Clinical trial results:
Coenzyme Q10 as treatment for Long Term COVID-19 (The QVID study)

Summary

EudraCT number	2020-005961-16
Trial protocol	DK
Global end of trial date	09 February 2022

Results information

Result version number	v1 (current)
This version publication date	06 May 2023
First version publication date	06 May 2023
Summary attachment (see zip file)	Hansen KS et al. High-dose coenzyme Q10 versus placebo..pdf (Hansen KS et al. High-dose coenzyme Q10 versus placebo..pdf)

Trial information

Trial identification

Sponsor protocol code	QVID-001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul-Jensens Blvd. 82, Aarhus N, Denmark, 8200
Public contact	Department of Infectious Diseases, Aarhus University Hospital, 0045 51513140, larsoest@rm.dk
Scientific contact	Department of Infectious Diseases, Aarhus University Hospital, 0045 51513140, larsoest@rm.dk

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	07 July 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of 6 weeks of CoQ10 treatment on the number and severity of self-reported symptoms in LTC patients

Protection of trial subjects:

All trial visits conducted in hospital setting in outpatient clinic with appropriate discretion. All data collected stored at protected hospital servers. During data analysis, pseudonymised data was used and social security numbers were never transfered from safe servers.
All patients provided written consent prior to any trial procedures or data collection.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 May 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	5 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 121
Worldwide total number of subjects	121
EEA total number of subjects	121

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)	119
From 65 to 84 years	2

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at the Department of Infectious Diseases at Aarhus University Hospital, Denmark. Participants were recruited from the PCC Outpatient Clinic at Aarhus University Hospital and Gødstrup Hospital, Denmark, directly or by letter invitation.

Pre-assignment

Screening details:

The following inclusion criteria were applied: >18 years of age; ability to give written informed consent; a history of SARS-CoV-2 infection based on either a PCR test or antibody test; and PCC-related symptoms that were diagnosed by a specialized infec- tious disease physician at the PCC Outpatient Clinic.

Period 1

Period 1 title	Period 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

Proper concealment of randomization was obtained by the use of an external randomization service (Clinical Trial Unit, Department of Clinical Medicine, Aarhus University, Denmark), who created the computer-generated sequence. The allocation list was stored in an electronic database with a concealed de-identification code, in case premature blinding was needed. This process was logged and monitored. Allocation lists were obtained by the pharmaceutical supplier for preparation of the study medicin

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

In this cross-over setting Arm A receives Coenzym Q10 in first period

Arm type	Experimental
Investigational medicinal product name	Coenzyme Q10
Investigational medicinal product code	
Other name	Ubiquinone
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100mg five times / day to enhance gastroinstenal uptake. Total day dose = 500mg.

Arm title	Arm B

Arm description:

In this cross-over setting Arm B receives placebo in first period

Arm type	Placebo
Investigational medicinal product name	Soy oil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo capsules administrated exactly like IMP: 1 capsule five times /day

Number of subjects in period 1	Arm A	Arm B
Started	59	62
Completed	59	60
Not completed	0	2
Consent withdrawn by subject	-	2

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

Proper concealment of randomization was obtained by the use of an external randomization service (Clinical Trial Unit, Department of Clinical Medicine, Aarhus University, Denmark), who created the computer-generated sequence. The allocation list was stored in an electronic database with a concealed de-identification code, in case premature blinding was needed. This process was logged and monitored. Allocation lists were obtained by the pharmaceutical supplier for preparation of the study medicin

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

In this cross-over setting arm A receives placebo in period 2

Arm type	Placebo
Investigational medicinal product name	Soy oil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 capsule five times / day

Arm title	Arm B

Arm description:

In this cross-over setting arm B receives Coenzyme Q10 in period 2

Arm type	Experimental
Investigational medicinal product name	Coenzyme Q10
Investigational medicinal product code	
Other name	Ubiquinone
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100mg five times / day to enhance gastroinstenal uptake. Total day dose = 500mg.

Number of subjects in period 2	Arm A	Arm B
Started	59	60
Completed	59	60

Baseline characteristics

Reporting groups	
Reporting group title	Period 1

Reporting group description: -

Reporting group values	Period 1	Total	
Number of subjects	121	121	
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)	119	119	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	47.95		
standard deviation	± 10.35	-	
Gender categorical Units: Subjects			
Female	91	91	
Male	30	30	
Smoking status Units: Subjects			
Never	78	78	
Former	36	36	
Current	7	7	
Hospital admission during acute COVID Units: Subjects			
Yes	18	18	
No	103	103	
Charlson Comorbidity Index Units: Subjects			
Score 0	62	62	
Score 1	40	40	
Score 2	16	16	
Score 3	2	2	
Score 4	1	1	
Vaccination status upon inclusion			
This categorical value refers to terms used at the time of the pandemic inclusion occured: "fully vaccinated" refers to having recieved first vaccination AND a booster and "partially vaccinated" to having recieved first vaccination, but no booster.			
Units: Subjects			

Fully vaccinated	102	102	
Partially vaccinated	13	13	
Not vaccinated	6	6	
Interval between acute COVID-19 and inclusion			
Units: days			
arithmetic mean	287.76		
standard deviation	± 118.88	-	
Post COVID-19 condition symptom score at baseline			
Units: points			
arithmetic mean	43.06		
standard deviation	± 16.0	-	
EQ-5D-5L quality of life index at baseline			
Units: index			
arithmetic mean	0.66		
standard deviation	± 0.12	-	
BMI			
Units: kg/m2			
arithmetic mean	28.02		
standard deviation	± 5.75	-	

Subject analysis sets

Subject analysis set title	Coenzyme Q10 vs placebo PCC score
Subject analysis set type	Full analysis

Subject analysis set description:

On average, the symptom scores were reduced by 5.18 points (95% CI: 3.40; 6.95) after the six-week treatment with CoQ10, compared to a reduction of 4.04 points (95% CI: 2.13; 5.96) after receiving placebo (Fig. 3A). After adjusting for sequence and period, the mean difference in the change in symptom scores be- tween CoQ10 and placebo was −1.18 (95% CI: −3.54; 1.17), indicating that on average the reduction in symptom score was 1.18 points larger after CoQ10 treatment compared to placebo; however, this difference was not significant (p = 0.32).

Subject analysis set title	Coenzyme Q10 vs placebo, EQ-5D-5L health index
Subject analysis set type	Full analysis

Subject analysis set description:

The estimated mean improvement in health index score was 0.04 (95% CI: 0.02; 0.06) and 0.03 (95% CI: 0.006; 0.05) after six weeks of CoQ10 treatment or placebo, respectively. After adjusting for period and sequence effect in the linear mixed-effects model, the estimated difference was 0.01 (95% CI: −0.02; 0.04), which was not statistically significant (p = 0.40).

Reporting group values	Coenzyme Q10 vs placebo PCC score	Coenzyme Q10 vs placebo, EQ-5D-5L health index	
Number of subjects	119	119	
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)	117	117	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	47.97	47.97	
standard deviation	± 10.42	± 10.42	
Gender categorical			
Units: Subjects			
Female	89	89	
Male	30	30	
Smoking status			
Units: Subjects			
Never	76	76	
Former	36	36	
Current	7	7	
Hospital admission during acute COVID			
Units: Subjects			
Yes	18	18	
No	101	101	
Charlson Comorbidity Index			
Units: Subjects			
Score 0	60	60	
Score 1	40	40	
Score 2	16	16	
Score 3	2	2	
Score 4	1	1	
Vaccination status upon inclusion			
This categorical value refers to terms used at the time of the pandemic inclusion occured: "fully vaccinated" refers to having recieved first vaccination AND a booster and "partially vaccinated" to having recieved first vaccination, but no booster.			
Units: Subjects			
Fully vaccinated	101	101	
Partially vaccinated	12	12	
Not vaccinated	6	6	
Interval between acute COVID-19 and inclusion			
Units: days			
arithmetic mean	288.55	288.55	
standard deviation	± 119.7	± 119.7	
Post COVID-19 condition symptom score at baseline			
Units: points			
arithmetic mean	43.06	43.06	
standard deviation	± 15.9	± 15.9	
EQ-5D-5L quality of life index at baseline			
Units: index			
arithmetic mean	0.66	0.66	
standard deviation	± 0.1	± 0.1	
BMI			
Units: kg/m2			
arithmetic mean	28.08	28.08	

standard deviation	± 5.8	± 5.8	

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
In this cross-over setting Arm A receives Coenzym Q10 in first period	
Reporting group title	Arm B
Reporting group description:	
In this cross-over setting Arm B receives placebo in first period	
Reporting group title	Arm A
Reporting group description:	
In this cross-over setting arm A receives placebo in period 2	
Reporting group title	Arm B
Reporting group description:	
In this cross-over setting arm B receives Coenzyme Q10 in period 2	
Subject analysis set title	Coenzyme Q10 vs placebo PCC score
Subject analysis set type	Full analysis
Subject analysis set description:	
On average, the symptom scores were reduced by 5.18 points (95% CI: 3.40; 6.95) after the six-week treatment with CoQ10, compared to a reduction of 4.04 points (95% CI: 2.13; 5.96) after receiving placebo (Fig. 3A). After adjusting for sequence and period, the mean difference in the change in symptom scores be- tween CoQ10 and placebo was −1.18 (95% CI: −3.54; 1.17), indicating that on average the reduction in symptom score was 1.18 points larger after CoQ10 treatment compared to placebo; however, this difference was not significant (p = 0.32).	
Subject analysis set title	Coenzyme Q10 vs placebo, EQ-5D-5L health index
Subject analysis set type	Full analysis
Subject analysis set description:	
The estimated mean improvement in health index score was 0.04 (95% CI: 0.02; 0.06) and 0.03 (95% CI: 0.006; 0.05) after six weeks of CoQ10 treatment or placebo, respectively. After adjusting for period and sequence effect in the linear mixed-effects model, the estimated difference was 0.01 (95% CI: −0.02; 0.04), which was not statistically significant (p = 0.40).	

Primary: Change in PCC symptom score

End point title	Change in PCC symptom score
End point description:	
The study course of 20 weeks (for each individual) comprised 5 visits at time point 0, 6, 10, 16 and 20 weeks. From 0-6 weeks arm A recieved coenzym Q10 and arm B received placebo. From week 10-16 arm A received placebo and arm B received coenzym Q10. In this crossover setting, the PCC score was measured by questionnaire at each visit, providing a picture of symptom burden. Change in symptom score to baseline for each period was used to compare effect of coenzym Q10 vs placebo.	
End point type	Primary
End point timeframe:	
6 weeks of treatment or placebo	

End point values	Arm A	Arm B	Arm A	Arm B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	60	59	60
Units: PCC score				
arithmetic mean (confidence interval 95%)	8.05 (5.73 to 10.37)	7.02 (4.7 to 9.33)	1.02 (-1.91 to 3.94)	2.35 (-0.19 to 4.89)

End point values	Coenzyme Q10 vs placebo PCC score			
Subject group type	Subject analysis set			
Number of subjects analysed	119			
Units: PCC score				
arithmetic mean (confidence interval 95%)	-1.18 (-3.54 to 1.17)			

Attachments (see zip file)	Time course of PCC-specific symptom scores and EQ-/Figure 3

Statistical analyses

Statistical analysis title	Mixed-effects model linear regression

Statistical analysis description:

To analyze the treatment effect of CoQ10 versus placebo and to quantify the period and sequence effects, we used a linear mixed-effects model with sequence, period, and treatment as two-level, fixed factors and participants as a random factor

Comparison groups	Arm A v Arm B v Arm A v Arm B
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Slope
Confidence interval	
level	95 %
sides	1-sided
Variability estimate	Standard deviation

Primary: Change in EQ-5D-5L health index

End point title	Change in EQ-5D-5L health index

End point description:

End point type	Primary

End point timeframe:

6 weeks of treatment or placebo

End point values	Arm A	Arm B	Arm A	Arm B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	60	59	60
Units: index				
arithmetic mean (confidence interval 95%)	0.05 (0.02 to 0.085)	0.04 (0.001 to 0.07)	0.02 (-0.006 to 0.04)	0.03 (0.003 to 0.05)

End point values	Coenzyme Q10 vs placebo, EQ-5D-5L health index			
Subject group type	Subject analysis set			
Number of subjects analysed	119			
Units: index				
arithmetic mean (confidence interval 95%)	0.01 (-0.02 to 0.04)			

Statistical analyses

Statistical analysis title	Mixed-effects model linear regression
Comparison groups	Arm A v Arm B v Arm A v Arm B v Coenzyme Q10 vs placebo, EQ-5D-5L health index
Number of subjects included in analysis	357
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Slope
Confidence interval	
level	95 %
sides	1-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose on day 1 of the study until 4 weeks after last dose (Coenzyme Q10 half-life is 48 hours).

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	5

Reporting groups

Reporting group title	All participants

Reporting group description: -

Serious adverse events	All participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 119 (1.68%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Skull X-ray	Additional description: Participant admitted to emergency department due to fall and subsequent severe headache. Skull x-ray normal. Participants' serum ethanol was elevated.		
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal behaviour	Additional description: Admitted to hospital due to suicidal thoughts. Unrelated to study drug. Participant had pre-existing depression and the event was caused by social circumstances.		
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	All participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 119 (10.92%)		
General disorders and administration site conditions			

Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	 1 / 119 (0.84%) 1 2 / 119 (1.68%) 2		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Heartburn subjects affected / exposed occurrences (all)	 2 / 119 (1.68%) 2 1 / 119 (0.84%) 1 9 / 119 (7.56%) 9 1 / 119 (0.84%) 1		
Musculoskeletal and connective tissue disorders Muscle pain subjects affected / exposed occurrences (all)	 1 / 119 (0.84%) 1		

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/36337437