



Clinical trial results:

A randomised, double-blind, placebo-controlled, single-centre phase IIb trial as part of the EU-funded UNISEC project to assess the immunogenicity and safety of different formulations and dosing regimens of FLU-v vaccine administered subcutaneously in healthy adults aged 18-60 years.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2015-001932-38 |
| Trial protocol | NL |
| Global end of trial date | 18 July 2017 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 12 April 2019 |
| First version publication date | 12 April 2019 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | FLU-v-003 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02962908 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | PepTcell |
| Sponsor organisation address | Central Point, 45 Beech Street, London, United Kingdom, EC2Y 8AD |
| Public contact | Gregory Stoloff, PepTcell Limited (trading as SEEK), 44 207 153 6575, gregory.stoloff@seekacure.com |
| Scientific contact | Dr Olga Pleguezuelos, PepTcell Limited (trading as SEEK), 44 207 153 6570, olga.pleguezuelos@seekacure.com |

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 | 30 April 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 18 July 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 July 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

(1) Cellular Immunogenicity

- To evaluate the cellular immune responses based on multi-parametric FACS analysis in all subjects at 0 and 42 and 180 days following FLU-v vaccination.
- To evaluate the cellular immune responses based on IFN- γ ELISA assays in all subjects at 0 and 42 and 180 days following FLU-v vaccination.

(2) Safety

- To evaluate the solicited AEs in all subjects until 21 days after the last dosing of the study vaccine (FLU-v).
- To evaluate the unsolicited AEs and SAEs in all subjects during the whole study period.

Protection of trial subjects:

Subjects were submitted to two subcutaneous injections and three blood samplings. If subjects showed influenza symptoms a nasopharyngeal swab was taken.

There were minimal risks to these procedures who were performed by trained personnel. Doctors and nurses were always available if subjects had any concerns or suffered any discomfort. Subjects were allowed to take over the counter anti-inflammatories to alleviate any adverse events post-vaccination. Subjects remained under observation for 30min post-vaccination.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 22 August 2016 |
| 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 | Netherlands: 175 |
| Worldwide total number of subjects | 175 |
| EEA total number of subjects | 175 |

Notes:

Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |

| | |
|--|-----|
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 175 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Healthy volunteers 18-60 years old were recruited from the Zwolle city of the Netherlands during the summer of 2016. Interested subjects were screened over the phone before being invited for the screening visit on Site.

Pre-assignment

Screening details:

195 subjects were screened, 3 were lost to follow up, 9 withdrew consent and 8 failed inclusion/exclusion criteria. 175 subjects were randomised. 1 subject in 1x adjuvanted FLU-v arm received the wrong treatment and could not be included in any arm for analysis leaving the total number as 174 subjects.

Period 1

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

Blinding implementation details:

The only personnel unblinded were those formulating the vaccine ready for administration and there were not involved in other trial-related activities. The appearance of the placebo and active treatments were the same and therefore no masking of the syringes was required. The randomisation codes remained in the pharmacy under locked key only accessible to unblinded personnel.

Arms

| | |
|------------------------------|-------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | 2x Non-adjuvanted FLU-v |

Arm description:

FLU-v on Day 0 and Day 21

FLU-v: Subcutaneous injection in the upper arm with 500 ug of FLU-v as 0.5ml suspension in 0.01M HCl and 0.01M NaOH

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | FLU-v |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

500micrograms in 0.5ml

| | |
|------------------|---------------------|
| Arm title | 1x Adjuvanted FLU-v |
|------------------|---------------------|

Arm description:

adjuvanted FLU-v on Day 0, saline (0.5mL) on Day 21

adjuvanted FLU-v: Subcutaneous injection in the upper arm with 500ug of FLU-v emulsified in 0.25ml of Montanide ISA-51 adjuvant (Seppic, France) and 0.25ml of water for injection

Saline: Subcutaneous injection in the upper arm with 0.5ml of saline

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|------------------------|
| Investigational medicinal product name | FLU-v |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Emulsion for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| 500ug in 0.5ml | |
| Arm title | Non-adjuvanted Placebo |
| Arm description: | |
| saline solution (0.5ml) on Day 0 and Day 21 | |
| Saline: Subcutaneous injection in the upper arm with 0.5ml of saline | |
| Arm type | Non-adjuvanted Placebo |
| No investigational medicinal product assigned in this arm | |
| Arm title | Adjuvanted Placebo |
| Arm description: | |
| Adjuvanted placebo on Day 0, saline (0.5mL) on Day 21 | |
| Adjuvanted placebo: Subcutaneous injection in the upper arm with an emulsion made with 0.25ml of Montanide | |
| ISA-51 adjuvant (Seppic, France) and 0.25ml of water for injection | |
| Saline: Subcutaneous injection in the upper arm with 0.5ml of saline | |
| Arm type | Adjuvanted Placebo |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 1 | 2x Non-adjuvanted FLU-v | 1x Adjuvanted FLU-v | Non-adjuvanted Placebo |
|---------------------------------------|-------------------------|---------------------|------------------------|
| Started | 58 | 58 | 32 |
| vaccination completed | 58 | 54 | 32 |
| day 42 sample collected | 58 | 51 | 32 |
| day 180 sample collected | 58 | 50 | 32 |
| Completed | 58 | 50 | 32 |
| Not completed | 0 | 8 | 0 |
| Consent withdrawn by subject | - | 3 | - |
| Physician decision | - | 1 | - |
| Lost to follow-up | - | 3 | - |
| Protocol deviation | - | 1 | - |

| Number of subjects in period 1 | Adjuvanted Placebo |
|---------------------------------------|--------------------|
| Started | 27 |
| vaccination completed | 26 |
| day 42 sample collected | 26 |
| day 180 sample collected | 24 |
| Completed | 24 |
| Not completed | 3 |
| Consent withdrawn by subject | 2 |

| | |
|--------------------|---|
| Physician decision | - |
| Lost to follow-up | 1 |
| Protocol deviation | - |

Baseline characteristics

Reporting groups

| | |
|---|-------------------------|
| Reporting group title | 2x Non-adjuvanted FLU-v |
| Reporting group description: FLU-v on Day 0 and Day 21 FLU-v: Subcutaneous injection in the upper arm with 500 ug of FLU-v as 0.5ml suspension in 0.01M HCl and 0.01M NaOH | |
| Reporting group title | 1x Adjuvanted FLU-v |
| Reporting group description: adjuvanted FLU-v on Day 0, saline (0.5mL) on Day 21 adjuvanted FLU-v: Subcutaneous injection in the upper arm with 500ug of FLU-v emulsified in 0.25ml of Montanide ISA-51 adjuvant (Seppic, France) and 0.25ml of water for injection Saline: Subcutaneous injection in the upper arm with 0.5ml of saline | |
| Reporting group title | Non-adjuvanted Placebo |
| Reporting group description: saline solution (0.5ml) on Day 0 and Day 21 Saline: Subcutaneous injection in the upper arm with 0.5ml of saline | |
| Reporting group title | Adjuvanted Placebo |
| Reporting group description: Adjuvanted placebo on Day 0, saline (0.5mL) on Day 21 Adjuvanted placebo: Subcutaneous injection in the upper arm with an emulsion made with 0.25ml of Montanide ISA-51 adjuvant (Seppic, France) and 0.25ml of water for injection Saline: Subcutaneous injection in the upper arm with 0.5ml of saline | |

| Reporting group values | 2x Non-adjuvanted FLU-v | 1x Adjuvanted FLU-v | Non-adjuvanted Placebo |
|--|-------------------------|---------------------|------------------------|
| Number of subjects | 58 | 58 | 32 |
| 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) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 58 | 58 | 32 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 40.02 | 40.12 | 41.19 |
| standard deviation | ± 13.691 | ± 12.221 | ± 12.458 |
| Gender categorical Units: Subjects | | | |
| Female | 36 | 31 | 18 |
| Male | 22 | 27 | 14 |

| | | | |
|------------------------|--------------------|-------|--|
| Reporting group values | Adjuvanted Placebo | Total | |
|------------------------|--------------------|-------|--|

| | | | |
|---|----------|-----|--|
| Number of subjects | 27 | 175 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 27 | 175 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 39.07 | | |
| standard deviation | ± 13.074 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 13 | 98 | |
| Male | 14 | 77 | |

Subject analysis sets

| | |
|----------------------------|------------------------|
| Subject analysis set title | Full analysis data set |
| Subject analysis set type | Full analysis |

Subject analysis set description:

The safety population includes all subjects that received at least one influenza injection

| Reporting group values | Full analysis data set | | |
|---|------------------------|--|--|
| Number of subjects | 167 | | |
| 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) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 167 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 40.11 | | |
| standard deviation | ± 12.847 | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 95 | | |

| | | | |
|------|----|--|--|
| Male | 72 | | |
|------|----|--|--|

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|--|
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End points

End points reporting groups

| | |
|-----------------------|-------------------------|
| Reporting group title | 2x Non-adjuvanted FLU-v |
|-----------------------|-------------------------|

Reporting group description:

FLU-v on Day 0 and Day 21

FLU-v: Subcutaneous injection in the upper arm with 500 ug of FLU-v as 0.5ml suspension in 0.01M HCl and 0.01M NaOH

| | |
|-----------------------|---------------------|
| Reporting group title | 1x Adjuvanted FLU-v |
|-----------------------|---------------------|

Reporting group description:

adjuvanted FLU-v on Day 0, saline (0.5mL) on Day 21

adjuvanted FLU-v: Subcutaneous injection in the upper arm with 500ug of FLU-v emulsified in 0.25ml of Montanide ISA-51 adjuvant (Seppic, France) and 0.25ml of water for injection

Saline: Subcutaneous injection in the upper arm with 0.5ml of saline

| | |
|-----------------------|------------------------|
| Reporting group title | Non-adjuvanted Placebo |
|-----------------------|------------------------|

Reporting group description:

saline solution (0.5ml) on Day 0 and Day 21

Saline: Subcutaneous injection in the upper arm with 0.5ml of saline

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

Reporting group description:

Adjuvanted placebo on Day 0, saline (0.5mL) on Day 21

Adjuvanted placebo: Subcutaneous injection in the upper arm with an emulsion made with 0.25ml of Montanide

ISA-51 adjuvant (Seppic, France) and 0.25ml of water for injection

Saline: Subcutaneous injection in the upper arm with 0.5ml of saline

| | |
|----------------------------|------------------------|
| Subject analysis set title | Full analysis data set |
|----------------------------|------------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

The safety population includes all subjects that received at least one influenza injection

Primary: Percentage of CD4+ TH1 Cytokine Responders

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|-----------------|--|
| End point title | Percentage of CD4+ TH1 Cytokine Responders |
|-----------------|--|

End point description:

To compare the number of subjects that showed at least a two-fold increase on day 42 and day 180 following vaccination in the number of CD4+T-cells secreting TH1 cytokines in all groups.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

prevaccination, day 42 (21 days after last vaccination) and day 180.

| End point values | 2x Non-adjuvanted FLU-v | 1x Adjuvanted FLU-v | Non-adjuvanted Placebo | Adjuvanted Placebo |
|--|-------------------------|---------------------|------------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 58 | 51 | 32 | 26 |
| Units: Percentage of subjects responders | | | | |
| number (not applicable) | | | | |
| IFN gamma CD4+ day 42 | 12.96 | 76 | 3.33 | 8.70 |
| TNF alpha CD4+ day 42 | 5.46 | 44 | 3.33 | 0 |

| | | | | |
|------------------------|-------|-------|------|------|
| IL-2 CD4+ day 42 | 1.82 | 56 | 3.33 | 0 |
| IFN gamm CD4+ day 180 | 14.29 | 63.27 | 6.67 | 4.76 |
| TNF alpha CD4+ day 180 | 3.57 | 24.49 | 3.33 | 0 |
| IL-2 CD4+ day 180 | 1.79 | 57.14 | 3.33 | 0 |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | IFNg day 42 nonadjuvanted FLUv vs nonadj placebo |
| Statistical analysis description: | |
| Comparison of IFNgamma responders on day 42. Differences considered significant if p-value <0.05. | |
| Comparison groups | 2x Non-adjuvanted FLU-v v Non-adjuvanted Placebo |
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.249 |
| Method | Chi-squared |

| | |
|--|--|
| Statistical analysis title | IFNg Adj-FLU-v vs AdjPlacebo day 42 |
| Statistical analysis description: | |
| Comparison of IFNgamma responders on day 42. Differences considered significant if pvalue <0.05. | |
| Comparison groups | 1x Adjuvanted FLU-v v Adjuvanted Placebo |
| Number of subjects included in analysis | 77 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Chi-squared |

| | |
|---|--|
| Statistical analysis title | TNF day 42 nonadjuvanted FLUv vs non-adj placebo |
| Statistical analysis description: | |
| Comparison of TNF alpha responders on day 42. Differences considered significant if pvalue <0.05. | |
| Comparison groups | 2x Non-adjuvanted FLU-v v Non-adjuvanted Placebo |
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 1 |
| Method | Fisher exact |

| | |
|--|--|
| Statistical analysis title | TNF day 42adjuvanted FLUv vs adj placebo |
| Statistical analysis description: | |
| Comparison of TNF alpha responders on day 42. Differences considered significant if pvalue | |

<0.05.

| | |
|---|--|
| Comparison groups | 1x Adjuvanted FLU-v v Adjuvanted Placebo |
| Number of subjects included in analysis | 77 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Chi-squared |

| | |
|-----------------------------------|--|
| Statistical analysis title | IL-2 day 42 nonadjuvanted FLUv vs nonadj placebo |
|-----------------------------------|--|

Statistical analysis description:

Comparison of IL-2 responders on day 42. Differences considered significant if p-value <0.05.

| | |
|---|--|
| Comparison groups | 2x Non-adjuvanted FLU-v v Non-adjuvanted Placebo |
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 1 |
| Method | Fisher exact |

| | |
|-----------------------------------|---|
| Statistical analysis title | IL-2 day 42adjuvanted FLUv vs adj placebo |
|-----------------------------------|---|

Statistical analysis description:

Comparison of IL-2 responders on day 42. Differences considered significant if p-value <0.05.

| | |
|---|--|
| Comparison groups | 1x Adjuvanted FLU-v v Adjuvanted Placebo |
| Number of subjects included in analysis | 77 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Chi-squared |

| | |
|-----------------------------------|---|
| Statistical analysis title | IFNg day 180 nonadjuvanted FLUv vs nonadj placebo |
|-----------------------------------|---|

Statistical analysis description:

Comparison of IFNgamma responders on day 180. Differences considered significant if pvalue <0.05.

| | |
|---|--|
| Comparison groups | 2x Non-adjuvanted FLU-v v Non-adjuvanted Placebo |
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.483 |
| Method | Fisher exact |
| Parameter estimate | Cox proportional hazard |

| | |
|--|---|
| Statistical analysis title | IFN γ day 180 adjuvanted FLUv vs adj placebo |
| Statistical analysis description: | |
| Comparison of IFN γ responders on day 180. Differences considered significant if p-value <0.05. | |
| Comparison groups | 1x Adjuvanted FLU-v v Adjuvanted Placebo |
| Number of subjects included in analysis | 77 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Chi-squared |

| | |
|---|---|
| Statistical analysis title | TNF day 180 nonadjuvanted FLUv vs non-adj placebo |
| Statistical analysis description: | |
| Comparison of TNF alpha responders on day 180. Differences considered significant if p-value <0.05. | |
| Comparison groups | 2x Non-adjuvanted FLU-v v Non-adjuvanted Placebo |
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 1 |
| Method | Fisher exact |

| | |
|---|--|
| Statistical analysis title | TNF day 180 adjuvanted FLUv vs adj placebo |
| Statistical analysis description: | |
| Comparison of TNF alpha responders on day 180. Differences considered significant if p-value <0.05. | |
| Comparison groups | 1x Adjuvanted FLU-v v Adjuvanted Placebo |
| Number of subjects included in analysis | 77 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.013 |
| Method | Fisher exact |

| | |
|--|--|
| Statistical analysis title | IL-2 day 180 nonadjuvanted FLUv vs non-adj placebo |
| Statistical analysis description: | |
| Comparison of IL-2 responders on day 180. Differences considered significant if p-value <0.05. | |
| Comparison groups | 2x Non-adjuvanted FLU-v v Non-adjuvanted Placebo |
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 1 |
| Method | Fisher exact |

| | |
|-----------------------------------|---|
| Statistical analysis title | IL-2 day 180 adjuvanted FLUv vs adj placebo |
|-----------------------------------|---|

Statistical analysis description:

Comparison of IL-2 responders on day 180. Differences considered significant if p-value <0.05.

| | |
|---|--|
| Comparison groups | 1x Adjuvanted FLU-v v Adjuvanted Placebo |
| Number of subjects included in analysis | 77 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Chi-squared |

Primary: Percentage of Responders on Day 42 and Day 180 for IFNgamma Secretion by PBMCs

| | |
|-----------------|--|
| End point title | Percentage of Responders on Day 42 and Day 180 for IFNgamma Secretion by PBMCs |
|-----------------|--|

End point description:

Responders were defined as subjects having at least a two-fold increase in the amount of IFNg secreted on day 42 and day 180 compared the amount secreted on day 0. IFNg was measured by ELISA

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

prevaccination (day 0) to postvaccination (day 42 and day 180)

| End point values | 2x Non-adjuvanted FLU-v | 1x Adjuvanted FLU-v | Non-adjuvanted Placebo | Adjuvanted Placebo |
|---|-------------------------|---------------------|------------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 58 | 51 | 32 | 26 |
| Units: percentage of responder subjects number (not applicable) | | | | |
| day 42 | 59.57 | 95.46 | 40.00 | 45.00 |
| day 180 | 45.83 | 93.02 | 56.52 | 55.00 |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | day 42 non-adj FLU-v vs Non-Adj placebo |
|----------------------------|---|

Statistical analysis description:

Comparison of number of responders on day 42. A subject was considered a "responder" if an increase of secreted IFNgamma of at least two fold was observed from day 0 to day 42.

| | |
|---|--|
| Comparison groups | 2x Non-adjuvanted FLU-v v Non-adjuvanted Placebo |
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.113 |
| Method | Chi-squared |

| | |
|--|--|
| Statistical analysis title | day 42 adjuvanted FLUv vs adj placebo |
| Statistical analysis description: | |
| Comparison of number of responders on day 42. A subject was considered a "responder" if an increase of secreted IFNgamma of at least two fold was observed from day 0 to day 42. | |
| Comparison groups | 1x Adjuvanted FLU-v v Adjuvanted Placebo |
| Number of subjects included in analysis | 77 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Fisher exact |

| | |
|--|--|
| Statistical analysis title | day 180 non-adj FLU-v vs Non-Adj placebo |
| Statistical analysis description: | |
| Comparison of number of responders on day 180. A subject was considered a "responder" if an increase of secreted IFNgamma of at least two fold was observed from day 0 to day 180. | |
| Comparison groups | 2x Non-adjuvanted FLU-v v Non-adjuvanted Placebo |
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.399 |
| Method | Chi-squared |

| | |
|--|--|
| Statistical analysis title | day 180 adjuvanted FLUv vs adj placebo |
| Statistical analysis description: | |
| Comparison of number of responders on day 180. A subject was considered a "responder" if an increase of secreted IFNgamma of at least two fold was observed from day 0 to day 180. | |
| Comparison groups | 1x Adjuvanted FLU-v v Adjuvanted Placebo |
| Number of subjects included in analysis | 77 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Fisher exact |

Secondary: Antibody Responses to FLU-v

| | |
|---|-----------------------------|
| End point title | Antibody Responses to FLU-v |
| End point description: | |
| To evaluate the humoral immune responses specific to FLU-v from baseline in all groups 42 and 180 days following FLU-v vaccination. Specific FLU-v IgG antibodies were measured by ELISA. The geometric mean for each treatment group was provided. | |
| End point type | Secondary |
| End point timeframe: | |
| prevaccination, day 42 (21 days after last vaccination) and day 180. | |
| Analysis Population | |

| End point values | 2x Non- adjuvanted FLU-v | 1x Adjuvanted FLU-v | Non- adjuvanted Placebo | Adjuvanted Placebo |
|---------------------------------|--------------------------------|------------------------|-------------------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 58 | 51 | 32 | 26 |
| Units: IgG ng/ml | | | | |
| geometric mean (standard error) | | | | |
| day 0 | 499.11 (± 103.19) | 362.86 (± 82.93) | 331.16 (± 59.00) | 371.89 (± 67.47) |
| day 42 | 2593.02 (± 1652.34) | 8740.48 (± 2432.9) | 336.37 (± 58.92) | 381.17 (± 61.18) |
| day 180 | 1276.34 (± 344.52) | 4769.16 (± 1131.67) | 344.88 (± 66.57) | 387.26 (± 61.48) |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | day 42 non-adj FLU-v vs Non-Adj placebo |
| Statistical analysis description: | |
| Comparison of geometric mean IgG titers specific to FLU-v antigens on day 42 postvaccination. | |
| Comparison groups | 2x Non-adjuvanted FLU-v v Non-adjuvanted Placebo |
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Wilcoxon (Mann-Whitney) |

| | |
|---|--|
| Statistical analysis title | day 42 adjuvanted FLUv vs adj placebo |
| Statistical analysis description: | |
| Comparison of geometric mean IgG titers specific to FLU-v antigens on day 42 postvaccination. | |
| Comparison groups | 1x Adjuvanted FLU-v v Adjuvanted Placebo |
| Number of subjects included in analysis | 77 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Wilcoxon (Mann-Whitney) |

| | |
|--|--|
| Statistical analysis title | day 180 non-adj FLU-v vs Non-Adj placebo |
| Statistical analysis description: | |
| Comparison of geometric mean IgG titers specific to FLU-v antigens on day 180 postvaccination. | |
| Comparison groups | 2x Non-adjuvanted FLU-v v Non-adjuvanted Placebo |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Cox proportional hazard |

| | |
|---|--|
| Statistical analysis title | day 180 adjuvanted FLUv vs adj placebo |
| Statistical analysis description: Comparison of geometric mean IgG titers specific to FLU-v antigens on day 180 postvaccination. | |
| Comparison groups | 1x Adjuvanted FLU-v v Adjuvanted Placebo |
| Number of subjects included in analysis | 77 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 |
| Method | Wilcoxon (Mann-Whitney) |

Other pre-specified: Percentage of subjects positive for influenza infection

| | |
|---|---|
| End point title | Percentage of subjects positive for influenza infection |
| End point description: During the influenza season (Dec 2016 to March 2017), fully vaccinated subjects will contact the trial center immediately if they feel unwell for 24h, with a sudden onset of flu-like symptoms. The medical staff will arrange for a nasopharyngeal swab to be performed if the subject has at least one respiratory (cough, sore throat, shortness of breath, runny nose, stuffy nose, sneezing and earache) and one systemic symptom (fever, malaise, headache and myalgia (muscle and joint pain)). Swabs should be taken from the reported subjects within 3 days from the trial center being contacted or within 4 days of the onset of symptoms, whatever time is shorter. | |
| End point type | Other pre-specified |
| End point timeframe: For up to 4 months during the influenza season | |

| End point values | 2x Non-adjuvanted FLU-v | 1x Adjuvanted FLU-v | Non-adjuvanted Placebo | Adjuvanted Placebo |
|-------------------------------|-------------------------|---------------------|------------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 58 | 51 | 32 | 26 |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| positive for influenza A | 5.2 | 7.8 | 6.3 | 19.2 |
| positive for influenza B | 0 | 2.0 | 3.1 | 3.8 |
| positive for influenza H1 | 0 | 0 | 0 | 0 |
| positive for influenza H3 | 5.2 | 7.8 | 6.3 | 19.2 |
| positive for any influenza | 5.2 | 9.8 | 9.4 | 23.1 |

| | | | | |
|-------------------------------|------------------------|--|--|--|
| End point values | Full analysis data set | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 167 | | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| positive for influenza A | 8.4 | | | |
| positive for influenza B | 1.8 | | | |
| positive for influenza H1 | 0 | | | |
| positive for influenza H3 | 8.4 | | | |
| positive for any influenza | 10.2 | | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Subjects tested positive for any influenza |
| Statistical analysis description: Differences in the infection rates against any of the strains tested between treatment group and corresponding placebo. | |
| Comparison groups | 2x Non-adjuvanted FLU-v v Non-adjuvanted Placebo |
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.662 |
| Method | Fisher exact |

| | |
|--|--|
| Statistical analysis title | subjects who tested positive for influenza |
| Statistical analysis description: Differences in the infection rates against any of the strains tested between treatment group and corresponding placebo. | |
| Comparison groups | 1x Adjuvanted FLU-v v Adjuvanted Placebo |
| Number of subjects included in analysis | 77 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.168 |
| Method | Fisher exact |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From vaccination to the end of the study

Adverse event reporting additional description:

Solicited Adverse Events were collected for 21 days after each vaccination. Subjects had to fill in the AEs diary card daily and return to the clinic on the next scheduled visit.

Unsolicited Adverse Events and Severe Adverse Events were collected at any time during the study directly to the PI or study doctor.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------------|
| Reporting group title | 2x Non-adjuvanted FLU-v |
|-----------------------|-------------------------|

Reporting group description:

FLU-v on Day 0 and Day 21

FLU-v: Subcutaneous injection in the upper arm with 500 ug of FLU-v as 0.5ml suspension in 0.01M HCl and 0.01M NaOH

| | |
|-----------------------|---------------------|
| Reporting group title | 1x Adjuvanted FLU-v |
|-----------------------|---------------------|

Reporting group description:

adjuvanted FLU-v on Day 0, saline (0.5mL) on Day 21

adjuvanted FLU-v: Subcutaneous injection in the upper arm with 500ug of FLU-v emulsified in 0.25ml of Montanide ISA-51 adjuvant (Seppic, France) and 0.25ml of water for injection

Saline: Subcutaneous injection in the upper arm with 0.5ml of saline

| | |
|-----------------------|------------------------|
| Reporting group title | Non-adjuvanted Placebo |
|-----------------------|------------------------|

Reporting group description:

saline solution (0.5ml) on Day 0 and Day 21

Saline: Subcutaneous injection in the upper arm with 0.5ml of saline

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

Reporting group description:

Adjuvanted placebo on Day 0, saline (0.5mL) on Day 21

Saline: Subcutaneous injection in the upper arm with 0.5ml of saline

Adjuvanted placebo: Subcutaneous injection in the upper arm with an emulsion made with 0.25ml of Montanide

ISA-51 adjuvant (Seppic, France) and 0.25ml of water for injection

| Serious adverse events | 2x Non-adjuvanted FLU-v | 1x Adjuvanted FLU-v | Non-adjuvanted Placebo |
|---|--|---------------------|------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 58 (3.45%) | 2 / 57 (3.51%) | 0 / 32 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| upper lim | Additional description: mild/ treatment unrelated, 16 day duration | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|----------------|----------------|
| subjects affected / exposed | 0 / 58 (0.00%) | 1 / 57 (1.75%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Abdominal hernia repair | Additional description: mild/ treatment unrelated, 1 day duration | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | 0 / 57 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Myocardial infarction | Additional description: severe/ unlikely related to treatment | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 58 (1.72%) | 0 / 57 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Depression | Additional description: moderate/ treatment unrelated | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 1 / 57 (1.75%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alcohol abuse | Additional description: moderate/ treatment unrelated | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 58 (0.00%) | 1 / 57 (1.75%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|--|--|--|
| Serious adverse events | Adjuvanted Placebo | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| upper lim | Additional description: mild/ treatment unrelated, 16 day duration | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|---|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| Abdominal hernia repair | Additional description: mild/ treatment unrelated, 1 day duration | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Myocardial infarction | Additional description: severe/ unlikely related to treatment | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Depression | Additional description: moderate/ treatment unrelated | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Alcohol abuse | Additional description: moderate/ treatment unrelated | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | 2x Non-adjuvanted FLU-v | 1x Adjuvanted FLU-v | Non-adjuvanted Placebo |
|---|-------------------------|---------------------|------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 49 / 58 (84.48%) | 54 / 57 (94.74%) | 28 / 32 (87.50%) |
| Nervous system disorders | | | |

| | | | |
|--|------------------|------------------|------------------|
| Headache | | | |
| subjects affected / exposed | 13 / 58 (22.41%) | 19 / 57 (33.33%) | 14 / 32 (43.75%) |
| occurrences (all) | 20 | 30 | 18 |
| Presyncope | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 58 (3.45%) | 3 / 57 (5.26%) | 1 / 32 (3.13%) |
| occurrences (all) | 2 | 4 | 1 |
| Blood and lymphatic system disorders | | | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 7 / 58 (12.07%) | 4 / 57 (7.02%) | 3 / 32 (9.38%) |
| occurrences (all) | 8 | 4 | 4 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 14 / 58 (24.14%) | 17 / 57 (29.82%) | 11 / 32 (34.38%) |
| occurrences (all) | 16 | 25 | 12 |
| Injection site haematoma | | | |
| subjects affected / exposed | 5 / 58 (8.62%) | 19 / 57 (33.33%) | 0 / 32 (0.00%) |
| occurrences (all) | 6 | 19 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 11 / 58 (18.97%) | 18 / 57 (31.58%) | 10 / 32 (31.25%) |
| occurrences (all) | 12 | 19 | 11 |
| Injection site erythema | | | |
| subjects affected / exposed | 13 / 58 (22.41%) | 38 / 57 (66.67%) | 0 / 32 (0.00%) |
| occurrences (all) | 15 | 40 | 0 |
| Injection site induration | | | |
| subjects affected / exposed | 16 / 58 (27.59%) | 49 / 57 (85.96%) | 0 / 32 (0.00%) |
| occurrences (all) | 18 | 49 | 0 |
| Injection site pain | | | |
| subjects affected / exposed | 4 / 58 (6.90%) | 39 / 57 (68.42%) | 4 / 32 (12.50%) |
| occurrences (all) | 6 | 46 | 4 |
| Injection site pruritus | | | |
| subjects affected / exposed | 9 / 58 (15.52%) | 22 / 57 (38.60%) | 0 / 32 (0.00%) |
| occurrences (all) | 10 | 23 | 0 |
| Injection site swelling | | | |
| subjects affected / exposed | 6 / 58 (10.34%) | 38 / 57 (66.67%) | 0 / 32 (0.00%) |
| occurrences (all) | 7 | 39 | 0 |

| | | | |
|---|------------------------|------------------------|------------------------|
| Injection site warmth subjects affected / exposed occurrences (all) | 7 / 58 (12.07%) 9 | 29 / 57 (50.88%) 30 | 1 / 32 (3.13%) 1 |
| Gastrointestinal disorders | | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 7 / 58 (12.07%) 7 | 7 / 57 (12.28%) 8 | 1 / 32 (3.13%) 2 |
| Vomiting subjects affected / exposed occurrences (all) | 3 / 58 (5.17%) 3 | 5 / 57 (8.77%) 6 | 2 / 32 (6.25%) 2 |
| Diarrhoea subjects affected / exposed occurrences (all) | 6 / 58 (10.34%) 8 | 8 / 57 (14.04%) 9 | 4 / 32 (12.50%) 4 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 16 / 58 (27.59%) 18 | 17 / 57 (29.82%) 20 | 8 / 32 (25.00%) 9 |
| Nasal congestion subjects affected / exposed occurrences (all) | 15 / 58 (25.86%) 16 | 11 / 57 (19.30%) 12 | 9 / 32 (28.13%) 12 |
| Pharyngitis subjects affected / exposed occurrences (all) | 21 / 58 (36.21%) 24 | 15 / 57 (26.32%) 19 | 14 / 32 (43.75%) 17 |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 20 / 58 (34.48%) 25 | 17 / 57 (29.82%) 19 | 14 / 32 (43.75%) 20 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus subjects affected / exposed occurrences (all) | 3 / 58 (5.17%) 3 | 3 / 57 (5.26%) 3 | 3 / 32 (9.38%) 3 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain subjects affected / exposed occurrences (all) | 5 / 58 (8.62%) 5 | 5 / 57 (8.77%) 7 | 6 / 32 (18.75%) 7 |
| Myalgia | | | |

| | | | |
|---|------------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 11 / 58 (18.97%) 12 | 9 / 57 (15.79%) 12 | 6 / 32 (18.75%) 6 |
| Pain in extremity subjects affected / exposed occurrences (all) | 2 / 58 (3.45%) 2 | 6 / 57 (10.53%) 6 | 0 / 32 (0.00%) 0 |
| Arthralgia subjects affected / exposed occurrences (all) | 4 / 58 (6.90%) 5 | 5 / 57 (8.77%) 6 | 1 / 32 (3.13%) 1 |
| Infections and infestations Herpes simplex alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 58 (3.45%) 2 | 2 / 57 (3.51%) 2 | 3 / 32 (9.38%) 3 |
| Upper respiratory tract infection alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 14 / 58 (24.14%) 15 | 14 / 57 (24.56%) 15 | 13 / 32 (40.63%) 14 |
| Metabolism and nutrition disorders Decreased appetite alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 58 (1.72%) 1 | 11 / 57 (19.30%) 12 | 0 / 32 (0.00%) 0 |

| | | | |
|---|------------------------|--|--|
| Non-serious adverse events | Adjuvanted Placebo | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 27 / 27 (100.00%) | | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 10 / 27 (37.04%) 13 | | |
| Presyncope alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 27 (3.70%) 1 | | |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|------------------------|--|--|
| Lymphadenopathy subjects affected / exposed occurrences (all) | 4 / 27 (14.81%) 4 | | |
| General disorders and administration site conditions | | | |
| Fatigue subjects affected / exposed occurrences (all) | 6 / 27 (22.22%) 6 | | |
| Injection site haematoma subjects affected / exposed occurrences (all) | 5 / 27 (18.52%) 5 | | |
| Influenza like illness subjects affected / exposed occurrences (all) | 9 / 27 (33.33%) 12 | | |
| Injection site erythema subjects affected / exposed occurrences (all) | 6 / 27 (22.22%) 6 | | |
| Injection site induration subjects affected / exposed occurrences (all) | 10 / 27 (37.04%) 11 | | |
| Injection site pain subjects affected / exposed occurrences (all) | 11 / 27 (40.74%) 12 | | |
| Injection site pruritus subjects affected / exposed occurrences (all) | 10 / 27 (37.04%) 14 | | |
| Injection site swelling subjects affected / exposed occurrences (all) | 7 / 27 (25.93%) 7 | | |
| Injection site warmth subjects affected / exposed occurrences (all) | 6 / 27 (22.22%) 7 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 2 | | |
| Vomiting | | | |

| | | | |
|--|----------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 2 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 3 / 27 (11.11%) 5 | | |
| Nasal congestion subjects affected / exposed occurrences (all) | 8 / 27 (29.63%) 9 | | |
| Pharyngitis subjects affected / exposed occurrences (all) | 7 / 27 (25.93%) 8 | | |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 6 / 27 (22.22%) 7 | | |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) | 1 / 27 (3.70%) 1 | | |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 2 | | |
| Myalgia subjects affected / exposed occurrences (all) | 4 / 27 (14.81%) 5 | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 2 | | |
| Arthralgia subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |
| Infections and infestations | | | |

| | | | |
|---|----------------------|--|--|
| Herpes simplex alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 27 (3.70%) 1 | | |
| Upper respiratory tract infection alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 6 / 27 (22.22%) 6 | | |
| Metabolism and nutrition disorders Decreased appetite alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 27 (3.70%) 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.

| |
|---|
| Recruitment stopped early at 175 subjects instead of 222. Dropout rate was lower than anticipated (4% vs 20%). The number of participants recruited was considered to be sufficient to provide statistically significant data in the primary endpoints. |
|---|

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28376743>