Clinical trial results:
Randomized placebo-controlled trial to investigate clinical efficacy, anti-inflammatory properties and safety of prednisolone in hand osteoarthritis: a proof-of-concept study

Summary

EudraCT number	2015-000687-33
Trial protocol	NL
Global end of trial date	02 July 2018

Results information

Result version number	v1 (current)
This version publication date	19 March 2022
First version publication date	19 March 2022

Trial information

Trial identification

Sponsor protocol code	HOPE

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Netherlands Trial Registry: NTR5263

Notes:

Sponsors

Sponsor organisation name	Leiden University Medical Center
Sponsor organisation address	Albinusdreef 2, Leiden, Netherlands,
Public contact	Principal investigator, Leiden University Medical Center, 0031 715263598,
Scientific contact	Principal investigator, Leiden University Medical Center, 0031 715263598,

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	02 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 July 2018
Global end of trial reached?	Yes
Global end of trial date	02 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to identify a new treatment to alleviate pain and diminish inflammation in patients with hand osteoarthritis with symptoms and signs of inflammation.

Protection of trial subjects:

Trial subjects were monitored very well during the study.

Background therapy:

Usual care

Evidence for comparator:

Since local inflammation is recognised as contributing to osteoarthritic
complaints, the Hand Osteoarthritis Prednisolone Efficacy (HOPE) study aimed to investigate the efficacy and safety
of short-term prednisolone in patients with painful hand osteoarthritis and synovial inflammation

Actual start date of recruitment	03 December 2015
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	Netherlands: 92
Worldwide total number of subjects	92
EEA total number of subjects	92

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)	70
From 65 to 84 years	22

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

We recruited eligible adults from rheumatology outpatient clinics at two sites in the Netherlands.

Pre-assignment

Screening details:

Symptomatic hand OA that fulfilled the ACR criteria and signs of inflammation in DIP/PIP joints. Required to have four or more DIP/PIP joints with OA nodes, >=1 DIP/PIP with soft swelling or erythema, >=1 DIP/PIP with positive power Doppler signal or synovial thickening >=grade 2, pain >=30/100 on VAS that flared after NSAID washout.

Period 1

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

Blinding implementation details:

Study medication (5 mg/mL oral prednisolone solution or placebo solution) was provided in sequentially numbered bottles. Prednisolone and placebo solutions were identical in appearance, smell, and taste. Patients, outcome assessors (not authors), and data analysts (FPBK and SB) remained masked for treatment allocation until the study database was locked.

Arms

Are arms mutually exclusive?	Yes
Arm title	Prednisolone

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Patients self-administered 2 mL of 5 mg/mL prednisolone solution (ie, a 10 mg dose)

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Patients self-administered 2 mL of placebo solution once daily for 6 weeks

Number of subjects in period 1	Prednisolone	Placebo
Started	46	46
Completed	42	42
Not completed	4	4
Consent withdrawn by subject	-	1
Adverse event, non-fatal	1	3
elective surgery	1	-
Lack of efficacy	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Prednisolone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Prednisolone	Placebo	Total
Number of subjects	46	46	92
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	62.2	65.6	
standard deviation	± 8.8	± 8.5	-
Gender categorical Units: Subjects			
Female	38	35	73
Male	8	11	19

End points

End points reporting groups

Reporting group title	Prednisolone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: VAS pain fingers

End point title	VAS pain fingers
End point description:	
End point type	Primary
End point timeframe:	
6 weeks	

End point values	Prednisolone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	46		
Units: 100				
arithmetic mean (standard deviation)	-21.5 (± 21.7)	-5.2 (± 24.3)		

Statistical analyses

Statistical analysis title	main analysis

Statistical analysis description:

We analysed all endpoints with generalised estimating equations, and we used robust standard errors and the working correlation structure specified as exchangeable. Data from all available timepoints were used. The independent variables included in our model were treatment group, visit number (categorical), interaction between treatment group and visit number, the baseline value of dependent variable (continuous), and study centre (categorical).

Comparison groups	Prednisolone v Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-16.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.1
upper limit	-6.9
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

14 weeks

Adverse event reporting additional description:

Safety
endpoints were the number of adverse events, serious
adverse events, withdrawals
because of adverse events,
and changes in blood glucose concentrations between baseline and week 2.

Assessment type	Systematic

Dictionary used

Dictionary name	none
Dictionary version	0

Reporting groups

Reporting group title	Prednisolone

Reporting group description: -

Reporting group title	Placebo

Reporting group description: -

Serious adverse events	Prednisolone	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 46 (2.17%)	4 / 46 (8.70%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
bowel surgery			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Reproductive system and breast disorders			
symptomatic uterine myomas requiring hysterectomy			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
infected traumatic leg haematoma requiring surgery			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Prednisolone	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 46 (93.48%)	43 / 46 (93.48%)	
Cardiac disorders			
Hypertension			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	
occurrences (all)	0	1	
Nervous system disorders			
headache dizziness or lightheadedness			
subjects affected / exposed	7 / 46 (15.22%)	5 / 46 (10.87%)	
occurrences (all)	7	5	
General disorders and administration site conditions			
other			
subjects affected / exposed	8 / 46 (17.39%)	6 / 46 (13.04%)	
occurrences (all)	8	6	
Psychiatric disorders			
hyperactivity or sleeping problems			
subjects affected / exposed	3 / 46 (6.52%)	0 / 46 (0.00%)	
occurrences (all)	3	0	
Endocrine disorders			
Hyperglycaemia			

subjects affected / exposed	1 / 46 (2.17%)	3 / 46 (6.52%)	
occurrences (all)	1	3	
Musculoskeletal and connective tissue disorders			
musculoskeletal or aspecific aches			
subjects affected / exposed	3 / 46 (6.52%)	3 / 46 (6.52%)	
occurrences (all)	3	3	
Infections and infestations			
all infections			
subjects affected / exposed	21 / 46 (45.65%)	25 / 46 (54.35%)	
occurrences (all)	21	25	

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