



Clinical trial results:

Effect of Intervention with DMR, GLP-1 and lifestyle intensification -in Subjects with insulin dePendent type 2 diabetes- on Insulin Requirement and mEtabolic parameters

Summary

EudraCT number	2017-000349-30
Trial protocol	NL
Global end of trial date	16 December 2020

Results information

Result version number	v1 (current)
This version publication date	18 April 2022
First version publication date	18 April 2022
Summary attachment (see zip file)	Published results INSPIRE (INSPIRE_manuscript_published_GIE.pdf)

Trial information

Trial identification

Sponsor protocol code	NL60669
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	ABR nummer: NL60669

Notes:

Sponsors

Sponsor organisation name	Amsterdam UMC
Sponsor organisation address	Meibergdreef 9 , Amsterdam , Netherlands, 1105 AZ
Public contact	Suzanne Meiring, Academic Medical Center, +31 21357593, s.meiring@amsterdamumc.nl
Scientific contact	Annieke van Baar, Academic Medical Center, +31 205661613, a.c.vanbaar@amc.nl

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	16 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2020
Global end of trial reached?	Yes
Global end of trial date	16 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this pilot study is to evaluate the efficacy of the Duodenal Mucosal Resurfacing procedure combined with GLP-1 administration and lifestyle intervention in subjects with insulindependent type 2 diabetes. Study success is defined as insulin independence at 6 months after DMR with an HbA1c level of $\leq 7.5\%$.

Protection of trial subjects:

Liraglutide is already approved for the treatment of type 2 diabetes. We used this medication in the same patient population and the same dosage as is registered.

Because side effects are minimal and mostly self-limiting, there were no additional measures taken for protection, because it was not necessary.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	12
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

3.1 Subject Recruitment

The investigational site (AMC) may utilize a number of methods to recruit potential subjects into the study including evaluation of existing subjects from their clinical practice, referrals from other physicians and recruitment via external advertising. Advertising materials need to be reviewed and approved by the Independent

Pre-assignment

Screening details:

1. Diagnosed with Type 2 Diabetes
2. 28 -75 years of age
3. Treatment with long acting insulin \leq 5 years
4. On daily long acting insulin dose \leq 1 U/kg
5. BMI \geq 24 and \leq 40 kg/m²
6. HbA1c \leq 8.0% (64 mmol/mol)
7. Fasting C-peptide \geq 0.5 nmol/L (1.5 ng/ml)

Period 1

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

Arms

Arm title	Overall trial
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Liraglutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1.8mg once daily

Number of subjects in period 1	Overall trial
Started	16
Completed	16

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	16	16	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
median	61		
inter-quartile range (Q1-Q3)	55 to 67	-	
Gender categorical			
Units: Subjects			
Female	6	6	
Male	10	10	
Duration of type 2 diabetes			
Units: years			
median	11		
inter-quartile range (Q1-Q3)	8 to 15	-	
BMI			
Units: kg/m2			
median	28.8		
inter-quartile range (Q1-Q3)	26.5 to 31.7	-	
HbA1c			
Units: percent			
median	7.5		
inter-quartile range (Q1-Q3)	7.1 to 7.9	-	
Fasting Plasma Glucose			
Units: mmol/l			
median	10.1		
inter-quartile range (Q1-Q3)	8.9 to 12	-	

Subject analysis sets

Subject analysis set title	Analysis complete trial population
Subject analysis set type	Full analysis

Subject analysis set description:

Complete patient population analysis. All patient were included in the analysis. All patients underwent DMR and started with liraglutide.

Reporting group values	Analysis complete trial population		
Number of subjects	16		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years median inter-quartile range (Q1-Q3)			
Gender categorical Units: Subjects			
Female	6		
Male	10		
Duration of type 2 diabetes Units: years median inter-quartile range (Q1-Q3)			
BMI Units: kg/m2 median inter-quartile range (Q1-Q3)			
HbA1c Units: percent median inter-quartile range (Q1-Q3)			
Fasting Plasma Glucose Units: mmol/l median inter-quartile range (Q1-Q3)			

End points

End points reporting groups

Reporting group title	Overall trial
Reporting group description: -	
Subject analysis set title	Analysis complete trial population
Subject analysis set type	Full analysis
Subject analysis set description:	
Complete patient population analysis. All patient were included in the analysis. All patients underwent DMR and started with liraglutide.	

Primary: % of patients HbA1c <7.6% at 6 months

End point title	% of patients HbA1c <7.6% at 6 months
End point description:	
End point type	Primary
End point timeframe:	
6 months after DMR	

End point values	Overall trial	Analysis complete trial population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	16	16		
Units: number of patients				
number (not applicable)	16	16		

Statistical analyses

Statistical analysis title	Analysis complete trial
Comparison groups	Overall trial v Analysis complete trial population
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

18 months

Assessment type	Systematic
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Dictionary used

Dictionary name	Toetsingonline
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Dictionary version	1
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Reporting groups

Reporting group title	Complete study population
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Reporting group description: -

Serious adverse events	Complete study population		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 16 (18.75%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Deep venous thrombosis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma exacerbation	Additional description: For which ER presentation/admission was necessary		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Ankle fracture			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia	Additional description: For which hospital admission was necessary		

subjects affected / exposed	1 / 16 (6.25%)		
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	Complete study population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 16 (93.75%)		
Vascular disorders			
Ulcer dig II left			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Orthostatic hypotension			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Iron deficiency anemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Dizziness			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Immune system disorders			
Hay fever			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 16 (31.25%)		
occurrences (all)	5		
Abdominal pain			
subjects affected / exposed	7 / 16 (43.75%)		
occurrences (all)	9		
Diarrhea			

subjects affected / exposed	7 / 16 (43.75%)		
occurrences (all)	8		
Superficial duodenal mucosal laesions	Additional description: prior to procedure and start medication		
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Obstipation			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Loss of appetite			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Dysphagia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Mild esofagitis	Additional description: Found during follow-up endoscopy		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Barrett segment	Additional description: Found during DMR procedure, follow-up planned		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Reflux			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Dark stool	Additional description: without alarm symptoms		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Asthma exacerbation			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Throat infection			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Renal and urinary disorders			

Benign cystic and prostate polyps subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 2		
Endocrine disorders Hyperglycemia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Musculoskeletal and connective tissue disorders			
Rotatorcuff rupture subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	Additional description: After cycling accident	
Dumbness en tingling limbs subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2		
Myalgia shoulders legs subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Muscle ache subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Infections and infestations			
Flu with flu-like symptoms subjects affected / exposed occurrences (all)	5 / 16 (31.25%) 6		
Testicular infection subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Conjunctivitis subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Fungal infection vagina subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Face infection subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		

Metabolism and nutrition disorders			
Low energy level			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 March 2018	Change in patient information sheet, regarding body material collection and storage.
14 December 2018	Addition of extra MRI assessment.
18 March 2019	Prolongation of the follow-up from 1 year to 2 years

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported