



Clinical trial results:

A monocentric, randomized, placebo-controlled double-blind clinical trial to assess the efficacy of Selenium in Morbus Basedow

Summary

EudraCT number	2010-022840-19
Trial protocol	DE
Global end of trial date	26 May 2015

Results information

Result version number	v1 (current)
This version publication date	26 January 2020
First version publication date	26 January 2020
Summary attachment (see zip file)	doi: 10.1210/jc.2017-01736 J Clin Endocrinol Metab, November 2017, 102(11):4333-4341 (2017_jc.2017-01736_SEBA.pdf)

Trial information

Trial identification

Sponsor protocol code	SEBA
-----------------------	------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University Medical Center Mainz
Sponsor organisation address	Langenbeckstreet 1, Mainz, Germany,
Public contact	Principal Investigator, University Medical Center Mainz, Dept. of Medicine I, 49 6131172290, kahaly@ukmainz.de
Scientific contact	Principal Investigator, Universitätsmedizin Mainz, Dept. of Medicine I, 49 6131172290, kahaly@ukmainz.de

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	13 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 May 2015
Global end of trial reached?	Yes
Global end of trial date	26 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- Response rate at week 24: comparison of the combination treatment of anti-thyroid drug and selenium vs. anti-thyroid monotherapy (compared to baseline).

Response rate is defined by euthyroidism:

normal fT3, fT4 and TSH and negative TSH-R-Ab.

- Relapse rate at week 36 (in both groups):

Relapse rate is defined by change of thyroid related hormones and -antibodies (TSH, fT3, fT4, TSH-R-Ab) compared to week 24.

Protection of trial subjects:

Patients were evaluated at baseline and 4, 12, 24 and 36 weeks after starting treatment.

Secondary outcomes were safety and tolerability of Se and MMI. Adverse events (AEs) were coded according to the standardized Medical Dictionary for Regulatory Activities (26) as recommended by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals

for Human Use (27). AEs were analyzed for alternative causes and judged for relatedness to intake of Se (side effects). AEs were followed up until a stable outcome could be documented or until the patient was lost to follow-up.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 January 2012
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	Germany: 70
Worldwide total number of subjects	70
EEA total number of subjects	70

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)	66
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Baseline assessments (general medical history, laboratory tests, physical examination, vital signs and thyroid investigations) could be performed up to 2 weeks before baseline (Screening period).

Results must be available and negative prior to administration of medication.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Blinding took place after the baseline period

Arms

Are arms mutually exclusive?	Yes
------------------------------	-----

Arm title	Baseline 1
------------------	------------

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet per day

Arm title	Selenium
------------------	----------

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Selenium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet per day

Number of subjects in period 1	Baseline 1	Selenium
Started	35	35
Completed	35	35

Period 2

Period 2 title	Treatment Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

A computer program generated a list and randomly allocated a patient number to one of the two treatment arms, starting with 001. Those numbers were also printed on the patient packs, packages, and blister cards, containing Se or placebo tablets, depending on the assigned number. Patients and site staff as well as monitors and clinical trial coordinators were blinded to identity of the Treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet per day

Arm title	Selenium
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Selenium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet per day

Number of subjects in period 2	Placebo	Selenium
Started	35	35
Completed	33	31
Not completed	2	4
subclinical hyperthyroidism	-	1
Consent withdrawn by subject	-	2
Pregnancy	1	-
Lost to follow-up	1	1

Baseline characteristics

End points

End points reporting groups

Reporting group title	Baseline 1
Reporting group description: -	
Reporting group title	Selenium
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Selenium
Reporting group description: -	

Primary: Response rate at week 24

End point title	Response rate at week 24
End point description:	
End point type	Primary
End point timeframe:	
baseline to week 24	

End point values	Placebo	Selenium		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	31		
Units: patients	27	25		

Statistical analyses

Statistical analysis title	Primary outcome
Statistical analysis description:	
Primary outcome response at week 24 was defined for each patient who appeared at the week 24 visit.	
Comparison groups	Placebo v Selenium
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	< 0.05 ^[2]
Method	Fisher exact
Parameter estimate	Odds ratio (OR)

Notes:

[1] - Comparison

[2] - All reported P values are two-sided. Significance level was set at 0.05.

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

From Baseline to visit 36 weeks

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

Dictionary used

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

Dictionary version	19.0
--------------------	------

Reporting groups

Reporting group title	Safety Analysis
-----------------------	-----------------

Reporting group description: -

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: Frequency threshold for reporting non-serious adverse Events was set at 5%. No AE occurred in more than 3 patients; a detailed safety analysis is given in the attached manuscript

Serious adverse events	Safety Analysis		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 70 (11.43%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Riding accident			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Eyelid operation			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breast operation			

subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhoid operation			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
anal sphincter repair			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
tachyarrhythmia absoluta			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
opticus neuropathy			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
hyperglycemia			
subjects affected / exposed	1 / 70 (1.43%)		
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	Safety Analysis		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 70 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 July 2013	Number of patients was increased from 50 to 70

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported