



Clinical trial results:

HERO:Hydroxychloroquine Effectiveness in Reducing Symptoms of hand OA, a randomised, double-blind, placebo-controlled trial

Summary

EudraCT number	2011-004300-38
Trial protocol	GB
Global end of trial date	18 October 2016

Results information

Result version number	v1 (current)
This version publication date	30 October 2020
First version publication date	30 October 2020
Summary attachment (see zip file)	HERO EOT report (AIME201803200-M171430.pdf)

Trial information

Trial identification

Sponsor protocol code	RR10/9390
-----------------------	-----------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Leeds
Sponsor organisation address	Worsley Building, Leeds, United Kingdom, LS2 9JT
Public contact	Sarah Kingsbury, University of Leeds, s.r.kingsbury@leeds.ac.uk
Scientific contact	Sarah Kingsbury, University of Leeds, s.r.kingsbury@leeds.ac.uk

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	18 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 October 2016
Global end of trial reached?	Yes
Global end of trial date	18 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary question to be answered by this study is whether hydroxychloroquine is an effective treatment for relieving pain in hand OA.

Protection of trial subjects:

sign Overview

HERO was an investigator-led, pragmatic, multicenter, superiority, randomized, 1:1 placebo-controlled trial. The research protocol (Part 1 of the Supplement, available at Annals.org) was approved by the Leeds East Research Ethics Committee and the U.K. Medicines and Healthcare Products Regulatory Agency and registered on ISRCTN (ISRCTN91859104). Participants were recruited from 24 September 2012 until 27 May 2014 and followed up for 12 months after randomization (follow-up completed 25 April 2015). All participants gave written informed consent before screening.

One was recruited before protocol registration (24 September 2012 vs. 17 October 2012); however, no changes were made to the protocol between these time points, so this participant is similar to all others

Background therapy:

Synovitis is believed to play a role in producing symptoms in persons with hand osteoarthritis, but data on slowacting anti-inflammatory treatments are sparse. Symptomatic hand osteoarthritis affects 4% to 31% of adults older than 70 years and 3% to 15% older than 60 years (1–7). Patients report chronic persistent pain and considerable difficulty with daily activities (8).

However, few therapies are effective, and their use is often limited by patients' comorbid conditions or toxicities (9–11). Consequently, primary and secondary care

physicians seek alternatives to improve quality of life for persons with this painful, disabling disease. Anecdotal reports suggest hydroxychloroquine (HCQ) as one such therapy. It has been used as an unlicensed treatment in many countries when other options have failed,

mainly for patients with "inflammatory" hand osteoarthritis (12, 13). An established drug treatment of inflammatory arthritides, such as rheumatoid arthritis (RA),

HCQ is supported by placebo-controlled trials showing its efficacy (as monotherapy and in combination with other RA drugs) and acceptable safety profile (14, 15).

Increasing evidence that inflammation is prevalent in osteoarthritis and may have a role in symptoms (16–20) and 3 small pilot studies suggesting reduction in hand pain with HCQ (21–23) provide a rationale for exploring the efficacy of HCQ in treating hand osteoarthritis.

The objective of the HERO (Hydroxychloroquine Effectiveness in Reducing symptoms of hand Osteoarthritis) trial was to test the hypothesis that HCQ is an effective symptomatic treatment when used in persons with

at least moderate symptomatic hand osteoarthritis and an inadequate response to current therapies, including nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids.

Evidence for comparator: -	
Actual start date of recruitment	01 June 2012
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	United Kingdom: 248
Worldwide total number of subjects	248
EEA total number of subjects	248

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)	134
From 65 to 84 years	112
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Participants

were recruited from 24 September 2012 until 27 May 2014 and followed up for 12 months after randomization (follow-up completed 25 April 2015). All participants gave written informed consent before screening.

Pre-assignment

Screening details:

Participants

were recruited from 24 September 2012 until 27 May 2014 and followed up for 12 months after randomization (follow-up completed 25 April 2015). All participants gave written informed consent before screening.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Hydroxychloroquine 6.5mg per day

Arm description:

HCQ

200, 300, or 400 mg, with dosage calculated according to ideal body weight for a maximum of 6.5 mg/kg per day

Arm type	Experimental
Investigational medicinal product name	Hydroxychloroquine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200, 300, or 400 mg, with dosage calculated according to ideal body weight for a maximum of 6.5 mg/kg per day

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

Arm description:

Placebo arm

Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Identical to IMP used in intervention arm

Number of subjects in period 1	Hydroxychloroquine 6.5mg per day	Placebo
Started	124	124
Completed	124	124

Baseline characteristics

Reporting groups

Reporting group title	Hydroxychloroquine 6.5mg per day
Reporting group description:	
HCQ 200, 300, or 400 mg, with dosage calculated according to ideal body weight for a maximum of 6.5 mg/kg per day	
Reporting group title	Placebo
Reporting group description:	
Placebo arm	

Reporting group values	Hydroxychloroquine 6.5mg per day	Placebo	Total
Number of subjects	124	124	248
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	62.8	62.5	
standard deviation	± 9.1	± 9.2	-
Gender categorical			
Units: Subjects			
Female	97	106	203
Male	27	18	45

End points

End points reporting groups

Reporting group title	Hydroxychloroquine 6.5mg per day
Reporting group description: HCQ 200, 300, or 400 mg, with dosage calculated according to ideal body weight for a maximum of 6.5 mg/kg per day	
Reporting group title	Placebo
Reporting group description: Placebo arm	

Primary: s average hand pain during the previous 2 weeks (on a 0- to 10-point numerical rating scale [NRS]) at 6 months

End point title	s average hand pain during the previous 2 weeks (on a 0- to 10-point numerical rating scale [NRS]) at 6 months ^[1]
End point description: : The primary end point was average hand pain during the previous 2 weeks (on a 0- to 10-point numerical rating scale [NRS]) at 6 months. Secondary end points included selfreported pain and function, grip strength, quality of life, radiographic structural change, and adverse events. Baseline ultrasonography was done.	
End point type	Primary
End point timeframe: 6 Months	

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: Please see attached results paper for all details of all final assessment patient figures, and statistical analysis performed in the trial.

End point values	Hydroxychloroquine 6.5mg per day	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	124		
Units: NRSI				
arithmetic mean (full range (min-max))	5.66 (5.13 to 6.19)	5.49 (4.96 to 6.02)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Staff asked participants about AEs at all visits, and physicians reviewed AEs for severity, duration, and relatedness to the investigational medicinal product.

Adverse event reporting additional description:

Serious AEs were defined according to prespecified criteria, as detailed in the protocol (Part 1 of the Supplement); assessed for causality and expectedness by a physician; and reported within 24 hours.

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

Dictionary used

Dictionary name	CTCAE
-----------------	-------

Dictionary version	4.0
--------------------	-----

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Please see attached results paper for all details of Adverse Event Data

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 July 2012	Amendment 2
18 September 2012	Amendment 4
20 December 2012	Amendment 5
28 June 2013	Amendment 7

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported