Clinical trial results:
Improved cardiovascular risk factors and inflammatory markers in Rheumatoid Arthritis and Systemic Lupus Erythematosus? New aspects of Hydroxychloroquine – an interventional study (HCQCVDRASLE)

Summary

EudraCT number	2014-005418-45
Trial protocol	SE
Global end of trial date	20 December 2016

Results information

Result version number	v1 (current)
This version publication date	27 November 2019
First version publication date	27 November 2019
Summary attachment (see zip file)	PosterHCQ (PosterHCQ 20180907.pdf)

Trial information

Trial identification

Sponsor protocol code	HCQCVDRASLE-1.1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Dep of Reumatology
Sponsor organisation address	Östersund Hospital, Östersund, Sweden,
Public contact	Christine Bengtsson, Östersund hospital, +46 703850636, christine.bengtsson@umu.se
Scientific contact	Christine Bengtsson, Östersund hospital, +46 703850636, christine.bengtsson@umu.se

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	20 December 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 December 2016
Global end of trial reached?	Yes
Global end of trial date	20 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effects of treatment with hydroxychloroquoine (HCQ) on traditional cardiovascular risk factor profile: blood lipid profile, B-glucose, blood pressure after 4 and 8 weeks in patients with RA and SLE.

Secondary objectives: To study the effect on vascular function, measured with pulse wave velocity (PWV) and inflammatory markers including CRP, cytokines, Calprotectin and Hyaluronan (HA).
To study the patient´s compliance to drug prescription and the occurring adverse events.

Protection of trial subjects:

The patients in highest risk for developing severe adverse reactions are excluded from the study. The adverse events and reactions occurring during the study are closely monitored and the actions will be taken to treat the reactions and mitigate the risk for worsening. The short period of drug treatment (8 weeks) will decrease the likeliness of developing long-term treatment adverse reactions.
To receive information in writing about the increased risk of CVD can worry the patient. However, we do have a strategy in answering the patients questions and also a structured plan for dealing with cardiovascular risk factors that need direct medical intervention. The patients will be able to reach the study nurse by phone at every site and if needed, the investiga-tor is available for answers. If risk factors for CVD are in need of direct investigation or medical treatment, the patient will be remitted for this as in clinical praxis.

Background therapy: -

Evidence for comparator:

Since we could not use a placebo arm, a delayed start for half of the patients was used and patients were randomised to one of these groups. However, all patients were included, sampled and interviewed at baseline. The rationale was that we would be able to exclude the impact of "care" from the results by comparing the first 4 weeks in patients who were cared for equally but with and without study drug. The variables of interest were investigated over time in the whole study group to evaluate the change over time.

Actual start date of recruitment	01 May 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	Sweden: 33
Worldwide total number of subjects	33
EEA total number of subjects	33

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)	32
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was started May 2015. However, due to one of the investigator´s faling ill with seroius disease, the study was postponed to 2016. Also the persons who had accepted the first time were contacted again for decision of participartion. Thus, the true recriutment period was May-August 2016

Pre-assignment

Screening details:

Total number screened: 39.
33 patients were randomized.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Arm title	8 w treatment

Arm description:

Both arms added in order to evaluate effect of study drug over eight weeks treatment. Group 1 started treatment w 1 to w8, Group 2 started with 4 w non-treatment and received 8 w treatment from w 5 to 12.

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

Dosage and administration details:

200 mg /day

Number of subjects in period 1	8 w treatment
Started	33
Completed	30
Not completed	3
Physician decision	1
Adverse event, non-fatal	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial
Reporting group description:	
33 patients were randomised but only 32 were started on stúdy drug due to suddenly up-coming medical problems.	

Reporting group values	Overall trial	Total	
Number of subjects	33	33	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	32	32	
From 65-84 years	1	1	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	29	29	
Male	4	4	

End points

End points reporting groups

Reporting group title	8 w treatment

Reporting group description:

Both arms added in order to evaluate effect of study drug over eight weeks treatment. Group 1 started treatment w 1 to w8, Group 2 started with 4 w non-treatment and received 8 w treatment from w 5 to 12.

Primary: Blood Lipid profile

End point title	Blood Lipid profile[1]

End point description:

The primary endpoint is to evaluate the effect on the blood lipids; total cholesterol, triglycerides, Low density lipoprotein (LDL), High density lipoprotein (HDL) and Apo lipoproteins (ApoA1, ApoB and Lp(a)) in patients with RA and SLE.
The analysis were performed at w0, w4 and w8.
Measurable units as per analys:
Toral cholesterol: mmol/L
Triglyceride: mmol/L
HDL: mmol/L
LDL: mmol/L
ApoA1: g/L
ApoB: g/L
Lp(a): nmol/L

End point type	Primary

End point timeframe:

A 0 w, after 4 and 8 weeks

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: Each patient is it´s own control. There is no comparison between groups. Non-parametric tests will be used. Mann-Whitneys test; when comparison between Groups. Statistical testing of multiple assessments over time; Kruskal-Wallis or Friedmans test and Wilcoxons test.

End point values	8 w treatment			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: units	33			

Attachments (see zip file)	Results Cholesterol-TG-ApoB- HbA1c/Results Cholesterol-TG- Results TG-HDL-ApoA1-Lp(a)/Results TG-HDL-ApoA1-Lp(a).png

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the time for patient conscent till he/she has completed the trial.	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.0
Reporting groups	
Reporting group title	8 w treatment
Reporting group description:	
Both arms added in order to evaluate effect of study drug over eight weeks treatment. Group 1 started treatment w 1 to w8, Group 2 started with 4 w non-treatment and received 8 w treatment from w 5 to 12.	

Serious adverse events	8 w treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 33 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	8 w treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 33 (66.67%)		
Injury, poisoning and procedural complications			
Brusing			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Bleeding due to intrauterin coil			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Cardiac disorders			
Murmur			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		

Nervous system disorders			
Headache			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Nervous system disorders Other, Migraine with aura			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	2		
Dysgeusia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Eye disorders			
Presbyopi			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Cataract operation			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Gastrointestinal disorders			
Gastroesophageal reflux disease			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Obstipation			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences (all)	3		
Stomach pain			

subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Rach			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Skin ulceration lower limb			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety, worsening			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Psychiatrik disorders Other, Nightmares			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Back pain			

subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Infections and infestations			
Infections and infestations Other, Herpes zoster			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
Upper respiratory infection			
subjects affected / exposed	5 / 33 (15.15%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 May 2016	Material extended with SLE-patients from Sunderby hospital

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported