



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 hydroxychloroquine (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 investigator 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 falling ill with serious disease, the study was postponed to 2016. Also the persons who had accepted the first time were contacted again for decision of participation. Thus, the true recruitment 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 | Hydroxycycloquine |
| 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 study 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 Wilcoxon's 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 consent 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 | | | |
| Bruising | | | |
| 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 occurrences (all) Nervous system disorders Other, Migraine with aura subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all) | 2 / 33 (6.06%) 2 1 / 33 (3.03%) 1 1 / 33 (3.03%) 2 1 / 33 (3.03%) 1 | | |
| General disorders and administration site conditions Chills subjects affected / exposed occurrences (all) | 1 / 33 (3.03%) 1 | | |
| Eye disorders Presbyopi subjects affected / exposed occurrences (all) Cataract operation subjects affected / exposed occurrences (all) | 1 / 33 (3.03%) 1 1 / 33 (3.03%) 1 | | |
| Gastrointestinal disorders Gastroesophageal reflux disease subjects affected / exposed occurrences (all) Obstipation subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Stomach pain | 1 / 33 (3.03%) 1 1 / 33 (3.03%) 1 3 / 33 (9.09%) 3 | | |

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

| | | | |
|---|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 33 (3.03%) 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