



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 continuous glucose monitoring).

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 medications 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 (\pm 0.4) | 3.2 (\pm 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 | BNNumber 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 | Mcneamar |
| 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 achieving 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 | <p>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.</p> <p>Amendment to Protocol:</p> <p>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.</p> <p>Impact on Study:</p> <p>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.</p> <p>Conclusion:</p> <p>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.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported