



Clinical trial results:

A Phase IIb, 2-Arm, Randomized, Double-blind, Placebo-Controlled, Multicentre Study to Optimize Diamyd® Therapy Administered into Lymph Nodes Combined with Oral Vitamin D to Investigate the Impact on the Progression of Type 1 diabetes

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2017-001861-25 |
| Trial protocol | SE CZ ES NL |
| Global end of trial date | 27 April 2021 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 13 October 2021 |
| First version publication date | 13 October 2021 |

Trial information

Trial identification

| | |
|-----------------------|------------------------|
| Sponsor protocol code | DIAGNODE-2 (D/P2/17/6) |
|-----------------------|------------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03345004 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Diamyd Medical AB |
| Sponsor organisation address | Kungsgatan 29, Stockholm, Sweden, SE-111 56 |
| Public contact | Clinical Study Director, Diamyd Medical AB, clinicaltrials@diamyd.com |
| Scientific contact | Clinical Study Director, Diamyd Medical AB, clinicaltrials@diamyd.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000609-PIP01-09 |
| 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 | 27 April 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 27 April 2021 |
| Global end of trial reached? | Yes |
| Global end of trial date | 27 April 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the efficacy of Diamyd, administered into lymph nodes in combination with an oral vitamin D regimen, compared to placebo in terms of preserving endogenous insulin secretion as measured by C-peptide.

Protection of trial subjects:

The final study protocol, including any substantial amendments and the final version of the subject information and consent form, were reviewed and approved by an Independent Ethics Committee and Competent Authorities prior to inclusion of subjects. The study was conducted in compliance with the protocol, regulatory requirements, good clinical practice (GCP) and the ethical principles of the latest revision of the Declaration of Helsinki as adopted by the World Medical Association. The investigator was responsible for giving the patients and his/her parents/caregivers full and adequate verbal and written information about the nature, purpose, possible risk and benefit of the study. Patients and, if applicable, his/her parents/caregivers were also notified that they were free to withdraw from the study at any time. The patients and parents/caregivers had reasonable time to read and understand the information before signing. The investigator was responsible for obtaining signed informed consent from all patients before including the patient in any study related procedures.

Background therapy:

Standard of care

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 17 December 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Netherlands: 2 |
| Country: Number of subjects enrolled | Spain: 43 |
| Country: Number of subjects enrolled | Sweden: 31 |
| Country: Number of subjects enrolled | Czech Republic: 33 |
| Worldwide total number of subjects | 109 |
| EEA total number of subjects | 109 |

Notes:

Subjects enrolled per age group

| | |
|--|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 | 0 |

| | |
|--|----|
| wk | |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 75 |
| Adults (18-64 years) | 34 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Patients were recruited at 18 sites in total, in Spain, Sweden, Czech Republic and the Netherlands. Patients were recruited from 07 December 2017 and the last patient's last visit was on 24 April 2021.

Pre-assignment

Screening details:

Inclusion: Patients aged 12-24 with type-1 diabetes diagnosed for at least 6 months with fasting C-peptide over 0.12 nmol/L and positive for GAD65A (<50,000 IU/mL) with adequate contraception. Exclusion: patients using immunosuppressants, anti-inflammatory drugs, anti-diabetics (other than insulin), vitamin D, with history of anaemia or epilepsy.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Main Study |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor |

Arms

| | |
|------------------------------|--------------------------------------|
| Are arms mutually exclusive? | No |
| Arm title | Diamyd + vitamin D (FAS, Main Study) |

Arm description: -

| | |
|--|----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Diamyd® intralymphatic injection |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intralymphatic use |

Dosage and administration details:

4 ug administered in the inguinal lymph node on Day 30, 60 and 90.

| | |
|--|--|
| Investigational medicinal product name | Vitamin D |
| Investigational medicinal product code | |
| Other name | D-vitaminolja ACO orala droppar, lösning, 80 IE/droppe |
| Pharmaceutical forms | Oral drops, solution |
| Routes of administration | Oral use |

Dosage and administration details:

2000 IU/day (25 drops á 80 IE/drop) from Day 1 to Day 120.

| | |
|------------------|---------------------------|
| Arm title | Placebo (FAS, Main Study) |
|------------------|---------------------------|

Arm description: -

| | |
|--|----------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo intralymphatic injection |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intralymphatic use |

Dosage and administration details:

Administered in the inguinal lymph node on Day 30, 60 and 90.

| | |
|--|--------------------|
| Investigational medicinal product name | Placebo oral drops |
| Investigational medicinal product code | |
| Other name | |

| | |
|--------------------------|----------------------|
| Pharmaceutical forms | Oral drops, solution |
| Routes of administration | Oral use |

Dosage and administration details:

Administered daily from Day 1 to Day 120.

| | |
|------------------|--|
| Arm title | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) |
|------------------|--|

Arm description: -

| | |
|--|----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Diamyd® intralymphatic injection |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intralymphatic use |

Dosage and administration details:

4 ug administered in the inguinal lymph node on Day 30, 60 and 90.

| | |
|--|--|
| Investigational medicinal product name | Vitamin D |
| Investigational medicinal product code | |
| Other name | D-vitaminolja ACO orala droppar, lösning, 80 IE/droppe |
| Pharmaceutical forms | Oral drops, solution |
| Routes of administration | Oral use |

Dosage and administration details:

2000 IU/day (25 drops á 80 IE/drop) from Day 1 to Day 120.

| | |
|------------------|-----------------------------------|
| Arm title | Placebo (HLA DR3-DQ2, Main Study) |
|------------------|-----------------------------------|

Arm description: -

| | |
|--|----------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo intralymphatic injection |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intralymphatic use |

Dosage and administration details:

Administered in the inguinal lymph node on Day 30, 60 and 90.

| | |
|--|----------------------|
| Investigational medicinal product name | Placebo oral drops |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral drops, solution |
| Routes of administration | Oral use |

Dosage and administration details:

Administered daily from Day 1 to Day 120.

| Number of subjects in period 1 | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) |
|--------------------------------|--------------------------------------|---------------------------|--|
| | | | |
| Started | 57 | 52 | 29 |
| Completed | 56 | 51 | 28 |
| Not completed | 1 | 1 | 1 |
| Physician decision | 1 | - | 1 |

| | | | |
|------------------------------|---|---|---|
| Consent withdrawn by subject | - | 1 | - |
|------------------------------|---|---|---|

| Number of subjects in period 1 | Placebo (HLA DR3-DQ2, Main Study) |
|--------------------------------|-----------------------------------|
| Started | 19 |
| Completed | 18 |
| Not completed | 1 |
| Physician decision | - |
| Consent withdrawn by subject | 1 |

Period 2

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

Arms

| | |
|------------------------------|--------------------------------|
| Are arms mutually exclusive? | No |
| Arm title | Diamyd + vitamin D (Extension) |

Arm description: -

| | |
|--|----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Diamyd® intralymphatic injection |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intralymphatic use |

Dosage and administration details:

4 ug administered in the inguinal lymph node on Day 30, 60 and 90.

| | |
|--|--|
| Investigational medicinal product name | Vitamin D |
| Investigational medicinal product code | |
| Other name | D-vitaminolja ACO orala droppar, lösning, 80 IE/droppe |
| Pharmaceutical forms | Oral drops, solution |
| Routes of administration | Oral use |

Dosage and administration details:

2000 IU/day (25 drops á 80 IE/drop) from Day 1 to Day 120.

| | |
|------------------|---------------------|
| Arm title | Placebo (Extension) |
|------------------|---------------------|

Arm description: -

| | |
|--|----------------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo intralymphatic injection |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intralymphatic use |

Dosage and administration details:

Administered in the inguinal lymph node on Day 30, 60 and 90.

| | |
|--|--|
| Investigational medicinal product name | Placebo oral drops |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral drops, solution |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Administered daily from Day 1 to Day 120. | |
| Arm title | Diamyd + vitamin D (HLA DR3-DQ2, Extension) |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Diamyd® intralymphatic injection |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intralymphatic use |
| Dosage and administration details: | |
| 4 ug administered in the inguinal lymph node on Day 30, 60 and 90. | |
| Investigational medicinal product name | Vitamin D |
| Investigational medicinal product code | |
| Other name | D-vitaminolja ACO orala droppar, lösning, 80 IE/droppe |
| Pharmaceutical forms | Oral drops, solution |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 2000 IU/day (25 drops á 80 IE/drop) from Day 1 to Day 120. | |
| Arm title | Placebo (HLA DR3-DQ2, Extension) |
| Arm description: - | |
| Arm type | Placebo |
| Investigational medicinal product name | Placebo intralymphatic injection |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intralymphatic use |
| Dosage and administration details: | |
| Administered in the inguinal lymph node on Day 30, 60 and 90. | |
| Investigational medicinal product name | Placebo oral drops |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral drops, solution |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Administered daily from Day 1 to Day 120. | |

| Number of subjects in period 2 | Diamyd + vitamin D (Extension) | Placebo (Extension) | Diamyd + vitamin D (HLA DR3-DQ2, Extension) |
|--------------------------------|-----------------------------------|---------------------|---|
| | | | |
| Started | 30 | 23 | 15 |
| Completed | 28 | 22 | 15 |
| Not completed | 2 | 1 | 0 |
| Lost to follow-up | 2 | 1 | - |

| Number of subjects in period 2 | Placebo (HLA DR3- DQ2, Extension) |
|--------------------------------|--------------------------------------|
| Started | 8 |
| Completed | 8 |
| Not completed | 0 |
| Lost to follow-up | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Main Study |
|-----------------------|------------|

Reporting group description: -

| Reporting group values | Main Study | Total | |
|--|------------|-------|--|
| Number of subjects | 109 | 109 | |
| 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) | 75 | 75 | |
| Adults (18-64 years) | 34 | 34 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 16.4 | | |
| standard deviation | ± 4.1 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 47 | 47 | |
| Male | 62 | 62 | |

End points

End points reporting groups

| | |
|--------------------------------|--|
| Reporting group title | Diamyd + vitamin D (FAS, Main Study) |
| Reporting group description: - | |
| Reporting group title | Placebo (FAS, Main Study) |
| Reporting group description: - | |
| Reporting group title | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) |
| Reporting group description: - | |
| Reporting group title | Placebo (HLA DR3-DQ2, Main Study) |
| Reporting group description: - | |
| Reporting group title | Diamyd + vitamin D (Extension) |
| Reporting group description: - | |
| Reporting group title | Placebo (Extension) |
| Reporting group description: - | |
| Reporting group title | Diamyd + vitamin D (HLA DR3-DQ2, Extension) |
| Reporting group description: - | |
| Reporting group title | Placebo (HLA DR3-DQ2, Extension) |
| Reporting group description: - | |

Primary: Change in C-peptide area under the curve (AUC)

| | |
|---|--|
| End point title | Change in C-peptide area under the curve (AUC) |
| End point description: | |
| Data is unitless as it is back-transformed from log scale. | |
| End point type | Primary |
| End point timeframe: | |
| Change between baseline and 15 months (Main Study reporting groups) or between baseline and 24 months (Extension Study reporting groups). | |

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) | Placebo (HLA DR3-DQ2, Main Study) |
|--------------------------------------|--------------------------------------|---------------------------|--|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 55 | 48 | 29 | 17 |
| Units: unitless | | | | |
| arithmetic mean (standard deviation) | 0.551 (\pm 1.715) | 0.506 (\pm 2.163) | 0.663 (\pm 1.511) | 0.425 (\pm 2.436) |

| End point values | Diamyd + vitamin D (Extension) | Placebo (Extension) | Diamyd + vitamin D (HLA DR3-DQ2, Extension) | Placebo (HLA DR3-DQ2, Extension) |
|-----------------------------|--------------------------------|---------------------|---|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 28 | 22 | 15 | 8 |

| | | | | |
|--------------------------------------|----------------------|----------------------|----------------------|----------------------|
| Units: unitless | | | | |
| arithmetic mean (standard deviation) | 0.376 (\pm 1.738) | 0.453 (\pm 1.914) | 0.449 (\pm 1.642) | 0.381 (\pm 1.706) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | MMRM of change in C-peptide AUC |
| Comparison groups | Diamyd + vitamin D (FAS, Main Study) v Placebo (FAS, Main Study) |
| Number of subjects included in analysis | 103 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5009 |
| Method | Mixed models analysis |
| Parameter estimate | Estimated ratio |
| Point estimate | 1.091 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.845 |
| upper limit | 1.408 |

| | |
|---|--|
| Statistical analysis title | MMRM of change in C-peptide AUC: HLA DR3-DQ2 |
| Comparison groups | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) v Placebo (HLA DR3-DQ2, Main Study) |
| Number of subjects included in analysis | 46 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0078 |
| Method | Mixed models analysis |
| Parameter estimate | Estimated ratio |
| Point estimate | 1.557 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.126 |
| upper limit | 2.153 |

| | |
|-----------------------------------|--|
| Statistical analysis title | MMRM of change in C-peptide AUC: Extension |
| Comparison groups | Diamyd + vitamin D (Extension) v Placebo (Extension) |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 50 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2215 |
| Method | Mixed models analysis |
| Parameter estimate | Estimated ratio |
| Point estimate | 0.807 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.569 |
| upper limit | 1.143 |

| | |
|---|--|
| Statistical analysis title | MMRM of change in C-peptide AUC: Extension DR3-DQ2 |
| Comparison groups | Diamyd + vitamin D (HLA DR3-DQ2, Extension) v Placebo (HLA DR3-DQ2, Extension) |
| Number of subjects included in analysis | 23 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4038 |
| Method | Mixed models analysis |
| Parameter estimate | Estimated ratio |
| Point estimate | 1.197 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.781 |
| upper limit | 1.834 |

Secondary: Change in Insulin-dose-adjusted HbA1c (IDAA1c)

| | |
|---|--|
| End point title | Change in Insulin-dose-adjusted HbA1c (IDAA1c) |
| End point description: | |
| | |
| End point type | Secondary |
| End point timeframe: | |
| Change between baseline and 15 months (Main Study reporting groups) or between baseline and 24 months (Extension Study reporting groups). | |

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) | Placebo (HLA DR3-DQ2, Main Study) |
|--------------------------------------|--------------------------------------|---------------------------|--|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 51 | 44 | 28 | 15 |
| Units: unitless | | | | |
| arithmetic mean (standard deviation) | 0.757 (\pm 1.851) | 0.377 (\pm 2.183) | 0.663 (\pm 1.627) | 0.667 (\pm 2.788) |

| End point values | Diamyd + vitamin D (Extension) | Placebo (Extension) | Diamyd + vitamin D (HLA DR3-DQ2, Extension) | Placebo (HLA DR3-DQ2, Extension) |
|--------------------------------------|--------------------------------|----------------------|---|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 22 | 13 | 8 |
| Units: unitless | | | | |
| arithmetic mean (standard deviation) | 1.327 (\pm 2.187) | 1.195 (\pm 1.881) | 1.402 (\pm 1.619) | 0.803 (\pm 2.481) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in HbA1c

| | |
|-----------------|-----------------|
| End point title | Change in HbA1c |
|-----------------|-----------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Change between baseline and 15 months (Main Study reporting groups) or between baseline and 24 months (Extension Study reporting groups).

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) | Placebo (HLA DR3-DQ2, Main Study) |
|--------------------------------------|--------------------------------------|---------------------------|--|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 56 | 51 | 29 | 18 |
| Units: mmol/mol haemoglobin | | | | |
| arithmetic mean (standard deviation) | 1.04 (\pm 15.87) | 0.53 (\pm 14.57) | 0.87 (\pm 14.34) | -0.98 (\pm 18.75) |

| End point values | Diamyd + vitamin D (Extension) | Placebo (Extension) | Diamyd + vitamin D (HLA DR3-DQ2, Extension) | Placebo (HLA DR3-DQ2, Extension) |
|------------------|--------------------------------|---------------------|---|----------------------------------|
|------------------|--------------------------------|---------------------|---|----------------------------------|

| | | | Extension) | |
|--------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 28 | 22 | 15 | 8 |
| Units: mmol/mol haemoglobin | | | | |
| arithmetic mean (standard deviation) | 3.94 (± 13.51) | 4.29 (± 14.40) | 6.00 (± 11.60) | 1.36 (± 21.07) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in daily exogenous insulin consumption

| | |
|---|---|
| End point title | Change in daily exogenous insulin consumption |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Change between baseline and 15 months (Main Study reporting groups) or between baseline and 24 months (Extension Study reporting groups). | |

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) | Placebo (HLA DR3-DQ2, Main Study) |
|--------------------------------------|--------------------------------------|---------------------------|--|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 51 | 44 | 28 | 15 |
| Units: IU/kg/24h | | | | |
| arithmetic mean (standard deviation) | 0.183 (± 0.285) | 0.094 (± 0.342) | 0.143 (± 0.196) | 0.153 (± 0.399) |

| End point values | Diamyd + vitamin D (Extension) | Placebo (Extension) | Diamyd + vitamin D (HLA DR3-DQ2, Extension) | Placebo (HLA DR3-DQ2, Extension) |
|--------------------------------------|--------------------------------|---------------------|---|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 22 | 13 | 8 |
| Units: IU/kg/24h | | | | |
| arithmetic mean (standard deviation) | 0.256 (± 0.342) | 0.201 (± 0.275) | 0.233 (± 0.317) | 0.173 (± 0.247) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in glycaemic variability

| | |
|-----------------|---------------------------------|
| End point title | Change in glycaemic variability |
|-----------------|---------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Change between baseline and 15 months (Main Study reporting groups) or between baseline and 24 months (Extension Study reporting groups).

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) | Placebo (HLA DR3-DQ2, Main Study) |
|--------------------------------------|--------------------------------------|---------------------------|--|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 49 | 39 | 25 | 12 |
| Units: per day | | | | |
| arithmetic mean (standard deviation) | | | | |
| 70-180 mg/dL (hours) | -2.479 (± 4.638) | -2.451 (± 4.012) | -1.724 (± 3.346) | -3.920 (± 4.090) |
| 50-70 mg/dL (hours) | -0.035 (± 2.416) | 0.197 (± 1.961) | 0.034 (± 2.992) | 0.581 (± 1.057) |
| <50 mg/dL (minutes) | 15.7 (± 46.4) | 9.0 (± 88.4) | 16.7 (± 59.3) | 48.1 (± 107.0) |

| End point values | Diamyd + vitamin D (Extension) | Placebo (Extension) | Diamyd + vitamin D (HLA DR3-DQ2, Extension) | Placebo (HLA DR3-DQ2, Extension) |
|--------------------------------------|--------------------------------|---------------------|---|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 16 | 13 | 6 |
| Units: per day | | | | |
| arithmetic mean (standard deviation) | | | | |
| 70-180 mg/dL (hours) | -3.104 (± 2.859) | -2.598 (± 4.295) | -2.643 (± 3.305) | -4.270 (± 4.420) |
| 50-70 mg/dL (hours) | -0.041 (± 2.142) | -0.185 (± 2.150) | -0.325 (± 2.529) | 0.159 (± 1.697) |
| <50 mg/dL (minutes) | 13.6 (± 47.2) | 18.6 (± 97.0) | 11.2 (± 56.0) | 46.7 (± 72.7) |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with IDAA1c ≤ 9

| | |
|-----------------|--|
| End point title | Proportion of patients with IDAA1c ≤ 9 |
|-----------------|--|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Proportion of patients at Month 15 (Main Study reporting groups) and at Month 24 (Extension Study reporting groups).

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) | Placebo (HLA DR3-DQ2, Main Study) |
|----------------------------------|--------------------------------------|---------------------------|--|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 51 | 44 | 28 | 15 |
| Units: percent | | | | |
| number (confidence interval 95%) | 62.7 (48.1 to 75.9) | 61.4 (45.5 to 75.6) | 78.6 (59.0 to 91.7) | 40.0 (16.3 to 67.7) |

| End point values | Diamyd + vitamin D (Extension) | Placebo (Extension) | Diamyd + vitamin D (HLA DR3-DQ2, Extension) | Placebo (HLA DR3-DQ2, Extension) |
|----------------------------------|--------------------------------|---------------------|---|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 22 | 13 | 8 |
| Units: percent | | | | |
| number (confidence interval 95%) | 60.9 (38.5 to 80.3) | 54.5 (32.2 to 75.6) | 69.2 (38.6 to 90.9) | 62.5 (24.5 to 91.5) |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with stimulated maximum C-peptide above 0.2 nmol/L

| | |
|-----------------|---|
| End point title | Proportion of patients with stimulated maximum C-peptide above 0.2 nmol/L |
|-----------------|---|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Proportion of patients at Month 15 (Main Study reporting groups) and at Month 24 (Extension Study reporting groups).

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) | Placebo (HLA DR3-DQ2, Main Study) |
|----------------------------------|--------------------------------------|---------------------------|--|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 55 | 49 | 29 | 17 |
| Units: percent | | | | |
| number (confidence interval 95%) | 92.7 (82.4 to 98.0) | 75.5 (61.1 to 86.7) | 96.6 (82.2 to 99.9) | 70.6 (44.0 to 89.7) |

| End point values | Diamyd + vitamin D (Extension) | Placebo (Extension) | Diamyd + vitamin D (HLA DR3-DQ2, Extension) | Placebo (HLA DR3-DQ2, Extension) |
|----------------------------------|--------------------------------|---------------------|---|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 28 | 22 | 15 | 8 |
| Units: percent | | | | |
| number (confidence interval 95%) | 75.0 (55.1 to 89.3) | 72.7 (49.8 to 89.3) | 80.0 (51.9 to 95.7) | 62.5 (24.5 to 91.5) |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with stimulated 90-minute C-peptide above 0.2 nmol/L

| | |
|-----------------|---|
| End point title | Proportion of patients with stimulated 90-minute C-peptide above 0.2 nmol/L |
|-----------------|---|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Proportion of patients at Month 15 (Main Study reporting groups) and at Month 24 (Extension Study reporting groups).

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) | Placebo (HLA DR3-DQ2, Main Study) |
|----------------------------------|--------------------------------------|---------------------------|--|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 55 | 49 | 29 | 17 |
| Units: percent | | | | |
| number (confidence interval 95%) | 87.3 (75.5 to 94.7) | 71.4 (56.7 to 83.4) | 96.6 (82.2 to 99.9) | 64.7 (38.3 to 85.8) |

| End point values | Diamyd + vitamin D (Extension) | Placebo (Extension) | Diamyd + vitamin D (HLA DR3-DQ2, Extension) | Placebo (HLA DR3-DQ2, Extension) |
|----------------------------------|--------------------------------|---------------------|---|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 27 | 22 | 14 | 8 |
| Units: percent | | | | |
| number (confidence interval 95%) | 70.4 (49.8 to 86.2) | 68.2 (45.1 to 86.1) | 71.4 (41.9 to 91.6) | 62.5 (24.5 to 91.5) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of self-reported episodes of severe hypoglycaemia

| | |
|-----------------|--|
| End point title | Number of self-reported episodes of severe hypoglycaemia |
|-----------------|--|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Between baseline and 15 months (Main Study reporting groups) or between baseline and 24 months (Extension Study reporting groups).

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) | Placebo (HLA DR3-DQ2, Main Study) |
|-----------------------------|--------------------------------------|---------------------------|--|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 57 | 52 | 29 | 19 |
| Units: episodes | 0 | 6 | 0 | 0 |

| End point values | Diamyd + vitamin D (Extension) | Placebo (Extension) | Diamyd + vitamin D (HLA DR3-DQ2, Extension) | Placebo (HLA DR3-DQ2, Extension) |
|-----------------------------|--------------------------------|---------------------|---|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 30 | 23 | 15 | 8 |
| Units: episodes | 0 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with at least 1 severe hypoglycaemic event

| | |
|--|---|
| End point title | Number of patients with at least 1 severe hypoglycaemic event |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Between baseline and 15 months (Main Study reporting groups) or between baseline and 24 months (Extension Study reporting groups). | |

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) | Placebo (HLA DR3-DQ2, Main Study) |
|-----------------------------|--------------------------------------|---------------------------|--|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 57 | 52 | 29 | 19 |
| Units: patients | 0 | 1 | 0 | 0 |

| End point values | Diamyd + vitamin D (Extension) | Placebo (Extension) | Diamyd + vitamin D (HLA DR3-DQ2, Extension) | Placebo (HLA DR3-DQ2, Extension) |
|-----------------------------|--------------------------------|---------------------|---|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 30 | 23 | 15 | 8 |
| Units: patients | 0 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in maximum C-peptide during MMTT

| | |
|---|---|
| End point title | Change in maximum C-peptide during MMTT |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Change between baseline and 15 months (Main Study reporting groups) or between baseline and 24 months (Extension Study reporting groups). | |

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) | Placebo (HLA DR3-DQ2, Main Study) |
|--------------------------------------|--------------------------------------|---------------------------|--|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 55 | 49 | 29 | 17 |
| Units: nmol/L | | | | |
| arithmetic mean (standard deviation) | -0.350 (± 0.463) | -0.300 (± 0.350) | -0.257 (± 0.400) | -0.277 (± 0.349) |

| End point values | Diamyd + vitamin D (Extension) | Placebo (Extension) | Diamyd + vitamin D (HLA DR3-DQ2, Extension) | Placebo (HLA DR3-DQ2, Extension) |
|--------------------------------------|--------------------------------|---------------------|---|----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 28 | 22 | 15 | 8 |
| Units: nmol/L | | | | |
| arithmetic mean (standard deviation) | -0.546 (± 0.295) | -0.403 (± 0.306) | -0.557 (± 0.319) | -0.520 (± 0.364) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fasting C-peptide

| | |
|-----------------|-----------------------------|
| End point title | Change in fasting C-peptide |
|-----------------|-----------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Change between baseline and 15 months (Main Study reporting groups) or between baseline and 24 months (Extension Study reporting groups).

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) | Placebo (HLA DR3-DQ2, Main Study) |
|--------------------------------------|--------------------------------------|---------------------------|--|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 55 | 49 | 29 | 17 |
| Units: nmol/L | | | | |
| arithmetic mean (standard deviation) | -0.115 (± 0.148) | -0.106 (± 0.169) | -0.081 (± 0.100) | -0.095 (± 0.190) |

| End point values | Diamyd + vitamin D (Extension) | Placebo (Extension) | Diamyd + vitamin D (HLA DR3-DQ2, Extension) | Placebo (HLA DR3-DQ2, Extension) |
|------------------|--------------------------------|---------------------|---|----------------------------------|
|------------------|--------------------------------|---------------------|---|----------------------------------|

| | | | Extension) | |
|--------------------------------------|------------------|------------------|------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 28 | 22 | 15 | 8 |
| Units: nmol/L | | | | |
| arithmetic mean (standard deviation) | -0.144 (± 0.160) | -0.139 (± 0.122) | -0.082 (± 0.119) | -0.150 (± 0.107) |

Statistical analyses

No statistical analyses for this end point

Secondary: C-peptide measured at 30, 60, 90 and 120 minutes during MMTT

| | |
|------------------------|--|
| End point title | C-peptide measured at 30, 60, 90 and 120 minutes during MMTT |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| At Month 15. | |

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (HLA DR3-DQ2, Main Study) | Placebo (HLA DR3-DQ2, Main Study) |
|--------------------------------------|--------------------------------------|---------------------------|--|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 55 | 49 | 29 | 19 |
| Units: nmol/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| 30 min | 0.376 (± 0.295) | 0.374 (± 0.330) | 0.659 (± 0.352) | 0.580 (± 0.282) |
| 60 min | 0.536 (± 0.383) | 0.495 (± 0.411) | 0.911 (± 0.393) | 0.715 (± 0.308) |
| 90 min | 0.645 (± 0.495) | 0.562 (± 0.438) | 1.016 (± 0.451) | 0.717 (± 0.318) |
| 120 min | 0.691 (± 0.542) | 0.590 (± 0.444) | 1.065 (± 0.430) | 0.728 (± 0.317) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in body weight and BMI

| | |
|------------------------|--|
| End point title | Change in body weight and BMI ^[1] |
| End point description: | |
| End point type | Secondary |

End point timeframe:

Change between baseline and 15 months (Main Study reporting groups) or between baseline and 24 months (Extension Study reporting groups).

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was summarised overall only, not further split by HLA subgroup.

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (Extension) | Placebo (Extension) |
|--------------------------------------|--------------------------------------|---------------------------|--------------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 56 | 51 | 28 | 22 |
| Units: unit(s) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Body weight (kg) | 4.3 (± 5.0) | 5.6 (± 5.4) | 6.5 (± 6.9) | 6.8 (± 6.8) |
| Body mass index (kg/m2) | 0.8 (± 1.4) | 1.3 (± 1.6) | 1.2 (± 1.9) | 1.9 (± 2.0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Injection site reactions

End point title Injection site reactions^[2]

End point description:

End point type Secondary

End point timeframe:

Change between baseline and 15 months (Main Study reporting groups)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was summarised overall only, not further split by HLA subgroup.

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | | |
|--|--------------------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 57 | 52 | | |
| Units: severe injection site reactions | 10 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Laboratory assessments

End point title Laboratory assessments^[3]

End point description:

Clinically significant abnormal results from laboratory measurements (haematology and clinical chemistry) and urinalysis.

End point type Secondary

End point timeframe:

From Screening until 15 months (Main Study reporting groups) or from Screening until 24 months (Extension Study reporting groups)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint was summarised overall only, not further split by HLA subgroup.

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (Extension) | Placebo (Extension) |
|--|--------------------------------------|---------------------------|--------------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 57 | 52 | 30 | 23 |
| Units: clinically significant abnormal results | 11 | 3 | 3 | 3 |

Statistical analyses

No statistical analyses for this end point

Secondary: Physical and neurological examination

End point title Physical and neurological examination^[4]

End point description:

End point type Secondary

End point timeframe:

From Screening until 15 months (Main Study reporting groups) or from Screening until 24 months (Extension Study reporting groups)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint was summarised overall only, not further split by HLA subgroup.

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (Extension) | Placebo (Extension) |
|--|--------------------------------------|---------------------------|--------------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 57 | 52 | 30 | 23 |
| Units: clinically significant abnormal results | | | | |
| Physical examination | 15 | 9 | 10 | 1 |
| Neurological examination | 4 | 0 | 4 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: GAD65A titer

End point title GAD65A titer^[5]

End point description:

Last assessment corresponds to Month 15 for the Main Study reporting groups and Month 24 for the Extension Study reporting groups

End point type Secondary

End point timeframe:

At baseline and 15 months (Main Study reporting groups) or at Baseline and 24 months (Extension Study reporting groups)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint was summarised overall only, not further split by HLA subgroup.

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (Extension) | Placebo (Extension) |
|--------------------------------------|--------------------------------------|---------------------------|--------------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 57 | 52 | 30 | 23 |
| Units: IU/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 731.3 (± 2302.9) | 627.3 (± 1829.9) | 677.8 (± 2060.8) | 168.0 (± 283.5) |
| Last assessment | 19941.2 (± 23083.6) | 19197.7 (± 22218.7) | 18972.5 (± 21432.4) | 18253.7 (± 21199.0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Vital signs (blood pressure)

End point title Vital signs (blood pressure)^[6]

End point description:

End point type Secondary

End point timeframe:

From Screening until 15 months (Main Study reporting groups) or from Screening until 24 months (Extension Study reporting groups)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint was summarised overall only, not further split by HLA subgroup.

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (Extension) | Placebo (Extension) |
|--|--------------------------------------|---------------------------|--------------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 57 | 52 | 30 | 23 |
| Units: clinically significant abnormal results | | | | |
| Systolic blood pressure | 0 | 0 | 0 | 0 |
| Diastolic blood pressure | 0 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of life: EQ-5D-5L

| | |
|-----------------|--|
| End point title | Quality of life: EQ-5D-5L ^[7] |
|-----------------|--|

End point description:

Last assessment corresponds to Month 15 for the Main Study reporting groups and Month 24 for the Extension Study reporting groups

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At baseline and 15 months (Main Study reporting groups) or at Baseline and 24 months (Extension Study reporting groups)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Endpoint was summarised overall only, not further split by HLA subgroup.

| End point values | Diamyd + vitamin D (FAS, Main Study) | Placebo (FAS, Main Study) | Diamyd + vitamin D (Extension) | Placebo (Extension) |
|---------------------------------------|--------------------------------------|---------------------------|--------------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 48 | 47 | 26 | 21 |
| Units: unitless | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| Baseline | 1.000 (0.922 to 1.000) | 1.000 (0.919 to 1.000) | 1.000 (0.922 to 1.000) | 1.000 (0.919 to 1.000) |
| Last assessment | 1.000 (0.919 to 1.000) | 1.000 (1.000 to 1.000) | 1.000 (0.919 to 1.000) | 1.000 (0.919 to 1.000) |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events, from start of Diamyd/Placebo treatment until Month 24.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Diamyd + vitamin D |
|-----------------------|--------------------|

Reporting group description: -

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events | Diamyd + vitamin D | Placebo | |
|---|--------------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 3 / 52 (5.77%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Jaw fracture | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 57 (0.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Diamyd + vitamin D | Placebo | |
|---|--------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 18 / 57 (31.58%) | 12 / 52 (23.08%) | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 57 (5.26%) | 3 / 52 (5.77%) | |
| occurrences (all) | 3 | 3 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 3 / 57 (5.26%) | 2 / 52 (3.85%) | |
| occurrences (all) | 4 | 2 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 10 / 57 (17.54%) | 10 / 52 (19.23%) | |
| occurrences (all) | 13 | 17 | |
| Viral infection | | | |
| subjects affected / exposed | 4 / 57 (7.02%) | 0 / 52 (0.00%) | |
| occurrences (all) | 4 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|--|
| 16 June 2017 | Amendment 1 included: <ul style="list-style-type: none">• Addition of new inclusion criterion• Clarification on all visits timing• Specification of c-peptid concentration at screening visit• Clarification on the physical examination outcome• Clarification on the lymph node injection side• Clarification on the relationship to study medication |
| 21 August 2017 | Amendment 4 included: <ul style="list-style-type: none">• Patients taking Vitamin D before screening had to stop it during trial (new exclusion criterion) |
| 28 June 2018 | Amendment 5 included: <ul style="list-style-type: none">• Addition of 2 sites in The Netherlands (new country)• Increase the number of total patients 106 instead of 80• Increase the recruitment period in 4 months (16 in total)• ICFs were updated |
| 18 June 2019 | Amendment 6 included: <ul style="list-style-type: none">• All patients that were ongoing, were asked to participate in the Extension Study Period which included Visit 8 at month 24.• Exploratory endpoints included all data collected at the 24-month follow-up visit• ICFs were updated for the patients that approved to participate in the Extension Study |
| 15 May 2020 | Amendment 7 included: <ul style="list-style-type: none">• Addition of key secondary endpoints to evaluate diabetic status• Correction of secondary endpoints and addition of new ones (body weight, body mass index and serological test for Covid-19)• Upgrade of analysis sets for statistical analysis• Upgrade of primary endpoint variable analysis; secondary efficacy endpoint variables analysis; secondary variables of diabetic status analysis; and exploratory endpoints variables analysis |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported