Clinical trial results:
Open Label trial to evaluate the tolerability of a combination therapy consisting of GAD-alum (Diamyd®), etanercept and vitamin D in children and adolescents newly diagnosed with type 1 diabetes

Summary

EudraCT number	2014-001323-76
Trial protocol	SE
Global end of trial date	25 February 2019

Results information

Result version number	v1 (current)
This version publication date	20 June 2019
First version publication date	20 June 2019

Trial information

Trial identification

Sponsor protocol code	EDCR_IIa

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02464033
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Linköping University
Sponsor organisation address	Crown Princess Victoria Children´s Hospital, Linköping, Sweden, 581 85
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	10 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 February 2019
Global end of trial reached?	Yes
Global end of trial date	25 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the tolerability of a combination therapy with Diamyd, vitamin D and etanercept

Protection of trial subjects:

To ensure subject safety a Safety Plan is in place describing the study specific safety measures that are to be taken during the study. This Safety Plan must be used in conjunction with this protocol.

The purpose of the Safety Plan is to ensure:
the safety of patients receiving etanercept, Diamyd and vitamin D treatment in the study.
that appropriately qualified medical personnel are readily available to advise on trial related medical questions or problems regarding the study drug treatment in the above mentioned study.
that study personnel are educated about know side effects of the study drug treatment and how to handle them.
that patients and their parents/legal guardian(s) are given information about possible side effects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2015
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	Sweden: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	9
Adolescents (12-17 years)	11

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

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

47 patients were screened and 20 entered 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	GAD-Alum+Vitamin D+Etanercept

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Diamyd
Investigational medicinal product code	
Other name	Recombinant Human Glutamic Acid Decarboxylase (rhGAD65)
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

GAD-alum 20 µg, administered subcutaneously in the stomach area at two occasions, each on Days 30 and 60 (Visits 3 and 4 respectively).

Investigational medicinal product name	Etanercept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Etanercept (Enbrel®) injected subcutaneously 0.8 mg/kg body weight (max 50 mg) once a week from Day 1 through Day 90 (3 months duration).

Investigational medicinal product name	Vitamin D
Investigational medicinal product code	
Other name	Cholecalciferol
Pharmaceutical forms	Oral drops
Routes of administration	Oral use

Dosage and administration details:

Vitamin D, administered as oral drops; 2000 IU per day (i.e. 25 drops per day) from Day 1 through Day 450 (15 months duration).

Number of subjects in period 1	GAD-Alum+Vitamin D+Etanercept
Started	20
Completed	20

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

Arms

Arm title	GAD-Alum+Vitamin D+Etanercept
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Diamyd
Investigational medicinal product code	
Other name	Recombinant Human Glutamic Acid Decarboxylase (rhGAD65)
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

2 subcutaneous injections of 20 µg Diamyd in a prime-and-boost regimen on Days 30 and 60

Investigational medicinal product name	Etanercept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

From Days 1-90 all patients receive etanercept (Enbrel) injected subcutaneously 0.8 mg/kg body weight (max 50 mg) once a week

Investigational medicinal product name	Vitamin D
Investigational medicinal product code	
Other name	Cholecalciferol
Pharmaceutical forms	Oral drops
Routes of administration	Oral use

Dosage and administration details:

All patients will from Day 1 receive 2 000 IU vitamin D per os per day during 15 months

Number of subjects in period 2	GAD-Alum+Vitamin D+Etanercept
Started	20
Completed	20

Baseline characteristics

Reporting groups

Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	20	20	
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)	9	9	
Adolescents (12-17 years)	11	11	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	12.36		
standard deviation	± 2.321	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	13	13	
Type 1 diabetes duration Units: days			
arithmetic mean	81.35		
standard deviation	± 22.091	-	
Body Mass Index (BMI) Units: kg/m2			
arithmetic mean	18.38		
standard deviation	± 2.141	-	

Subject analysis sets

Subject analysis set title	Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Population included all enrolled patients who received at least one dose of study drug and had at least one safety/tolerability evaluation. It was used for prior and concomitant diseases/medications and analysis safety/tolerability variables.

Subject analysis set title	Total
Subject analysis set type	Full analysis

Subject analysis set description:

The Total Population included all patients who had consented for the study. It was used for patient

listings, patient disposition and demographics.

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Intention-to-Treat Population included all enrolled patients who received at least one dose of study drug and had at least one efficacy evaluation. It was used for primary analysis of efficacy variables (diabetes-related parameters).

Subject analysis set title	PP
Subject analysis set type	Per protocol

Subject analysis set description:

The Per Protocol Population was a subset of ITT Population and included patients' all study visits that followed the study protocol without any major violations.

Reporting group values	Safety	Total	ITT
Number of subjects	20	20	20
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	9	9	9
Adolescents (12-17 years)	11	11	11
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	12.36	12.36	12.36
standard deviation	± 2.321	± 2.321	± 2.321
Gender categorical Units: Subjects			
Female	7	7	7
Male	13	13	13
Type 1 diabetes duration Units: days			
arithmetic mean	81.35	81.35	81.35
standard deviation	± 22.091	± 22.091	± 22.091
Body Mass Index (BMI) Units: kg/m2			
arithmetic mean	18.38	18.38	18.38
standard deviation	± 2.141	± 2.141	± 2.141

Reporting group values	PP		
Number of subjects	20		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		

Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	9		
Adolescents (12-17 years)	11		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean	12.36		
standard deviation	± 2.321		
Gender categorical			
Units: Subjects			
Female	7		
Male	13		
Type 1 diabetes duration			
Units: days			
arithmetic mean	81.35		
standard deviation	± 22.091		
Body Mass Index (BMI)			
Units: kg/m2			
arithmetic mean	18.38		
standard deviation	± 2.141		

End points

End points reporting groups

Reporting group title	GAD-Alum+Vitamin D+Etanercept
Reporting group description: -	
Reporting group title	GAD-Alum+Vitamin D+Etanercept
Reporting group description: -	
Subject analysis set title	Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Population included all enrolled patients who received at least one dose of study drug and had at least one safety/tolerability evaluation. It was used for prior and concomitant diseases/medications and analysis safety/tolerability variables.	
Subject analysis set title	Total
Subject analysis set type	Full analysis
Subject analysis set description:	
The Total Population included all patients who had consented for the study. It was used for patient listings, patient disposition and demographics.	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The Intention-to-Treat Population included all enrolled patients who received at least one dose of study drug and had at least one efficacy evaluation. It was used for primary analysis of efficacy variables (diabetes-related parameters).	
Subject analysis set title	PP
Subject analysis set type	Per protocol
Subject analysis set description:	
The Per Protocol Population was a subset of ITT Population and included patients' all study visits that followed the study protocol without any major violations.	

Primary: Reactions of the injection site

End point title	Reactions of the injection site[1]
End point description:	
Reactions of the injection site (Erythema, Oedema, Haematoma, Tenderness, Pain, Itching, Other). Inspection of injection site 60 minutes after GAD-Alum injection by investigator or nurse	
End point type	Primary
End point timeframe:	
1 months	

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: This was an uncontrolled open study and no formal statistical analyses were pre-specified.

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Number of subjects	3			

Statistical analyses

No statistical analyses for this end point

Primary: Reactions of the injection site

End point title	Reactions of the injection site[2]

End point description:

Reactions of the injection site (Erythema, Oedema, Haematoma, Tenderness, Pain, Itching, Other). Inspection of injection site 60 minutes after GAD-Alum injection by investigator or nurse

End point type	Primary

End point timeframe:

2 months

Notes:

[2] - 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: This was an uncontrolled open study and no formal statistical analyses were pre-specified.

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Number of subjects	5			

Statistical analyses

No statistical analyses for this end point

Primary: Physical examinations, including neurological assessments.

End point title	Physical examinations, including neurological assessments.[3]

End point description:

Physical examinations, including neurological assessments. Number of patients with any abnormal findings after baseline.

End point type	Primary

End point timeframe:

Overall treatment

Notes:

[3] - 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: This was an uncontrolled open study and no formal statistical analyses were pre-specified.

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Number of patients	6			

Statistical analyses

No statistical analyses for this end point

Primary: Laboratory Measurements

End point title	Laboratory Measurements[4]

End point description:

Laboratory Measurements. Number of patients with clinically significant laboratory findings during the study.

End point type	Primary

End point timeframe:

Overall treatment

Notes:

[4] - 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: This was an uncontrolled open study and no formal statistical analyses were pre-specified.

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Number of subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: GAD65AB titer (GADA) change from baseline

End point title	GAD65AB titer (GADA) change from baseline[5]

End point description:

GAD65AB = Antibodies to GAD with molecular mass 65000

End point type	Primary

End point timeframe:

6 months

Notes:

[5] - 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: This was an uncontrolled open study and no formal statistical analyses were pre-specified.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: U/mL				
arithmetic mean (standard deviation)	2509.41 (± 4866.515)			

Statistical analyses

No statistical analyses for this end point

Primary: GAD65AB titer (GADA) change from baseline.

End point title	GAD65AB titer (GADA) change from baseline.[6]

End point description:

GAD65AB = Antibodies to GAD with molecular mass 65000

End point type	Primary

End point timeframe:

15 months

Notes:

[6] - 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: This was an uncontrolled open study and no formal statistical analyses were pre-specified.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: U/mL				
arithmetic mean (standard deviation)	1036.19 (± 2527.249)			

Statistical analyses

No statistical analyses for this end point

Primary: GAD65AB titer (GADA) change from baseline

End point title	GAD65AB titer (GADA) change from baseline[7]

End point description:

GAD65AB = Antibodies to GAD with molecular mass 65000

End point type	Primary

End point timeframe:

30 months

Notes:

[7] - 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: This was an uncontrolled open study and no formal statistical analyses were pre-specified.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: U/mL				
arithmetic mean (standard deviation)	347.01 (± 1564.466)			

Statistical analyses

No statistical analyses for this end point

Primary: Infections

End point title	Infections[8]

End point description:

Number of patients with an infection reported as Adverse Event related to study treatment (GAD-alum and/or Etanercept)

End point type	Primary

End point timeframe:

Overall treatment

Notes:

[8] - 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: This was an uncontrolled open study and no formal statistical analyses were pre-specified.

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Number of subjects	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Weighted mean C-peptide: (AUC mean 0-120 min) during an MMTT, change from baseline

End point title	Weighted mean C-peptide: (AUC mean 0-120 min) during an MMTT, change from baseline

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	18			
Units: nmol/L*min				
arithmetic mean (standard deviation)	-0.09 (± 0.153)			

Statistical analyses

No statistical analyses for this end point

Secondary: Weighted mean C-peptide: (AUC mean 0-120 min) during an MMTT, change from baseline

End point title	Weighted mean C-peptide: (AUC mean 0-120 min) during an MMTT, change from baseline

End point description:

End point type	Secondary

End point timeframe:

15 months

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: nmol/L*min				
arithmetic mean (standard deviation)	-0.30 (± 0.158)			

Statistical analyses

No statistical analyses for this end point

Secondary: Weighted mean C-peptide: (AUC mean 0-120 min) during an MMTT, change from baseline

End point title	Weighted mean C-peptide: (AUC mean 0-120 min) during an MMTT, change from baseline

End point description:

End point type	Secondary

End point timeframe:

30 months

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	19			
Units: nmol/L*min				
arithmetic mean (standard deviation)	-0.40 (± 0.168)			

Statistical analyses

No statistical analyses for this end point

Secondary: Stimulated maximum C-peptide level above 0.2 nmol/L

End point title	Stimulated maximum C-peptide level above 0.2 nmol/L

End point description:	
Proportion of patients with a stimulated maximum C-peptide level above 0.2 nmol/L	
End point type	Secondary
End point timeframe:	
6 months	

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Number of subjects	17			

Statistical analyses

No statistical analyses for this end point

Secondary: Stimulated maximum C-peptide level above 0.2 nmol/L	
End point title	Stimulated maximum C-peptide level above 0.2 nmol/L
End point description:	
Proportion of patients with a stimulated maximum C-peptide level above 0.2 nmol/L	
End point type	Secondary
End point timeframe:	
15 months	

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Number of subjects	14			

Statistical analyses

No statistical analyses for this end point

Secondary: Stimulated maximum C-peptide level above 0.2 nmol/L	
End point title	Stimulated maximum C-peptide level above 0.2 nmol/L
End point description:	
Proportion of patients with a stimulated maximum C-peptide level above 0.2 nmol/L	
End point type	Secondary
End point timeframe:	
30 months	

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Number of subjects	8			

Statistical analyses

No statistical analyses for this end point

Secondary: Hemoglobin A1c (HbA1c), change from baseline

End point title	Hemoglobin A1c (HbA1c), change from baseline

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: mmol/mol				
arithmetic mean (standard deviation)	0.80 (± 8.433)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hemoglobin A1c (HbA1c), change from baseline

End point title	Hemoglobin A1c (HbA1c), change from baseline

End point description:

End point type	Secondary

End point timeframe:

15 months

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: mmol/mol				
arithmetic mean (standard deviation)	6.15 (± 12.495)			

Statistical analyses

No statistical analyses for this end point

Secondary: Hemoglobin A1c (HbA1c), change from baseline

End point title	Hemoglobin A1c (HbA1c), change from baseline

End point description:

End point type	Secondary

End point timeframe:

30 months

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: mmol/mol				
arithmetic mean (standard deviation)	7.55 (± 11.213)			

Statistical analyses

No statistical analyses for this end point

Secondary: Exogenous 24-hour insulin dose per kg body weight and 24 hours average, change from baseline

End point title	Exogenous 24-hour insulin dose per kg body weight and 24 hours average, change from baseline

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: IU				
arithmetic mean (standard deviation)	0.01 (± 0.249)			

Statistical analyses

No statistical analyses for this end point

Secondary: Exogenous 24-hour insulin dose per kg body weight and 24 hours average, change from baseline

End point title	Exogenous 24-hour insulin dose per kg body weight and 24 hours average, change from baseline

End point description:

End point type	Secondary

End point timeframe:

15 months

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: IU				
arithmetic mean (standard deviation)	0.25 (± 0.342)			

Statistical analyses

No statistical analyses for this end point

Secondary: Exogenous 24-hour insulin dose per kg body weight and 24 hours average, change from baseline

End point title	Exogenous 24-hour insulin dose per kg body weight and 24 hours average, change from baseline

End point description:

End point type	Secondary

End point timeframe:

30 months

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: IU				
arithmetic mean (standard deviation)	0.42 (± 0.333)			

Statistical analyses

No statistical analyses for this end point

Secondary: C-peptide: Stimulated, 90 minute value, change from baseline

End point title	C-peptide: Stimulated, 90 minute value, change from baseline

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	18			
Units: nmol/L				
arithmetic mean (standard deviation)	-0.09 (± 0.233)			

Statistical analyses

No statistical analyses for this end point

Secondary: C-peptide: Stimulated, 90 minute value, change from baseline

End point title	C-peptide: Stimulated, 90 minute value, change from baseline

End point description:

End point type	Secondary

End point timeframe:

15 months

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: nmol/L				
arithmetic mean (standard deviation)	-0.35 (± 0.231)			

Statistical analyses

No statistical analyses for this end point

Secondary: C-peptide: Stimulated, 90 minute value, change from baseline

End point title	C-peptide: Stimulated, 90 minute value, change from baseline

End point description:

End point type	Secondary

End point timeframe:

30 months

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	19			
Units: nmol/L				
arithmetic mean (standard deviation)	-0.49 (± 0.221)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in fasting C-peptide concentrations

End point title	Changes in fasting C-peptide concentrations

End point description:

Change from baseline in fasting C-peptide concentrations

End point type	Secondary

End point timeframe:

Month 6

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: nmol/L				
arithmetic mean (standard deviation)	-0.02 (± 0.083)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in fasting C-peptide concentrations

End point title	Changes in fasting C-peptide concentrations

End point description:

Change from baseline in fasting C-peptide concentrations

End point type	Secondary

End point timeframe:

Month 15

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: nmol/L				
arithmetic mean (standard deviation)	-0.10 (± 0.091)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in fasting C-peptide concentration

End point title	Changes in fasting C-peptide concentration

End point description:

Changes from baseline in fasting C-peptide concentrations

End point type	Secondary

End point timeframe:

Month 30

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: nmol/L				
arithmetic mean (standard deviation)	-0.15 (± 0.093)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall trial	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	GAD-Alum+Vitamin D+Etanercept

Reporting group description: -

Serious adverse events	GAD-Alum+Vitamin D+Etanercept		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	GAD-Alum+Vitamin D+Etanercept		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)		
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	13 / 20 (65.00%)		
occurrences (all)	20		
Pyrexia			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Gastrointestinal disorders			

Diarrhoea subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		
Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Viral infection subjects affected / exposed occurrences (all)	9 / 20 (45.00%) 11 2 / 20 (10.00%) 2 13 / 20 (65.00%) 30 8 / 20 (40.00%) 15		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported