



Clinical trial results:

DIAPREV-IT Diabetes Prevention Immune Tolerance.

A double-blind, randomized investigator-initiated study to determine the safety and the effect of Diamyd® on the progression to type 1 diabetes in children with multiple islet cell autoantibodies.

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2008-007484-16 |
| Trial protocol | SE |
| Global end of trial date | 31 January 2017 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 09 April 2020 |
| First version publication date | 09 April 2020 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | DIAPREV/2008 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01122446 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Skåne University Hospital |
| Sponsor organisation address | Jan Waldenströms gata 35, hus 60, Malmö, Sweden, |
| Public contact | Helena Elding Larsson, Skåne University Hospital, 46 040-337676, helena.larsson@med.lu.se |
| Scientific contact | Helena Elding Larsson, Skåne University Hospital, 46 040-337676, helena.larsson@med.lu.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 | 22 June 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 31 January 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 January 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to demonstrate that Diamyd® is safe in children at risk for type 1 diabetes from 4 years of age. The subjects will be followed for 5 years.

Protection of trial subjects:

After the injection of Diamyd/placebo at visits 1 and 2, each trial participant was to remain at the study clinic for at least 1h and monitored by the study personnel. Additionally, the participants were offered to stay at the clinic for an additional 2h or contact the investigator by phone.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 01 April 2009 |
| 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: 50 |
| Worldwide total number of subjects | 50 |
| EEA total number of subjects | 50 |

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) | 48 |
| Adolescents (12-17 years) | 2 |
| 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:

55 children were screened for participation. Of those, 4 did not fulfil the inclusion criteria of positive autoantibodies to GAD65 (GADA) and at least one more islet autoantibody, or had already developed diabetes at screening. For one child, the parents changed their mind about participation and withdrew the child before the first treatment.

Period 1

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

Arms

| | |
|------------------------------|--------|
| Are arms mutually exclusive? | Yes |
| Arm title | Diamyd |

Arm description:

ALUM-rhGAD65

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Diamyd |
| Investigational medicinal product code | |
| Other name | ALUM-rhGAD65 |
| Pharmaceutical forms | Concentrate and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

2 subcutaneous injections of 20 microgram each

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description: -

| | |
|--|--|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

2 injections

| Number of subjects in period 1 | Diamyd | Placebo |
|---------------------------------------|--------|---------|
| Started | 25 | 25 |
| Completed | 25 | 25 |

| | |
|--|--|
| Period 2 | |
| Period 2 title | Treatment follow-up |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst |
| Arms | |
| Are arms mutually exclusive? | Yes |
| Arm title | Diamyd |
| Arm description: | |
| ALUM-rhGAD65 | |
| Arm type | Experimental |
| Investigational medicinal product name | Diamyd |
| Investigational medicinal product code | |
| Other name | ALUM-rhGAD65 |
| Pharmaceutical forms | Concentrate for solution for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| 2 subcutaneous injections of 20 microgram each | |
| Arm title | Placebo |
| Arm description: - | |
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate and solvent for solution for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| 2 subcutaneous injections | |

| Number of subjects in period 2 | Diamyd | Placebo |
|--------------------------------|--------|---------|
| Started | 25 | 25 |
| Completed | 25 | 25 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------|
| Reporting group title | Diamyd |
| Reporting group description: | |
| ALUM-rhGAD65 | |
| Reporting group title | Placebo |
| Reporting group description: - | |

| Reporting group values | Diamyd | Placebo | Total |
|---|-------------|-------------|-------|
| Number of subjects | 25 | 25 | 50 |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years | | | |
| median | 6.0 | 5.0 | |
| full range (min-max) | 4.1 to 15.1 | 4.0 to 17.9 | - |
| Gender categorical Units: Subjects | | | |
| Female | 11 | 12 | 23 |
| Male | 14 | 13 | 27 |
| Population source Units: Subjects | | | |
| General population | 16 | 18 | 34 |
| First degree relative | 9 | 7 | 16 |
| Stratum Units: Subjects | | | |
| 2 positive antibodies | 7 | 7 | 14 |
| 3-6 positive antibodies | 18 | 18 | 36 |
| GADA Units: Subjects | | | |
| Positive | 25 | 25 | 50 |
| Negative | 0 | 0 | 0 |
| Glucose tolerance Units: Subjects | | | |
| Impaired | 13 | 13 | 26 |
| Normal | 12 | 12 | 24 |
| OGTT fasting C-peptide Units: nmol/L | | | |
| arithmetic mean | 0.21 | 0.18 | |
| standard deviation | ± 0.1 | ± 0.09 | - |
| OGTT 2 hour C-peptide Units: nmol/L | | | |
| arithmetic mean | 1.22 | 1.09 | |
| standard deviation | ± 0.46 | ± 0.6 | - |
| OGTT AUC C-peptide Units: nmol/L | | | |

| | | | |
|--|--------------------|--------------------|---|
| arithmetic mean standard deviation | 146.98 ± 62.12 | 134.82 ± 55.36 | - |
| OGTT fasting glucose Units: mmol/L arithmetic mean standard deviation | 4.74 ± 0.49 | 4.67 ± 0.56 | - |
| OGTT 2 hour glucose Units: mmol/L arithmetic mean standard deviation | 6.88 ± 1.61 | 6.82 ± 2.12 | - |
| OGTT AUC glucose Units: mmol/L arithmetic mean standard deviation | 938.72 ± 190.87 | 989.63 ± 207.07 | - |
| HbA1c Units: mmol/mol arithmetic mean standard deviation | 32.76 ± 3.13 | 33.84 ± 3.52 | - |

End points

End points reporting groups

| | |
|--------------------------------|---------|
| Reporting group title | Diamyd |
| Reporting group description: | |
| ALUM-rhGAD65 | |
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | Diamyd |
| Reporting group description: | |
| ALUM-rhGAD65 | |
| Reporting group title | Placebo |
| Reporting group description: - | |

Primary: Frequency of type 1 diabetes

| | |
|------------------------|------------------------------|
| End point title | Frequency of type 1 diabetes |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| 5 years | |

| End point values | Diamyd | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 25 | 25 | | |
| Units: Days | 8 | 10 | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Progression to type 1 diabetes |
| Comparison groups | Diamyd v Placebo |
| Number of subjects included in analysis | 50 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.574 ^[1] |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.3 |
| upper limit | 1.94 |

Notes:

[1] - Difference between treatment in time to type 1 diabetes

Secondary: Change from baseline in FPIR (First-phase Insulin Response)

| | |
|-----------------|---|
| End point title | Change from baseline in FPIR (First-phase Insulin Response) |
|-----------------|---|

End point description:

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

End point timeframe:

5 years

| End point values | Diamyd | Placebo | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 15 | 15 | | |
| Units: Unknown | | | | |
| arithmetic mean (standard deviation) | 89.60 (\pm 63.60) | 97.60 (\pm 63.15) | | |

Statistical analyses

| | |
|----------------------------|------------------------------|
| Statistical analysis title | Change from baseline in FPIR |
|----------------------------|------------------------------|

| | |
|-------------------|------------------|
| Comparison groups | Diamyd v Placebo |
|-------------------|------------------|

| | |
|---|----|
| Number of subjects included in analysis | 30 |
|---|----|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|-------------|
| Analysis type | superiority |
|---------------|-------------|

| | |
|---------|------------|
| P-value | = 0.94 [2] |
|---------|------------|

| | |
|--------|-----------------------|
| Method | Mixed models analysis |
|--------|-----------------------|

Notes:

[2] - Difference between the treatment groups

Secondary: Change from baseline in fasting C-peptide

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

End point description:

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

End point timeframe:

5 years

| End point values | Diamyd | Placebo | | |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 15 | | |
| Units: Unknown | | | | |
| arithmetic mean (standard deviation) | 0.45 (\pm 0.16) | 0.48 (\pm 0.25) | | |

Statistical analyses

| Statistical analysis title | Change from baseline in fasting C-peptide |
|---|---|
| Comparison groups | Diamyd v Placebo |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.366 |
| Method | Mixed models analysis |

Secondary: Change from baseline in 120-minutes C-peptide

| | |
|------------------------|---|
| End point title | Change from baseline in 120-minutes C-peptide |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 5 years | |

| End point values | Diamyd | Placebo | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 15 | | |
| Units: Unknown | | | | |
| arithmetic mean (standard deviation) | 1.45 (\pm 0.5) | 1.58 (\pm 0.7) | | |

Statistical analyses

| Statistical analysis title | Change from baseline in 120-minutes C-peptide |
|---|---|
| Comparison groups | Diamyd v Placebo |
| Number of subjects included in analysis | 31 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.384 ^[3] |
| Method | Mixed models analysis |

Notes:

[3] - Difference between the treatments

Secondary: Change from baseline in AUC C-peptide

| | |
|-----------------|---------------------------------------|
| End point title | Change from baseline in AUC C-peptide |
|-----------------|---------------------------------------|

End point description:

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

End point timeframe:

5 years

| End point values | Diamyd | Placebo | | |
|--------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 15 | | |
| Units: Unknown | | | | |
| arithmetic mean (standard deviation) | 184.14 (\pm 65.59) | 183.23 (\pm 64.78) | | |

Statistical analyses

| | |
|-----------------------------------|---------------------------------------|
| Statistical analysis title | Change from baseline in AUC C-peptide |
|-----------------------------------|---------------------------------------|

| | |
|-------------------|------------------|
| Comparison groups | Placebo v Diamyd |
|-------------------|------------------|

| | |
|---|----|
| Number of subjects included in analysis | 31 |
|---|----|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|-------------|
| Analysis type | superiority |
|---------------|-------------|

| | |
|---------|------------------------|
| P-value | = 0.308 ^[4] |
|---------|------------------------|

| | |
|--------|-----------------------|
| Method | Mixed models analysis |
|--------|-----------------------|

Notes:

[4] - Difference between the treatments

Secondary: Change from baseline in fasting glucose

| | |
|-----------------|---|
| End point title | Change from baseline in fasting glucose |
|-----------------|---|

End point description:

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

End point timeframe:

5 years

| End point values | Diamyd | Placebo | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 15 | | |
| Units: Unknown | | | | |
| arithmetic mean (standard deviation) | 5.36 (± 0.39) | 5.29 (± 0.5) | | |

Statistical analyses

| Statistical analysis title | Change from baseline in fasting glucose |
|---|---|
| Comparison groups | Diamyd v Placebo |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5 [5] |
| Method | Mixed models analysis |

Notes:

[5] - Difference between treatments

Secondary: Change from baseline in 120-minutes glucose

| | |
|------------------------|---|
| End point title | Change from baseline in 120-minutes glucose |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 5 years | |

| End point values | Diamyd | Placebo | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 15 | | |
| Units: Unknown | | | | |
| arithmetic mean (standard deviation) | 7.04 (± 3.11) | 6.67 (± 2.38) | | |

Statistical analyses

| Statistical analysis title | Change from baseline in AUC glucose |
|---|-------------------------------------|
| Comparison groups | Diamyd v Placebo |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.565 [6] |
| Method | Mixed models analysis |

Notes:

[6] - Difference between the treatments

Secondary: Change from baseline in HbA1c

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

End point description:

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

End point timeframe:

5 years

| End point values | Diamyd | Placebo | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 16 | | |
| Units: Unknown | | | | |
| arithmetic mean (standard deviation) | 34.00 (± 3.12) | 34.56 (± 4.23) | | |

Statistical analyses

| | |
|---|-------------------------------|
| Statistical analysis title | Change from baseline in HbA1c |
| Comparison groups | Diamyd v Placebo |
| Number of subjects included in analysis | 32 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.151 |
| Method | Mixed models analysis |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From randomization up to 5 year follow-up or diagnosis of type 1 diabetes.

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 19 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | Diamyd |
|-----------------------|--------|

Reporting group description:

ALUM-rhGAD65

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

Reporting group description:

Placebo

| Serious adverse events | Diamyd | Placebo | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 2 / 25 (8.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Upper limb fracture | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 1 / 25 (4.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 1 / 25 (4.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 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 | Placebo | |
|---|-------------------|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 25 / 25 (100.00%) | 25 / 25 (100.00%) | |
| Injury, poisoning and procedural complications | | | |
| Upper limb fracture | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | 3 / 25 (12.00%) | |
| occurrences (all) | 3 | 3 | |
| Vaccination complication | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 5 / 25 (20.00%) | |
| occurrences (all) | 1 | 5 | |
| Fall | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 3 / 25 (12.00%) | |
| occurrences (all) | 0 | 3 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 7 / 25 (28.00%) | 6 / 25 (24.00%) | |
| occurrences (all) | 54 | 17 | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 1 / 25 (4.00%) | |
| occurrences (all) | 1 | 2 | |
| Migraine | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 1 / 25 (4.00%) | |
| occurrences (all) | 1 | 19 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 1 / 25 (4.00%) | |
| occurrences (all) | 3 | 4 | |
| Injection site reaction | | | |
| subjects affected / exposed | 24 / 25 (96.00%) | 23 / 25 (92.00%) | |
| occurrences (all) | 43 | 43 | |
| Malaise | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 1 / 25 (4.00%) | |
| occurrences (all) | 2 | 1 | |
| Pyrexia | | | |
| subjects affected / exposed | 10 / 25 (40.00%) | 19 / 25 (76.00%) | |
| occurrences (all) | 29 | 43 | |

| | | | |
|---|-----------------|-----------------|--|
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | 0 / 25 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Seasonal allergy | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | 2 / 25 (8.00%) | |
| occurrences (all) | 6 | 2 | |
| Coeliac disease | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | 2 / 25 (8.00%) | |
| occurrences (all) | 2 | 2 | |
| Ear and labyrinth disorders | | | |
| Ear pain | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 2 / 25 (8.00%) | |
| occurrences (all) | 0 | 2 | |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 6 / 25 (24.00%) | 5 / 25 (20.00%) | |
| occurrences (all) | 10 | 11 | |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | 1 / 25 (4.00%) | |
| occurrences (all) | 3 | 1 | |
| Vomiting | | | |
| subjects affected / exposed | 4 / 25 (16.00%) | 5 / 25 (20.00%) | |
| occurrences (all) | 5 | 7 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | 4 / 25 (16.00%) | |
| occurrences (all) | 25 | 18 | |
| Cough | | | |
| subjects affected / exposed | 6 / 25 (24.00%) | 5 / 25 (20.00%) | |
| occurrences (all) | 16 | 12 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | 3 / 25 (12.00%) | |
| occurrences (all) | 5 | 5 | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|-------------------------|------------------------|--|
| Growing pains subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 2 / 25 (8.00%) 7 | |
| Infections and infestations | | | |
| Ear infection subjects affected / exposed occurrences (all) | 3 / 25 (12.00%) 5 | 6 / 25 (24.00%) 11 | |
| Enterobiasis subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 8 | 2 / 25 (8.00%) 4 | |
| Gastroenteritis subjects affected / exposed occurrences (all) | 19 / 25 (76.00%) 41 | 17 / 25 (68.00%) 29 | |
| Influenza subjects affected / exposed occurrences (all) | 7 / 25 (28.00%) 9 | 4 / 25 (16.00%) 4 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 21 / 25 (84.00%) 117 | 21 / 25 (84.00%) 92 | |
| Otitis media subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 3 / 25 (12.00%) 3 | |
| Pneumonia subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 2 / 25 (8.00%) 2 | |
| Scarlet fever subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 2 / 25 (8.00%) 2 | |
| Tonsillitis subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 2 | 7 / 25 (28.00%) 10 | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 13 / 25 (52.00%) 19 | 9 / 25 (36.00%) 11 | |
| Varicella | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 6 / 25 (24.00%) | 6 / 25 (24.00%) | |
| occurrences (all) | 6 | 6 | |
| Viral infection | | | |
| subjects affected / exposed | 7 / 25 (28.00%) | 2 / 25 (8.00%) | |
| occurrences (all) | 13 | 3 | |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 4 / 25 (16.00%) | |
| occurrences (all) | 0 | 4 | |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 2 / 25 (8.00%) | |
| occurrences (all) | 0 | 2 | |

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

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/2346994>

<http://www.ncbi.nlm.nih.gov/pubmed/25381193>

<http://www.ncbi.nlm.nih.gov/pubmed/29171140>