Clinical trial results:
Effects on pain of infiltration by a combination of hyaluronic acid and corticoids versus corticoids alone in rhizarthrosis.

Summary

EudraCT number	2017-002298-20
Trial protocol	FR
Global end of trial date	16 December 2021

Results information

Result version number	v1 (current)
This version publication date	30 June 2023
First version publication date	30 June 2023

Trial information

Trial identification

Sponsor protocol code	CHD046-17

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03431584
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Centre Hospitalier Départemental Vendée
Sponsor organisation address	Boulevard Stéphane Moreau , La Roche-sur-Yon, France, 85000
Public contact	Dr Grégoire CORMIER , Centre Hospitalier Départemental Vendée, promotion.urc@chd-vendee.fr
Scientific contact	Dr Grégoire CORMIER , Centre Hospitalier Départemental Vendée, promotion.urc@chd-vendee.fr

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	31 May 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 March 2021
Global end of trial reached?	Yes
Global end of trial date	16 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of the association hyaluronic acid+steroids versus saline+steroids in patients with painful rhizarthrosis despite medical therapy.

Protection of trial subjects:

All adverse events or reactions (except tjose specified in the protocol), wether expected or unexpected, seriou or not, were collected in the eCRF.
The follow-up of serious events or adverse reaction was ensured until resolution or consolidation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 May 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 150
Worldwide total number of subjects	150
EEA total number of subjects	150

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)	85
From 65 to 84 years	65

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

254 patients were screened for inclusion 150 patient signed an informed consent and were randomised but 1 patient lost to follow-up after infiltration

Pre-assignment

Screening details:

254 patients were screened

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

Patient "blinding" was ensure with the placement of a sterile field, vertically on an infusion stand before injection by the physician

Arms

Are arms mutually exclusive?	Yes
Arm title	betamethasone and hyaluronic acid

Arm description:

0.5 ml of CTC (betamethasone) and 0.5 ml of HA (hyaluronic acid)

Arm type	Experimental
Investigational medicinal product name	Betamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intraarticular use

Dosage and administration details:

0.5 mL (7 mg/mL)

Investigational medicinal product name	Hyaluronic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intraarterial use

Dosage and administration details:

0.5mL (8mg/ mL)

Arm title	betamethasone and saline

Arm description:

0.5 ml of CTC (betamethasone) and 0.5 ml of saline

Arm type	Active comparator
Investigational medicinal product name	Betamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details: 0.5 mL (7 mg/ mL)	
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for...
Routes of administration	Intraarticular use

Dosage and administration details:

0.5 mL (NaCL 0.9%)

Number of subjects in period 1[1]	betamethasone and hyaluronic acid	betamethasone and saline
Started	73	76
M1 - intermediate visit	73	76
M3 - intermediate visit	73	73
M6 - intermediate visit	72	71
M12 - End of study	65	69
Completed	65	69
Not completed	8	7
Adverse event, serious fatal	-	1
Physician decision	1	-
Consent withdrawn by subject	1	4
visit canceled	3	1
Lost to follow-up	3	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One patient in the "betamethasone & hyaluronic acid" group was lost to follow-up after infiltration. 149 patients were included for analysis

Baseline characteristics

Reporting groups	
Reporting group title	betamethasone and hyaluronic acid
Reporting group description:	
0.5 ml of CTC (betamethasone) and 0.5 ml of HA (hyaluronic acid)	
Reporting group title	betamethasone and saline
Reporting group description:	
0.5 ml of CTC (betamethasone) and 0.5 ml of saline	

Reporting group values	betamethasone and hyaluronic acid	betamethasone and saline	Total
Number of subjects	73	76	149
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	44	41	85
From 65-84 years	29	35	64
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	61.8	61.9	
standard deviation	± 9.3	± 8.9	-
Gender categorical Units: Subjects			
Female	61	62	123
Male	12	14	26

End points

End points reporting groups

Reporting group title	betamethasone and hyaluronic acid
Reporting group description: 0.5 ml of CTC (betamethasone) and 0.5 ml of HA (hyaluronic acid)	
Reporting group title	betamethasone and saline
Reporting group description: 0.5 ml of CTC (betamethasone) and 0.5 ml of saline	

Primary: effectiveness of thumb infiltration

End point title	effectiveness of thumb infiltration
End point description: The endpoint was the intensity of pain at the base of the thumb during activity at 3 months. This evaluation was done by asking the following question: "During the last week, how would you estimate the average intensity of pain caused by osteoarthritis of your thumb during activity?" in order to have a standardization of its collection.	
End point type	Primary
End point timeframe: M3	

End point values	betamethasone and hyaluronic acid	betamethasone and saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	73		
Units: centimeter				
least squares mean (confidence interval 95%)	-2.65 (-3.29 to -2.01)	-1.66 (-2.29 to -1.03)		

Statistical analyses

Statistical analysis title	effectiveness of thumb infiltration
Comparison groups	betamethasone and hyaluronic acid v betamethasone and saline
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Mixed models analysis

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From randomisation (intervention) until end of participation of patient (M12)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	betamethasone and hyaluronic acid
Reporting group description:	
0.5 ml of CTC (betamethasone) and 0.5 ml of HA (hyaluronic acid)	
Reporting group title	betamethasone and saline
Reporting group description:	
0.5 ml of CTC (betamethasone) and 0.5 ml of saline	

Serious adverse events	betamethasone and hyaluronic acid	betamethasone and saline	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 73 (15.07%)	16 / 76 (21.05%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
LEUKAEMIA			
subjects affected / exposed	0 / 73 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
OVARIAN CANCER			
subjects affected / exposed	1 / 73 (1.37%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYOGENIC GRANULOMA			
subjects affected / exposed	1 / 73 (1.37%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
PELVIC FRACTURE			

subjects affected / exposed	1 / 73 (1.37%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TOXICITY TO VARIOUS AGENTS			
subjects affected / exposed	1 / 73 (1.37%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	1 / 73 (1.37%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
JOINT ARTHROPLASTY			
subjects affected / exposed	0 / 73 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRAPEZIECTOMY			
subjects affected / exposed	0 / 73 (0.00%)	2 / 76 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
CARPAL TUNNEL SYNDROME			
subjects affected / exposed	2 / 73 (2.74%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	0 / 73 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
CATARACT			

subjects affected / exposed	1 / 73 (1.37%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
PANCREATITIS			
subjects affected / exposed	0 / 73 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
ALCOHOL ABUSE			
subjects affected / exposed	1 / 73 (1.37%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 73 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 73 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
OSTEOARTHRITIS			
subjects affected / exposed	2 / 73 (2.74%)	5 / 76 (6.58%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 73 (1.37%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ROTATOR CUFF SYNDROME			

subjects affected / exposed	1 / 73 (1.37%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TENOSYNOVITIS STENOSANS			
subjects affected / exposed	0 / 73 (0.00%)	1 / 76 (1.32%)	
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: 5 %

Non-serious adverse events	betamethasone and hyaluronic acid	betamethasone and saline	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 73 (21.92%)	21 / 76 (27.63%)	
Nervous system disorders			
MIGRAINE			
subjects affected / exposed	3 / 73 (4.11%)	0 / 76 (0.00%)	
occurrences (all)	3	0	
SCIATICA			
subjects affected / exposed	1 / 73 (1.37%)	0 / 76 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
PERIPHERAL SWELLING			
subjects affected / exposed	1 / 73 (1.37%)	1 / 76 (1.32%)	
occurrences (all)	1	1	
MALAISE			
subjects affected / exposed	0 / 73 (0.00%)	1 / 76 (1.32%)	
occurrences (all)	0	1	
INJECTION SITE HAEMATOMA			
subjects affected / exposed	0 / 73 (0.00%)	1 / 76 (1.32%)	
occurrences (all)	0	1	
INJECTION SITE ATROPHY			
subjects affected / exposed	0 / 73 (0.00%)	1 / 76 (1.32%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			

ARTHRALGIA			
subjects affected / exposed	2 / 73 (2.74%)	1 / 76 (1.32%)	
occurrences (all)	2	1	
BACK PAIN			
subjects affected / exposed	0 / 73 (0.00%)	2 / 76 (2.63%)	
occurrences (all)	0	2	
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 73 (0.00%)	1 / 76 (1.32%)	
occurrences (all)	0	1	
PAIN IN EXTREMITY			
subjects affected / exposed	10 / 73 (13.70%)	13 / 76 (17.11%)	
occurrences (all)	11	14	
TENDON DISORDER			
subjects affected / exposed	0 / 73 (0.00%)	1 / 76 (1.32%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 March 2018	clarification of treatment kit labeling
11 November 2018	treatment kits will no longer be dispensed by the pharmacy but will be available in the services
12 November 2019	extended inclusion period (additional 18 months)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported