Clinical trial results:
DIAGNODE-B, A Phase I/II Open Label Pilot Study to evaluate the safety and feasibility of an additional intralymphatic booster administration of GAD-alum (Diamyd®) in individuals with Type 1 diabetes

Summary

EudraCT number	2021-005441-32
Trial protocol	SE
Global end of trial date	29 August 2023

Results information

Result version number	v1 (current)
This version publication date	12 May 2024
First version publication date	12 May 2024

Trial information

Trial identification

Sponsor protocol code	DIAGNODE-B

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05351879
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Linköping University
Sponsor organisation address	Crown Princess Victoria Children´s Hospital and Div of Pediatrics, Department of Biomedical and Cli, Linköping, Sweden, 58183
Public contact	Johnny Ludvigsson, Linköping University, Johnny.Ludvigsson@liu.se
Scientific contact	Johnny Ludvigsson, Linköping University, Johnny.Ludvigsson@liu.se

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	07 March 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 August 2023
Global end of trial reached?	Yes
Global end of trial date	29 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate feasibility and safety of administering an additional intralymphatic booster dose of Diamyd.

Protection of trial subjects:

After the injection of Diamyd each trial participant was to remain at the study clinic for at least 1 h and monitored by the study personnel.

Background therapy:

All patients was to continue to receive standard of care treatment for Type 1 diabetes during the study.

Evidence for comparator: -

Actual start date of recruitment	15 December 2021
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	Sweden: 6
Worldwide total number of subjects	6
EEA total number of subjects	6

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)	1
Adults (18-64 years)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In total, 6 patients (2 from the DIAGNODE-1 cohort and 4 from the DIAGNODE-2 cohort) were screened for the study and all met the eligibility criteria and were enrolled in the study.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	ALUM-rhGAD65 + Vitamin D

Arm description:

All patients received one dose of Diamyd 4 µg as a 0.1 mL intralymphatic injection into an inguinal lymph node. Vitamin D (cholecalciferol 2000 IE) was administered as tablets 2000 IU daily.

Arm type	Experimental
Investigational medicinal product name	Diamyd
Investigational medicinal product code	
Other name	ALUM-rhGAD65
Pharmaceutical forms	Solution for injection
Routes of administration	Intralymphatic use

Dosage and administration details:

GAD-alum (Diamyd®; 4 µg) was administered as a 0.1 mL intralymphatic injection into an inguinal lymph node.

Investigational medicinal product name	Vitamin D
Investigational medicinal product code	
Other name	Caliciferol
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Commercially available vitamin D (cholecalciferol; trade name Divisun® 2000 IE) was administered as tablets 2000 IU daily.

Number of subjects in period 1	ALUM-rhGAD65 + Vitamin D
Started	6
Completed	6

Period 2	
Period 2 title	Overall Study
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	ALUM-rhGAD65 + Vitamin D

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Diamyd
Investigational medicinal product code	
Other name	ALUM-rhGAD65
Pharmaceutical forms	Solution for injection
Routes of administration	Intralymphatic use

Dosage and administration details:

GAD-alum (Diamyd®; 4 µg) was administered as a 0.1 mL intralymphatic injection into an inguinal lymph node.

Investigational medicinal product name	Vitamin D
Investigational medicinal product code	
Other name	Caliciferol
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Commercially available vitamin D (cholecalciferol; trade name Divisun® 2000 IE) was administered as tablets 2000 IU daily.

Number of subjects in period 2	ALUM-rhGAD65 + Vitamin D
Started	6
Completed	6

Baseline characteristics

Reporting groups

Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	6	6	
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)	1	1	
Adults (18-64 years)	5	5	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	23.3		
standard deviation	± 5.1	-	
Gender categorical Units: Subjects			
Female	2	2	
Male	4	4	
Time since type 1 diagnosis Units: month			
median	54.5		
full range (min-max)	44 to 76	-	
Time since last Diamyd injection Units: month			
median	43		
full range (min-max)	38 to 48	-	

End points

End points reporting groups

Reporting group title	ALUM-rhGAD65 + Vitamin D

Reporting group description:

All patients received one dose of Diamyd 4 µg as a 0.1 mL intralymphatic injection into an inguinal lymph node. Vitamin D (cholecalciferol 2000 IE) was administered as tablets 2000 IU daily.

Reporting group title	ALUM-rhGAD65 + Vitamin D

Reporting group description: -

Primary: Injection site reactions

End point title	Injection site reactions[1]

End point description:

End point type	Primary

End point timeframe:

From enrollment up to 1 year after the booster injection

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Too few patients and no comparator arm to enable statistical analysis.

End point values	ALUM-rhGAD65 + Vitamin D			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Number of patients	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in C-peptide (AUCmean 0-120 min) during MMTT from baseline to 12 months

End point title	Change in C-peptide (AUCmean 0-120 min) during MMTT from baseline to 12 months

End point description:

Change ratio

End point type	Secondary

End point timeframe:

Change from baseline to 12 months

End point values	ALUM-rhGAD65 + Vitamin D			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: nmol/L/min				
median (full range (min-max))	0.636 (0.333 to 0.895)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in HbA1c from baseline to 12 months

End point title	Change in HbA1c from baseline to 12 months

End point description:

End point type	Secondary

End point timeframe:

From baseline to month 12

End point values	ALUM-rhGAD65 + Vitamin D			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: mmol/mol				
arithmetic mean (standard deviation)	2.3 (± 4.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in daily exogenous insulin consumption from baseline to 12 months

End point title	Change in daily exogenous insulin consumption from baseline to 12 months

End point description:

End point type	Secondary

End point timeframe:

From baseline to month 12

End point values	ALUM-rhGAD65 + Vitamin D			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: IU/kg				
arithmetic mean (standard deviation)	-0.147 (± 0.17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in IDAA1C (Insulin-dose-adjusted HbA1c levels) from baseline to 12 months

End point title	Change in IDAA1C (Insulin-dose-adjusted HbA1c levels) from baseline to 12 months

End point description:

End point type	Secondary

End point timeframe:

From baseline to month 12

End point values	ALUM-rhGAD65 + Vitamin D			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: mmol/mol				
arithmetic mean (standard deviation)	-0.4 (± 0.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in time in glycemic target range 3.9 to 10 mmol/L (70 to 180 mg/dL) from baseline to 12 months

End point title	Change in time in glycemic target range 3.9 to 10 mmol/L (70 to 180 mg/dL) from baseline to 12 months

End point description:

End point type	Secondary

End point timeframe:

From baseline to month 12

End point values	ALUM-rhGAD65 + Vitamin D			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hours				
arithmetic mean (standard deviation)	12.9 (± 66.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in time in hyperglycemic range > 10 mmol/L (> 180 mg/dL) from baseline to 12 months

End point title	Change in time in hyperglycemic range > 10 mmol/L (> 180 mg/dL) from baseline to 12 months

End point description:

End point type	Secondary

End point timeframe:

From baseline to month 12

End point values	ALUM-rhGAD65 + Vitamin D			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hours				
arithmetic mean (standard deviation)	-26.8 (± 25.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From enrollment up to 1 year after the booster injection.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26

Reporting groups	
Reporting group title	ALUM-rhGAD65 + Vitamin D
Reporting group description: All patients received one dose of Diamyd 4 µg as a 0.1 mL intralymphatic injection into an inguinal lymph node. Vitamin D (cholecalciferol 2000 IE) was administered as tablets 2000 IU daily.	

Serious adverse events	ALUM-rhGAD65 + Vitamin D		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	ALUM-rhGAD65 + Vitamin D		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)		
Injury, poisoning and procedural complications			
Joint injury			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Pyrexia			

subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 3		
Musculoskeletal and connective tissue disorders Myositis subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	 2 / 6 (33.33%) 2 1 / 6 (16.67%) 2		
Metabolism and nutrition disorders Obesity subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The main limitation of the present pilot study is the low number of participants, and the results obtained herein, especially the efficacy results, should therefore be taken with caution.

Notes: