# 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<br>Units: Subjects | | | |
| Adults (18-64 years) | 20 | 20 | 40 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 47 | 46 | |
| standard deviation | ± 6.4 | ± 5.7 | - |
| Gender categorical<br>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 | 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 | 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