



## Clinical trial results:

**Randomized, controlled, multi-center trial to evaluate the efficacy and safety of a Flurbiprofen 40 mg cutaneous hydrogel medicated plaster vs. placebo and vs. a marketed active comparator in the local symptomatic and short-term treatment of pain in acute strains, sprains or bruises of the soft tissues following blunt trauma, e.g. sports injuries**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2020-005217-41 |
| Trial protocol           | DE             |
| Global end of trial date | 16 August 2022 |

### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 11 October 2023 |
| First version publication date | 11 October 2023 |

### Trial information

#### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | 51-03FPAEU |
|-----------------------|------------|

#### Additional study identifiers

|                                    |   |
|------------------------------------|---|
| ISRCTN number                      | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN)   | - |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Lead Chemical Company  |
| Sponsor organisation address | 77-3 Himata, Toyama-city Toyama, Japan, 930-0912   |
| Public contact               | Ilias Zontiros, Dr. Regenold GmbH, +49 76328226270, <a href="mailto:ilias.zontiros@regenold.com">ilias.zontiros@regenold.com</a> |
| Scientific contact           | Ilias Zontiros, Dr. Regenold GmbH, +49 76328226270, <a href="mailto:ilias.zontiros@regenold.com">ilias.zontiros@regenold.com</a> |

Notes:

### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                |
|--|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 12 June 2023   |
| Is this the analysis of the primary completion data? | No             |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 16 August 2022 |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

To determine efficacy and safety of a flurbiprofen 40 mg cutaneous hydrogel medicated plaster (Test) compared to placebo and to a marketed active comparator in patients with acute strains, sprains or bruises (contusions) of the soft tissues following blunt trauma, e.g. sports injuries.  
To demonstrate that the Test plaster is superior to placebo, is comparable to the active comparator, and that the Test plaster has acceptable local tolerability.

Protection of trial subjects:

This clinical study was designed and was implemented and reported in accordance with the ICH Harmonized Tripartite Guidelines for Good Clinical Practice E6 (R2) [European Medicines Agency 2016], with applicable local regulations (including European Directive 2001/20/EC, US Code of Federal Regulations Title 21, and Japanese Ministry of Health, Labor, and Welfare), and with the ethical principles laid down in the Declaration of Helsinki. Informed consent was obtained in writing prior to any trial-related activities. Subjects were monitored for adverse events throughout participation in the trial.

Background therapy:

Concomitant therapies allowed during the study:

- Rescue medication (paracetamol, 500 mg tablets) except for the 6 hours prior to visit 5 (72 h).
- Standard care by rest, ice, compression (non-occlusive bandage), or elevation (RICE) could have been considered following discussion with the Investigator.

Concomitant therapies prohibited during the study:

- Use of systemic or topical NSAIDs, analgesics (other than paracetamol), opioids, corticosteroids (except for topical treatment of bronchial asthma), heparin, or psychotropic agents.

The Investigator instructed the patient to notify the study center about any new medications and significant non-drug therapies (i.e. RICE) he/she took after the start of the study drug. All medications and significant non-drug therapies taken during the 30 days prior to Visit 1 (0h, Day 1) (including physical therapy and blood transfusions) or administered after the patient started treatment with study drug were listed on the Concomitant medications/Significant nondrug therapies CRF page. An AE CRF page was also completed, if appropriate.

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 09 November 2021 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |              |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Germany: 312 |
| Worldwide total number of subjects   | 312          |
| EEA total number of subjects         | 312          |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 3   |
| Adults (18-64 years)                      | 303 |
| From 65 to 84 years                       | 6   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Overall, 312 healthy (151 female and 161 male) subjects were randomised. In total 310 out of 312 study participants (99.36 %) were Caucasian.

The trial was performed in 5 centers in Germany.

### Pre-assignment

Screening details:

Subjects were eligible for enrollment according to the trial inclusion and exclusion criteria.

### Period 1

|                              |  |
|------------------------------|--|
| Period 1 title               | Intervention (overall period)                          |
| Is this the baseline period? | Yes  |
| Allocation method            | Randomised - controlled                                |
| Blinding used                | Double blind   |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Assessor |

Blinding implementation details:

Double-blind with respect to flurbiprofen and placebo formulations. Patients, investigator staff, persons performing the assessments, monitors, data analysts blinded until data base close. With respect to the active comparator, full blinding of patients and investigators could not be completely assured due to slight differences between Test and the Diclofenac-ratiopharm Schmerzpfaster. Measures were put in place to ensure that the opportunity was limited to become aware of treatment allocation.

### Arms

|                              |                     |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes                 |
| <b>Arm title</b>             | Flurbiprofen (Test) |

Arm description:

Flurbiprofen 40 mg cutaneous hydrogel medicated plaster was applied topically to the injury side once every 12 hours.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Flurbiprofen 40 mg cutaneous hydrogel medicated plaster |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Transdermal patch                                       |
| Routes of administration               | Cutaneous use, Local use , Transdermal use              |

Dosage and administration details:

The Test product 'Flurbiprofen 40 mg cutaneous hydrogel medicated plaster' was applied topically to the injured site twice daily (i.e., every 12 hours) for 7 days.

Overall, subjects were exposed to 560 mg Flurbiprofen (7\*2\*40 mg).

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

Arm description:

The placebo plaster that did not contain the active ingredient but the excipients used in the placebo formulation were identical to the ones used in the Test formulation.

The placebo plaster was applied topically to the injury side once every 12 hours.

|  |  |
|--|--|
| Arm type                               | Placebo                                    |
| Investigational medicinal product name | Placebo plaster                            |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Transdermal patch                          |
| Routes of administration               | Cutaneous use, Local use , Transdermal use |

Dosage and administration details:

A single placebo plaster was applied topically to the injured site twice daily (i.e., every 12 hours) for 7 days.

|  |   |
|--|---|
| <b>Arm title</b>   | Active comparator                         |
| <p>Arm description:</p> <p>Diclofenac-ratiopharm Schmerzpfaster containing 140 mg of diclofenac sodium were used as marketed active comparator and had been purchased from the German market. Samples originated from normal production batches. No modifications were made to the authorized product other than clinical re-packaging and labelling. There was complete over-labelling of the sachets in order to conceal the branded labelling.</p> <p>The active comparator plaster was applied topically to the injury side once every 12 hours.</p> |   |
| Arm type   | Experimental                              |
| Investigational medicinal product name   | Diclofenac-ratiopharm Schmerzpfaster      |
| Investigational medicinal product code   |   |
| Other name   |   |
| Pharmaceutical forms   | Transdermal patch                         |
| Routes of administration   | Cutaneous use, Transdermal use, Local use |
| <p>Dosage and administration details:</p> <p>A single Diclofenac-ratiopharm plaster (diclofenac sodium 140 mg) was applied topically to the injured site twice daily (i.e., every 12 hours) for 7 days.</p> <p>Overall, subjects were exposed to 1960 mg Diclofenac (7*2*140 mg).</p>  |   |

| <b>Number of subjects in period 1</b> | Flurbiprofen (Test) | Placebo | Active comparator |
|---------------------------------------|---------------------|---------|-------------------|
| Started                               | 156                 | 78      | 78                |
| Completed                             | 156                 | 78      | 78                |

## Baseline characteristics

### Reporting groups

| Reporting group title          | Intervention |
|--------------------------------|--------------|
| Reporting group description: - |              |

| Reporting group values    | Intervention | Total |  |
|---------------------------|--------------|-------|--|
| Number of subjects        | 312          | 312   |  |
| Age categorical           |              |       |  |
| Units: Subjects           |              |       |  |
| Adolescents (12-17 years) | 3            | 3     |  |
| Adults (18-64 years)      | 303          | 303   |  |
| From 65-84 years          | 6            | 6     |  |
| Age continuous            |              |       |  |
| Units: years              |              |       |  |
| arithmetic mean           | 36.6         |       |  |
| standard deviation        | ± 13.3       | -     |  |
| Gender categorical        |              |       |  |
| Units: Subjects           |              |       |  |
| Female                    | 151          | 151   |  |
| Male                      | 161          | 161   |  |

### Subject analysis sets

| Subject analysis set title | Full Analysis Set (FAS) |
|----------------------------|-------------------------|
| Subject analysis set type  | Full analysis           |

Subject analysis set description:

The Full Analysis Set (FAS) was all randomized patients who received at least one dose of study drug. The FAS population was primary population for the analysis of efficacy. Any exclusions from the FAS population were made and documented before unblinding (e.g., never used study medication, randomized twice). Additional secondary populations could have been defined before unblinding

| Reporting group values    | Full Analysis Set (FAS) |  |  |
|---------------------------|-------------------------|--|--|
| Number of subjects        | 312                     |  |  |
| Age categorical           |                         |  |  |
| Units: Subjects           |                         |  |  |
| Adolescents (12-17 years) | 3                       |  |  |
| Adults (18-64 years)      | 303                     |  |  |
| From 65-84 years          | 6                       |  |  |
| Age continuous            |                         |  |  |
| Units: years              |                         |  |  |
| arithmetic mean           | 36.6                    |  |  |
| standard deviation        | ± 13.3                  |  |  |
| Gender categorical        |                         |  |  |
| Units: Subjects           |                         |  |  |
| Female                    | 151                     |  |  |
| Male                      | 161                     |  |  |

## End points

### End points reporting groups

|   |                         |
|---|-------------------------|
| Reporting group title   | Flurbiprofen (Test)     |
| Reporting group description:<br>Flurbiprofen 40 mg cutaneous hydrogel medicated plaster was applied topically to the injury side once every 12 hours.   |                         |
| Reporting group title   | Placebo                 |
| Reporting group description:<br>The placebo plaster that did not contain the active ingredient but the excipients used in the placebo formulation were identical to the ones used in the Test formulation.<br>The placebo plaster was applied topically to the injury side once every 12 hours.   |                         |
| Reporting group title   | Active comparator       |
| Reporting group description:<br>Diclofenac-ratiopharm Schmerzplaster containing 140 mg of diclofenac sodium were used as marketed active comparator and had been purchased from the German market. Samples originated from normal production batches. No modifications were made to the authorized product other than clinical re-packaging and labelling. There was complete over-labelling of the sachets in order to conceal the branded labelling.<br>The active comparator plaster was applied topically to the injury side once every 12 hours. |                         |
| Subject analysis set title  | Full Analysis Set (FAS) |
| Subject analysis set type   | Full analysis           |
| Subject analysis set description:<br>The Full Analysis Set (FAS) was all randomized patients who received at least one dose of study drug. The FAS population was primary population for the analysis of efficacy. Any exclusions from the FAS population were made and documented before unblinding (e.g., never used study medication, randomized twice). Additional secondary populations could have been defined before unblinding  |                         |

### Primary: Pain-on-movement (POM)

|  |                        |
|--|------------------------|
| End point title  | Pain-on-movement (POM) |
| End point description:<br>The primary efficacy outcome was pain-on-movement on VAS (using a 100 mm VAS from 0 = "no pain" to 100 = "extreme pain") at 72 hours ( $\pm 4$ h) after initiating treatment in the Full Analysis Set (FAS) population.<br>POM was induced by the same subject-specific standardised passive movement, and/or investigator-derived manipulation of the nearest joint. To standardize the procedure for the assessment of POM a special movement could have been performed by the patient, where possible, either for the upper limb or the lower limb depending on which limb was injured. |                        |
| End point type   | Primary                |
| End point timeframe:<br>72 hours after initiating treatment (visit 5)  |                        |

| End point values                     | Flurbiprofen (Test) | Placebo             | Active comparator   |  |
|--------------------------------------|---------------------|---------------------|---------------------|--|
| Subject group type                   | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed          | 156                 | 78                  | 78                  |  |
| Units: millimetre(s)                 |                     |                     |                     |  |
| arithmetic mean (standard deviation) | 14.1 ( $\pm 13.1$ ) | 30.1 ( $\pm 18.0$ ) | 14.4 ( $\pm 12.6$ ) |  |

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Treatment comparison - Test vs. comparator |
| Comparison groups                       | Active comparator v Flurbiprofen (Test)    |
| Number of subjects included in analysis | 234  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           | non-inferiority                            |
| P-value                                 | = 0.8304                                   |
| Method                                  | ANCOVA                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | -3.3592                                    |
| upper limit                             | 4.1805                                     |

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Treatment comparison - Test vs. placebo |
| Comparison groups                       | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis | 234                                     |
| Analysis specification                  | Pre-specified                           |
| Analysis type                           | superiority                             |
| P-value                                 | < 0.0001                                |
| Method                                  | ANCOVA                                  |
| Confidence interval                     |   |
| level                                   | 95 %                                    |
| sides                                   | 2-sided                                 |
| lower limit                             | -19.7516                                |
| upper limit                             | -12.2702                                |

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Treatment comparison - Comparator vs. placebo |
| Comparison groups                       | Placebo v Active comparator                   |
| Number of subjects included in analysis | 156   |
| Analysis specification                  | Pre-specified                                 |
| Analysis type                           | superiority                                   |
| P-value                                 | < 0.0001                                      |
| Method                                  | ANCOVA  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided                                       |
| lower limit                             | -20.7851                                      |
| upper limit                             | -12.058                                       |

## Secondary: Pain-on-movement (POM) at visit 1

|                 |                                   |
|-----------------|-----------------------------------|
| End point title | Pain-on-movement (POM) at visit 1 |
|-----------------|-----------------------------------|



End point description:

As secondary endpoints POM measured by VAS at baseline.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Visit 1

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: millimetre(s)                 |                     |                 |                   |  |
| arithmetic mean (standard deviation) | 69.1 (± 7.3)        | 69.0 (± 7.5)    | 70.7 (± 8.4)      |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pain-on-movement (POM) at visit 2

|                 |                                   |
|-----------------|-----------------------------------|
| End point title | Pain-on-movement (POM) at visit 2 |
|-----------------|-----------------------------------|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Visit 2 (12 hours)

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: millimetre(s)                 |                     |                 |                   |  |
| arithmetic mean (standard deviation) | 56.4 (± 11.9)       | 59.9 (± 11.3)   | 57.3 (± 14.5)     |  |

### Statistical analyses

|                            |  |
|----------------------------|--|
| Statistical analysis title | Treatment comparison - Test vs. comparator |
|----------------------------|--|

|                   |   |
|-------------------|---|
| Comparison groups | Flurbiprofen (Test) v Active comparator |
|-------------------|---|

|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 234             |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | non-inferiority |
| P-value                                 | = 0.6328        |
| Method                                  | ANCOVA          |
| Confidence interval                     |                 |
| level                                   | 95 %            |
| sides                                   | 2-sided         |
| lower limit                             | -1.8162         |
| upper limit                             | 2.9825          |

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Treatment comparison - Test vs. placebo |
| Comparison groups                       | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis | 234                                     |
| Analysis specification                  | Pre-specified                           |
| Analysis type                           | superiority                             |
| P-value                                 | = 0.0022                                |
| Method                                  | ANCOVA                                  |
| Confidence interval                     |   |
| level                                   | 95 %                                    |
| sides                                   | 2-sided                                 |
| lower limit                             | -6.1233                                 |
| upper limit                             | -1.3617                                 |

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Treatment comparison - Comparator vs. placebo |
| Comparison groups                       | Placebo v Active comparator                   |
| Number of subjects included in analysis | 156   |
| Analysis specification                  | Pre-specified                                 |
| Analysis type                           | superiority                                   |
| P-value                                 | = 0.0024                                      |
| Method                                  | ANCOVA  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided                                       |
| lower limit                             | -7.1028                                       |
| upper limit                             | -1.5485                                       |

### Secondary: Pain-on-movement (POM) at visit 3

|                        |                                   |
|------------------------|-----------------------------------|
| End point title        | Pain-on-movement (POM) at visit 3 |
| End point description: |                                   |
|                        |                                   |
| End point type         | Secondary                         |
| End point timeframe:   |                                   |
| Visit 3 (24 hours)     |                                   |

| <b>End point values</b>              | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: millimetre(s)                 |                     |                 |                   |  |
| arithmetic mean (standard deviation) | 44.1 (± 15.3)       | 52.8 (± 15.9)   | 45.9 (± 17.0)     |  |

## Statistical analyses

| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. comparator |
|---|--|
| Statistical analysis description:<br>Pain-on-movement VAS - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |  |
| Comparison groups   | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis   | 234  |
| Analysis specification  | Pre-specified                              |
| Analysis type   | non-inferiority                            |
| P-value   | = 0.9006                                   |
| Method  | ANCOVA                                     |
| Confidence interval   |  |
| level   | 95 %                                       |
| sides   | 2-sided                                    |
| lower limit   | -3.5159                                    |
| upper limit   | 3.0957                                     |

| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. placebo |
|---|---|
| Statistical analysis description:<br>Pain-on-movement VAS - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups   | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis   | 234                                     |
| Analysis specification  | Pre-specified                           |
| Analysis type   | superiority                             |
| P-value   | < 0.0001                                |
| Method  | ANCOVA                                  |
| Confidence interval   |   |
| level   | 95 %                                    |
| sides   | 2-sided                                 |
| lower limit   | -12.0788                                |
| upper limit   | -5.5184                                 |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Treatment comparison - Comparator vs. placebo |
| Statistical analysis description:<br>Pain-on-movement VAS - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups   | Placebo v Active comparator                   |
| Number of subjects included in analysis   | 156   |
| Analysis specification  | Pre-specified                                 |
| Analysis type   | superiority                                   |
| P-value   | < 0.0001                                      |
| Method  | ANCOVA  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided                                       |
| lower limit   | -12.4149                                      |
| upper limit   | -4.7621                                       |

### Secondary: Pain-on-movement (POM) at visit 4

|                        |                                   |
|------------------------|-----------------------------------|
| End point title        | Pain-on-movement (POM) at visit 4 |
| End point description: |                                   |
| End point type         | Secondary                         |
| End point timeframe:   |                                   |
| Visit 4 (48 hours)     |                                   |

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: millimetre(s)                 |                     |                 |                   |  |
| arithmetic mean (standard deviation) | 26.8 (± 15.4)       | 41.3 (± 16.7)   | 27.8 (± 15.5)     |  |

### Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. comparator |
| Statistical analysis description:<br>Pain-on-movement VAS - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |  |
| Comparison groups   | Flurbiprofen (Test) v Active comparator    |

|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 234             |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | non-inferiority |
| P-value                                 | = 0.99          |
| Method                                  | ANCOVA          |
| Confidence interval                     |                 |
| level                                   | 95 %            |
| sides                                   | 2-sided         |
| lower limit                             | -4.0998         |
| upper limit                             | 4.0479          |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Test vs. placebo |
| Statistical analysis description:  |   |
| Pain-on-movement VAS - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups  | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis  | 234                                     |
| Analysis specification   | Pre-specified                           |
| Analysis type  | superiority                             |
| P-value  | < 0.0001                                |
| Method   | ANCOVA                                  |
| Confidence interval  |   |
| level  | 95 %                                    |
| sides  | 2-sided                                 |
| lower limit  | -18.7044                                |
| upper limit  | -10.6197                                |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Comparator vs. placebo |
| Statistical analysis description:  |   |
| Pain-on-movement VAS - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups  | Placebo v Active comparator                   |
| Number of subjects included in analysis  | 156   |
| Analysis specification   | Pre-specified                                 |
| Analysis type  | superiority                                   |
| P-value  | < 0.0001                                      |
| Method   | ANCOVA  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided                                       |
| lower limit  | -19.3515                                      |
| upper limit  | -9.9207                                       |

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## Secondary: Pain-on-movement (POM) at visit 6

|                        |                                   |
|------------------------|-----------------------------------|
| End point title        | Pain-on-movement (POM) at visit 6 |
| End point description: |                                   |
| End point type         | Secondary                         |
| End point timeframe:   |                                   |
| Visit 6 (96 hours)     |                                   |

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: millimetre(s)                 |                     |                 |                   |  |
| arithmetic mean (standard deviation) | 7.1 (± 10.0)        | 19.8 (± 16.7)   | 6.6 (± 9.6)       |  |

## Statistical analyses

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Treatment comparison - Test vs. comparator |
| Statistical analysis description:  |  |
| Pain-on-movement VAS - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |  |
| Comparison groups  | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis  | 234  |
| Analysis specification   | Pre-specified                              |
| Analysis type  | non-inferiority                            |
| P-value  | = 0.563                                    |
| Method   | ANCOVA                                     |
| Confidence interval  |  |
| level  | 95 %                                       |
| sides  | 2-sided                                    |
| lower limit  | -2.2394                                    |
| upper limit  | 4.1067                                     |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Test vs. placebo |
| Statistical analysis description:  |   |
| Pain-on-movement VAS - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups  | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis  | 234                                     |
| Analysis specification   | Pre-specified                           |
| Analysis type  | superiority                             |
| P-value  | < 0.0001                                |
| Method   | ANCOVA                                  |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -15.852 |
| upper limit         | -9.555  |

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | Treatment comparison - Comparator vs. placebo |
|-----------------------------------|---|

Statistical analysis description:

Pain-on-movement VAS - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS

|   |                             |
|---|-----------------------------|
| Comparison groups                       | Placebo v Active comparator |
| Number of subjects included in analysis | 156                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority                 |
| P-value                                 | < 0.0001                    |
| Method                                  | ANCOVA                      |

|                     |          |
|---------------------|----------|
| Confidence interval |          |
| level               | 95 %     |
| sides               | 2-sided  |
| lower limit         | -17.3099 |
| upper limit         | -9.9645  |

## Secondary: Pain-on-movement (POM) at visit 7

|                 |                                   |
|-----------------|-----------------------------------|
| End point title | Pain-on-movement (POM) at visit 7 |
|-----------------|-----------------------------------|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Visit 7 (168 hours)

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: millimetre(s)                 |                     |                 |                   |  |
| arithmetic mean (standard deviation) | 1.2 (± 4.4)         | 8.1 (± 12.9)    | 1.6 (± 5.8)       |  |

## Statistical analyses

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Treatment comparison - Test vs. comparator |
|-----------------------------------|--|

Statistical analysis description:

Pain-on-movement VAS - treatment comparison by Visit – ANCOVA considering baseline value as

covariate including type-III tests of fixed effects, FAS

|   |   |
|---|---|
| Comparison groups                       | Flurbiprofen (Test) v Active comparator |
| Number of subjects included in analysis | 234                                     |
| Analysis specification                  | Pre-specified                           |
| Analysis type                           | non-inferiority                         |
| P-value                                 | = 0.7804                                |
| Method                                  | ANCOVA                                  |
| Confidence interval                     |   |
| level                                   | 95 %                                    |
| sides                                   | 2-sided                                 |
| lower limit                             | -2.3616                                 |
| upper limit                             | 1.7751                                  |

---

**Statistical analysis title**

Treatment comparison - Test vs. placebo

Statistical analysis description:

Pain-on-movement VAS - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Flurbiprofen (Test) v Placebo |
| Number of subjects included in analysis | 234                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | superiority                   |
| P-value                                 | < 0.0001                      |
| Method                                  | ANCOVA                        |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -8.9704                       |
| upper limit                             | -4.8656                       |

---

**Statistical analysis title**

Treatment comparison - Comparator vs. placebo

Statistical analysis description:

Pain-on-movement VAS - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS

|   |                             |
|---|-----------------------------|
| Comparison groups                       | Placebo v Active comparator |
| Number of subjects included in analysis | 156                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority                 |
| P-value                                 | < 0.0001                    |
| Method                                  | ANCOVA                      |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | -9.0189                     |
| upper limit                             | -4.2306                     |



**Secondary: AUC for POM on VAS - visit 3**

|  |                              |
|--|------------------------------|
| End point title  | AUC for POM on VAS - visit 3 |
| End point description:<br>For POM on VAS, partial AUCs were calculated based on the raw VAS values and actual times of scheduled visits. |                              |
| End point type   | Secondary                    |
| End point timeframe:<br>Visit 3 (24 hours)   |                              |

| End point values                     | Flurbiprofen (Test)                   | Placebo                               | Active comparator                     |  |
|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|--|
| Subject group type                   | Reporting group                       | Reporting group                       | Reporting group                       |  |
| Number of subjects analysed          | 156                                   | 78                                    | 78                                    |  |
| Units: mm*h                          |                                       |                                       |                                       |  |
| arithmetic mean (standard deviation) | 1358.2489316<br>0 (±<br>233.62331908) | 1444.6832265<br>0 (±<br>235.21685419) | 1387.3344017<br>0 (±<br>306.75795742) |  |

**Statistical analyses**

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. comparator |
| Statistical analysis description:<br>Pain-on-movement AUC - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |  |
| Comparison groups   | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis   | 234  |
| Analysis specification  | Pre-specified                              |
| Analysis type   | non-inferiority                            |
| P-value   | = 0.7287                                   |
| Method  | ANCOVA                                     |
| Confidence interval   |  |
| level   | 95 %                                       |
| sides   | 2-sided                                    |
| lower limit   | -36.967                                    |
| upper limit   | 52.8055                                    |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. placebo |
| Statistical analysis description:<br>Pain-on-movement AUC - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups   | Flurbiprofen (Test) v Placebo           |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 234           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | superiority   |
| P-value                                 | < 0.0001      |
| Method                                  | ANCOVA        |
| Confidence interval                     |               |
| level                                   | 95 %          |
| sides                                   | 2-sided       |
| lower limit                             | -134.4        |
| upper limit                             | -45.3194      |

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Treatment comparison - Comparator vs. placebo |
| Comparison groups                       | Placebo v Active comparator                   |
| Number of subjects included in analysis | 156   |
| Analysis specification                  | Pre-specified                                 |
| Analysis type                           | superiority                                   |
| P-value                                 | = 0.0003                                      |
| Method                                  | ANCOVA  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided                                       |
| lower limit                             | -149.73                                       |
| upper limit                             | -45.8228                                      |

#### Secondary: AUC for POM on VAS - visit 4

|                        |                              |
|------------------------|------------------------------|
| End point title        | AUC for POM on VAS - visit 4 |
| End point description: |                              |
| End point type         | Secondary                    |
| End point timeframe:   |                              |
| Visit 4 (48 hours)     |                              |

| End point values                     | Flurbiprofen (Test)                   | Placebo                               | Active comparator                     |  |
|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|--|
| Subject group type                   | Reporting group                       | Reporting group                       | Reporting group                       |  |
| Number of subjects analysed          | 156                                   | 78                                    | 78                                    |  |
| Units: mm*h                          |                                       |                                       |                                       |  |
| arithmetic mean (standard deviation) | 2178.7155449<br>0 (±<br>525.38989828) | 2528.7019231<br>0 (±<br>553.90662209) | 2235.7366453<br>0 (±<br>634.90203041) |  |

## Statistical analyses

| Statistical analysis title   | Treatment comparison - Test vs. comparator |
|--|--|
| Statistical analysis description:  |  |
| Pain-on-movement AUC - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |  |
| Comparison groups  | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis  | 234  |
| Analysis specification   | Pre-specified                              |
| Analysis type  | non-inferiority                            |
| P-value  | = 0.8854                                   |
| Method   | ANCOVA                                     |
| Confidence interval  |  |
| level  | 95 %                                       |
| sides  | 2-sided                                    |
| lower limit  | -112.8                                     |
| upper limit  | 130.64                                     |

| Statistical analysis title   | Treatment comparison - Test vs. placebo |
|--|---|
| Statistical analysis description:  |   |
| Pain-on-movement AUC - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups  | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis  | 234                                     |
| Analysis specification   | Pre-specified                           |
| Analysis type  | superiority                             |
| P-value  | < 0.0001                                |
| Method   | ANCOVA                                  |
| Confidence interval  |   |
| level  | 95 %                                    |
| sides  | 2-sided                                 |
| lower limit  | -477.26                                 |
| upper limit  | -235.71                                 |

| Statistical analysis title   | Treatment comparison - Comparator vs. placebo |
|--|---|
| Statistical analysis description:  |   |
| Pain-on-movement AUC - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups  | Placebo v Active comparator                   |
| Number of subjects included in analysis  | 156   |
| Analysis specification   | Pre-specified                                 |
| Analysis type  | superiority                                   |
| P-value  | < 0.0001                                      |
| Method   | ANCOVA  |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -506.29 |
| upper limit         | -224.52 |

### Secondary: AUC for POM on VAS - visit 5

|                        |                              |
|------------------------|------------------------------|
| End point title        | AUC for POM on VAS - visit 5 |
| End point description: |                              |
| End point type         | Secondary                    |
| End point timeframe:   |                              |
| Visit 5 (72 hours)     |                              |

| End point values                     | Flurbiprofen (Test)                   | Placebo                               | Active comparator                     |  |
|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|--|
| Subject group type                   | Reporting group                       | Reporting group                       | Reporting group                       |  |
| Number of subjects analysed          | 156                                   | 78                                    | 78                                    |  |
| Units: mm*h                          |                                       |                                       |                                       |  |
| arithmetic mean (standard deviation) | 2672.7868590<br>0 (±<br>806.58571556) | 3393.5897436<br>0 (±<br>931.53411720) | 2746.6175214<br>0 (±<br>931.50009354) |  |

### Statistical analyses

|  |  |
|--|--|
| Statistical analysis title   | Treatment comparison - Test vs. comparator |
| Statistical analysis description:  |  |
| Pain-on-movement AUC - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |  |
| Comparison groups  | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis  | 234  |
| Analysis specification   | Pre-specified                              |
| Analysis type  | non-inferiority                            |
| P-value  | = 0.9012                                   |
| Method   | ANCOVA                                     |
| Confidence interval  |  |
| level  | 95 %                                       |
| sides  | 2-sided                                    |
| lower limit  | -191.65                                    |
| upper limit  | 217.49                                     |

|                            |   |
|----------------------------|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
|----------------------------|---|

Statistical analysis description:

Pain-on-movement AUC - treatment comparison by Visit - ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Flurbiprofen (Test) v Placebo |
| Number of subjects included in analysis | 234                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | superiority                   |
| P-value                                 | < 0.0001                      |
| Method                                  | ANCOVA                        |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -931.97                       |
| upper limit                             | -526                          |

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Treatment comparison - Comparator vs. placebo |
| Comparison groups                       | Active comparator v Placebo                   |
| Number of subjects included in analysis | 156   |
| Analysis specification                  | Pre-specified                                 |
| Analysis type                           | superiority                                   |
| P-value                                 | < 0.0001                                      |
| Method                                  | ANCOVA  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided                                       |
| lower limit                             | -978.68                                       |
| upper limit                             | -505.12                                       |

**Secondary: AUC for POM on VAS - visit 6**

|                        |                              |
|------------------------|------------------------------|
| End point title        | AUC for POM on VAS - visit 6 |
| End point description: |                              |
| End point type         | Secondary                    |
| End point timeframe:   |                              |
| Visit 6 ( hours)       |                              |

| End point values                     | Flurbiprofen (Test)                        | Placebo                                    | Active comparator                          |  |
|--------------------------------------|--|--|--|--|
| Subject group type                   | Reporting group                            | Reporting group                            | Reporting group                            |  |
| Number of subjects analysed          | 156  | 78   | 78   |  |
| Units: mm*h                          |  |  |  |  |
| arithmetic mean (standard deviation) | 2927.6875000<br>0 (±<br>1019.6457770<br>0) | 3992.6244658<br>0 (±<br>1288.8013982<br>0) | 2997.7211538<br>0 (±<br>1141.1062394<br>0) |  |

## Statistical analyses

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Treatment comparison - Test vs. comparator |
| Statistical analysis description:  |  |
| Pain-on-movement AUC - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |  |
| Comparison groups  | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis  | 234  |
| Analysis specification   | Pre-specified                              |
| Analysis type  | non-inferiority                            |
| P-value  | = 0.8306                                   |
| Method   | ANCOVA                                     |
| Confidence interval  |  |
| level  | 95 %                                       |
| sides  | 2-sided                                    |
| lower limit  | -243.89                                    |
| upper limit  | 303.45                                     |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Test vs. placebo |
| Statistical analysis description:  |   |
| Pain-on-movement AUC - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups  | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis  | 234                                     |
| Analysis specification   | Pre-specified                           |
| Analysis type  | superiority                             |
| P-value  | < 0.0001                                |
| Method   | ANCOVA                                  |
| Confidence interval  |   |
| level  | 95 %                                    |
| sides  | 2-sided                                 |
| lower limit  | -1344.89                                |
| upper limit  | -801.78                                 |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Comparator vs. placebo |
| Statistical analysis description:  |   |
| Pain-on-movement AUC - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups  | Placebo v Active comparator                   |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 156           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | superiority   |
| P-value                                 | < 0.0001      |
| Method                                  | ANCOVA        |
| Confidence interval                     |               |
| level                                   | 95 %          |
| sides                                   | 2-sided       |
| lower limit                             | -1419.89      |
| upper limit                             | -786.35       |

### Secondary: POM - Time to meaningful reduction (30%)

|  |  |
|--|--|
| End point title  | POM - Time to meaningful reduction (30%) |
| End point description:   |  |
| End point type   | Secondary                                |
| End point timeframe:   |  |
| Time to meaningful (30 %) reduction of pain was calculated as 30 % reduction of baseline POM respectively, based on the VAS values measured for POM at the study visits. |  |

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: hour                          |                     |                 |                   |  |
| arithmetic mean (standard deviation) | 34.0 (± 20.5)       | 53.4 (± 28.3)   | 33.7 (± 16.8)     |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: POM - Time to optimal reduction (50%)

|   |                                       |
|---|---------------------------------------|
| End point title   | POM - Time to optimal reduction (50%) |
| End point description:  |                                       |
| End point type  | Secondary                             |
| End point timeframe:  |                                       |
| Time to optimal (50 %) reduction of pain was calculated as 50 % reduction of baseline POM respectively, based on the VAS values measured for POM at the study visits. |                                       |

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 72              | 78                |  |
| Units: hour                          |                     |                 |                   |  |
| arithmetic mean (standard deviation) | 53.7 (± 28.1)       | 83.0 (± 44.8)   | 51.8 (± 25.5)     |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: POM - Time to complete resolution of pain

|  |   |
|--|---|
| End point title  | POM - Time to complete resolution of pain |
| End point description:   |   |
| End point type   | Secondary                                 |
| End point timeframe:   |   |
| Time to complete (100 %) resolution of pain was calculated as 100 % reduction of baseline POM, based on the VAS values measured for POM at the study visits. |   |

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 127                 | 42              | 59                |  |
| Units: hour                          |                     |                 |                   |  |
| arithmetic mean (standard deviation) | 122.1 (± 45.3)      | 130.3 (± 43.4)  | 118.4 (± 46.3)    |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pain-at-rest (PAR) - visit 2

|  |                              |
|--|------------------------------|
| End point title  | Pain-at-rest (PAR) - visit 2 |
| End point description:   |                              |
| The patients' pain-at-rest (PAR) was assessed at baseline, V2 (12 h), V3 (24 h), V4 (48 h), V5 (72 h) and V6 (96 h) using a 100 mm VAS from 0 = "no pain" to 100 = "extreme pain" in response to the question:<br>"How would you describe the pain in the injured area at rest?"<br>From the assessments of PAR at baseline (screening visit) vs. all later visits the change from baseline was calculated as pain intensity difference (PID). |                              |
| End point type   | Secondary                    |
| End point timeframe:   |                              |
| Visit 2 (12 hours)   |                              |



| <b>End point values</b>              | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: millimetre(s)                 |                     |                 |                   |  |
| arithmetic mean (standard deviation) | -5.2 (± 5.5)        | -3.0 (± 3.2)    | -4.6 (± 4.5)      |  |

## Statistical analyses

| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. comparator |
|---|--|
| Statistical analysis description:<br>Pain-at-rest PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate, FAS |  |
| Comparison groups   | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis   | 234  |
| Analysis specification  | Pre-specified                              |
| Analysis type   | non-inferiority                            |
| P-value   | = 0.3229                                   |
| Method  | ANCOVA                                     |
| Confidence interval   |  |
| level   | 95 %                                       |
| sides   | 2-sided                                    |
| lower limit   | -1.5102                                    |
| upper limit   | 0.4992                                     |

| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. placebo |
|---|---|
| Statistical analysis description:<br>Pain-at-rest PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate, FAS |   |
| Comparison groups   | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis   | 234                                     |
| Analysis specification  | Pre-specified                           |
| Analysis type   | superiority                             |
| P-value   | < 0.0001                                |
| Method  | ANCOVA                                  |
| Confidence interval   |   |
| level   | 95 %                                    |
| sides   | 2-sided                                 |
| lower limit   | -3.0523                                 |
| upper limit   | -1.0475                                 |

| <b>Statistical analysis title</b> | Treatment comparison - Comparator vs. placebo |
|-----------------------------------|---|
|-----------------------------------|---|

**Statistical analysis description:**

Pain-at-rest PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate, FAS

|   |   |
|---|---|
| Comparison groups                       | Active comparator v Flurbiprofen (Test) |
| Number of subjects included in analysis | 234                                     |
| Analysis specification                  | Pre-specified                           |
| Analysis type                           | superiority                             |
| P-value                                 | = 0.0094                                |
| Method                                  | ANCOVA                                  |
| Confidence interval                     |   |
| level                                   | 95 %                                    |
| sides                                   | 2-sided                                 |
| lower limit                             | -2.7078                                 |
| upper limit                             | -0.381                                  |

**Secondary: Pain-at-rest (PAR) - visit 3**

|                 |                              |
|-----------------|------------------------------|
| End point title | Pain-at-rest (PAR) - visit 3 |
|-----------------|------------------------------|

**End point description:**

The patients' pain-at-rest (PAR) was assessed at baseline, V2 (12 h), V3 (24 h), V4 (48 h), V5 (72 h) and V6 (96 h) using a 100 mm VAS from 0 = "no pain" to 100 = "extreme pain" in response to the question:

"How would you describe the pain in the injured area at rest?"

From the assessments of PAR at baseline (screening visit) vs. all later visits the change from baseline was calculated as pain intensity difference (PID).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Visit 3 (24 hours)

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: hour                          |                     |                 |                   |  |
| arithmetic mean (standard deviation) | -9.5 (± 7.1)        | -6.1 (± 5.3)    | -9.5 (± 7.1)      |  |

**Statistical analyses**

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Treatment comparison - Test vs. comparator |
|-----------------------------------|--|

**Statistical analysis description:**

Pain-at-rest PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate, FAS

|                   |   |
|-------------------|---|
| Comparison groups | Flurbiprofen (Test) v Active comparator |
|-------------------|---|

|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 234             |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | non-inferiority |
| P-value                                 | = 0.8666        |
| Method                                  | ANCOVA          |
| Confidence interval                     |                 |
| level                                   | 95 %            |
| sides                                   | 2-sided         |
| lower limit                             | -1.0727         |
| upper limit                             | 1.2731          |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Test vs. placebo |
| Statistical analysis description:  |   |
| Pain-at-rest PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate, FAS |   |
| Comparison groups  | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis  | 234                                     |
| Analysis specification   | Pre-specified                           |
| Analysis type  | superiority                             |
| P-value  | < 0.0001                                |
| Method   | ANCOVA                                  |
| Confidence interval  |   |
| level  | 95 %                                    |
| sides  | 2-sided                                 |
| lower limit  | -4.3931                                 |
| upper limit  | -2.0526                                 |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Comparator vs. placebo |
| Statistical analysis description:  |   |
| Pain-at-rest PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate, FAS |   |
| Comparison groups  | Placebo v Active comparator                   |
| Number of subjects included in analysis  | 156   |
| Analysis specification   | Pre-specified                                 |
| Analysis type  | superiority                                   |
| P-value  | < 0.0001                                      |
| Method   | ANCOVA  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided                                       |
| lower limit  | -4.6812                                       |
| upper limit  | -1.9648                                       |

## Secondary: Pain-at-rest (PAR) - visit 4

|                 |                              |
|-----------------|------------------------------|
| End point title | Pain-at-rest (PAR) - visit 4 |
|-----------------|------------------------------|

End point description:

The patients' pain-at-rest (PAR) was assessed at baseline, V2 (12 h), V3 (24 h), V4 (48 h), V5 (72 h) and V6 (96 h) using a 100 mm VAS from 0 = "no pain" to 100 = "extreme pain" in response to the question:

"How would you describe the pain in the injured area at rest?"

From the assessments of PAR at baseline (screening visit) vs. all later visits the change from baseline was calculated as pain intensity difference (PID).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Visit 4 (48 hours)

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: millimetre(s)                 |                     |                 |                   |  |
| arithmetic mean (standard deviation) | -13.6 (± 6.9)       | -9.2 (± 5.6)    | -13.1 (± 6.6)     |  |

## Statistical analyses

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Treatment comparison - Test vs. comparator |
|-----------------------------------|--|

Statistical analysis description:

Pain-at-rest PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate, FAS

|   |   |
|---|---|
| Comparison groups                       | Flurbiprofen (Test) v Active comparator |
| Number of subjects included in analysis | 234                                     |
| Analysis specification                  | Pre-specified                           |
| Analysis type                           | non-inferiority                         |
| P-value                                 | = 0.4581                                |
| Method                                  | ANCOVA                                  |
| Confidence interval                     |   |
| level                                   | 95 %                                    |
| sides                                   | 2-sided                                 |
| lower limit                             | -1.3767                                 |
| upper limit                             | 0.6221                                  |

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | Treatment comparison - Test vs. placebo |
|-----------------------------------|---|

Statistical analysis description:

Pain-at-rest PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate, FAS

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Flurbiprofen (Test) v Placebo |
| Number of subjects included in analysis | 234                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | superiority                   |
| P-value                                 | < 0.0001                      |
| Method                                  | ANCOVA                        |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -5.195  |
| upper limit         | -3.2007 |

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | Treatment comparison - Comparator vs. placebo |
|-----------------------------------|---|

Statistical analysis description:

Pain-at-rest PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate, FAS

|   |                             |
|---|-----------------------------|
| Comparison groups                       | Active comparator v Placebo |
| Number of subjects included in analysis | 156                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority                 |
| P-value                                 | < 0.0001                    |
| Method                                  | ANCOVA                      |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -4.9778 |
| upper limit         | -2.6632 |

## Secondary: Pain-at-rest (PAR) - visit 5

|                 |                              |
|-----------------|------------------------------|
| End point title | Pain-at-rest (PAR) - visit 5 |
|-----------------|------------------------------|

End point description:

The patients' pain-at-rest (PAR) was assessed at baseline, V2 (12 h), V3 (24 h), V4 (48 h), V5 (72 h) and V6 (96 h) using a 100 mm VAS from 0 = "no pain" to 100 = "extreme pain" in response to the question:

"How would you describe the pain in the injured area at rest?"

From the assessments of PAR at baseline (screening visit) vs. all later visits the change from baseline was calculated as pain intensity difference (PID).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Visit 5 (72 hours)

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: millimetre(s)                 |                     |                 |                   |  |
| arithmetic mean (standard deviation) | -15.1 (± 6.8)       | -12.1 (± 6.4)   | -15.1 (± 6.6)     |  |

## Statistical analyses

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Treatment comparison - Test vs. comparator |
| Statistical analysis description:  |  |
| Pain-at-rest PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate, FAS |  |
| Comparison groups  | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis  | 234  |
| Analysis specification   | Pre-specified                              |
| Analysis type  | non-inferiority                            |
| P-value  | = 0.7393                                   |
| Method   | ANCOVA                                     |
| Confidence interval  |  |
| level  | 95 %                                       |
| sides  | 2-sided                                    |
| lower limit  | -0.6497                                    |
| upper limit  | 0.9144                                     |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Test vs. placebo |
| Statistical analysis description:  |   |
| Pain-at-rest PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate, FAS |   |
| Comparison groups  | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis  | 234                                     |
| Analysis specification   | Pre-specified                           |
| Analysis type  | superiority                             |
| P-value  | < 0.0001                                |
| Method   | ANCOVA                                  |
| Confidence interval  |   |
| level  | 95 %                                    |
| sides  | 2-sided                                 |
| lower limit  | -3.4906                                 |
| upper limit  | -1.9299                                 |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Comparator vs. placebo |
| Statistical analysis description:  |   |
| Pain-at-rest PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate, FAS |   |
| Comparison groups  | Active comparator v Placebo                   |
| Number of subjects included in analysis  | 156   |
| Analysis specification   | Pre-specified                                 |
| Analysis type  | superiority                                   |
| P-value  | < 0.0001                                      |
| Method   | ANCOVA  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided                                       |
| lower limit  | -3.7483                                       |
| upper limit  | -1.937  |

## Secondary: Pain-at-rest (PAR) - visit 6

|                 |                              |
|-----------------|------------------------------|
| End point title | Pain-at-rest (PAR) - visit 6 |
|-----------------|------------------------------|

End point description:

The patients' pain-at-rest (PAR) was assessed at baseline, V2 (12 h), V3 (24 h), V4 (48 h), V5 (72 h) and V6 (96 h) using a 100 mm VAS from 0 = "no pain" to 100 = "extreme pain" in response to the question:

"How would you describe the pain in the injured area at rest?"

From the assessments of PAR at baseline (screening visit) vs. all later visits the change from baseline was calculated as pain intensity difference (PID).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Visit 6 (96 hours)

| End point values                     | Flurbiprofen (Test) | Placebo            | Active comparator  |  |
|--------------------------------------|---------------------|--------------------|--------------------|--|
| Subject group type                   | Reporting group     | Reporting group    | Reporting group    |  |
| Number of subjects analysed          | 156                 | 78                 | 78                 |  |
| Units: millimetre(s)                 |                     |                    |                    |  |
| arithmetic mean (standard deviation) | -16.0 ( $\pm$ 6.7)  | -13.8 ( $\pm$ 6.3) | -15.8 ( $\pm$ 6.6) |  |

## Statistical analyses

|                            |  |
|----------------------------|--|
| Statistical analysis title | Treatment comparison - Test vs. comparator |
|----------------------------|--|

Statistical analysis description:

Pain-at-rest PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate, FAS

|                   |   |
|-------------------|---|
| Comparison groups | Flurbiprofen (Test) v Active comparator |
|-------------------|---|

|   |     |
|---|-----|
| Number of subjects included in analysis | 234 |
|---|-----|

|                        |               |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

|               |                 |
|---------------|-----------------|
| Analysis type | non-inferiority |
|---------------|-----------------|

|         |          |
|---------|----------|
| P-value | = 0.5641 |
|---------|----------|

|        |        |
|--------|--------|
| Method | ANCOVA |
|--------|--------|

Confidence interval

|       |      |
|-------|------|
| level | 95 % |
|-------|------|

|       |         |
|-------|---------|
| sides | 2-sided |
|-------|---------|

|             |         |
|-------------|---------|
| lower limit | -0.7271 |
|-------------|---------|

|             |        |
|-------------|--------|
| upper limit | 0.3972 |
|-------------|--------|

|                            |   |
|----------------------------|---|
| Statistical analysis title | Treatment comparison - Comparator vs. placebo |
|----------------------------|---|

Statistical analysis description:

Pain-at-rest PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate, FAS

|                   |                             |
|-------------------|-----------------------------|
| Comparison groups | Active comparator v Placebo |
|-------------------|-----------------------------|

|   |               |
|---|---------------|
| Number of subjects included in analysis | 156           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | superiority   |
| P-value                                 | < 0.0001      |
| Method                                  | ANCOVA        |
| Confidence interval                     |               |
| level                                   | 95 %          |
| sides                                   | 2-sided       |
| lower limit                             | -2.4747       |
| upper limit                             | -1.1728       |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Test vs. placebo |
| Statistical analysis description:  |   |
| Pain-at-rest PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate, FAS |   |
| Comparison groups  | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis  | 234                                     |
| Analysis specification   | Pre-specified                           |
| Analysis type  | superiority                             |
| P-value  | < 0.0001                                |
| Method   | ANCOVA                                  |
| Confidence interval  |   |
| level  | 95 %                                    |
| sides  | 2-sided                                 |
| lower limit  | -2.5495                                 |
| upper limit  | -1.4278                                 |

|   |                                |
|---|--------------------------------|
| <b>Secondary: POM - responder rate - visit 5</b>  |                                |
| End point title   | POM - responder rate - visit 5 |
| End point description:  |                                |
| The responder rate was defined as the number of patients achieving at least 50% reduction from baseline in the VAS score for POM at 72 hours. |                                |
| End point type  | Secondary                      |
| End point timeframe:  |                                |
| Visit 5 (72 hours)  |                                |

| <b>End point values</b>     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|-----------------------------|---------------------|-----------------|-------------------|--|
| Subject group type          | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed | 156                 | 78              | 78                |  |
| Units: Yes                  | 142                 | 43              | 73                |  |



## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. comparator |
| Statistical analysis description:<br>POM Responder - response at Visit 5 (72 h) stratified by center - frequency analysis including 95% CI and CMH test of general association, FAS |  |
| Comparison groups   | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis   | 234  |
| Analysis specification  | Pre-specified                              |
| Analysis type   | non-inferiority                            |
| P-value   | = 0.4982                                   |
| Method  | Cochran-Mantel-Haenszel                    |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. placebo |
| Statistical analysis description:<br>POM Responder - response at Visit 5 (72 h) stratified by center - frequency analysis including 95% CI and CMH test of general association, FAS |   |
| Comparison groups   | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis   | 234                                     |
| Analysis specification  | Pre-specified                           |
| Analysis type   | superiority                             |
| P-value   | < 0.0001                                |
| Method  | Cochran-Mantel-Haenszel                 |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Treatment comparison - Comparator vs. placebo |
| Statistical analysis description:<br>POM Responder - response at Visit 5 (72 h) stratified by center - frequency analysis including 95% CI and CMH test of general association, FAS |   |
| Comparison groups   | Placebo v Active comparator                   |
| Number of subjects included in analysis   | 156   |
| Analysis specification  | Pre-specified                                 |
| Analysis type   | superiority                                   |
| P-value   | < 0.0001                                      |
| Method  | Cochran-Mantel-Haenszel                       |

## Secondary: POM - Pain Intensity Difference (PID) - visit 2

|  |   |
|--|---|
| End point title  | POM - Pain Intensity Difference (PID) - visit 2 |
| End point description:<br>PID (Pain Intensity Difference calculated as reduction in VAS for POM from baseline) was a derived parameter calculated from POM data and used as secondary endpoint. Negative PID values indicate pain reduction. |   |
| End point type   | Secondary                                       |
| End point timeframe:<br>Visit 2 (12 hours)   |   |

| <b>End point values</b>              | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: millimetre(s)                 |                     |                 |                   |  |
| arithmetic mean (standard deviation) | -12.8 (± 10.7)      | -9.1 (± 9.1)    | -13.4 (± 11.3)    |  |

## Statistical analyses

| <b>Statistical analysis title</b>  | Treatment comparison - Test vs. comparator |
|--|--|
| Statistical analysis description:  |  |
| Pain-on-movement PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |  |
| Comparison groups  | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis  | 234  |
| Analysis specification   | Pre-specified                              |
| Analysis type  | non-inferiority                            |
| P-value  | = 0.6328                                   |
| Method   | ANCOVA                                     |
| Confidence interval  |  |
| level  | 95 %                                       |
| sides  | 2-sided                                    |
| lower limit  | -1.8162                                    |
| upper limit  | 2.9825                                     |

| <b>Statistical analysis title</b>  | Treatment comparison - Test vs. placebo |
|--|---|
| Statistical analysis description:  |   |
| Pain-on-movement PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups  | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis  | 234                                     |
| Analysis specification   | Pre-specified                           |
| Analysis type  | superiority                             |
| P-value  | = 0.0022                                |
| Method   | ANCOVA                                  |
| Confidence interval  |   |
| level  | 95 %                                    |
| sides  | 2-sided                                 |
| lower limit  | -6.1233                                 |
| upper limit  | -1.3617                                 |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Treatment comparison - Comparator vs. placebo |
| Statistical analysis description:<br>Pain-on-movement PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups   | Placebo v Active comparator                   |
| Number of subjects included in analysis   | 156   |
| Analysis specification  | Pre-specified                                 |
| Analysis type   | superiority                                   |
| P-value   | = 0.0024                                      |
| Method  | ANCOVA  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided                                       |
| lower limit   | -7.1028                                       |
| upper limit   | -1.5485                                       |

### Secondary: POM - Pain Intensity Difference (PID) - visit 3

|  |   |
|--|---|
| End point title  | POM - Pain Intensity Difference (PID) - visit 3 |
| End point description:<br>PID (Pain Intensity Difference calculated as reduction in VAS for POM from baseline) was a derived parameter calculated from POM data and used as secondary endpoint. Negative PID values indicate pain reduction. |   |
| End point type   | Secondary                                       |
| End point timeframe:<br>Visit 3 (24 hours)   |   |

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: millimetre(s)                 |                     |                 |                   |  |
| arithmetic mean (standard deviation) | -25.0 (± 14.4)      | -16.3 (± 13.7)  | -24.8 (± 13.4)    |  |

### Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. comparator |
| Statistical analysis description:<br>Pain-on-movement PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |  |
| Comparison groups   | Flurbiprofen (Test) v Active comparator    |

|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 234             |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | non-inferiority |
| P-value                                 | = 0.9006        |
| Method                                  | ANCOVA          |
| Confidence interval                     |                 |
| level                                   | 95 %            |
| sides                                   | 2-sided         |
| lower limit                             | -3.5159         |
| upper limit                             | 3.0957          |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. placebo |
| Statistical analysis description:<br>Pain-on-movement PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups   | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis   | 234                                     |
| Analysis specification  | Pre-specified                           |
| Analysis type   | superiority                             |
| P-value   | < 0.0001                                |
| Method  | ANCOVA                                  |
| Confidence interval   |   |
| level   | 95 %                                    |
| sides   | 2-sided                                 |
| lower limit   | -12.0788                                |
| upper limit   | -5.5184                                 |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Treatment comparison - Comparator vs. placebo |
| Statistical analysis description:<br>Pain-on-movement PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups   | Placebo v Active comparator                   |
| Number of subjects included in analysis   | 156   |
| Analysis specification  | Pre-specified                                 |
| Analysis type   | superiority                                   |
| P-value   | < 0.0001                                      |
| Method  | ANCOVA  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided                                       |
| lower limit   | -12.4149                                      |
| upper limit   | -4.7621                                       |

---

## Secondary: POM - Pain Intensity Difference (PID) - visit 4

|  |   |
|--|---|
| End point title  | POM - Pain Intensity Difference (PID) - visit 4 |
| End point description:<br>PID (Pain Intensity Difference calculated as reduction in VAS for POM from baseline) was a derived parameter calculated from POM data and used as secondary endpoint. Negative PID values indicate pain reduction. |   |
| End point type   | Secondary                                       |
| End point timeframe:<br>Visit 4 (48 hours)   |   |

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: millimetre(s)                 |                     |                 |                   |  |
| arithmetic mean (standard deviation) | -42.3 (± 16.2)      | -27.7 (± 15.1)  | -42.8 (± 13.0)    |  |

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. comparator |
| Statistical analysis description:<br>Pain-on-movement PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |  |
| Comparison groups   | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis   | 234  |
| Analysis specification  | Pre-specified                              |
| Analysis type   | non-inferiority                            |
| P-value   | = 0.99                                     |
| Method  | ANCOVA                                     |
| Confidence interval   |  |
| level   | 95 %                                       |
| sides   | 2-sided                                    |
| lower limit   | -4.0998                                    |
| upper limit   | 4.0479                                     |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. placebo |
| Statistical analysis description:<br>Pain-on-movement PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups   | Flurbiprofen (Test) v Placebo           |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 234           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | superiority   |
| P-value                                 | < 0.0001      |
| Method                                  | ANCOVA        |
| Confidence interval                     |               |
| level                                   | 95 %          |
| sides                                   | 2-sided       |
| lower limit                             | -18.7044      |
| upper limit                             | -10.6197      |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Comparator vs. placebo |
| Statistical analysis description:  |   |
| Pain-on-movement PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups  | Placebo v Active comparator                   |
| Number of subjects included in analysis  | 156   |
| Analysis specification   | Pre-specified                                 |
| Analysis type  | superiority                                   |
| P-value  | < 0.0001                                      |
| Method   | ANCOVA  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided                                       |
| lower limit  | -19.3515                                      |
| upper limit  | -9.9207                                       |

|  |   |
|--|---|
| <b>Secondary: POM - Pain Intensity Difference (PID) - visit 5</b>  |   |
| End point title  | POM - Pain Intensity Difference (PID) - visit 5 |
| End point description:   |   |
| PID (Pain Intensity Difference calculated as reduction in VAS for POM from baseline) was a derived parameter calculated from POM data and used as secondary endpoint. Negative PID values indicate pain reduction. |   |
| End point type   | Secondary                                       |
| End point timeframe:   |   |
| Visit 5 (72 hours)   |   |

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: millimetre(s)                 |                     |                 |                   |  |
| arithmetic mean (standard deviation) | -55.0 (± 14.7)      | -38.9 (± 16.8)  | -56.3 (± 11.4)    |  |

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. comparator |
| Statistical analysis description:<br>Pain-on-movement PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |  |
| Comparison groups   | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis   | 234  |
| Analysis specification  | Pre-specified                              |
| Analysis type   | non-inferiority                            |
| P-value   | = 0.8304                                   |
| Method  | ANCOVA                                     |
| Confidence interval   |  |
| level   | 95 %                                       |
| sides   | 2-sided                                    |
| lower limit   | -3.3592                                    |
| upper limit   | 4.1805                                     |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. placebo |
| Statistical analysis description:<br>Pain-on-movement PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups   | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis   | 234                                     |
| Analysis specification  | Pre-specified                           |
| Analysis type   | superiority                             |
| P-value   | < 0.0001                                |
| Method  | ANCOVA                                  |
| Confidence interval   |   |
| level   | 95 %                                    |
| sides   | 2-sided                                 |
| lower limit   | -19.7516                                |
| upper limit   | -12.2702                                |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Treatment comparison - Comparator vs. placebo |
| Statistical analysis description:<br>Pain-on-movement PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups   | Placebo v Active comparator                   |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 156           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | superiority   |
| P-value                                 | < 0.0001      |
| Method                                  | ANCOVA        |
| Confidence interval                     |               |
| level                                   | 95 %          |
| sides                                   | 2-sided       |
| lower limit                             | -20.7851      |
| upper limit                             | -12.058       |

### Secondary: POM - Pain Intensity Difference (PID) - visit 6

|                        |   |
|------------------------|---|
| End point title        | POM - Pain Intensity Difference (PID) - visit 6 |
| End point description: |   |
| End point type         | Secondary                                       |
| End point timeframe:   |   |
| Visit 6 (96 hours)     |   |

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 156                 | 78              | 78                |  |
| Units: millimetre(s)                 |                     |                 |                   |  |
| arithmetic mean (standard deviation) | -62.0 (± 12.2)      | -49.2 (± 16.7)  | -64.1 (± 10.2)    |  |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | Treatment comparison - Test vs. comparator   |
| Statistical analysis description:       |  |
|   | Pain-on-movement PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |
| Comparison groups                       | Flurbiprofen (Test) v Active comparator  |
| Number of subjects included in analysis | 234  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | non-inferiority  |
| P-value                                 | = 0.563  |
| Method                                  | ANCOVA   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -2.2394  |
| upper limit                             | 4.1067   |



|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. placebo |
| Statistical analysis description:<br>Pain-on-movement PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups   | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis   | 234                                     |
| Analysis specification  | Pre-specified                           |
| Analysis type   | superiority                             |
| P-value   | < 0.0001                                |
| Method  | ANCOVA                                  |
| Confidence interval   |   |
| level   | 95 %                                    |
| sides   | 2-sided                                 |
| lower limit   | -15.852                                 |
| upper limit   | -9.555                                  |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Treatment comparison - Comparator vs. placebo |
| Statistical analysis description:<br>Pain-on-movement PID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups   | Active comparator v Placebo                   |
| Number of subjects included in analysis   | 156   |
| Analysis specification  | Pre-specified                                 |
| Analysis type   | superiority                                   |
| P-value   | < 0.0001                                      |
| Method  | ANCOVA  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided                                       |
| lower limit   | -17.3099                                      |
| upper limit   | -9.9645                                       |

|   |  |
|---|--|
| <b>Secondary: POM - SPID (Sum of Pain Intensity Differences) - visit 3</b>  |  |
| End point title   | POM - SPID (Sum of Pain Intensity Differences) - visit 3 |
| End point description:<br>SPID (Sum of Pain Intensity Differences) was derived parameter calculated from POM data and used as secondary endpoint. Negative SPID values indicate pain reduction. SPID was calculated as the time-weighted sum of pain intensity differences. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Visit 3 (24 hours)  |  |

| <b>End point values</b>              | Flurbiprofen (Test)               | Placebo                           | Active comparator                 |  |
|--------------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|--|
| Subject group type                   | Reporting group                   | Reporting group                   | Reporting group                   |  |
| Number of subjects analysed          | 156                               | 78                                | 78                                |  |
| Units: millimetre(s)                 |                                   |                                   |                                   |  |
| arithmetic mean (standard deviation) | -300.52029910<br>(± 195.36163866) | -211.62446580<br>(± 171.29802329) | -308.97329060<br>(± 205.46802941) |  |

## Statistical analyses

| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. comparator |
|---|--|
| Statistical analysis description:   |  |
| Pain-on-movement SPID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |  |
| Comparison groups   | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis   | 234  |
| Analysis specification  | Pre-specified                              |
| Analysis type   | non-inferiority                            |
| P-value   | = 0.7287                                   |
| Method  | ANCOVA                                     |
| Confidence interval   |  |
| level   | 95 %                                       |
| sides   | 2-sided                                    |
| lower limit   | -36.967                                    |
| upper limit   | 52.8055                                    |

| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. placebo |
|---|---|
| Statistical analysis description:   |   |
| Pain-on-movement SPID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups   | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis   | 234                                     |
| Analysis specification  | Pre-specified                           |
| Analysis type   | superiority                             |
| P-value   | < 0.0001                                |
| Method  | ANCOVA                                  |
| Confidence interval   |   |
| level   | 95 %                                    |
| sides   | 2-sided                                 |
| lower limit   | -134.4                                  |
| upper limit   | -45.3194                                |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Comparator vs. placebo |
| Statistical analysis description:<br>Pain-on-movement SPID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups  | Placebo v Active comparator                   |
| Number of subjects included in analysis  | 156   |
| Analysis specification   | Pre-specified                                 |
| Analysis type  | superiority                                   |
| P-value  | = 0.0003                                      |
| Method   | ANCOVA  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided                                       |
| lower limit  | -149.73                                       |
| upper limit  | -45.8228                                      |

## Secondary: POM - SPID (Sum of Pain Intensity Differences) - visit 4

|   |  |
|---|--|
| End point title   | POM - SPID (Sum of Pain Intensity Differences) - visit 4 |
| End point description:<br>SPID (Sum of Pain Intensity Differences) was derived parameter calculated from POM data and used as secondary endpoint. Negative SPID values indicate pain reduction. SPID was calculated as the time-weighted sum of pain intensity differences. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Visit 4 (48 hours)  |  |

| End point values                     | Flurbiprofen (Test)       | Placebo                              | Active comparator         |  |
|--------------------------------------|---------------------------|--------------------------------------|---------------------------|--|
| Subject group type                   | Reporting group           | Reporting group                      | Reporting group           |  |
| Number of subjects analysed          | 156                       | 78                                   | 78                        |  |
| Units: millimetre(s)                 |                           |                                      |                           |  |
| arithmetic mean (standard deviation) | -<br>1138.8229170<br>0 (± | -783.91346150<br>(±<br>456.89601944) | -<br>1156.8787390<br>0 (± |  |

## Statistical analyses

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Treatment comparison - Test vs. comparator |
| Statistical analysis description:<br>Pain-on-movement SPID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |  |
| Comparison groups  | Flurbiprofen (Test) v Active comparator    |

|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 234             |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | non-inferiority |
| P-value                                 | = 0.8854        |
| Method                                  | ANCOVA          |
| Confidence interval                     |                 |
| level                                   | 95 %            |
| sides                                   | 2-sided         |
| lower limit                             | -112.8          |
| upper limit                             | 130.64          |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Test vs. placebo |
| Statistical analysis description:<br>Pain-on-movement SPID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups  | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis  | 234                                     |
| Analysis specification   | Pre-specified                           |
| Analysis type  | superiority                             |
| P-value  | < 0.0001                                |
| Method   | ANCOVA                                  |
| Confidence interval  |   |
| level  | 95 %                                    |
| sides  | 2-sided                                 |
| lower limit  | -477.26                                 |
| upper limit  | -235.71                                 |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Comparator vs. placebo |
| Statistical analysis description:<br>Pain-on-movement SPID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups  | Placebo v Active comparator                   |
| Number of subjects included in analysis  | 156   |
| Analysis specification   | Pre-specified                                 |
| Analysis type  | superiority                                   |
| P-value  | < 0.0001                                      |
| Method   | ANCOVA  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided                                       |
| lower limit  | -506.29                                       |
| upper limit  | -224.52                                       |

---

## Secondary: POM - SPID (Sum of Pain Intensity Differences) - visit 5

|   |  |
|---|--|
| End point title   | POM - SPID (Sum of Pain Intensity Differences) - visit 5 |
| End point description:  |  |
| SPID (Sum of Pain Intensity Differences) was derived parameter calculated from POM data and used as secondary endpoint. Negative SPID values indicate pain reduction. SPID was calculated as the time-weighted sum of pain intensity differences. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Visit 5 (72 hours)  |  |

| End point values                     | Flurbiprofen (Test)       | Placebo                   | Active comparator         |  |
|--------------------------------------|---------------------------|---------------------------|---------------------------|--|
| Subject group type                   | Reporting group           | Reporting group           | Reporting group           |  |
| Number of subjects analysed          | 156                       | 78                        | 78                        |  |
| Units: millimetre(s)                 |                           |                           |                           |  |
| arithmetic mean (standard deviation) | -<br>2303.5208330<br>0 (± | -<br>1575.3333330<br>0 (± | -<br>2342.3055560<br>0 (± |  |

### Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. comparator |
| Statistical analysis description:   |  |
| Pain-on-movement SPID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |  |
| Comparison groups   | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis   | 234  |
| Analysis specification  | Pre-specified                              |
| Analysis type   | non-inferiority                            |
| P-value   | = 0.9012                                   |
| Method  | ANCOVA                                     |
| Confidence interval   |  |
| level   | 95 %                                       |
| sides   | 2-sided                                    |
| lower limit   | -191.65                                    |
| upper limit   | 217.49                                     |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Treatment comparison - Test vs. placebo |
| Statistical analysis description:   |   |
| Pain-on-movement SPID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups   | Flurbiprofen (Test) v Placebo           |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 234           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | superiority   |
| P-value                                 | < 0.0001      |
| Method                                  | ANCOVA        |
| Confidence interval                     |               |
| level                                   | 95 %          |
| sides                                   | 2-sided       |
| lower limit                             | -931.97       |
| upper limit                             | -526          |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Comparator vs. placebo |
| Statistical analysis description:<br>Pain-on-movement SPID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups  | Placebo v Active comparator                   |
| Number of subjects included in analysis  | 156   |
| Analysis specification   | Pre-specified                                 |
| Analysis type  | superiority                                   |
| P-value  | < 0.0001                                      |
| Method   | ANCOVA  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided                                       |
| lower limit  | -978.68                                       |
| upper limit  | -505.12                                       |

|   |  |
|---|--|
| <b>Secondary: POM - SPID (Sum of Pain Intensity Differences) - visit 6</b>  |  |
| End point title   | POM - SPID (Sum of Pain Intensity Differences) - visit 6 |
| End point description:<br>SPID (Sum of Pain Intensity Differences) was derived parameter calculated from POM data and used as secondary endpoint. Negative SPID values indicate pain reduction. SPID was calculated as the time-weighted sum of pain intensity differences. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Visit 6 (96 hours)  |  |

| End point values                     | Flurbiprofen (Test)                       | Placebo                                   | Active comparator         |  |
|--------------------------------------|---|---|---------------------------|--|
| Subject group type                   | Reporting group                           | Reporting group                           | Reporting group           |  |
| Number of subjects analysed          | 156                                       | 78  | 78                        |  |
| Units: millimetre(s)                 |   |   |                           |  |
| arithmetic mean (standard deviation) | -<br>3707.3894230<br>0 (±<br>1083.2468793 | -<br>2632.6063030<br>0 (±<br>1143.5024923 | -<br>3787.5096150<br>0 (± |  |

## Statistical analyses

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Treatment comparison - Test vs. comparator |
| Statistical analysis description:<br>Pain-on-movement SPID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |  |
| Comparison groups  | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis  | 234  |
| Analysis specification   | Pre-specified                              |
| Analysis type  | non-inferiority                            |
| P-value  | = 0.8306                                   |
| Method   | ANCOVA                                     |
| Confidence interval  |  |
| level  | 95 %                                       |
| sides  | 2-sided                                    |
| lower limit  | -243.89                                    |
| upper limit  | 303.45                                     |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Test vs. placebo |
| Statistical analysis description:<br>Pain-on-movement SPID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups  | Flurbiprofen (Test) v Placebo           |
| Number of subjects included in analysis  | 234                                     |
| Analysis specification   | Pre-specified                           |
| Analysis type  | superiority                             |
| P-value  | < 0.0001                                |
| Method   | ANCOVA                                  |
| Confidence interval  |   |
| level  | 95 %                                    |
| sides  | 2-sided                                 |
| lower limit  | -1344.89                                |
| upper limit  | -801.78                                 |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Treatment comparison - Comparator vs. placebo |
| Statistical analysis description:<br>Pain-on-movement SPID - treatment comparison by Visit – ANCOVA considering baseline value as covariate including type-III tests of fixed effects, FAS |   |
| Comparison groups  | Placebo v Active comparator                   |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 156           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | superiority   |
| P-value                                 | < 0.0001      |
| Method                                  | ANCOVA        |
| Confidence interval                     |               |
| level                                   | 95 %          |
| sides                                   | 2-sided       |
| lower limit                             | -1419.89      |
| upper limit                             | -786.35       |

### Secondary: Time to resolution of tissue injury/contusion in days

|   |   |
|---|---|
| End point title   | Time to resolution of tissue injury/contusion in days |
| End point description:  |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| Resolution of soft tissue injury/contusion was assessed by the Investigator at the final study visit. The date was documented and used to derive the time span between "date of visit V1" and "date of resolution". |   |

| End point values                     | Flurbiprofen (Test) | Placebo         | Active comparator |  |
|--------------------------------------|---------------------|-----------------|-------------------|--|
| Subject group type                   | Reporting group     | Reporting group | Reporting group   |  |
| Number of subjects analysed          | 154                 | 78              | 77                |  |
| Units: day                           |                     |                 |                   |  |
| arithmetic mean (standard deviation) | 5.9 (± 1.9)         | 7.9 (± 2.9)     | 6.1 (± 2.5)       |  |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title  | Treatment comparison - Test vs. comparator |
| Statistical analysis description:   |  |
| Resolution of tissue injury – Time to resolution by treatment – log-rank test stratified by center, FAS |  |
| Comparison groups   | Flurbiprofen (Test) v Active comparator    |
| Number of subjects included in analysis   | 231  |
| Analysis specification  | Pre-specified                              |
| Analysis type   | non-inferiority                            |
| P-value   | = 0.7691                                   |
| Method  | Logrank                                    |

|                            |   |
|----------------------------|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
|----------------------------|---|



Statistical analysis description:

Resolution of tissue injury – Time to resolution by treatment – log-rank test stratified by center, FAS

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Flurbiprofen (Test) v Placebo |
| Number of subjects included in analysis | 232                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | superiority                   |
| P-value                                 | < 0.0001                      |
| Method                                  | Logrank                       |

---

**Statistical analysis title**

Treatment comparison - Comparator vs. placebo

Statistical analysis description:

Resolution of tissue injury – Time to resolution by treatment – log-rank test stratified by center, FAS

|   |                             |
|---|-----------------------------|
| Comparison groups                       | Placebo v Active comparator |
| Number of subjects included in analysis | 155                         |
| Analysis specification                  | Pre-specified               |
| Analysis type                           | superiority                 |
| P-value                                 | < 0.0001                    |
| Method                                  | Logrank                     |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were evaluated at every visit (except randomisation visit).

Adverse event reporting additional description:

The Safety Analysis Set (SAF) was used for the evaluation of adverse events.

The SAF included all randomized patients who received at least one dose of the study drug.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Flurbiprofen (Test) |
|-----------------------|---------------------|

Reporting group description:

Flurbiprofen 40 mg cutaneous hydrogel medicated plaster was applied topically to the injury side once every 12 hours.

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

The placebo plaster was applied topically to the injury side once every 12 hours.

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Active comparator |
|-----------------------|-------------------|

Reporting group description:

The active comparator plaster was applied topically to the injury side once every 12 hours.

| Serious adverse events                            | Flurbiprofen (Test) | Placebo        | Active comparator |
|---|---------------------|----------------|-------------------|
| Total subjects affected by serious adverse events |                     |                |                   |
| subjects affected / exposed                       | 0 / 156 (0.00%)     | 0 / 78 (0.00%) | 0 / 78 (0.00%)    |
| number of deaths (all causes)                     | 0                   | 0              | 0                 |
| number of deaths resulting from adverse events    | 0                   | 0              | 0                 |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events                            | Flurbiprofen (Test) | Placebo        | Active comparator |
|---|---------------------|----------------|-------------------|
| Total subjects affected by non-serious adverse events |                     |                |                   |
| subjects affected / exposed                           | 1 / 156 (0.64%)     | 1 / 78 (1.28%) | 5 / 78 (6.41%)    |
| General disorders and administration site conditions  |                     |                |                   |
| Application site erythema                             |                     |                |                   |
| subjects affected / exposed                           | 0 / 156 (0.00%)     | 0 / 78 (0.00%) | 1 / 78 (1.28%)    |
| occurrences (all)                                     | 0                   | 0              | 1                 |
| Application site joint erythema                       |                     |                |                   |

|  |                      |                     |                     |
|--|----------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 156 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 2 / 78 (2.56%)<br>2 |
| Application site rash<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 156 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 1 / 78 (1.28%)<br>1 |
| Immune system disorders<br>Immunisation reaction<br>subjects affected / exposed<br>occurrences (all)     | 0 / 156 (0.00%)<br>0 | 1 / 78 (1.28%)<br>1 | 0 / 78 (0.00%)<br>0 |
| Infections and infestations<br>Asymptomatic COVID-19<br>subjects affected / exposed<br>occurrences (all) | 1 / 156 (0.64%)<br>1 | 0 / 78 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 |
| Coronavirus infection<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 156 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0 | 1 / 78 (1.28%)<br>1 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported