Clinical trial results:
Fast-Acting Insulin Aspart and Insulin Pump Settings:
“THE FAST PUMP SETTING STUDY”

Summary

EudraCT number	2020-001158-23
Trial protocol	DK
Global end of trial date	06 June 2023

Results information

Result version number	v1 (current)
This version publication date	22 November 2024
First version publication date	22 November 2024

Trial information

Trial identification

Sponsor protocol code	U1111-1243-4058

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04620967
WHO universal trial number (UTN)	U1111-1243-4058

Notes:

Sponsors

Sponsor organisation name	Steno Diabetes Center Copenhagen
Sponsor organisation address	Borgmester Ib Juuls Vej 83, Herlev, Denmark, 2730
Public contact	Kirsten Nørgaard, Steno Diabetes Center Copenhagen, +45 27131011, kirsten.noergaard@regionh.dk
Scientific contact	Kirsten Nørgaard, Steno Diabetes Center Copenhagen, +45 27131011, kirsten.noergaard@regionh.dk

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	06 September 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 June 2023
Global end of trial reached?	Yes
Global end of trial date	06 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the CGM-derived time in range (3.9-10.0 mmol/l) during the last two weeks of the 16-week interventions with Fiasp versus NovoRapid

Protection of trial subjects:

N/A

Background therapy:

All participants used their regular treatment modality (insulin pump therapy including contiunous glucose monitorering).

Evidence for comparator:

N/A

Actual start date of recruitment	01 November 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	Denmark: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	33
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from Steno Diabetes Center Copenhagen, Denmark, from February 2021 to June 2023

Pre-assignment

Screening details:

After providing oral and written informed consent, participants completed a screening visit for assessment of the eligibility criteria. Procedures included routine blood sampling, physical examination, review of medical history and edications as well as registration of baseline characteristics.

Period 1

Period 1 title	Study period (overall) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

The randomization codes were produced by Novo Nordisk who also provided the study medication in sealed and coded vials with a dispensing unit number. Unblinded staff, who were not involved in any other study activities, ensured the correct treatment allocation and dispensing of the study medication.

Arms

Are arms mutually exclusive?	No
Arm title	Faster aspart --> Insulin aspart

Arm description:

First went through 16-weeks of faster aspart (Fiasp® 100 U/mL; Novo Nordisk, Bagsværd, Denmark) then 16-weeks of insulin aspart (Iasp® 100 U/mL; Novo Nordisk, Bagsværd, Denmark)

Arm type	Experimental
Investigational medicinal product name	Faster-acting Insulin aspart
Investigational medicinal product code	A10AB05
Other name	Fiasp
Pharmaceutical forms	Solution for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Vial, 10 ml/vial, 100 U/ml, solution for subcutaneous injection.

Investigational medicinal product name	Insulin aspart
Investigational medicinal product code	A10AB05
Other name	Novorapid
Pharmaceutical forms	Solution for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Vial, 10 ml/vial, 100 U/ml, solution for subcutaneous injection.

Arm title	Insulin Aspart --> Faster aspart

Arm description:

First 16-weeks of insulin aspart (NovoRapid® 100 U/mL; Novo Nordisk, Bagsværd, Denmark then 16-weeks of insulin aspart (Iasp® 100 U/mL; Novo Nordisk, Bagsværd, Denmark)

Arm type	Active comparator

Investigational medicinal product name	Insulin aspart
Investigational medicinal product code	A10AB05
Other name	Novorapid
Pharmaceutical forms	Solution for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Vial, 10 ml/vial, 100 U/ml, solution for subcutaneous injection.

Investigational medicinal product name	Faster-acting Insulin aspart
Investigational medicinal product code	A10AB05
Other name	Fiasp
Pharmaceutical forms	Solution for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Vial, 10 ml/vial, 100 U/ml, solution for subcutaneous injection.

Number of subjects in period 1	Faster aspart --> Insulin aspart	Insulin Aspart --> Faster aspart
Started	20	20
Completed	20	19
Not completed	0	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Study period (overall)

Reporting group description: -

Reporting group values	Study period (overall)	Total	
Number of subjects	40	40	
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)	33	33	
From 65-84 years	7	7	
85 years and over	0	0	
Age continuous Units: years			
median	54		
inter-quartile range (Q1-Q3)	44 to 61	-	
Gender categorical Units: Subjects			
Female	20	20	
Male	20	20	
Previous faster insulin aspart users Units: Subjects			
Number of fiasp users	6	6	
Number of iasp users	34	34	
Insulin pump device Units: Subjects			
Medtronic MiniMed 640G	33	33	
Omnipod Dash	7	7	
CGM device type Units: Subjects			
Medtronic Guardian Sensor 3	32	32	
Medtronic Guardian Connect	0	0	
Dexcom G5	1	1	
Dexcom G6	7	7	
BMI			
Body mass index			
Units: kg/m2			
median	25.7		
inter-quartile range (Q1-Q3)	24.5 to 30.3	-	
HbA1c			

Hemoglobin A1c			
Units: mmol/mol			
median	59		
inter-quartile range (Q1-Q3)	55 to 65	-	
Diabetes duration			
Units: years			
median	27		
inter-quartile range (Q1-Q3)	20 to 34	-	
Insulin pump use			
Units: years			
median	11		
inter-quartile range (Q1-Q3)	7 to 13	-	
CGM use			
Units: years			
median	6		
inter-quartile range (Q1-Q3)	3 to 9	-	
Total daily insulin dosis			
Units: IU			
median	37		
inter-quartile range (Q1-Q3)	29 to 52	-	

End points

End points reporting groups

Reporting group title	Faster aspart --> Insulin aspart
Reporting group description:	
First went through 16-weeks of faster aspart (Fiasp® 100 U/mL; Novo Nordisk, Bagsværd, Denmark) then 16-weeks of insulin aspart (Iasp® 100 U/mL; Novo Nordisk, Bagsværd, Denmark)	
Reporting group title	Insulin Aspart --> Faster aspart
Reporting group description:	
First 16-weeks of insulin aspart (NovoRapid® 100 U/mL; Novo Nordisk, Bagsværd, Denmark then 16-weeks of insulin aspart (Iasp® 100 U/mL; Novo Nordisk, Bagsværd, Denmark)	

Primary: Time in range (3.9-10.0 mmol/l)

End point title	Time in range (3.9-10.0 mmol/l)
End point description:	
Assessed by CGM	
End point type	Primary
End point timeframe:	
During the last two weeks of the 16-week interventions with Fiasp vs. Iasp	

End point values	Faster aspart --> Insulin aspart	Insulin Aspart --> Faster aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: percent				
arithmetic mean (standard deviation)	65.8 (± 11.5)	63.9 (± 11.9)		

Statistical analyses

Statistical analysis title	Difference between interventions
Statistical analysis description:	
All analyses followed intention to treat principles, meaning all participants that were randomized after screening were included in the analyses. A linear mixed effect model with treatment and period as fixed effects and participant as random effect was used to compare the interventions.	
Comparison groups	Faster aspart --> Insulin aspart v Insulin Aspart --> Faster aspart
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.23
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-2.11

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.59
upper limit	1.35
Variability estimate	Standard deviation
Dispersion value	1.74

Secondary: Time below range (< 3.9 mmol/l)

End point title	Time below range (< 3.9 mmol/l)
End point description:	
CGM assessed	
End point type	Secondary
End point timeframe:	
The last two weeks of each treatment period	

End point values	Faster aspart --> Insulin aspart	Insulin Aspart --> Faster aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: percent				
arithmetic mean (standard deviation)	2.3 (± 1.5)	2.9 (± 2.1)		

Statistical analyses

Statistical analysis title	Difference between interventions
Statistical analysis description:	
All analyses followed intention to treat principles, meaning all participants that were randomized after screening were included in the analyses. A linear mixed effect model with treatment and period as fixed effects and participant as random effect was used to compare the interventions.	
Comparison groups	Faster aspart --> Insulin aspart v Insulin Aspart --> Faster aspart
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.82
upper limit	3

Variability estimate	Standard deviation
Dispersion value	1.6

Secondary: Time above range (>10.0 mmol/l)

End point title	Time above range (>10.0 mmol/l)
End point description:	
CGM assessed	
End point type	Secondary
End point timeframe:	
The last two weeks of each treatment period	

End point values	Faster aspart --> Insulin aspart	Insulin Aspart --> Faster aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: percent				
arithmetic mean (standard deviation)	31.9 (± 12.4)	33.2 (± 13.0)		

Statistical analyses

Statistical analysis title	Difference between interventions
Statistical analysis description:	
All analyses followed intention to treat principles, meaning all participants that were randomized after screening were included in the analyses. A linear mixed effect model with treatment and period as fixed effects and participant as random effect was used to compare the interventions.	
Comparison groups	Faster aspart --> Insulin aspart v Insulin Aspart --> Faster aspart
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.35
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.99
upper limit	5.38
Variability estimate	Standard deviation
Dispersion value	1.85

Secondary: Mean sensor glucose

End point title	Mean sensor glucose
End point description: CGM assessed.	
End point type	Secondary
End point timeframe: The last two week of each treatment period	

End point values	Faster aspart --> Insulin aspart	Insulin Aspart --> Faster aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: mmol/L				
arithmetic mean (standard deviation)	8.9 (± 1.0)	9.0 (± 1.1)		

Statistical analyses

Statistical analysis title	Difference between interventions
Statistical analysis description: All analyses followed intention to treat principles, meaning all participants that were randomized after screening were included in the analyses. A linear mixed effect model with treatment and period as fixed effects and participant as random effect was used to compare the interventions.	
Comparison groups	Faster aspart --> Insulin aspart v Insulin Aspart --> Faster aspart
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.35
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.45
Variability estimate	Standard deviation
Dispersion value	0.15

Secondary: Standard deviation

End point title	Standard deviation
End point description: cgm assessed	
End point type	Secondary

End point timeframe:

The last two of each treatment period

End point values	Faster aspart --> Insulin aspart	Insulin Aspart --> Faster aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: mmol/L				
arithmetic mean (standard deviation)	3.0 (± 0.4)	3.2 (± 0.6)		

Statistical analyses

Statistical analysis title	Difference between interventions

Statistical analysis description:

All analyses followed intention to treat principles, meaning all participants that were randomized after screening were included in the analyses. A linear mixed effect model with treatment and period as fixed effects and participant as random effect was used to compare the interventions.

Comparison groups	Faster aspart --> Insulin aspart v Insulin Aspart --> Faster aspart
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Mixed models analysis
Parameter estimate	Median difference (net)
Point estimate	0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.37
Variability estimate	Standard deviation
Dispersion value	0.08

Secondary: Coefficient of variation

End point title	Coefficient of variation

End point description:

CGM assessed

End point type	Secondary

End point timeframe:

The last two weeks of each treatment period

End point values	Faster aspart --> Insulin aspart	Insulin Aspart --> Faster aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: percent				
arithmetic mean (standard deviation)	34.0 (± 3.7)	35.9 (± 4.9)		

Statistical analyses

Statistical analysis title	Difference between interventions
Comparison groups	Faster aspart --> Insulin aspart v Insulin Aspart --> Faster aspart
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	3.25
Variability estimate	Standard deviation
Dispersion value	0.73

Secondary: Glucose management index (GMI)

End point title	Glucose management index (GMI)
End point description:	
CGM assessed	
End point type	Secondary
End point timeframe:	
The last two weeks of each treatment period	

End point values	Faster aspart --> Insulin aspart	Insulin Aspart --> Faster aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: mmol/mol				
arithmetic mean (standard deviation)	54.4 (± 4.5)	55.0 (± 5.3)		

Statistical analyses

Statistical analysis title	Difference between interventions
Statistical analysis description:	
All analyses followed intention to treat principles, meaning all participants that were randomized after screening were included in the analyses. A linear mixed effect model with treatment and period as fixed effects and participant as random effect was used to compare the interventions.	
Comparison groups	Faster aspart --> Insulin aspart v Insulin Aspart --> Faster aspart
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.35
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	2.11
Variability estimate	Standard deviation
Dispersion value	0.7

Secondary: Glucose risk index

End point title	Glucose risk index
End point description:	
CGM assessed	
End point type	Secondary
End point timeframe:	
The last two weeks of each treatment period	

End point values	Faster aspart --> Insulin aspart	Insulin Aspart --> Faster aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: unit(s)				
arithmetic mean (standard deviation)	37.0 (± 11.5)	41.1 (± 11.9)		

Statistical analyses

Statistical analysis title	Difference between interventions
Statistical analysis description:	
All analyses followed intention to treat principles, meaning all participants that were randomized after screening were included in the analyses. A linear mixed effect model with treatment and period as fixed effects and participant as random effect was used to compare the interventions.	
Comparison groups	Faster aspart --> Insulin aspart v Insulin Aspart --> Faster aspart
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.06
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	4.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	8.18
Variability estimate	Standard deviation
Dispersion value	2.05

Secondary: Obtained recommendation of TIR > 70%

End point title	Obtained recommendation of TIR > 70%
End point description:	
cgm assessed	
End point type	Secondary
End point timeframe:	
The last two weeks of each treatment period	

End point values	Faster aspart --> Insulin aspart	Insulin Aspart --> Faster aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Number of participants	15	13		

Statistical analyses

Statistical analysis title	BNumber of participants achivieng goal
Statistical analysis description:	
Binary outcomes were analyzed by a McNemar test or general linear regression model with mixed effects.	
Comparison groups	Faster aspart --> Insulin aspart v Insulin Aspart --> Faster aspart
Number of subjects included in analysis	40
Analysis specification	Post-hoc
Analysis type	superiority
P-value	> 0.9999
Method	Mcnemar
Parameter estimate	Log odds ratio
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.474
upper limit	1.48

Secondary: Obtained recommendation TAR < 25%

End point title	Obtained recommendation TAR < 25%
End point description:	
CGM assessed	
End point type	Secondary
End point timeframe:	
The last two week of each treatment period	

End point values	Faster aspart --> Insulin aspart	Insulin Aspart --> Faster aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Number of participants	22	22		

Statistical analyses

Statistical analysis title	Number of participants achivieng goal
Statistical analysis description:	
Binary outcomes were analyzed by a McNemar test or general linear regression model with mixed effects	
Comparison groups	Faster aspart --> Insulin aspart v Insulin Aspart --> Faster aspart

Number of subjects included in analysis	40
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.37
Method	Mcnemar
Parameter estimate	Log odds ratio
Point estimate	0.099
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1

Secondary: Obtained recommendation of TBR < 4%

End point title	Obtained recommendation of TBR < 4%

End point description:

End point type	Secondary

End point timeframe:

The last two weeks of treatment period

End point values	Faster aspart --> Insulin aspart	Insulin Aspart --> Faster aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Number of participants	36	34		

Statistical analyses

Statistical analysis title	Number of participants achivieng goal

Statistical analysis description:

Binary outcomes were analyzed by a McNemar test or general linear regression model with mixed effects

Comparison groups	Faster aspart --> Insulin aspart v Insulin Aspart --> Faster aspart
Number of subjects included in analysis	40
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.48
Method	Mcnemar
Parameter estimate	Log odds ratio
Point estimate	0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	1.78

Secondary: HbA1c

End point title	HbA1c
End point description:	
End point type	Secondary
End point timeframe:	
Taken at start and end of each intervention period	

End point values	Faster aspart --> Insulin aspart	Insulin Aspart --> Faster aspart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: mmol/mol				
geometric mean (standard deviation)	57.5 (± 6.9)	58.0 (± 6.6)		

Statistical analyses

Statistical analysis title	Difference between interventions
Comparison groups	Faster aspart --> Insulin aspart v Insulin Aspart --> Faster aspart
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7421
upper limit	1.78
Variability estimate	Standard deviation
Dispersion value	0.6

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From screening to end of study, involving a total of 16 week for the first period, 16 week for the second period and more than three week for the washout.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	1

Reporting groups

Reporting group title	Faster aspart

Reporting group description:

16-weeks of faster aspart (Fiasp® 100 U/mL; Novo Nordisk, Bagsværd, Denmark)

Reporting group title	Insulin Aspart

Reporting group description:

16-weeks of insulin aspart (NovoRapid® 100 U/mL; Novo Nordisk, Bagsværd, Denmark

Serious adverse events	Faster aspart	Insulin Aspart	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 40 (2.50%)	3 / 40 (7.50%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Endocrine disorders			
SAE overall			
subjects affected / exposed	1 / 40 (2.50%)	3 / 40 (7.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Faster aspart	Insulin Aspart	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 40 (75.00%)	25 / 40 (62.50%)	
Endocrine disorders			
Adverse event			
subjects affected / exposed	30 / 40 (75.00%)	25 / 40 (62.50%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 March 2023	A change in the supply of investigational medication occurred during the study. Novo Nordisk was no longer able to supply investigational medication (FiASP) for the study participants. Their clinical packaging services no longer supported FiASP, meaning they could not provide medication with an expiry date beyond March 22, 2023. Amendment to Protocol: To address this issue, the decision was made internally to purchase FiASP as commercial stock and perform the blinding procedures in-house. The sponsor and investigator thoroughly assessed this change and concluded that there was no additional risk to participants associated with the adjustment. The integrity of the blinding process was maintained under this new arrangement. Impact on Study: This amendment did not affect the primary or secondary endpoints, study design, or safety profile. The study timeline remained unchanged, with the study expected to be completed by May 30, 2023. Conclusion: This protocol amendment was implemented to ensure continuity in the supply of investigational medication while maintaining the integrity of the study. There was no impact on participant safety or study outcomes as a result of this change.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported