 | 01-201 | TJ | LEFT KNEE | NA |
| 01-702 | 01-202 | FP | RIGHT SHOULDER | NA |
| 01-703 | 01-203 | BA | RIGHT SHOULDER | NA |
| 01-704 | 01-204 | BS | RIGHT SHOULDER | NA |
| 01-721 | 01-221 | LC | LUMBAR | NA |
| 01-722 | 01-222 | CM | CERVICAL | NA |
| 01-723 | 01-223 | RM | LUMBAR | NA |
| 01-724 | 01-224 | MM | RIGHT SHOULDER | NA |
| 01-725 | 01-225 | TE | RIGHT SHOULDER | NA |
| 01-726 | 01-226 | CH | LEFT BUTTOCK | NA |
| 01-727 | 01-227 | SM | CERVICAL | NA |
| 01-728 | 01-228 | DP | RIGHT ANKLE | NA |
| 01-729 | 01-229 | BM | CERVICAL | NA |
| 01-730 | 01-230 | VM | LEFT BUTTOCK | NA |
| 01-731 | 01-231 | MG | RIGHT KNEE | NA |
| 01-732 | 01-232 | FJ | RIGHT HEMIFACE | NA |
| 01-733 | 01-233 | TT | LEFT KNEE | NA |
| 01-734 | 01-234 | VM | RIGHT MAMMARY ZONE | NA |
| 01-735 | 01-235 | GJ | RIGHT KNEE | NA |
| 01-736 | 01-236 | GL | RIGHT HIP | NA |
| 01-737 | 01-237 | CA | RIGHT KNEE | NA |
| 01-738 | 01-238 | GP | LEFT KNEE | NA |
| 01-739 | 01-239 | BN | LEFT KNEE | NA |
| 01-740 | 01-240 | BM | LUMBAR | NA |
| 01-741 | 01-241 | BZ | RIGHT SHOULDER | NA |
| 01-742 | 01-242 | PP | LUMBAR | NA |
| 01-743 | 01-243 | DM | LEFT ANKLE | NA |
| 01-744 | 01-244 | GY | LUMBAR | NA |
| 01-745 | 01-245 | GR | RIGHT KNEE | NA |
| 01-746 | 01-246 | GM | RIGHT ELBOW | NA |
| 01-747 | 01-247 | BC | CERVICAL | NA |
| 01-748 | 01-248 | RM | LEFT KNEE | NA |
| 01-749 | 01-249 | LA | RIGHT HIP | NA |
| 01-750 | 01-250 | FC | CERVICAL | NA |
| 01-751 | 01-251 | LE | RIGHT SHOULDER | NA |
| 01-752 | 01-252 | DV | BACKBONE | NA |
| 01-753 | 01-253 | PC | UNDER FEET | NA |
| 01-760 | 01-260 | FE | RIGHT KNEE | NA |
| 01-761 | 01-261 | VP | LEFT KNEE | NA |
| 01-762 | 01-262 | BA | RIGHT KNEE | NA |
| 01-763 | 01-263 | GB | LUMBAR | NA |
| 01-764 | 01-264 | MS | LUMBAR | NA |
| 01-765 | 01-265 | AM | CERVICAL | NA |
| 01-766 | 01-266 | RV | RIGHT KNEE | NA |
| 01-767 | 01-267 | BJ | RIGHT KNEE | NA |
| 01-768 | 01-268 | RE | RIGHT HAND | NA |
| 01-769 | 01-269 | GH | LUMBAR | NA |
| 01-770 | 01-270 | VF | RIGHT SHOULDER | NA |
| 01-790 | 01-290 | VJ | RIGHT KNEE | NA |
| 01-791 | 01-291 | CA | LEFT SHOULDER | NA |
| 01-792 | 01-292 | OR | LUMBAR | NA |
| 01-793 | 01-293 | MS | RIGHT KNEE | NA |
| 01-794 | 01-294 | RP | LEFT KNEE | NA |
| 01-795 | 01-295 | CM | CERVICAL | NA |
| 01-796 | 01-296 | VN | LEFT FOOT | NA |
| 01-797 | 01-297 | BC | LEFT RIBBING | NA |
| 01-798 | 01-298 | MJ | RIGHT SHOULDER | NA |
| 01-799 | 01-299 | CJ | CERVICAL | NA |
| 01-820 | 01-320 | CC | RIGHT HAND | NA |
| 01-821 | 01-321 | FS | RIGHT HIP | NA |
| 01-822 | 01-322 | TA | RIGHT SHOULDER | NA |
| 01-823 | 01-323 | NM | CERVICAL | NA |
| 01-824 | 01-324 | GF | LEFT HAND | NA |
| 01-825 | 01-325 | GM | RIGHT ANKLE | NA |
| 01-826 | 01-326 | VY | LEFT SHOULDER | NA |
| 01-827 | 01-327 | BB | LUMBAR | NA |

| Subject identification | | | Final location of the patchs | Time to obtain pain relief (if inferior to 5 minutes) |
|---|---|---|---|---|
| Screening number | Randomisation # | Initials | | |
| 01-828 | 01-328 | BA | RIGHT KNEE | NA |
| 01-829 | 01-329 | GS | RIGHT HAND | NA |
| 01-830 | 01-330 | LM | LEFT KNEE | NA |
| 01-831 | 01-331 | GY | DORSAL | NA |
| 01-832 | 01-332 | PG | RIGHT THUMB | NA |
| 01-833 | 01-333 | BS | LUMBAR | NA |
| 01-834 | 01-334 | TJ | LEFT SHOULDER | NA |
| 01-835 | 01-335 | JJ | LUMBAR | NA |
| 01-840 | 01-340 | MA | LUMBAR | NA |
| 01-841 | 01-341 | BV | CERVICAL | NA |
| 01-842 | 01-342 | TY | LEFT UPPER LIMB | NA |
| 01-843 | 01-343 | GJ | LUMBAR | NA |
| 01-844 | 01-344 | MD | LUMBAR | NA |
| 01-845 | 01-345 | GC | CERVICAL | NA |
| 01-846 | 01-346 | RC | RHIGHT KNEE | NA |
| 01-847 | 01-347 | DB | LUMBAR | NA |
| 01-849 | 01-349 | VP | CERVICAL | NA |
| 01-850 | 01-350 | GP | RIGHT KNEE | NA |
| 01-851 | 01-351 | TR | LEFT SHOULDER | NA |
| 01-852 | 01-352 | TG | LEFT SHOULDER | NA |
| 01-853 | 01-353 | YC | SHOULDER | NA |
| 01-854 | 01-354 | SJ | LUMBAR | NA |
| 01-855 | 01-355 | GG | LEFT HIP | NA |
| 01-856 | 01-356 | VC | LUMBAR | NA |
| 04-702 | 04-102 | ZS | RIGHT KNEE | NA |
| 04-703 | 04-103 | TD | UNDER FOOT | NA |
| 04-704 | 04-104 | BP | BUTTOCKS | NA |
| 04-705 | 04-105 | SK | RIGHT FEET | NA |
| 04-706 | 04-106 | SJ | LEFT HAND | NA |
| 04-707 | 04-107 | GJ | LEFT SHOULDER | NA |
| 04-708 | 04-108 | DB | UPPER DORSAL | NA |
| 04-709 | 04-109 | DM | LUMBAR | NA |
| 04-710 | 04-110 | BL | LEFT HIP | NA |
| 04-711 | 04-111 | NJ | LUMBAR | NA |

### 16.2.5 Data on treatment adherence or on drug concentration (if available)

Not applicable.

### 16.2.6 Individual Efficacy Response data

## Pain scores on the EVA scale

| Subject identification | | Batch number | Pain score on T0 (mm) | Pain score on T5 minutes | Pain score on T15 minutes | Pain score on T1 hour |
|---|---|---|---|---|---|---|
| Randomisation # | Initials | | | | | |
| 01-201 | TJ | RDEYH38-FR | 50 | 30 | 0 | 0 |
| 01-202 | FP | RDEYH36-FR | 100 | 100 | 80 | 70 |
| 01-203 | BA | RDEYH36-FR | 60 | 60 | 60 | 30 |
| 01-204 | BS | RDEYH38-FR | 60 | 60 | 60 | 60 |
| 01-221 | LC | RDEYH36-FR | 50 | 30 | 10 | 10 |
| 01-222 | CM | RDEYH36-FR | 60 | 60 | 40 | 20 |
| 01-223 | RM | RDEYH36-FR | 70 | 70 | 70 | 60 |
| 01-224 | MM | RDEYH36-FR | 50 | 20 | 20 | 10 |
| 01-225 | TE | RDEYH38-FR | 50 | 50 | 50 | 50 |
| 01-226 | CH | RDEYH38-FR | 60 | 60 | 50 | 30 |
| 01-227 | SM | RDEYH38-FR | 50 | 50 | 50 | 45 |
| 01-228 | DP | RDEYH36-FR | 50 | 50 | 30 | 20 |
| 01-229 | BM | RDEYH36-FR | 70 | 70 | 60 | 20 |
| 01-230 | VM | RDEYH38-FR | 60 | 60 | 60 | 0 |
| 01-231 | MG | RDEYH36-FR | 50 | 40 | 30 | 30 |
| 01-232 | FJ | RDEYH36-FR | 80 | 70 | 50 | 10 |
| 01-233 | TT | RDEYH38-FR | 60 | 60 | 60 | 60 |
| 01-234 | VM | RDEYH36-FR | 50 | 40 | 20 | 20 |
| 01-235 | GJ | RDEYH36-FR | 70 | 60 | 20 | 10 |
| 01-236 | GL | RDEYH38-FR | 50 | 35 | 30 | 20 |
| 01-237 | CA | RDEYH38-FR | 60 | 50 | 45 | 30 |
| 01-238 | GP | RDEYH36-FR | 60 | 60 | 40 | 20 |
| 01-239 | BN | RDEYH38-FR | 50 | 40 | 20 | 10 |
| 01-240 | BM | RDEYH36-FR | 60 | 30 | 10 | 10 |
| 01-241 | BZ | RDEYH38-FR | 90 | 60 | 50 | 50 |
| 01-242 | PP | RDEYH36-FR | 70 | 70 | 40 | 40 |
| 01-243 | DM | RDEYH38-FR | 50 | 10 | 10 | 0 |
| 01-244 | GY | RDEYH38-FR | 50 | 50 | 50 | 40 |
| 01-245 | GR | RDEYH36-FR | 50 | 50 | 30 | 10 |
| 01-246 | GM | RDEYH36-FR | 50 | 30 | 0 | 0 |
| 01-247 | BC | RDEYH38-FR | 50 | 50 | 50 | 50 |
| 01-248 | RM | RDEYH38-FR | 70 | 70 | 70 | 70 |
| 01-249 | LA | RDEYH36-FR | 70 | 70 | 30 | 0 |
| 01-250 | FC | RDEYH36-FR | 80 | 80 | 40 | 20 |
| 01-251 | LE | RDEYH36-FR | 70 | 60 | 50 | 0 |
| 01-252 | DV | RDEYH38-FR | 60 | 60 | 60 | 60 |
| 01-253 | PC | RDEYH38-FR | 50 | 50 | 50 | 50 |
| 01-260 | FE | RDEYH36-FR | 50 | 40 | 50 | 50 |
| 01-261 | VP | RDEYH36-FR | 50 | 30 | 20 | 0 |
| 01-262 | BA | RDEYH38-FR | 70 | 30 | 20 | 10 |
| 01-263 | GB | RDEYH38-FR | 70 | 50 | 40 | 50 |
| 01-264 | MS | RDEYH36-FR | 50 | 30 | 30 | 30 |
| 01-265 | AM | RDEYH38-FR | 80 | 80 | 80 | 80 |
| 01-266 | RV | RDEYH38-FR | 60 | 60 | 60 | 60 |
| 01-267 | BJ | RDEYH38-FR | 60 | 60 | 60 | 60 |
| 01-268 | RE | RDEYH36-FR | 70 | 70 | 50 | 20 |
| 01-269 | GH | RDEYH38-FR | 50 | 50 | 40 | 40 |
| 01-270 | VF | RDEYH36-FR | 70 | 70 | 40 | 40 |
| 01-290 | VJ | RDEYH38-FR | 50 | 40 | 40 | 35 |
| 01-291 | CA | RDEYH38-FR | 60 | 30 | 20 | 10 |
| 01-292 | OR | RDEYH38-FR | 80 | 70 | 70 | 70 |
| 01-293 | MS | RDEYH36-FR | 50 | 20 | 10 | 0 |
| 01-294 | RP | RDEYH36-FR | 50 | 40 | 40 | 10 |
| 01-295 | CM | RDEYH36-FR | 70 | 60 | 40 | 30 |
| 01-296 | VN | RDEYH36-FR | 50 | 50 | 20 | 20 |
| 01-297 | BC | RDEYH36-FR | 80 | 80 | 60 | 50 |
| 01-298 | MJ | RDEYH36-FR | 70 | 70 | 40 | 20 |
| 01-299 | CJ | RDEYH36-FR | 70 | 40 | 20 | 0 |
| 01-320 | CC | RDEYH38-FR | 80 | 80 | 80 | 80 |
| 01-321 | FS | RDEYH38-FR | 60 | 40 | 50 | 50 |
| 01-322 | TA | RDEYH38-FR | 80 | 70 | 70 | 70 |
| 01-323 | NM | RDEYH36-FR | 80 | 80 | 50 | 0 |
| 01-324 | GF | RDEYH38-FR | 90 | 90 | 100 | 100 |
| 01-325 | GM | RDEYH38-FR | 50 | 20 | 20 | 20 |
| 01-326 | VY | RDEYH38-FR | 50 | 40 | 60 | 50 |
| 01-327 | BB | RDEYH38-FR | 50 | 40 | 25 | 50 |

| Subject identification | | Batch number | Pain score on T0 (mm) | Pain score on T5 minutes | Pain score on T15 minutes | Pain score on T1 hour |
|---|---|---|---|---|---|---|
| Randomisation # | Initials | | | | | |
| 01-328 | BA | RDEYH38-FR | 70 | 40 | 60 | 70 |
| 01-329 | GS | RDEYH38-FR | 50 | 40 | 40 | 40 |
| 01-330 | LM | RDEYH38-FR | 50 | 40 | 40 | 60 |
| 01-331 | GY | RDEYH36-FR | 70 | 70 | 30 | 10 |
| 01-332 | PG | RDEYH38-FR | 50 | 50 | 50 | 50 |
| 01-333 | BS | RDEYH36-FR | 80 | 70 | 20 | 20 |
| 01-334 | TJ | RDEYH36-FR | 60 | 50 | 30 | 0 |
| 01-335 | JJ | RDEYH36-FR | 70 | 60 | 40 | 10 |
| 01-340 | MA | RDEYH38-FR | 80 | 80 | 80 | 90 |
| 01-341 | BV | RDEYH36-FR | 50 | 40 | 20 | 0 |
| 01-342 | TY | RDEYH38-FR | 50 | 50 | 50 | 50 |
| 01-343 | GJ | RDEYH36-FR | 50 | 40 | 25 | 10 |
| 01-344 | MD | RDEYH36-FR | 80 | 50 | 50 | 40 |
| 01-345 | GC | RDEYH36-FR | 60 | 60 | 40 | 20 |
| 01-346 | RC | RDEYH38-FR | 70 | 70 | 70 | 70 |
| 01-347 | DB | RDEYH36-FR | 100 | 70 | 50 | 15 |
| 01-349 | VP | RDEYH38-FR | 50 | 50 | 50 | 50 |
| 01-350 | GP | RDEYH36-FR | 50 | 50 | 50 | 50 |
| 01-351 | TR | RDEYH38-FR | 50 | 50 | 50 | 50 |
| 01-352 | TG | RDEYH38-FR | 70 | 70 | 70 | 70 |
| 01-353 | YC | RDEYH36-FR | 80 | 80 | 70 | 80 |
| 01-354 | SJ | RDEYH38-FR | 60 | 20 | 20 | 20 |
| 01-355 | GG | RDEYH38-FR | 50 | 50 | 50 | 50 |
| 01-356 | VC | RDEYH36-FR | 50 | 50 | 40 | 40 |
| 04-102 | ZS | RDEYH38-FR | 55 | 35 | 35 | 30 |
| 04-103 | TD | RDEYH38-FR | 50 | 40 | 20 | 20 |
| 04-104 | BP | RDEYH36-FR | 50 | 30 | 30 | 10 |
| 04-105 | SK | RDEYH38-FR | 50 | 30 | 30 | 50 |
| 04-106 | SJ | RDEYH36-FR | 70 | 20 | 40 | 40 |
| 04-107 | GJ | RDEYH36-FR | 90 | 60 | 50 | 40 |
| 04-108 | DB | RDEYH36-FR | 60 | 40 | 40 | 40 |
| 04-109 | DM | RDEYH38-FR | 50 | 30 | 30 | 20 |
| 04-110 | BL | RDEYH38-FR | 50 | 50 | 50 | 50 |
| 04-111 | NJ | RDEYH36-FR | 50 | 40 | 35 | 25 |

### 16.2.7 Adverse event listings (each subject) and concomitant treatments

*16.2.7.1 Adverse event listing*

No adverse event occurred during the study.

*16.2.7.2 Concomitant treatments listing*

No treatment was taken during the study.

### 16.2.8 Listing of individual laboratory measurements by subject, when required by regulatory authorities

Not applicable.

### 16.2.9 Case report forms

*16.2.9.1 CRFs of deaths, other serious adverse events and withdrawals for AE*

Not applicable

*16.2.9.2 Other CRFs submitted*

Not applicable.

## 16.3 Other Individual subject data listings (US Archival Listings)

Not applicable.