# Clinical trial results:
# A Phase II, Open-Label, Single-Arm, Multicenter Study to Evaluate the Safety and Immunogenicity of a Trivalent, Surface Antigen Inactivated Subunit Influenza Virus Vaccine (Agrippal®) in Healthy Adults

## Summary

| | |
|---|---|
| EudraCT number | 2013-000545-39 |
| Trial protocol | BE |
| Global end of trial date | 20 August 2013 |

### Results information

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 28 July 2016 |
| First version publication date | 18 November 2014 |
| Version creation reason | • Correction of full data set<br>Required for the re-QC project because of the EudraCT system glitch and possible updates to results may be required.<br>Moreover, a change in system user for this study is necessary. |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | V71_34S |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01879553 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Novartis Vaccines and Diagnostics S.r.l. |
| Sponsor organisation address | Via Fiorentina, 1, Siena, Italy, 53100 |
| Public contact | Michelangelo Barone, Novartis Vaccines and Diagnostics S.r.l., +39 0577243516, michelangelo.barone@novartis.com |
| Scientific contact | Michelangelo Barone, Novartis Vaccines and Diagnostics S.r.l., +39 0577243516, michelangelo.barone@novartis.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 | 04 September 2013 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 20 August 2013 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Immunogenicity Objective
To evaluate the antibody response to each influenza vaccine antigen after vaccination with the TIV vaccine, as measured by single radial hemolysis (SRH) or hemagglutination inhibition (HI) assay in accordance with Guidance CPMP/BWP/214/96

Safety Objective
To evaluate the safety of TIV in adult subjects in compliance with the requirements of the current European Union recommendations for clinical trials related to yearly licensing of influenza vaccines (CPMP/BWP/214/96)

Protection of trial subjects:

This clinical study was designed, implemented and reported in accordance with the ICH Harmonized Tripartite Guidelines for GCP, with applicable local regulations, including the European Directive 2001/20/EC, the US CFR Title 21, and the Japanese Ministry of Health, Labor, and Welfare, Novartis codes on the protection of human rights, and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 29 July 2013 |
| 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 | Belgium: 126 |
| Worldwide total number of subjects | 126 |
| EEA total number of subjects | 126 |

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) | 75 |
| From 65 to 84 years | 50 |
| 85 years and over | 1 |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled from one study center in Belgium.

### Pre-assignment

Screening details:

All enrolled subjects were included in study.

### Period 1

| | |
|---|---|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | TIV (18 to ≤ 60 Years) |

Arm description:

Adult subjects 18 to ≤60 years received one dose of a trivalent, surface antigen inactivated subunit influenza virus vaccine (TIV) formulation 2013/2014 Northern Hemisphere.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | trivalent influenza virus vaccine (surface antigen, inactivated, egg-derived) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Vaccination consisted of one 0.5 mL dose administered IM in the deltoid muscle, preferably of the non-dominant arm.

| | |
|---|---|
| **Arm title** | TIV (≥ 61 Years) |

Arm description:

Adult subjects ≥61 years received one dose of a trivalent, surface antigen inactivated subunit influenza virus vaccine (TIV) formulation 2013/2014 Northern Hemisphere.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | trivalent influenza virus vaccine (surface antigen, inactivated, egg-derived) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Vaccination consisted of one 0.5 mL dose administered IM in the deltoid muscle, preferably of the non-dominant arm.

| **Number of subjects in period 1** | TIV (18 to ≤ 60 Years) | TIV (≥ 61 Years) |
|---|---|---|
| Started | 63 | 63 |
| Completed | 62 | 63 |
| Not completed | 1 | 0 |
| Consent withdrawn by subject | 1 | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | TIV (18 to ≤ 60 Years) |
| Reporting group description: | |
| Adult subjects 18 to ≤60 years received one dose of a trivalent, surface antigen inactivated subunit influenza virus vaccine (TIV) formulation 2013/2014 Northern Hemisphere. | |
| Reporting group title | TIV (≥ 61 Years) |
| Reporting group description: | |
| Adult subjects ≥61 years received one dose of a trivalent, surface antigen inactivated subunit influenza virus vaccine (TIV) formulation 2013/2014 Northern Hemisphere. | |

| Reporting group values | TIV (18 to ≤ 60 Years) | TIV (≥ 61 Years) | Total |
|---|---|---|---|
| Number of subjects | 63 | 63 | 126 |
| Age categorical<br>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) | 63 | 12 | 75 |
| From 65-84 years | 0 | 50 | 50 |
| 85 years and over | 0 | 1 | 1 |
| Adults (18 to ≤ 60 Years) | 0 | 0 | 0 |
| Adults (≥ 61 Years) | 0 | 0 | 0 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 40 | 29 | 69 |
| Male | 23 | 34 | 57 |

| Subject analysis sets | |
|---|---|
| Subject analysis set title | Enrolled Set |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| All screened subjects who provided informed consent and provided demographic and/or baseline screening assessments and received a 'Subject ID'. | |
| Subject analysis set title | Per Protocol Set |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| All subjects who have received study vaccination and provided immunogenicity data both at baseline and after vaccination, and were not excluded due to reasons defined prior to unblinding or analysis. | |
| Subject analysis set title | Safety Set (solicited AEs and other solicited events) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| All subjects in the Exposed Set who provided postvaccination reactogenicity data. | |

| | |
|---|---|
| Subject analysis set title | Safety Set (unsolicited AEs) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

All subjects in the Exposed Set who had postvaccination unsolicited AE records.

| **Reporting group values** | Enrolled Set | Per Protocol Set | Safety Set (solicited AEs and other solicited events) |
|---|---|---|---|
| Number of subjects | 126 | 124 | 126 |
| Age categorical<br>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) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Adults (18 to ≤ 60 Years) | 63 | 61 | 63 |
| Adults (≥ 61 Years) | 63 | 63 | 63 |
| Gender categorical<br>Units: Subjects | | | |
| Female | | | |
| Male | | | |

| **Reporting group values** | Safety Set (unsolicited AEs) | | |
|---|---|---|---|
| Number of subjects | 126 | | |
| Age categorical<br>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) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Adults (18 to ≤ 60 Years) | 63 | | |
| Adults (≥ 61 Years) | 63 | | |
| Gender categorical<br>Units: Subjects | | | |
| Female | | | |
| Male | | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | TIV (18 to ≤ 60 Years) |
| Reporting group description: | |
| Adult subjects 18 to ≤60 years received one dose of a trivalent, surface antigen inactivated subunit influenza virus vaccine (TIV) formulation 2013/2014 Northern Hemisphere. | |
| Reporting group title | TIV (≥ 61 Years) |
| Reporting group description: | |
| Adult subjects ≥61 years received one dose of a trivalent, surface antigen inactivated subunit influenza virus vaccine (TIV) formulation 2013/2014 Northern Hemisphere. | |
| Subject analysis set title | Enrolled Set |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| All screened subjects who provided informed consent and provided demographic and/or baseline screening assessments and received a 'Subject ID'. | |
| Subject analysis set title | Per Protocol Set |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| All subjects who have received study vaccination and provided immunogenicity data both at baseline and after vaccination, and were not excluded due to reasons defined prior to unblinding or analysis. | |
| Subject analysis set title | Safety Set (solicited AEs and other solicited events) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| All subjects in the Exposed Set who provided postvaccination reactogenicity data. | |
| Subject analysis set title | Safety Set (unsolicited AEs) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| All subjects in the Exposed Set who had postvaccination unsolicited AE records. | |

### Primary: Percentages of Subjects With Single Radial Hemolysis (SRH) Areas ≥25mm2, Against Each of Three Vaccine Strains After Receiving One Dose of TIV

| | |
|---|---|
| End point title | Percentages of Subjects With Single Radial Hemolysis (SRH) Areas ≥25mm2, Against Each of Three Vaccine Strains After Receiving One Dose of TIV[1] |
| End point description: | |
| Immunogenicity was assessed in terms of percentages of subjects in both age groups with SRH areas ≥25mm2 against each of the three vaccine strains, three weeks after receiving one dose of TIV.<br>The related European (CHMP) criterion for the assessment of immunogenicity is met if the percentage of subjects achieving post vaccination SRH areas ≥ 25mm2 is >70% for adults aged 18 to ≤60 years and >60% for subjects aged ≥61 years. | |
| End point type | Primary |
| End point timeframe: | |
| Day 22 post vaccination | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistical analysis done.

| End point values | TIV (18 to ≤ 60 Years) | TIV (≥ 61 Years) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 61 | 63 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Day 1 (H1N1 strain) | 52 (39 to 65) | 41 (29 to 54) | | |
| Day 22 (H1N1 strain) | 100 (94 to 100) | 78 (66 to 87) | | |
| Day 1 (H3N2 strain) | 31 (20 to 44) | 46 (33 to 59) | | |
| Day 22 (H3N2 strain) | 92 (82 to 97) | 78 (66 to 87) | | |
| Day 1 (B strain) | 38 (26 to 51) | 67 (54 to 78) | | |
| Day 22 (B strain) | 92 (82 to 97) | 89 (78 to 95) | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Percentages of Subjects With Seroconversion or Significant Increase in SRH Area, against Each of Three Vaccine Strains After Receiving One Dose of TIV

| End point title | Percentages of Subjects With Seroconversion or Significant Increase in SRH Area, against Each of Three Vaccine Strains After Receiving One Dose of TIV[2] |
|---|---|

End point description:

Immunogenicity was assessed in terms of percentages of subjects in both age groups achieving seroconversion or significant increase by SRH area against each of the three vaccine strains, three weeks after receiving one dose of TIV.
Seroconversion is defined as percentage of subjects with a pre vaccination SRH area ≤4mm2 achieving a post vaccination SRH area ≥25 mm2. Significant increase is defined as percentage of subjects with a pre-vaccination SRH area >4mm2 achieving at least 50% increase in post vaccination SRH area.
The related European (CHMP) criterion for the assessment of immunogenicity is met if >40% for adults aged 18 to ≤60 years and >30% for subjects aged ≥61 years achieve seroconversion or significant increase in post-vaccination SRH areas.

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

End point timeframe:

Day 22 post vaccination

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistical analysis done.

| End point values | TIV (18 to ≤ 60 Years) | TIV (≥ 61 Years) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 61 | 63 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| H1N1 strain | 69 (56 to 80) | 49 (36 to 62) | | |
| H3N2 strain | 70 (57 to 81) | 43 (30 to 56) | | |
| B strain | 70 (57 to 81) | 30 (19 to 43) | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Geometric Mean Ratio of Post Vaccination Versus Pre Vaccination GMAs, After one Dose of TIV

| End point title | Geometric Mean Ratio of Post Vaccination Versus Pre Vaccination GMAs, After one Dose of TIV[3] |
|---|---|

End point description:

The antibody responses were evaluated in terms of GMRs of post vaccination GMAs to pre vaccination GMAs against each of the three vaccine strains, three weeks after receiving one dose of TIV.
The related European (CHMP) criterion for the assessment of immunogenicity is met if the GMR day 22/day 1 is >2.5 for adults aged 18 to ≤60 years and > 2.0 in for subjects aged ≥61 years.

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

End point timeframe:

Day 22 post vaccination

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistical analysis done.

| End point values | TIV (18 to ≤ 60 Years) | TIV (≥ 61 Years) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 61 | 63 | | |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H1N1 strain | 3.41 (2.51 to 4.63) | 1.85 (1.52 to 2.25) | | |
| H3N2 strain | 3.07 (2.45 to 3.85) | 1.74 (1.46 to 2.08) | | |
| B strain | 2.06 (1.75 to 2.42) | 1.49 (1.29 to 1.73) | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentages of Subjects With Haemagglutination Inhibition (HI) Titers ≥40, against Each of Three Vaccine Strains After Receiving One Dose of TIV

| End point title | Percentages of Subjects With Haemagglutination Inhibition (HI) Titers ≥40, against Each of Three Vaccine Strains After Receiving One Dose of TIV[4] |
|---|---|

End point description:

Immunogenicity was assessed in terms of percentages of subjects in both age groups with HI titers ≥40, against each of the three vaccine strains, three weeks after receiving one dose of TIV.
The related European (CHMP) criterion for the assessment of immunogenicity is met if the percentage of subjects achieving HI titers ≥ 40 is >70% for adults aged 18 to ≤60 years and >60% for subjects aged ≥61 years.

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

End point timeframe:

Day 22 post vaccination

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistical analysis done.

| End point values | TIV (18 to ≤ 60 Years) | TIV (≥ 61 Years) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 61 | 63 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Day 1 (H1N1 strain) | 59 (46 to 71) | 60 (47 to 72) | | |
| Day 22 (H1N1 strain) | 100 (94 to 100) | 90 (80 to 96) | | |
| Day 1 (H3N2 strain) | 66 (52 to 77) | 86 (75 to 93) | | |
| Day 22 (H3N2 strain) | 100 (94 to 100) | 98 (91 to 100) | | |
| Day 1 (B strain) | 66 (52 to 77) | 70 (57 to 81) | | |
| Day 22 (B strain) | 98 (91 to 100) | 89 (78 to 95) | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentages of Subjects With Seroconversion or Significant Increase in HI Antibody Titers After Receiving One Dose of TIV

| End point title | Percentages of Subjects With Seroconversion or Significant Increase in HI Antibody Titers After Receiving One Dose of TIV[5] |
|---|---|

End point description:

Immunogenicity was assessed in terms of percentages of subjects in both age groups achieving seroconversion or significant increase in HI antibody titers after receiving one dose of TIV. Seroconversion is defined as percentage of subjects with a pre vaccination HI titer <10 to a post vaccination titer ≥40. Significant increase is defined as percentage of subjects with a pre vaccination HI titer ≥10 to at least a 4-fold increase in post vaccination HI antibody titers.
The related European (CHMP) criterion for the assessment of immunogenicity is met if >40% for adults aged 18 to ≤60 years and >30% for subjects aged ≥61 years achieve seroconversion or significant increase in post-vaccination HI titers.

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

End point timeframe:

Day 22 post vaccination

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistical analysis done.

| End point values | TIV (18 to ≤ 60 Years) | TIV (≥ 61 Years) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 61 | 63 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| H1N1 strain | 64 (51 to 76) | 32 (21 to 45) | | |

| | | | | |
|---|---|---|---|---|
| H3N2 strain | 64 (51 to 76) | 16 (8 to 27) | | |
| B strain | 52 (39 to 65) | 13 (6 to 23) | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Geometric Mean Ratio of Post Vaccination Versus Pre Vaccination HI Antibody Titers, After Receiving One Dose of TIV

| End point title | Geometric Mean Ratio of Post Vaccination Versus Pre Vaccination HI Antibody Titers, After Receiving One Dose of TIV[6] |
|---|---|

End point description:

The antibody responses following one dose of TIV were evaluated in terms of GMRs of post vaccination against pre vaccination geometric mean HI titers against each of the three vaccine strains, three weeks after receiving one dose of TIV.
The related European (CHMP) criterion for the assessment of immunogenicity is met if the GMR day 22/day 1 is >2.5 for adults aged 18 to ≤60 years and > 2.0 for subjects aged ≥61 years.

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

End point timeframe:

Day 22 post vaccination

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistical analysis done.

| End point values | TIV (18 to ≤ 60 Years) | TIV (≥ 61 Years) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 61 | 63 | | |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H1N1 strain | 9.65 (5.96 to 16) | 2.6 (1.97 to 3.45) | | |
| H3N2 strain | 8.47 (5.44 to 13) | 1.85 (1.37 to 2.5) | | |
| B strain | 4.56 (3.26 to 6.37) | 1.49 (1.22 to 1.83) | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of Subjects Reporting Unsolicited Adverse Events After Receiving One Dose of TIV

| End point title | Number of Subjects Reporting Unsolicited Adverse Events After Receiving One Dose of TIV[7] |
|---|---|

End point description:

The number of subjects in both age groups reporting any unsolicited AEs (between Day 1 to 4), serious adverse events (SAEs), medically attended AEs, AEs leading to premature withdrawal (Day 1 to Day 22), after receiving one dose of TIV is reported.

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

End point timeframe:

Day 1 to Day 22 post vaccination

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: There were no statistical analysis done.

| **End point values** | TIV (18 to ≤ 60 Years) | TIV (≥ 61 Years) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 63 | 63 | | |
| Units: Subjects | | | | |
| Any AE (Day 1 to 4) | 10 | 8 | | |
| At least Possibly related AE | 9 | 6 | | |
| Any SAE | 0 | 0 | | |
| At least Possibly related SAE | 0 | 0 | | |
| Medically attended AE | 0 | 0 | | |
| AE leading to discontinuation | 0 | 0 | | |
| Death | 0 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects Reporting Solicited Adverse Events After

| End point title | Number of Subjects Reporting Solicited Adverse Events After[8] |
|---|---|

End point description:

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

End point timeframe:

Day 1 to Day 4 post vaccination

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistical analysis done.

| **End point values** | TIV (18 to ≤ 60 Years) | TIV (≥ 61 Years) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 63 | | |
| Units: Subjects | | | | |
| Any Local | 38 | 18 | | |
| Injection site induration | 13 | 9 | | |
| Injection site erythema | 10 | 8 | | |
| Injection site ecchymosis | 4 | 1 | | |
| Injection site pain | 34 | 12 | | |

| | | | | |
|---|---|---|---|---|
| Any Systemic | 17 | 10 | | |
| Shivering/Chills | 0 | 0 | | |
| Myalgia | 1 | 1 | | |
| Arthralgia | 0 | 1 | | |
| Fatigue | 15 | 8 | | |
| Headache | 5 | 3 | | |
| Malaise | 2 | 4 | | |
| Fever (≥ 38°C) | 0 | 0 | | |
| Prophylactic use of analgesics/antipyretics | 0 | 0 | | |
| Therapeutic use of analgesics/antipyretics | 2 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All solicited AEs and unsolicited AEs were collected from Day1 to Day 4; all unsolicited SAEs, medically attended AEs, AEs leading to withdrawal from the study were collected from Day 1 to Day 22.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 16.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | TIV (≥ 61 Years) |

Reporting group description:

Adult subjects ≥61 years received one dose of a trivalent, surface antigen inactivated subunit influenza virus vaccine (TIV) formulation 2013/2014 Northern Hemisphere.

| | |
|---|---|
| Reporting group title | TIV (18 to ≤ 60 Years) |

Reporting group description:

Adult subjects 18 to ≤60 years received one dose of a trivalent, surface antigen inactivated subunit influenza virus vaccine (TIV) formulation 2013/2014 Northern Hemisphere.

| **Serious adverse events** | TIV (≥ 61 Years) | TIV (18 to ≤ 60 Years) | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 63 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

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

| **Non-serious adverse events** | TIV (≥ 61 Years) | TIV (18 to ≤ 60 Years) | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 27 / 63 (42.86%) | 41 / 63 (65.08%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 5 / 63 (7.94%) | |
| occurrences (all) | 3 | 5 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 8 / 63 (12.70%) | 15 / 63 (23.81%) | |
| occurrences (all) | 8 | 17 | |

| | | | |
|---|---|---|---|
| Injection site erythema | | | |
| subjects affected / exposed | 9 / 63 (14.29%) | 9 / 63 (14.29%) | |
| occurrences (all) | 17 | 16 | |
| Injection site haemorrhage | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 4 / 63 (6.35%) | |
| occurrences (all) | 2 | 8 | |
| Injection site induration | | | |
| subjects affected / exposed | 8 / 63 (12.70%) | 11 / 63 (17.46%) | |
| occurrences (all) | 12 | 19 | |
| Injection site pain | | | |
| subjects affected / exposed | 16 / 63 (25.40%) | 35 / 63 (55.56%) | |
| occurrences (all) | 16 | 36 | |
| Malaise | | | |
| subjects affected / exposed | 5 / 63 (7.94%) | 2 / 63 (3.17%) | |
| occurrences (all) | 5 | 3 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported