Clinical trial results:
A PHASE 2, SINGLE-CENTRE, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL-GROUP, EFFICACY AND SAFETY STUDY OF ZOLEDRONATE IN SUBJECTS WITH EROSIVE 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	17.6	15.8	
full range (min-max)	3 to 27	2 to 29	-
HAQ disability index			
Units: unit(s)			
arithmetic mean	0.325	0.4	
full range (min-max)	0.25 to 0.375	0.25 to 0.625	-
VAS disease activity			
standardised 100mm Likert scale			
Units: unit(s)			
arithmetic mean	64.6	60.8	
full range (min-max)	44 to 78	44 to 82	-
AUSCAN			
Units: unit(s)			
arithmetic mean	19.43	18.97	
full range (min-max)	17.45 to 20.67	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	1 / 10 (10.00%)		
occurrences (all)	1		
Tooth extraction			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Middle ear disorder			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Ear discomfort			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Tinnitus			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
vertigo			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

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