Clinical trial results:
Evaluation of the efficacy and tolerability of long-term administration of Acetyl-L-Carnitine in the treatment of HIV related lipodystrophy. Parallel-group, randomized, double blind, placebo-controlled study.

Summary

EudraCT number	2005-004665-42
Trial protocol	IT
Global end of trial date	20 January 2009

Results information

Result version number	v1 (current)
This version publication date	05 November 2020
First version publication date	05 November 2020

Trial information

Trial identification

Sponsor protocol code	ST 200 DS 05-002

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Sigma Tau
Sponsor organisation address	Viale Shakespeare 47, Rome, Italy,
Public contact	Serena Principe, Alfasigma, serena.principe@alfasigma.com
Scientific contact	Serena Principe, Alfasigma, serena.principe@alfasigma.com

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 October 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 January 2009
Global end of trial reached?	Yes
Global end of trial date	20 January 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is the evaluation of the efficacy and tolerability of Acetyl-L-Carnitine administered at the dose of 3 g/die for 48 weeks in patients affected by HIV related lipodystrophy. The primary objective consists in the variation of the following parameters:

- Homeostasis Model of Assessment (HOMA), i.e. the evaluation of the ratio between glycemia and insulinemia.
- Mitochondrial DNA content of CD4 and CD8 cells.

Protection of trial subjects:

The study was performed in accordance with the Declaration of Helsinki, GCP guidelines and applicable normative dispositions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 September 2006
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	Italy: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	40
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study consisted of a screening period of up to 4 weeks.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Acetyl-L-Carnitine arm

Arm description:

Patients randomized to this arm of the study were treated with Acetyl-L-Carnitine granules for oral solution.

Arm type	Experimental
Investigational medicinal product name	Acetyl-L-Carnitine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral solution
Routes of administration	Oral use

Dosage and administration details:

Patients randomized to this arm of the study were treated with Acetyl-L-Carnitine granules for oral solution administered orally in one 1 g sachet tris in die (after breakfast, after lunch and after dinner) for 48 weeks.

Arm title	Placebo

Arm description:

Patients randomized to this arm of the study were treated with placebo.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral solution
Routes of administration	Oral use

Dosage and administration details:

Patients randomized to this arm of the study were treated with Placebo granules for oral solution administered orally in one sachet tris in die (after breakfast, after lunch and after dinner) for 48 weeks.

Number of subjects in period 1	Acetyl-L-Carnitine arm	Placebo
Started	20	20
Completed	15	14
Not completed	5	6
Drop out	5	6

Baseline characteristics

Reporting groups	
Reporting group title	Acetyl-L-Carnitine arm
Reporting group description:	
Patients randomized to this arm of the study were treated with Acetyl-L-Carnitine granules for oral solution.	
Reporting group title	Placebo
Reporting group description:	
Patients randomized to this arm of the study were treated with placebo.	

Reporting group values	Acetyl-L-Carnitine arm	Placebo	Total
Number of subjects	20	20	40
Age categorical Units: Subjects			
Adults (18-64 years)	20	20	40
Age continuous Units: years			
arithmetic mean	47	46	
standard deviation	± 6.4	± 5.7	-
Gender categorical Units: Subjects			
Female	4	2	6
Male	16	18	34

End points

End points reporting groups

Reporting group title	Acetyl-L-Carnitine arm
Reporting group description:	
Patients randomized to this arm of the study were treated with Acetyl-L-Carnitine granules for oral solution.	
Reporting group title	Placebo
Reporting group description:	
Patients randomized to this arm of the study were treated with placebo.	
Subject analysis set title	Per protocol Acetyl-L-Carnitine
Subject analysis set type	Per protocol
Subject analysis set description:	
The Per Protocol (PP) population includes all patients who completed the study. The PP Population is the primary population for the efficacy analysis	
Subject analysis set title	Per Protocol Placebo
Subject analysis set type	Per protocol
Subject analysis set description:	
The Per Protocol (PP) population includes all patients who completed the study. The PP Population is the primary population for the efficacy analysis.	

Primary: Homeostasis Model of Assessment (HOMA) variation

End point title	Homeostasis Model of Assessment (HOMA) variation
End point description:	
HOMA absolute change at visit 4 (after 48 ± 2 weeks of treatment) vs visit 1 (baseline).	

End point type	Primary
End point timeframe:	
46-54 weeks.	

End point values	Per protocol Acetyl-L-Carnitine	Per Protocol Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	14		
Units: HOMA absolute change				
arithmetic mean (standard deviation)	-0.19 (± 1.52)	1.25 (± 9.51)		

Statistical analyses

Statistical analysis title	Efficacy statistical analysis
Comparison groups	Per protocol Acetyl-L-Carnitine v Per Protocol Placebo

Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	
P-value	≤ 0.05
Method	Welch two sample t-test

Primary: CD4 mitochondrial DNA content variation

End point title	CD4 mitochondrial DNA content variation

End point description:

End point type	Primary

End point timeframe:

46-50 weeks

End point values	Per protocol Acetyl-L-Carnitine	Per Protocol Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	14		
Units: CD4 mit. DNA content absolute change				
arithmetic mean (standard deviation)	-26.9 (± 93.6)	8.2 (± 91.8)		

Statistical analyses

Statistical analysis title	Efficacy statistical analysis
Comparison groups	Per protocol Acetyl-L-Carnitine v Per Protocol Placebo
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	Welch two sample t-test

Primary: CD8 mitochondrial DNA content variation

End point title	CD8 mitochondrial DNA content variation

End point description:

End point type	Primary

End point timeframe:

46-50 weeks

End point values	Per protocol Acetyl-L-Carnitine	Per Protocol Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	14		
Units: CD8 mit. DNA content absolute change				
arithmetic mean (standard deviation)	-37.1 (± 81.6)	-40.8 (± 160.5)		

Statistical analyses

Statistical analysis title	Efficacy statistical analysis
Comparison groups	Per protocol Acetyl-L-Carnitine v Per Protocol Placebo
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	Welch two sample t-test

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 46-50 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	ND
Dictionary version	ND

Reporting groups	
Reporting group title	ITT population

Reporting group description: -

Serious adverse events	ITT population		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 40 (7.50%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix carcinoma			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Acute hepatitis C			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	ITT population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 40 (75.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Thyroid cyst			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Sinusitis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Cardiac disorders			
Arteriosclerosis coronary artery			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Bundle branch block right			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Aortic dilatation			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Hyperamylasaemia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Proteinuria			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Hyperglycaemia			

subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Leukocyturia subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Iron deficiency anaemia subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	6 / 40 (15.00%) 6		
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Gastroenteritis subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Inguinal hernia subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Gastritis subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Dyspepsia subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
Constipation subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Hepatobiliary disorders			
Hepatic steatosis subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 3		
Renal and urinary disorders			

Renal colic			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Osteoporosis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Osteopenia			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	5		
Rotator cuff syndrome			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Infections and infestations			
Penile wart			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperinsulinaemia			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Diabetes mellitus			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Dyslipidaemia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Insulin resistance			

subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Hypovitaminosis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 June 2006	Changes in some administrative informations
14 July 2008	Change of the CRO

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported