



Clinical trial results:

Phase IIb Study of the Efficacy of FLU-v, a Broad Spectrum Influenza Vaccine in an H1N1 Influenza Healthy Human Challenge Model.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2016-002134-74 |
| Trial protocol | GB |
| Global end of trial date | 25 May 2017 |

Results information

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

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | FLU-v-004 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03180801 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | PepTcell Ltd (t/a SEEK) |
| Sponsor organisation address | Central Point, 45 Beech Street, London, United Kingdom, EC2Y 8AD |
| Public contact | Gregory Stoloff, PepTcell Ltd (t/a SEEK), +44 207 153 6575, gregory.stoloff@seekacure.com |
| Scientific contact | Dr Olga Pleguezuelos, PepTcell Ltd (t/a 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 | 24 April 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 31 March 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 25 May 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To determine the effect of FLU-v on reducing the incidence of Mild to Moderate Influenza Disease (MMID) defined as detectable viral shedding plus at least one symptom of influenza.

Protection of trial subjects:

Subjects were submitted to two subcutaneous injections with vaccine or placebo, blood samplings, intranasal inoculation with influenza virus and nasal swabs.

There were minimal risks to these procedures as they 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.

Subjects were closely monitored under quarantine after inoculation with influenza virus. The virus was GMP manufactured, dosage was optimised in previous clinical trials approved by the FDA sponsored by NIAID-NIH, US.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 18 July 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 | United Kingdom: 153 |
| Worldwide total number of subjects | 153 |
| EEA total number of subjects | 153 |

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) | 153 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Recruitment took place at two UK sites, London and Manchester, during Q3 and Q4 of 2017.

Pre-assignment

Screening details:

Only subjects with an HAI<40 for the influenza challenge strain at the time of screening were allowed to enrol the study.

Period 1

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

Blinding implementation details:

Only pharmacy staff responsible for vaccine formulation were unblinded. The randomisation codes were kept locked in the pharmacy and only unblinded staff had access to them.

The placebo and active doses were identical in appearance, thus there was no need for masking the contents of the syringe.

Arms

| | |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Adjuvanted Placebo |

Arm description:

Received two doses of adjuvanted placebo 21 days apart and 21 days after the last vaccination were inoculated with influenza.

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

Dosage and administration details:

0.5ml of water in oil emulsion composed of 0.25ml of Montanide ISA-51 adjuvant (Seppic, France) and 0.25ml of water for injection.

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

Arm description:

Subjects received one dose of adjuvanted FLU-v and 21 days later a dose of adjuvanted placebo, followed by intranasal influenza inoculation 21 days after that.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Adjuvanted placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Emulsion for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.5ml of water in oil emulsion composed of 0.25ml of Montanide ISA-51 adjuvant (Seppic, France) and 0.25ml of water for injection.

| | |
|--|------------------|
| Investigational medicinal product name | Adjuvanted FLU-v |
| Investigational medicinal product code | |
| Other name | |

| | |
|--|------------------------|
| Pharmaceutical forms | Emulsion for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| 500 micrograms of FLU-v reconstituted in 0.25ml of Montanide ISA-51 adjuvant (Seppic, France) and emulsified with 0.25ml of water for injection. | |
| Arm title | 2x Adjuvanted FLU-v |
| Arm description: | |
| Subjects received two doses of adjuvanted FLU-v 21 days apart, and 21 days after the last dose were intranasally inoculated with influenza. | |
| Arm type | Experimental |
| Investigational medicinal product name | Adjuvanted placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Emulsion for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| 0.5ml of water in oil emulsion composed of 0.25ml of Montanide ISA-51 adjuvant (Seppic, France) and 0.25ml of water for injection. | |
| Investigational medicinal product name | Adjuvanted FLU-v |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Emulsion for injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| 500 micrograms of FLU-v reconstituted in 0.25ml of Montanide ISA-51 adjuvant (Seppic, France) and emulsified with 0.25ml of water for injection. | |

| Number of subjects in period 1 | Adjuvanted Placebo | 1x adjuvanted FLU-v | 2x Adjuvanted FLU-v |
|---------------------------------------|--------------------|---------------------|---------------------|
| Started | 50 | 52 | 51 |
| Vaccinated | 50 | 48 | 48 |
| Completed | 42 | 40 | 41 |
| Not completed | 8 | 12 | 10 |
| Consent withdrawn by subject | 2 | 2 | 1 |
| Physician decision | 3 | 3 | 1 |
| Adverse event, non-fatal | 1 | - | 2 |
| Non-compliance | 1 | 4 | - |
| Lost to follow-up | - | 2 | 3 |
| inoculation target reached | 1 | 1 | 3 |

Baseline characteristics

Reporting groups

| | |
|---|---------------------|
| Reporting group title | Adjuvanted Placebo |
| Reporting group description: Received two doses of adjuvanted placebo 21 days apart and 21 days after the last vaccination were inoculated with influenza. | |
| Reporting group title | 1x adjuvanted FLU-v |
| Reporting group description: Subjects received one dose of adjuvanted FLU-v and 21 days later a dose of adjuvanted placebo, followed by intranasal influenza inoculation 21 days after that. | |
| Reporting group title | 2x Adjuvanted FLU-v |
| Reporting group description: Subjects received two doses of adjuvanted FLU-v 21 days apart, and 21 days after the last dose were intranasally inoculated with influenza. | |

| Reporting group values | Adjuvanted Placebo | 1x adjuvanted FLU-v | 2x Adjuvanted FLU-v |
|---|--------------------|---------------------|---------------------|
| Number of subjects | 50 | 52 | 51 |
| 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) | 50 | 52 | 51 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 28.9 | 30.2 | 27.6 |
| standard deviation | ± 7.6 | ± 9.3 | ± 8.7 |
| Gender categorical Units: Subjects | | | |
| Female | 17 | 19 | 14 |
| Male | 33 | 33 | 37 |

| Reporting group values | Total | | |
|---|-------|--|--|
| Number of subjects | 153 | | |
| 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) | 153 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 50 | | |
| Male | 103 | | |

Subject analysis sets

| | |
|----------------------------|---------------------------|
| Subject analysis set title | Placebo Efficacy analysis |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

ITT includes those participants in the adjuvanted placebo group who received both vaccination and challenge with an influenza virus.

| | |
|----------------------------|---------------------------|
| Subject analysis set title | 1xFLU-v Efficacy analysis |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Includes all subjects in the 1 dose adjuvanted FLU-v group who completed the vaccinations and were challenge with influenza.

| | |
|----------------------------|---------------------------|
| Subject analysis set title | 2xFLU-v efficacy analysis |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Includes all subjects in the 2 dose adjuvanted FLU-v who completed all vaccinations and were challenged with influenza.

| Reporting group values | Placebo Efficacy analysis | 1xFLU-v Efficacy analysis | 2xFLU-v efficacy analysis |
|--|---------------------------|---------------------------|---------------------------|
| Number of subjects | 42 | 40 | 41 |
| 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) | 42 | 40 | 41 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 28.8 | 29.9 | 27.4 |
| standard deviation | ± 7.5 | ± 8.9 | ± 9.2 |

| | | | |
|--------------------|----|----|----|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 13 | 12 | 11 |
| Male | 29 | 28 | 30 |

End points

End points reporting groups

| | |
|---|---------------------------|
| Reporting group title | Adjuvanted Placebo |
| Reporting group description: Received two doses of adjuvanted placebo 21 days apart and 21 days after the last vaccination were inoculated with influenza. | |
| Reporting group title | 1x adjuvanted FLU-v |
| Reporting group description: Subjects received one dose of adjuvanted FLU-v and 21 days later a dose of adjuvanted placebo, followed by intranasal influenza inoculation 21 days after that. | |
| Reporting group title | 2x Adjuvanted FLU-v |
| Reporting group description: Subjects received two doses of adjuvanted FLU-v 21 days apart, and 21 days after the last dose were intranasally inoculated with influenza. | |
| Subject analysis set title | Placebo Efficacy analysis |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: ITT includes those participants in the adjuvanted placebo group who received both vaccination and challenge with an influenza virus. | |
| Subject analysis set title | 1xFLU-v Efficacy analysis |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Includes all subjects in the 1 dose adjuvanted FLU-v group who completed the vaccinations and were challenge with influenza. | |
| Subject analysis set title | 2xFLU-v efficacy analysis |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Includes all subjects in the 2 dose adjuvanted FLU-v who completed all vaccinations and were challenged with influenza. | |

Primary: Incidence of MMID

| | |
|--|-------------------|
| End point title | Incidence of MMID |
| End point description: To determine the effect of FLU-v on reducing the incidence of Mild to Moderate Influenza Disease (MMID) defined as detectable viral shedding plus at least one symptom of influenza. This analysis was done in the ITT population which included all subjects that completed vaccination and inoculation milestones. | |
| End point type | Primary |
| End point timeframe: From 24h post-viral inoculation (Day 1) until the end of the quarantine phase on Day 7 | |

| End point values | Placebo Efficacy analysis | 1xFLU-v Efficacy analysis | 2xFLU-v efficacy analysis | |
|-----------------------------|---------------------------|---------------------------|---------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 42 | 40 | 41 | |
| Units: Number of subjects | | | | |
| Positive for MMID | 23 | 13 | 15 | |

| | | | | |
|-------------------|----|----|----|--|
| Negative for MMID | 19 | 27 | 26 | |
|-------------------|----|----|----|--|

Statistical analyses

| | |
|-----------------------------------|------------------------------------|
| Statistical analysis title | 1xFLU-v vs Placebo: incidence MMID |
|-----------------------------------|------------------------------------|

Statistical analysis description:

One-sided Fisher exact test is used to test if vaccine group has lower MMID rate.

| | |
|---|---|
| Comparison groups | Placebo Efficacy analysis v 1xFLU-v Efficacy analysis |
| Number of subjects included in analysis | 82 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0349 ^[1] |
| Method | Fisher exact |

Notes:

[1] - P-value<0.05 was considered significant, therefore the difference in the incidence of MMID in the 1xFLU-v group compared to placebo is significant.

| | |
|-----------------------------------|---------------------------------------|
| Statistical analysis title | 2xFLU-v vs Placebo: Incidence of MMID |
|-----------------------------------|---------------------------------------|

Statistical analysis description:

One-sided Fisher exact test is used to test if vaccine group has lower MMID rate.

| | |
|---|---|
| Comparison groups | Placebo Efficacy analysis v 2xFLU-v efficacy analysis |
| Number of subjects included in analysis | 83 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0745 ^[2] |
| Method | Fisher exact |

Notes:

[2] - P-value<0.05 was considered significant. The p-value obtained shows that difference in incidence of MMID between the 2xFLU-v and Placebo is not quite significant.

Primary: Incidence of Treatment Emergent AEs

| | |
|-----------------|-------------------------------------|
| End point title | Incidence of Treatment Emergent AEs |
|-----------------|-------------------------------------|

End point description:

To determine the safety and tolerability of FLU-v by means of recording the incidence of TEAEs.

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

End point timeframe:

From the first administration of treatment to the end of the study.

| End point values | Adjuvanted Placebo | 1x adjuvanted FLU-v | 2x Adjuvanted FLU-v | |
|----------------------------------|--------------------|---------------------|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 52 | 51 | |
| Units: number of TEAEs | | | | |
| arithmetic mean (standard error) | | | | |
| Overall | 1.86 (± 0.26) | 1.38 (± 0.24) | 2.35 (± 0.27) | |

| | | | | |
|------------------|--------------------|--------------------|--------------------|--|
| Pre-inoculation | 1.00 (\pm 0.21) | 0.81 (\pm 0.13) | 1.51 (\pm 0.19) | |
| Post-inoculation | 0.86 (\pm 0.16) | 0.58 (\pm 0.15) | 0.84 (\pm 0.16) | |

Statistical analyses

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Comparison of TEAEs pre-inoculation |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

One sided Fisher's exact test is used to test if AE rates of vaccine group is higher than the placebo group.

| | |
|---|--|
| Comparison groups | Adjuvanted Placebo v 1x adjuvanted FLU-v |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6474 ^[3] |
| Method | Fisher exact |

Notes:

[3] - The difference in pre-inoculation TEAEs is not significant.

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Comparison of TEAEs pre-inoculation |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

One sided Fisher's exact test is used to test if AE rates of vaccine group is higher than the placebo group.

| | |
|---|--|
| Comparison groups | Adjuvanted Placebo v 2x Adjuvanted FLU-v |
| Number of subjects included in analysis | 101 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9995 ^[4] |
| Method | Fisher exact |

Notes:

[4] - The difference in pre-inoculation TEAEs is not significant.

| | |
|-----------------------------------|--------------------------------------|
| Statistical analysis title | Comparison of TEAEs post-inoculation |
|-----------------------------------|--------------------------------------|

Statistical analysis description:

One sided Fisher's exact test is used to test if AE rates of vaccine group is higher than the placebo group.

| | |
|---|--|
| Comparison groups | Adjuvanted Placebo v 1x adjuvanted FLU-v |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.024 ^[5] |
| Method | Fisher exact |

Notes:

[5] - The lower rate of post-inoculation TEAEs in the 1xFLU-v group compared to placebo is significant.

| | |
|-----------------------------------|--------------------------------------|
| Statistical analysis title | Comparison of TEAEs post-inoculation |
|-----------------------------------|--------------------------------------|

Statistical analysis description:

One sided Fisher's exact test is used to test if AE rates of vaccine group is higher than the placebo group.

| | |
|---|--|
| Comparison groups | Adjuvanted Placebo v 2x Adjuvanted FLU-v |
| Number of subjects included in analysis | 101 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.186 ^[6] |
| Method | Fisher exact |

Notes:

[6] - The difference in post-inoculation TEAEs in the 2xFLU-v group compared to placebo is not significant.

Primary: TEAEs relatedness and severity

| | |
|-----------------|---|
| End point title | TEAEs relatedness and severity ^[7] |
|-----------------|---|

End point description:

Number of subjects with one or more AE are reported by severity and relatedness to vaccine or challenge virus inoculation.

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

End point timeframe:

From the day the first treatment was administered until the end of the study.

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: No statistical analysis were performed only summary numeration of the TEAEs in the different categories of relatedness and severity.

| End point values | Adjuvanted Placebo | 1x adjuvanted FLU-v | 2x Adjuvanted FLU-v | |
|---|--------------------|---------------------|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 52 | 51 | |
| Units: Number of subjects | | | | |
| Subjects with TEAEs definitely related to vaccine | 7 | 24 | 29 | |
| Subjects with TEAEs probably related to vaccine | 1 | 0 | 6 | |
| Subjects with TEAEs possibly related to vaccine | 3 | 2 | 3 | |
| Subjects with TEAEs definitely related to virus | 1 | 0 | 0 | |
| Subjects with TEAEs probably related to virus | 3 | 1 | 1 | |
| Subjects with TEAEs possibly related to virus | 4 | 3 | 6 | |
| Subjects with mild TEAEs | 37 | 33 | 42 | |
| Subjects with moderate TEAEs | 13 | 4 | 11 | |
| Subjects with severe TEAEs | 0 | 1 | 3 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of symptomatic and asymptomatic subjects

| | |
|-----------------|---|
| End point title | Number of symptomatic and asymptomatic subjects |
|-----------------|---|

End point description:

Number of subjects experiencing no symptoms, at least one influenza symptom and at least two influenza symptoms.

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

End point timeframe:

Quarantine period from day 1 to day 7

| End point values | Placebo Efficacy analysis | 1xFLU-v Efficacy analysis | 2xFLU-v efficacy analysis | |
|-----------------------------|---------------------------------|---------------------------------|---------------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 42 | 40 | 41 | |
| Units: Number of subjects | | | | |
| no symptoms | 5 | 6 | 11 | |
| at least one symptom | 37 | 34 | 30 | |
| at least two symptoms | 27 | 16 | 23 | |

Statistical analyses

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | At least one symptom |
|-----------------------------------|----------------------|

Statistical analysis description:

One-sided Fisher exact test is used to test if vaccine group has lower rate of "at least one symptom" than placebo.

| | |
|-------------------|---|
| Comparison groups | 1xFLU-v Efficacy analysis v Placebo Efficacy analysis |
|-------------------|---|

| | |
|---|----|
| Number of subjects included in analysis | 82 |
|---|----|

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

| | |
|---------------|-------|
| Analysis type | other |
|---------------|-------|

| | |
|---------|-------------------------|
| P-value | = 0.4648 ^[8] |
|---------|-------------------------|

| | |
|--------|--------------|
| Method | Fisher exact |
|--------|--------------|

Notes:

[8] - Differences with a P-value<0.05 were considered significant. The results of this analysis are not significant.

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | At least one symptom |
|-----------------------------------|----------------------|

Statistical analysis description:

One-sided Fisher exact test is used to test if vaccine group has lower rate of "at least one symptom" than placebo.

| | |
|-------------------|---|
| Comparison groups | Placebo Efficacy analysis v 2xFLU-v efficacy analysis |
|-------------------|---|

| | |
|---|----|
| Number of subjects included in analysis | 83 |
|---|----|

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

| | |
|---------------|-------|
| Analysis type | other |
|---------------|-------|

| | |
|---------|-------------------------|
| P-value | = 0.0736 ^[9] |
|---------|-------------------------|

| | |
|--------|--------------|
| Method | Fisher exact |
|--------|--------------|

Notes:

[9] - Differences with a P-value<0.05 were considered significant. The results of this analysis are not quite significant.

| | |
|-----------------------------------|-----------------------|
| Statistical analysis title | At least two symptoms |
|-----------------------------------|-----------------------|

Statistical analysis description:

One-sided Fisher exact test is used to test if vaccine group has lower rate of "at least two symptoms" than placebo.

| | |
|---|---|
| Comparison groups | Placebo Efficacy analysis v 1xFLU-v Efficacy analysis |
| Number of subjects included in analysis | 82 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0235 ^[10] |
| Method | Fisher exact |

Notes:

[10] - Differences with a P-value<0.05 were considered significant. The results of this analysis are significant.

| | |
|-----------------------------------|-----------------------|
| Statistical analysis title | At least two symptoms |
|-----------------------------------|-----------------------|

Statistical analysis description:

One-sided Fisher exact test is used to test if vaccine group has lower rate of "at least two symptoms" than placebo.

| | |
|---|---|
| Comparison groups | Placebo Efficacy analysis v 2xFLU-v efficacy analysis |
| Number of subjects included in analysis | 83 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2955 ^[11] |
| Method | Fisher exact |

Notes:

[11] - Differences with a P-value<0.05 were considered significant. The results of this analysis are not significant.

| | |
|-----------------------------------|-------------|
| Statistical analysis title | No symptoms |
|-----------------------------------|-------------|

Statistical analysis description:

One-sided Fisher exact test is used to test if vaccine group has lower rate of "no symptoms" than placebo.

| | |
|---|---|
| Comparison groups | Placebo Efficacy analysis v 1xFLU-v Efficacy analysis |
| Number of subjects included in analysis | 82 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | > 0.05 ^[12] |
| Method | Fisher exact |

Notes:

[12] - Differences were considered significant if P-value<0.05. The results show that the differences in this analysis are not significant.

| | |
|-----------------------------------|-------------|
| Statistical analysis title | No symptoms |
|-----------------------------------|-------------|

Statistical analysis description:

One-sided Fisher exact test is used to test if vaccine group has lower rate of "no symptoms" than placebo.

| | |
|---|---|
| Comparison groups | Placebo Efficacy analysis v 2xFLU-v efficacy analysis |
| Number of subjects included in analysis | 83 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | > 0.05 ^[13] |
| Method | Fisher exact |

Notes:

[13] - Differences were considered significant if P-value<0.05. The results show that the differences in this analysis are not significant.

Secondary: Number of subjects with detectable viral shedding

| | |
|---|---|
| End point title | Number of subjects with detectable viral shedding |
| End point description: Subjects were swabbed intranasally daily in the morning and evening. Swabs were tested for the presence of virus using a Respiratory Pathogen Panel (RPP) Luminex test. If influenza virus was detected then the subject was positive for shedding. | |
| End point type | Secondary |
| End point timeframe: Quarantine period from day 1 to day 7. | |

| End point values | Placebo Efficacy analysis | 1xFLU-v Efficacy analysis | 2xFLU-v efficacy analysis | |
|-----------------------------|---------------------------------|---------------------------------|---------------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 42 | 40 | 41 | |
| Units: Number of subjects | 23 | 15 | 18 | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | incidence of viral shedding |
| Statistical analysis description: One-sided Fisher exact test is used to test if vaccine group has lower rate of shedding compared to placebo. | |
| Comparison groups | 1xFLU-v Efficacy analysis v Placebo Efficacy analysis |
| Number of subjects included in analysis | 82 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0891 ^[14] |
| Method | Fisher exact |

Notes:

[14] - Differences were considered significant if the p-value<0.05. In this analysis the difference is not quite significant.

| | |
|---|---|
| Statistical analysis title | incidence of viral shedding |
| Statistical analysis description: One-sided Fisher exact test is used to test if vaccine group has lower rate of shedding compared to placebo. | |
| Comparison groups | Placebo Efficacy analysis v 2xFLU-v efficacy analysis |
| Number of subjects included in analysis | 83 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2208 ^[15] |
| Method | Fisher exact |

Notes:

[15] - Differences were considered significant if the p-value<0.05. In this analysis the difference is not significant.

Secondary: Shedding duration

| | |
|-----------------|-------------------|
| End point title | Shedding duration |
|-----------------|-------------------|

End point description:

Number of days from day 1 with a positive test for viral shedding in nasal swabs tested by Luminex RPP assay.

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

End point timeframe:

Starting from evening of Day 1 post-inoculation up to Day 7.

| End point values | Placebo Efficacy analysis | 1xFLU-v Efficacy analysis | 2xFLU-v efficacy analysis | |
|----------------------------------|---------------------------|---------------------------|---------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 42 | 40 | 41 | |
| Units: days | | | | |
| arithmetic mean (standard error) | 1.95 (± 0.3574) | 1.20 (± 0.3084) | 1.90 (± 0.3917) | |

Statistical analyses

| | |
|----------------------------|-------------------|
| Statistical analysis title | Shedding duration |
|----------------------------|-------------------|

Statistical analysis description:

One-sided Wilcoxon test is used to test if vaccine group has shorter shedding duration than placebo.

| | |
|-------------------|---|
| Comparison groups | Placebo Efficacy analysis v 1xFLU-v Efficacy analysis |
|-------------------|---|

| | |
|---|----|
| Number of subjects included in analysis | 82 |
|---|----|

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

| | |
|---------------|-------|
| Analysis type | other |
|---------------|-------|

| | |
|---------|--------------------------|
| P-value | = 0.0501 ^[16] |
|---------|--------------------------|

| | |
|--------|-------------------------|
| Method | Wilcoxon (Mann-Whitney) |
|--------|-------------------------|

Notes:

[16] - Differences are considered significant if the p-value<0.05. This analysis indicates that the difference is almost significant.

| | |
|----------------------------|-------------------|
| Statistical analysis title | Shedding duration |
|----------------------------|-------------------|

Statistical analysis description:

One-sided Wilcoxon test is used to test if vaccine group has shorter shedding duration than placebo.

| | |
|-------------------|---|
| Comparison groups | Placebo Efficacy analysis v 2xFLU-v efficacy analysis |
|-------------------|---|

| | |
|---|----|
| Number of subjects included in analysis | 83 |
|---|----|

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

| | |
|---------------|-------|
| Analysis type | other |
|---------------|-------|

| | |
|---------|--------------------------|
| P-value | = 0.3139 ^[17] |
|---------|--------------------------|

| | |
|--------|-------------------------|
| Method | Wilcoxon (Mann-Whitney) |
|--------|-------------------------|

Notes:

[17] - Differences are considered significant if the p-value<0.05. This analysis indicates that the difference is not significant.

Secondary: Total viral shedding

| | |
|-----------------|----------------------|
| End point title | Total viral shedding |
|-----------------|----------------------|

End point description:

Subjects were swabbed daily (morning and evening) whilst under quarantine. The swabs were tested by RT-PCR to measure the number of copies of viral genetic material.

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

End point timeframe:

Starting from evening of Day 1 post-inoculation up to Day 7.

| End point values | Placebo Efficacy analysis | 1xFLU-v Efficacy analysis | 2xFLU-v efficacy analysis | |
|-----------------------------------|---------------------------|---------------------------|---------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 42 | 40 | 40 | |
| Units: hours*log10 copy number/ml | | | | |
| arithmetic mean (standard error) | 153.67 (± 33.39) | 98.47 (± 27.39) | 138.79 (± 31.73) | |

Statistical analyses

| | |
|----------------------------|----------------------------|
| Statistical analysis title | Total viral shedding (AUC) |
|----------------------------|----------------------------|

Statistical analysis description:

One-sided Wilcoxon test is used to test if vaccine group has smaller shedding AUC than the placebo.

| | |
|-------------------|---|
| Comparison groups | Placebo Efficacy analysis v 1xFLU-v Efficacy analysis |
|-------------------|---|

| | |
|---|----|
| Number of subjects included in analysis | 82 |
|---|----|

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

| | |
|---------------|-------|
| Analysis type | other |
|---------------|-------|

| | |
|---------|--------------------------|
| P-value | = 0.1018 ^[18] |
|---------|--------------------------|

| | |
|--------|-------------------------|
| Method | Wilcoxon (Mann-Whitney) |
|--------|-------------------------|

Notes:

[18] - Differences were considered significant if p-value<0.05. The difference in this analysis is not quite significant.

| | |
|----------------------------|----------------------------|
| Statistical analysis title | Total viral shedding (AUC) |
|----------------------------|----------------------------|

Statistical analysis description:

One-sided Wilcoxon test is used to test if vaccine group has smaller shedding AUC than the placebo.

| | |
|-------------------|---|
| Comparison groups | Placebo Efficacy analysis v 2xFLU-v efficacy analysis |
|-------------------|---|

| | |
|---|----|
| Number of subjects included in analysis | 82 |
|---|----|

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

| | |
|---------------|-------|
| Analysis type | other |
|---------------|-------|

| | |
|---------|--------------------------|
| P-value | = 0.4808 ^[19] |
|---------|--------------------------|

| | |
|--------|-------------------------|
| Method | Wilcoxon (Mann-Whitney) |
|--------|-------------------------|

Notes:

[19] - Differences were considered significant if $p\text{-value} < 0.05$. The difference in this analysis is not significant.

Secondary: Peak viral shedding

| | |
|-----------------|---------------------|
| End point title | Peak viral shedding |
|-----------------|---------------------|

End point description:

The highest RT-qPCR (log10 copy number/ml) recorded for each subject under quarantine.

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

End point timeframe:

Starting from evening of Day 1 post-inoculation up to Day 7.

| End point values | Placebo Efficacy analysis | 1xFLU-v Efficacy analysis | 2xFLU-v efficacy analysis | |
|----------------------------------|---------------------------|---------------------------|---------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 42 | 40 | 41 | |
| Units: log10 copy number/ml | | | | |
| arithmetic mean (standard error) | 2.24 (\pm 0.40) | 1.54 (\pm 0.39) | 2.28 (\pm 0.42) | |

Statistical analyses

| | |
|----------------------------|---------------------|
| Statistical analysis title | Peak viral shedding |
|----------------------------|---------------------|

Statistical analysis description:

One-sided Wilcoxon test is used to test if vaccine group has lower peak viral shedding than the placebo.

| | |
|-------------------|---|
| Comparison groups | Placebo Efficacy analysis v 1xFLU-v Efficacy analysis |
|-------------------|---|

| | |
|---|----|
| Number of subjects included in analysis | 82 |
|---|----|

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

| | |
|---------------|-------|
| Analysis type | other |
|---------------|-------|

| | |
|---------|-------------------------|
| P-value | = 0.128 ^[20] |
|---------|-------------------------|

| | |
|--------|-------------------------|
| Method | Wilcoxon (Mann-Whitney) |
|--------|-------------------------|

Notes:

[20] - Differences are considered significant if $p\text{-value} < 0.05$. The difference in this analysis is not quite significant.

| | |
|----------------------------|---------------------|
| Statistical analysis title | Peak viral shedding |
|----------------------------|---------------------|

Statistical analysis description:

One-sided Wilcoxon test is used to test if vaccine group has lower peak viral shedding than the placebo.

| | |
|-------------------|---|
| Comparison groups | Placebo Efficacy analysis v 2xFLU-v efficacy analysis |
|-------------------|---|

| | |
|---|----|
| Number of subjects included in analysis | 83 |
|---|----|

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

| | |
|---------------|-------|
| Analysis type | other |
|---------------|-------|

| | |
|---------|--------------------------|
| P-value | = 0.6007 ^[21] |
|---------|--------------------------|

| | |
|--------|-------------------------|
| Method | Wilcoxon (Mann-Whitney) |
|--------|-------------------------|

Notes:

[21] - Differences are considered significant if $p\text{-value} < 0.05$. The difference in this analysis is not significant.

Secondary: Symptom duration

| | |
|-----------------|------------------|
| End point title | Symptom duration |
|-----------------|------------------|

End point description:

Number of symptomatic days as per physician's assessment.

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

End point timeframe:

Starting from evening of Day 1 post-inoculation up to Day 7.

| End point values | Placebo Efficacy analysis | 1xFLU-v Efficacy analysis | 2xFLU-v efficacy analysis | |
|----------------------------------|---------------------------|---------------------------|---------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 42 | 40 | 41 | |
| Units: days | | | | |
| arithmetic mean (standard error) | 3.26 (± 0.37) | 2.67 (± 0.35) | 2.76 (± 0.37) | |

Statistical analyses

| | |
|----------------------------|----------------------|
| Statistical analysis title | Duration of symptoms |
|----------------------------|----------------------|

Statistical analysis description:

One-sided Wilcoxon test is used to test if vaccine group has shorter duration of symptoms than the placebo.

| | |
|-------------------|---|
| Comparison groups | Placebo Efficacy analysis v 1xFLU-v Efficacy analysis |
|-------------------|---|

| | |
|---|----|
| Number of subjects included in analysis | 82 |
|---|----|

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

| | |
|---------------|-------|
| Analysis type | other |
|---------------|-------|

| | |
|---------|--------------------------|
| P-value | = 0.1416 ^[22] |
|---------|--------------------------|

| | |
|--------|-------------------------|
| Method | Wilcoxon (Mann-Whitney) |
|--------|-------------------------|

Notes:

[22] - Differences are considered significant when p-value<0.05. The difference in this analysis is not quite significant.

| | |
|----------------------------|----------------------|
| Statistical analysis title | Duration of symptoms |
|----------------------------|----------------------|

Statistical analysis description:

One-sided Wilcoxon test is used to test if vaccine group has shorter duration of symptoms than the placebo.

| | |
|-------------------|---|
| Comparison groups | Placebo Efficacy analysis v 2xFLU-v efficacy analysis |
|-------------------|---|

| | |
|---|----|
| Number of subjects included in analysis | 83 |
|---|----|

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

| | |
|---------------|-------|
| Analysis type | other |
|---------------|-------|

| | |
|---------|--------------------------|
| P-value | = 0.1469 ^[23] |
|---------|--------------------------|

| | |
|--------|-------------------------|
| Method | Wilcoxon (Mann-Whitney) |
|--------|-------------------------|

Notes:

[23] - Differences are considered significant when p-value<0.05. The difference in this analysis is not quite significant.

Secondary: Average number of symptoms experienced

| | |
|-----------------|--|
| End point title | Average number of symptoms experienced |
|-----------------|--|

| | |
|---|-----------|
| End point description: | |
| Sum of symptoms experienced divided by the number of days in which symptoms were collected. | |
| End point type | Secondary |
| End point timeframe: | |
| Starting from evening of Day 1 post-inoculation up to Day 7. | |

| End point values | Placebo Efficacy analysis | 1xFLU-v Efficacy analysis | 2xFLU-v efficacy analysis | |
|----------------------------------|---------------------------|---------------------------|---------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 42 | 40 | 41 | |
| Units: number of symptoms | | | | |
| arithmetic mean (standard error) | 2.57 (± 0.33) | 2.08 (± 0.32) | 2.51 (± 0.41) | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Total average symptoms experienced |
| Statistical analysis description: | |
| One-sided Wilcoxon test is used to test if vaccine group has fewer number of symptoms than placebo. | |
| Comparison groups | Placebo Efficacy analysis v 1xFLU-v Efficacy analysis |
| Number of subjects included in analysis | 82 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0795 ^[24] |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[24] - Differences are considered significant if p-value<0.05. The difference in this analysis is not quite significant.

| | |
|---|---|
| Statistical analysis title | Total average symptoms experienced |
| Statistical analysis description: | |
| One-sided Wilcoxon test is used to test if vaccine group has fewer number of symptoms than placebo. | |
| Comparison groups | Placebo Efficacy analysis v 2xFLU-v efficacy analysis |
| Number of subjects included in analysis | 83 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.271 ^[25] |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[25] - Differences are considered significant if p-value<0.05. The difference in this analysis is not significant.

Secondary: Peak number of symptoms

| | |
|--|-------------------------|
| End point title | Peak number of symptoms |
| End point description: | |
| The highest number of symptoms recorded in a time point as per physician's assessment. | |
| End point type | Secondary |

End point timeframe:

Starting from evening of Day 1 post-inoculation up to Day 7.

| End point values | Placebo Efficacy analysis | 1xFLU-v Efficacy analysis | 2xFLU-v efficacy analysis | |
|----------------------------------|---------------------------------|---------------------------------|---------------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 42 | 40 | 41 | |
| Units: number of symptoms | | | | |
| arithmetic mean (standard error) | 2.12 (\pm 0.26) | 1.68 (\pm 0.22) | 1.88 (\pm 0.28) | |

Statistical analyses

| Statistical analysis title | Peak number of symptoms |
|----------------------------|-------------------------|
|----------------------------|-------------------------|

Statistical analysis description:

One-sided Wilcoxon test is used to test if vaccine group has fewer peak number of symptoms than placebo.

| | |
|---|---|
| Comparison groups | Placebo Efficacy analysis v 1xFLU-v Efficacy analysis |
| Number of subjects included in analysis | 82 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0985 ^[26] |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[26] - Differences are considered significant if p-value<0.05. The difference in this analysis is not quite significant.

| Statistical analysis title | Peak number of symptoms |
|----------------------------|-------------------------|
|----------------------------|-------------------------|

Statistical analysis description:

One-sided Wilcoxon test is used to test if vaccine group has fewer peak number of symptoms than placebo.

| | |
|---|---|
| Comparison groups | Placebo Efficacy analysis v 2xFLU-v efficacy analysis |
| Number of subjects included in analysis | 83 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.178 ^[27] |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[27] - Differences are considered significant if p-value<0.05. The difference in this analysis is not significant.

Secondary: Self-assessed symptom severity score (FLU-PRO)

| | |
|-----------------|--|
| End point title | Self-assessed symptom severity score (FLU-PRO) |
|-----------------|--|

End point description:

The mean of self-assessed daily symptom score over all study quarantine days.

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

End point timeframe:

Starting from evening of Day 1 post-inoculation up to Day 7.

| End point values | Placebo Efficacy analysis | 1xFLU-v Efficacy analysis | 2xFLU-v efficacy analysis | |
|----------------------------------|---------------------------------|---------------------------------|---------------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 42 | 40 | 41 | |
| Units: symptom score | | | | |
| arithmetic mean (standard error) | 0.05 (\pm 0.01) | 0.03 (\pm 0.01) | 0.04 (\pm 0.01) | |

Statistical analyses

| Statistical analysis title | Total symptom score (FLU-PRO) |
|---|---|
| Statistical analysis description: One-sided Wilcoxon test is used to test if vaccine group has lower FluPro scores than placebo. | |
| Comparison groups | Placebo Efficacy analysis v 1xFLU-v Efficacy analysis |
| Number of subjects included in analysis | 82 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0638 ^[28] |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[28] - Differences are considered significant if p-value<0.05. The difference in this analysis is not quite significant.

| Statistical analysis title | Total symptom score (FLU-PRO) |
|---|---|
| Statistical analysis description: One-sided Wilcoxon test is used to test if vaccine group has lower FluPro scores than placebo. | |
| Comparison groups | Placebo Efficacy analysis v 2xFLU-v efficacy analysis |
| Number of subjects included in analysis | 83 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.2009 ^[29] |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[29] - Differences are considered significant if p-value<0.05. The difference in this analysis is not significant.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of first administration of vaccine to the date of inoculation with the challenge virus.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

Reporting groups

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

Reporting group description:

Received two doses of adjuvanted placebo 21 days apart and 21 days after the last vaccination were inoculated with influenza.

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

Reporting group description:

Subjects received one dose of adjuvanted FLU-v and 21 days later a dose of adjuvanted placebo, followed by intranasal influenza inoculation 21 days after that.

| | |
|-----------------------|---------------------|
| Reporting group title | 2x Adjuvanted FLU-v |
|-----------------------|---------------------|

Reporting group description:

Subjects received two doses of adjuvanted FLU-v 21 days apart, and 21 days after the last dose were intranasally inoculated with influenza.

| Serious adverse events | Adjuvanted Placebo | 1x adjuvanted FLU-v | 2x Adjuvanted FLU-v |
|---|--------------------|---------------------|---------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 0 / 52 (0.00%) | 0 / 51 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |

Frequency threshold for reporting non-serious adverse events: 4 %

| Non-serious adverse events | Adjuvanted Placebo | 1x adjuvanted FLU-v | 2x Adjuvanted FLU-v |
|---|--------------------|---------------------|---------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 40 / 50 (80.00%) | 33 / 52 (63.46%) | 45 / 51 (88.24%) |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | 0 / 52 (0.00%) | 2 / 51 (3.92%) |
| occurrences (all) | 3 | 0 | 2 |
| Aspartate aminotransferase increased | | | |

| | | | |
|--|------------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 3 / 50 (6.00%) 3 | 0 / 52 (0.00%) 0 | 2 / 51 (3.92%) 2 |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 2 / 50 (4.00%) 2 | 0 / 52 (0.00%) 0 | 0 / 51 (0.00%) 0 |
| Nervous system disorders | | | |
| Dizziness subjects affected / exposed occurrences (all) | 4 / 50 (8.00%) 4 | 2 / 52 (3.85%) 2 | 2 / 51 (3.92%) 2 |
| Headache subjects affected / exposed occurrences (all) | 11 / 50 (22.00%) 11 | 5 / 52 (9.62%) 5 | 13 / 51 (25.49%) 13 |
| Blood and lymphatic system disorders | | | |
| Neutropenia subjects affected / exposed occurrences (all) | 0 / 50 (0.00%) 0 | 0 / 52 (0.00%) 0 | 3 / 51 (5.88%) 3 |
| General disorders and administration site conditions | | | |
| Injection site induration subjects affected / exposed occurrences (all) | 9 / 50 (18.00%) 9 | 24 / 52 (46.15%) 24 | 31 / 51 (60.78%) 31 |
| Injection site pain subjects affected / exposed occurrences (all) | 0 / 50 (0.00%) 0 | 1 / 52 (1.92%) 1 | 3 / 51 (5.88%) 3 |
| Gastrointestinal disorders | | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 3 / 50 (6.00%) 3 | 1 / 52 (1.92%) 1 | 1 / 51 (1.96%) 1 |
| Nausea subjects affected / exposed occurrences (all) | 1 / 50 (2.00%) 1 | 0 / 52 (0.00%) 0 | 3 / 51 (5.88%) 3 |
| Toothache alternative assessment type: Non- systematic subjects affected / exposed occurrences (all) | 0 / 50 (0.00%) 0 | 0 / 52 (0.00%) 0 | 3 / 51 (5.88%) 3 |
| Reproductive system and breast disorders | | | |

| | | | |
|---|---|--|--|
| Dysmenorrhoea subjects affected / exposed occurrences (all) | 3 / 50 (6.00%) 3 | 2 / 52 (3.85%) 2 | 1 / 51 (1.96%) 1 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 0 / 50 (0.00%) 0 | 3 / 52 (5.77%) 3 | 0 / 51 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all) | 0 / 50 (0.00%) 0 | 3 / 52 (5.77%) 3 | 0 / 51 (0.00%) 0 |
| Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Oral herpes alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Laceration alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 50 (0.00%) 0 6 / 50 (12.00%) 6 1 / 50 (2.00%) 1 14 / 50 (28.00%) 14 2 / 50 (4.00%) 2 | 0 / 52 (0.00%) 0 0 / 52 (0.00%) 0 1 / 52 (1.92%) 1 9 / 52 (17.31%) 9 0 / 52 (0.00%) 0 | 3 / 51 (5.88%) 3 3 / 51 (5.88%) 3 3 / 51 (5.88%) 3 8 / 51 (15.69%) 8 0 / 51 (0.00%) 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 26 September 2016 | Section 7.2; Inclusion Criteria 9: Clarification to participant asthma history prior to entry into study. Section 7.2; Inclusion Criteria 11: Clarification on the time-point for acquiring a subject's medical history from their GP. Section 18.7.1; Informed consent procedure: Amended to include Investigator or delegate to conduct participant consenting. Section 18.7.3; Information for General Practitioners: Amendment to the requirement for participant's medical history from their GP. |
| 18 April 2017 | Pages 1, 6 and 12 updated to reflect change in PI. Section 6.3.1 and throughout updated to reflect exploratory endpoints may be reported separately from CSR. Section 9.3.1 correction for consistency that subjects will be admitted to the Quarantine unit with a minimum 20 days not 21 days post second vaccination. Section 9.3.1 and throughout a clarification that serology test and result must be available within 90 days of Day 0 inoculation Section 13.1.2 inspection of the eyes removed from mandatory list in directed physical examination. Section 13.2.2 language inserted to state how missing Flu-PRO data will be handled. |

Notes:

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/17668898>

<http://www.ncbi.nlm.nih.gov/pubmed/2257516>

<http://www.ncbi.nlm.nih.gov/pubmed/25994549>

<http://www.ncbi.nlm.nih.gov/pubmed/26084515>

<http://www.ncbi.nlm.nih.gov/pubmed/25416753>