



Clinical trial results:

A PHASE 2, SINGLE-CENTRE, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL-GROUP, EFFICACY AND SAFETY STUDY OF ZOLEDRONATE IN SUBJECTS WITH EROSIIVE HAND OSTEOARTHRITIS

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2010-019110-24 |
| Trial protocol | DE |
| Global end of trial date | 18 December 2013 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 02 August 2020 |
| First version publication date | 02 August 2020 |

Trial information

Trial identification

| | |
|-----------------------|---------------|
| Sponsor protocol code | CZOL446HDE43T |
|-----------------------|---------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Universitätsklinikum Erlangen |
| Sponsor organisation address | Maximiliansplatz 2, Erlangen, Germany, 91054 |
| Public contact | Medizinische Klinik 3, Universitätsklinikum Erlangen, Universitätsklinikum Erlangen, juergen.rech@uk-erlangen.de |
| Scientific contact | Medizinische Klinik 3, Universitätsklinikum Erlangen, Universitätsklinikum Erlangen, juergen.rech@uk-erlangen.de |

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 | 29 November 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 29 November 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 December 2013 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the 90-day symptomatic efficacy of a single dose of zoledronate (Aclasta ®) 5 mg IV, compared to placebo, for the treatment of erosive hand osteoarthritis

Protection of trial subjects:

none

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 06 October 2011 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Germany: 10 |
| Worldwide total number of subjects | 10 |
| EEA total number of subjects | 10 |

Notes:

Subjects enrolled per age group

| | |
|---|---|
| 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) | 0 |
| Adults (18-64 years) | 7 |
| From 65 to 84 years | 3 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

single centre (Medizinische Klinik 3, Universitätsklinikum Erlangen)

Pre-assignment

Screening details:

11 subjects screened, 1 Screening failure due to positive RF

Period 1

| | |
|------------------------------|---------------------------------------|
| Period 1 title | Treatment period |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|-------------|
| Arm title | Zoledronate |
|------------------|-------------|

Arm description:

subjects received one single dose of 5mg zoledronate iv

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Zoledronate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous drip use |

Dosage and administration details:

one single dose of 5mg i.v. as intravenous drip (30min)

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

subjects received one single dose of placebo iv

| | |
|--|-----------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous drip use |

Dosage and administration details:

one single dose as intravenous drip (30min)

| Number of subjects in period 1 | Zoledronate | Placebo |
|--------------------------------|-------------|---------|
| Started | 5 | 5 |
| Completed | 5 | 5 |

Period 2

| | |
|------------------------------|---------------------------------------|
| Period 2 title | Follow-up |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer |

Arms

| | |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Zoledronate |

Arm description:

subjects received one single dose of 5mg zoledronate iv

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Zoledronate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous drip use |

Dosage and administration details:

one single dose of 5mg i.v. as intravenous drip (30min)

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

subjects received one single dose of placebo iv

| | |
|--|-----------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous drip use |

Dosage and administration details:

one single dose as intravenous drip (30min)

| Number of subjects in period 2 | Zoledronate | Placebo |
|---------------------------------------|-------------|---------|
| Started | 5 | 5 |
| Completed | 5 | 5 |

Baseline characteristics

Reporting groups

| | |
|---|-------------|
| Reporting group title | Zoledronate |
| Reporting group description: subjects received one single dose of 5mg zoledronate iv | |
| Reporting group title | Placebo |
| Reporting group description: subjects received one single dose of placebo iv | |

| Reporting group values | Zoledronate | Placebo | Total |
|---|-------------|----------|-------|
| Number of subjects | 5 | 5 | 10 |
| Age categorical Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 0 |
| Newborns (0-27 days) | | | 0 |
| Infants and toddlers (28 days-23 months) | | | 0 |
| Children (2-11 years) | | | 0 |
| Adolescents (12-17 years) | | | 0 |
| Adults (18-64 years) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 58.8 | 62.2 | |
| full range (min-max) | 52 to 72 | 55 to 76 | - |
| Gender categorical Units: Subjects | | | |
| Female | 3 | 3 | 6 |
| Male | 2 | 2 | 4 |
| Prior NSAID use Units: Subjects | | | |
| used | 1 | 2 | 3 |
| not used | 4 | 3 | 7 |
| Duration of disease Units: years | | | |
| arithmetic mean | 7 | 11.2 | |
| full range (min-max) | 4 to 14 | 4 to 23 | - |
| SJC | | | |
| sum score swollen Joints at baseline | | | |
| Units: unit(s) | | | |
| arithmetic mean | 8.8 | 6.6 | |
| full range (min-max) | 2 to 28 | 2 to 14 | - |
| TJC | | | |
| sum score tender Joints at baseline | | | |
| Units: unit(s) | | | |

| | | | |
|---|-------------------------|-------------------------|---|
| arithmetic mean full range (min-max) | 17.6 3 to 27 | 15.8 2 to 29 | - |
| HAQ disability index Units: unit(s) arithmetic mean full range (min-max) | 0.325 0.25 to 0.375 | 0.4 0.25 to 0.625 | - |
| VAS disease activity | | | |
| standardised 100mm Likert scale | | | |
| Units: unit(s) arithmetic mean full range (min-max) | 64.6 44 to 78 | 60.8 44 to 82 | - |
| AUSCAN Units: unit(s) arithmetic mean full range (min-max) | 19.43 17.45 to 20.67 | 18.97 14.84 to 21.84 | - |

End points

End points reporting groups

| | |
|---|-------------|
| Reporting group title | Zoledronate |
| Reporting group description: subjects received one single dose of 5mg zoledronate iv | |
| Reporting group title | Placebo |
| Reporting group description: subjects received one single dose of placebo iv | |
| Reporting group title | Zoledronate |
| Reporting group description: subjects received one single dose of 5mg zoledronate iv | |
| Reporting group title | Placebo |
| Reporting group description: subjects received one single dose of placebo iv | |

Primary: AUSCAN

| | |
|-----------------------------|-----------------------|
| End point title | AUSCAN ^[1] |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| End of study visit (day 91) | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Due to the small number of subjects only descriptive analysis

| End point values | Zoledronate | Placebo | | |
|--|-----------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5 | 5 | | |
| Units: unit(s) | | | | |
| arithmetic mean (full range (min-max)) | 15.37 (8.20 to 21.45) | 18.76 (14.95 to 24.34) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: SJC

| | |
|---|-----------|
| End point title | SJC |
| End point description: sum score swollen Joints at EoS | |
| End point type | Secondary |
| End point timeframe: | |
| End of study visit (day 91) | |

| End point values | Zoledronate | Placebo | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5 | 5 | | |
| Units: number | | | | |
| arithmetic mean (full range (min-max)) | 5.2 (4 to 9) | 8.8 (1 to 28) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: TJC

| | |
|--------------------------------|-----------|
| End point title | TJC |
| End point description: | |
| sum score tender Joints at EoS | |
| End point type | Secondary |
| End point timeframe: | |
| End of study vsisit (day 91) | |

| End point values | Zoledronate | Placebo | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5 | 5 | | |
| Units: number | | | | |
| arithmetic mean (full range (min-max)) | 17 (5 to 36) | 6.7 (2 to 14) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: HAQ disability index

| | |
|-----------------------------|----------------------|
| End point title | HAQ disability index |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| End of study visit (day 91) | |

| End point values | Zoledronate | Placebo | | |
|--|--------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5 | 5 | | |
| Units: unit(s) | | | | |
| arithmetic mean (full range (min-max)) | 0.3 (0.125 to 0.5) | 0.425 (0.25 to 0.625) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: VAS disease activity

| | |
|-----------------------------|----------------------|
| End point title | VAS disease activity |
| End point description: | |
| 100mm Likert scale | |
| End point type | Secondary |
| End point timeframe: | |
| End of study visit (day 91) | |

| End point values | Zoledronate | Placebo | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5 | 5 | | |
| Units: unit(s) | | | | |
| arithmetic mean (full range (min-max)) | 28.5 (13 to 48) | 48.8 (21 to 87) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

from enrolment to end of study visit (day 91)

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | All subjects |
|-----------------------|--------------|

Reporting group description: -

| Serious adverse events | All subjects | | |
|--|-----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | All subjects | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 10 / 10 (100.00%) | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Surgical and medical procedures | | | |

| | | | |
|--|----------------------|--|--|
| Endodontic procedure subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | | |
| Tooth extraction subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | | |
| Syncope subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | | |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | | |
| Chest pain subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | | |
| Influenza like illness subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | | |
| Ear and labyrinth disorders Middle ear disorder subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | | |
| Ear discomfort subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | | |
| Tinnitus subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | | |
| vertigo subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | | |

| | | | |
|--|--|--|--|
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 | | |
| Psychiatric disorders Sleep disorder subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | | |
| Musculoskeletal and connective tissue disorders Pain in jaw subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Bursitis subjects affected / exposed occurrences (all) Musculoskeletal pain subjects affected / exposed occurrences (all) Spinal pain subjects affected / exposed occurrences (all) Bone pain subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 | | |
| Infections and infestations Nasopharyngitis | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |
| Helicobacter gastritis | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--------------------------------------|
| 29 April 2011 | Rescue medication with acetaminophen |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

clinical Trial was prematurely ended due to slow recruitment

Notes: