



Clinical trial results:

Clinical study of the efficacy of liquid (drops) versus classic (tablets) formulations of levothyroxine in replacement therapy of adults with clinical hypothyroidism.

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2017-001760-38 |
| Trial protocol | GR |
| Global end of trial date | 31 October 2018 |

Results information

| | |
|-----------------------------------|---|
| Result version number | v1 (current) |
| This version publication date | 14 November 2021 |
| First version publication date | 14 November 2021 |
| Summary attachment (see zip file) | DOI: 10.1159/000508216 (Therapeutic Equivalence of a New Preparation.pdf) |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | T4drops-02 |
|-----------------------|------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Uni-Pharma Kleon Tsetis Pharmaceutical Laboratories SA |
| Sponsor organisation address | 14th Km National Road 1, Kifissia, Greece, 14564 |
| Public contact | Regulatory Affairs department, Uni-Pharma Kleon Tsetis Pharmaceutical Laboratories S.A., 30 2108072512374, soumelas@uni-pharma.gr |
| Scientific contact | Regulatory Affairs department, Uni-Pharma Kleon Tsetis Pharmaceutical Laboratories S.A., 2108072512 2108072512374, soumelas@uni-pharma.gr |

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 | 01 November 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 31 October 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 October 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Scope of the present study is to investigate whether there is equivalent efficacy between replacement therapy of a new LT4 formulation in liquid form (oral drops) versus the classic form (tablets) in adult patients with clinical permanent hypothyroidism.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator:

Use of the tablet Levothyroxine formulation of the same manufacturer (T4® tablets by Uni-Pharma).

| | |
|---|----------------|
| Actual start date of recruitment | 31 August 2017 |
| 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 | Greece: 50 |
| Worldwide total number of subjects | 50 |
| EEA total number of subjects | 50 |

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) | 50 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The first patient was admitted to the study on 19.09.2017 and the date of last visit of last patient was 31.10.2018.

Pre-assignment

Screening details:

1. Patients diagnosed with clinically permanent hypothyroidism
 2. 20-60 years
 3. Patients who are already receiving replacement therapy with levothyroxine tablets
- At the time of screening, many of the patients were taking levo tablets other than T4® so due to possible different bioequivalence between the products, patients were switched to T4®

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | First visit |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | No |
| Arm title | Tablets |

Arm description:

The levothyroxine preparation that the patient was receiving prior to entering the study was switched to T4® tablets (group A), , in the same dose

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | T4 tablets |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

At the same dosage the patients used to receive prior to entering the study

| | |
|------------------|---------------|
| Arm title | T4 Oral drops |
|------------------|---------------|

Arm description:

The levothyroxine preparation that the patient was receiving prior to entering the study was switched either to T4® drops (group B), in the same dose

| | |
|--|----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | T4 100µg/ml oral drops, solution |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral drops, solution |
| Routes of administration | Oral use |

Dosage and administration details:

At the same Levothyroxine dose the patient was receiving prior to entering the study

| Number of subjects in period 1 | Tablets | T4 Oral drops |
|--------------------------------|---------|---------------|
| Started | 25 | 25 |
| Completed | 22 | 22 |
| Not completed | 3 | 3 |
| Lost to follow-up | 3 | 3 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Second visit |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | No |
| Arm title | T4 Tablets |

Arm description:

At the second visit, if the TSH levels were within the target range, the patient was switched from the tablet to the liquid form with the same dose

| | |
|--|----------------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | T4 100µg/ml oral drops, solution |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral drops, solution |
| Routes of administration | Oral use |

Dosage and administration details:

At the second visit, if the TSH levels were within the target range, the patient was switched from the tablet to the liquid form with the same dose

| | |
|------------------|---------------|
| Arm title | T4 Oral drops |
|------------------|---------------|

Arm description:

At the second visit, if the TSH levels were within the target range, the patient was switched from the oral drops to the tablet form with the same dose

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | T4 tablets |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

At the second visit, if the TSH levels were within the target range, the patient was switched from the oral drops to the tablet form with the same dose

| Number of subjects in period 2 | T4 Tablets | T4 Oral drops |
|---------------------------------------|------------|---------------|
| Started | 22 | 22 |
| Completed | 21 | 18 |
| Not completed | 1 | 4 |
| Protocol deviation | 1 | 4 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | First visit |
|-----------------------|-------------|

Reporting group description: -

| Reporting group values | First visit | Total | |
|---|-------------|-------|--|
| Number of subjects | 50 | 50 | |
| 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) | 50 | 50 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 42.4 | | |
| standard deviation | ± 12.5 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 41 | 41 | |
| Male | 9 | 9 | |

End points

End points reporting groups

| | |
|---|---------------|
| Reporting group title | Tablets |
| Reporting group description: The levothyroxine preparation that the patient was receiving prior to entering the study was switched to T4® tablets (group A), , in the same dose | |
| Reporting group title | T4 Oral drops |
| Reporting group description: The levothyroxine preparation that the patient was receiving prior to entering the study was switched either to T4® drops (group B), in the same dose | |
| Reporting group title | T4 Tablets |
| Reporting group description: At the second visit, if the TSH levels were within the target range, the patient was switched from the tablet to the liquid form with the same dose | |
| Reporting group title | T4 Oral drops |
| Reporting group description: At the second visit, if the TSH levels were within the target range, the patient was switched from the oral drops to the tablet form with the same dose | |

Primary: TSH-Oral drops

| | |
|--|-------------------------------|
| End point title | TSH-Oral drops ^[1] |
| End point description: | |
| End point type | Primary |
| End point timeframe: After 10±2 weeks of treatment | |
| Notes: [1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This was a cross-over design | |

| End point values | Tablets | T4 Oral drops | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 18 | | |
| Units: mIU/L | | | | |
| arithmetic mean (standard deviation) | 1.901 (± 0.957) | 2.076 (± 1.334) | | |

Statistical analyses

| | |
|----------------------------|-------------------------|
| Statistical analysis title | Paired samples t test |
| Comparison groups | Tablets v T4 Oral drops |

| | |
|---|-----------------|
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.05 |
| Method | ANOVA |

Primary: TSH-T4 tablets

| | |
|-----------------|-------------------------------|
| End point title | TSH-T4 tablets ^[2] |
|-----------------|-------------------------------|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

After 10 ± 2 weeks of treatment

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This was a cross-over design

| End point values | T4 Oral drops | T4 Tablets | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 21 | | |
| Units: mIU/L | | | | |
| arithmetic mean (standard deviation) | 1.901 (± 0.957) | 1.759 (± 1.104) | | |

Statistical analyses

| | |
|---|----------------------------|
| Statistical analysis title | Paired samples t test |
| Comparison groups | T4 Oral drops v T4 Tablets |
| Number of subjects included in analysis | 43 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.05 |
| Method | ANOVA |

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Whole study

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|----|
| Dictionary version | 20 |
|--------------------|----|

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious AEs reported

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