



Clinical trial results:

Adjustment of insulin Degludec to Reduce post-Exercise (nocturnal) hypoglycaemia in people with diabetes – the ADREM study

Summary

EudraCT number	2019-004222-22
Trial protocol	NL
Global end of trial date	02 September 2021

Results information

Result version number	v1 (current)
This version publication date	16 September 2022
First version publication date	16 September 2022

Trial information

Trial identification

Sponsor protocol code	U1111-1235-6899
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Radboud University Medical Center
Sponsor organisation address	Geert Grooteplein Zuid 10, Nijmegen, Netherlands, 6525 GA
Public contact	research physician, Radboud University Medical Center, +31 243618819, evertine.abbink@radboudumc.nl
Scientific contact	research physician, Radboud University Medical Center, +31 243618819, evertine.abbink@radboudumc.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	30 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 September 2021
Global end of trial reached?	Yes
Global end of trial date	02 September 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effect of three degludec dosing regimens on the risk of post-exercise nocturnal hypoglycaemia (time spent in glucose range ≤ 3.8 mmol/l, 00:00 to 05:59h) in type 1 diabetes mellitus patients at elevated risk of hypoglycaemia.

Protection of trial subjects:

Insulin degludec has a generally favourable safety profile. The drug is approved by the Dutch medicines evaluation board and is generally well tolerated. In total 15 blood samples will be taken. The total blood volume taken will be approximately 300 ml during a total period of 10 weeks. Needles used to draw blood may cause inconvenience or pain at the insertion site. During the screening and the long visits an intravenous cannula will be inserted to limit the number of venous punctures. The risk classification was assessed as low.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 September 2020
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	Netherlands: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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)	18
From 65 to 84 years	0

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

Participants were recruited from the outpatient clinic of the Radboud University Medical Center and Rijnstate hospital, via social media and websites of patient associations.

Pre-assignment

Screening details:

A total of 19 participants were screened, 18 of whom were included. One participant was withdrawn after screening because of personal reasons unrelated to the study. First inclusion: 22-9-2020. Last inclusion: 10-6-2021. After eligibility, patients not on degludec were transferred to it at least 28 days before first exercise day.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	ADREM-CON

Arm description:

No adjustment of insulin degludec

Arm type	No adjustment
Investigational medicinal product name	Insulin Degludec
Investigational medicinal product code	EU/1/12/807/001
Other name	Tresiba
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Individualized dosage, administer once daily. No dose reduction on the exercise day

Arm title	ADREM-D40
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Arm description:

40% dose reduction of insulin degludec

Arm type	40% dose reduction
Investigational medicinal product name	Insulin Degludec
Investigational medicinal product code	EU/1/12/807/001
Other name	Tresiba
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Individualized dosage, administer once daily. A 40% dose reduction on the exercise day

Arm title	ADREM-D20-PP
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Arm description:

8h postponement and 20% dose reduction of insulin degludec

Arm type	8h postponement and 20% dose reduction
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Investigational medicinal product name	Insulin Degludec
Investigational medicinal product code	EU/1/12/807/001
Other name	Tresiba
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Individualized dosage, administer once daily. An 8-hour postponement and 20% dose reduction on the exercise day.

Number of subjects in period 1	ADREM-CON	ADREM-D40	ADREM-D20-PP
Started	18	18	18
Completed	18	18	18

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	18	18	
Age categorical			
Inclusion criterium: adults aged 18-60 years			
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)	18	18	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	6	6	
Male	12	12	

End points

End points reporting groups

Reporting group title	ADREM-CON
Reporting group description: No adjustment of insulin degludec	
Reporting group title	ADREM-D40
Reporting group description: 40% dose reduction of insulin degludec	
Reporting group title	ADREM-D20-PP
Reporting group description: 8h postponement and 20% dose reduction of insulin degludec	

Primary: Amount of people spending time in hypoglycaemic range (i.e. glucose <3.9 mmol/l) during the night (00:00 to 05:59h) following the exercise day measured by continuous glucose monitoring

End point title	Amount of people spending time in hypoglycaemic range (i.e. glucose <3.9 mmol/l) during the night (00:00 to 05:59h) following the exercise day measured by continuous glucose monitoring
End point description:	
End point type	Primary
End point timeframe: The night (00:00 to 05:59h) following the exercise day	

End point values	ADREM-CON	ADREM-D40	ADREM-D20-PP	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	18	
Units: yes/no				
Yes	3	1	1	
No	15	17	17	

Statistical analyses

Statistical analysis title	Logistic random effects model
Statistical analysis description: We used random effects models to account for the three measurements for each participant with period and treatment as independent variables.	
Comparison groups	ADREM-CON v ADREM-D40 v ADREM-D20-PP

Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	< 0.05
Method	Logistic random effects model
Parameter estimate	Count

Notes:

[1] - Subjects in this analysis: 18

Adverse events

Adverse events information

Timeframe for reporting adverse events:

22-9-2020 / 2-9-2021

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25
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Reporting groups

Reporting group title	ADREM-CON
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Reporting group description:

No adjustment of insulin degludec

Reporting group title	ADREM-D40
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Reporting group description:

40% dose reduction of insulin degludec

Reporting group title	ADREM-D20-PP
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Reporting group description:

8h postponement and 20% dose reduction of insulin degludec

Serious adverse events	ADREM-CON	ADREM-D40	ADREM-D20-PP
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

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

Non-serious adverse events	ADREM-CON	ADREM-D40	ADREM-D20-PP
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 18 (5.56%)	1 / 18 (5.56%)	0 / 18 (0.00%)
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0

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