Clinical trial results:
A multicentre, open-label switch study to investigate the necessity of dose adjustment after switching from L-Thyroxine Christiaens® to the new levothyroxine sodium test formulation in (near) total thyroidectomised patients.

Summary

EudraCT number	2012-005732-28
Trial protocol	BE
Global end of trial date	23 June 2014

Results information

Result version number	v1 (current)
This version publication date	04 March 2016
First version publication date	08 July 2015

Trial information

Trial identification

Sponsor protocol code	LE-9999-401-BE

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01916304
WHO universal trial number (UTN)	U1111-1145-3526

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	One Takeda Parkway, Deerfield, IL, United States, 60015
Public contact	Medical Director, Clinical Science, Takeda, +1 877-825-3327, trialdisclosures@takeda.com
Scientific contact	Medical Director, Clinical Science, Takeda, +1 877-825-3327, trialdisclosures@takeda.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	09 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 June 2014
Global end of trial reached?	Yes
Global end of trial date	23 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to investigate the effect of switching participants taking levothyroxine to a new formulation.

Protection of trial subjects:

All participants were required to read and sign an informed consent form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 July 2013
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	Belgium: 101
Worldwide total number of subjects	101
EEA total number of subjects	101

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)	78
From 65 to 84 years	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 8 investigative sites in Belgium from 02 July 2013 to 23 June 2014.

Pre-assignment

Screening details:

Participants with a diagnosis of Primary Hypothyroidism were switched from treatment with L-Thyroxine Christiaens® to treatment with new levothyroxine sodium 25-225 µg.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Levothyroxine sodium new formulation

Arm description:

Levothyroxine (25-225 µg), tablets, orally, once daily for up to 12 to 20 weeks. Dose administered depends on the thyroid stimulating hormone level.

Arm type	Experimental
Investigational medicinal product name	levothyroxine sodium new formulation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 to 225 µg once daily (dose dependent on TSH level) for 12 to 20 weeks.

Number of subjects in period 1	Levothyroxine sodium new formulation
Started	101
Safety Set	101
Intent-to-Treat Set	84
Completed	84
Not completed	17
Screening failure	17

Baseline characteristics

Reporting groups	
Reporting group title	Levothyroxine sodium new formulation
Reporting group description:	
Levothyroxine (25-225 µg), tablets, orally, once daily for up to 12 to 20 weeks. Dose administered depends on the thyroid stimulating hormone level.	

Reporting group values	Levothyroxine sodium new formulation	Total	
Number of subjects	101	101	
Age, Customized Units: participants			
<65 years	78	78	
≥ 65 years	23	23	
Age Continuous Units: years			
arithmetic mean	54.1		
standard deviation	± 12.17	-	
Gender, Male/Female Units: participants			
Female	72	72	
Male	29	29	
Region of Enrollment Units: Subjects			
Belgium	101	101	
Weight			
Weight data was available for 100 participants.			
Units: kg			
arithmetic mean	76.9		
standard deviation	± 18.05	-	
Height			
Height data was available for 96 participants.			
Units: cm			
arithmetic mean	168.4		
standard deviation	± 8.57	-	
Investigator Reported Body Mass Index (BMI)			
Investigator reported BMI data was available for 93 participants.			
Units: kg/m^2			
arithmetic mean	27.2		
standard deviation	± 5.98	-	
Calculated BMI			
Calculated BMI data was available for 96 participants.			
Units: kg/m^2			
arithmetic mean	27.1		
standard deviation	± 6	-	

End points

End points reporting groups

Reporting group title	Levothyroxine sodium new formulation

Reporting group description:

Levothyroxine (25-225 µg), tablets, orally, once daily for up to 12 to 20 weeks. Dose administered depends on the thyroid stimulating hormone level.

Primary: Percentage of Participants that Do Not Need a Change of Dose

End point title	Percentage of Participants that Do Not Need a Change of

End point description:

Dose change was determined by physician according to their clinical judgement.

End point type	Primary

End point timeframe:

2 months (± 2 weeks) after switch to sodium formulation.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis is not reported for this outcome measure.

End point values	Levothyroxine sodium new formulation			
Subject group type	Reporting group			
Number of subjects analysed	82			
Units: percentage of participants				
number (confidence interval 95%)	32.9 (23.7 to 43.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Magnitude of the Change in Daily Dose Needed

End point title	Magnitude of the Change in Daily Dose Needed

End point description:

Magnitude was determined via a change table which provides the percentage of participants that needed a change in Daily Dose (µg/day) of -25 µg, -12.5 µg, -6.25 µg, -5.35 µg, 0 µg or +12.5 µg.

End point type	Secondary

End point timeframe:

2 months (± 2 weeks) after switch to sodium formulation.

End point values	Levothyroxine sodium new formulation			
Subject group type	Reporting group			
Number of subjects analysed	82			
Units: percentage of participants				
number (not applicable)				
-25 µg change	19.51			
-12.5 µg change	42.68			
-6.25 µg change	1.22			
-5.35 µg change	1.22			
0 µg change	32.93			
+12.5 µg change	2.44			

Statistical analyses

No statistical analyses for this end point

Secondary: Relative Percent Change from Baseline in Serum Thyroid Stimulating Hormone

End point title	Relative Percent Change from Baseline in Serum Thyroid Stimulating Hormone

End point description:

Blood samples were collected and samples were analyzed according to the local Quality System. A negative change from Baseline indicated improvement.

End point type	Secondary

End point timeframe:

Baseline, Month 2 (± 2 weeks) and Month 4 (± 4 weeks) after inclusion into study.

End point values	Levothyroxine sodium new formulation			
Subject group type	Reporting group			
Number of subjects analysed	83			
Units: percent change				
median (inter-quartile range (Q1-Q3))				
Month 2	-74.5 (-89.5 to 50.6)			
Month 4 (n=82)	-54 (-75.1 to -15.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants that Obtained a Thyroid Stimulating Hormone (TSH) Between 0.4-2.5 mU/L

End point title	Percentage of Participants that Obtained a Thyroid Stimulating Hormone (TSH) Between 0.4-2.5 mU/L

End point description:

Blood samples were collected and samples were analyzed according to the local Quality System.

End point type	Secondary

End point timeframe:

Month 4 (± 4 weeks) after inclusion into study.

End point values	Levothyroxine sodium new formulation			
Subject group type	Reporting group			
Number of subjects analysed	82			
Units: percentage of participants				
number (not applicable)	57.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Serum Thyroid Stimulating Hormone Values

End point title	Absolute Serum Thyroid Stimulating Hormone Values

End point description:

Blood samples were collected and samples were analyzed according to the local Quality System.
Participants from the intent-to-treat population, all enrolled participants, with data available for analysis.

End point type	Secondary

End point timeframe:

Baseline, Month 2 (± 2 weeks) and Month 4 (± 4 weeks) after inclusion into study.

End point values	Levothyroxine sodium new formulation			
Subject group type	Reporting group			
Number of subjects analysed	84			
Units: mIU/mL				
arithmetic mean (standard deviation)				
Baseline	1.2 (± 0.59)			
Month 2 (n=83)	0.6 (± 1.69)			
Month 4 (n=82)	0.9 (± 1.09)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Study inclusion to recovery or final status is known of adverse drug reactions (ADRs) [up to 5 months]

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Levothyroxine sodium new formulation

Reporting group description:

Levothyroxine (25-225 µg), tablets, orally, once daily for up to 12 to 20 weeks. Dose administered depends on the thyroid stimulating hormone level.

Serious adverse events	Levothyroxine sodium new formulation		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 101 (6.93%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Catheterisation cardiac			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Post procedural haematoma			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Bladder catheterisation			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hysterectomy			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mastectomy			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Salivary gland resection			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin lesion			
subjects affected / exposed	1 / 101 (0.99%)		
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	Levothyroxine sodium new formulation		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 101 (6.93%)		
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	7 / 101 (6.93%) 9		

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