



## 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
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#### 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:

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**Results analysis stage**

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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:

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**General information about the trial**

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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:

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**Population of trial subjects**

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**Subjects enrolled per country**

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Country: Number of subjects enrolled	Italy: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

Notes:

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**Subjects enrolled per age group**

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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
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## 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
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<b>Arm title</b>	Acetyl-L-Carnitine arm
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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.

<b>Arm title</b>	Placebo
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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.

<b>Number of subjects in period 1</b>	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
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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
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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 $48 \pm 2$ 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 ( $\pm$ 1.52)	1.25 ( $\pm$ 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

<b>Statistical analysis title</b>	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	



<b>End point values</b>	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

<b>Statistical analysis title</b>	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
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### Dictionary used

Dictionary name	ND
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Dictionary version	ND
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### Reporting groups

Reporting group title	ITT population
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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 %

<b>Non-serious adverse events</b>	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 occurrences (all)	1 / 40 (2.50%) 1		
Respiratory, thoracic and mediastinal disorders Sinusitis subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Investigations Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Cardiac disorders Arteriosclerosis coronary artery subjects affected / exposed occurrences (all)  Bundle branch block right subjects affected / exposed occurrences (all)  Aortic dilatation subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 3  2 / 40 (5.00%) 2  1 / 40 (2.50%) 1		
Blood and lymphatic system disorders Hyperamylasaemia subjects affected / exposed occurrences (all)  Proteinuria subjects affected / exposed occurrences (all)  Hyperglycaemia	2 / 40 (5.00%) 2  1 / 40 (2.50%) 1		

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

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

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:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported