ClinicalTrials.gov PRS

ClinicalTrials.gov ID: NCT00560066

Study Identification

Unique Protocol ID:	V58P14
Brief Title:	Safety of a Influenza Vaccine Produced Either in Mammalian Cell Culture or in Embryonated Hen Eggs in Adults and Elderly With and Without Underlying Medical Conditions, and Immunogenicity in a Subset of Subjects With Underlying Medical Conditions
Official Title:	A Phase IV, Multi-Center, Active-Controlled, Observer-Blind Study to Evaluate the Safety of a Trivalent Subunit Influenza Vaccine Produced Either in Mammalian Cell Culture (Optaflu®) or in Embryonated Hen Eggs (Agrippal®) in Adults and Elderly With and Without Underlying Medical Conditions, and to Evaluate the Immunogenicity in a Subset of Subjects With Underlying Medical Conditions
Secondary IDs:	2007-002872-32

Study Status

Record Verification:	April 2013
Overall Status:	Completed
Study Start:	November 2007
Primary Completion:	July 2008 [Actual]
Study Completion:	July 2008 [Actual]

Sponsor/Collaborators

Sponsor:	Novartis Vaccines
Responsible Party:	Sponsor
Collaborators:	Novartis Vaccines

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes Delayed Posting? No
IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: S 7/2007 Board Name: LÄK Brandenburg Board Affiliation: Board of physicians, Brandenburg Phone: 0355 78010-53 Email:
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Germany: Paul-Ehrlich-Institute

Study Description

Brief Summary:	Evaluation of the safety of Trivalent Subunit Influenza Vaccine Produced either in Mammalian Cell Culture or in embryonated Hen Eggs in subjects 18 years of age and above with and without underlying medical conditions and evaluation of the immunogenicity in a subset of subjects with underlying medical conditions, compared to an egg-based vaccine in a post marketing setting.
Detailed Description:	

Conditions

Conditions:	Seasonal Influenza Vaccine
Keywords:	influenza vaccine

Study Design

Study Type:	Interventional
Primary Purpose:	Prevention
Study Phase:	Phase 4

Intervention Model:	Single Group Assignment
Number of Arms:	2
Masking:	Single Blind (Subject)
Allocation:	Randomized
Endpoint Classification:	Safety Study
Enrollment:	1398 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: cTIV Subjects received one vaccination of cell culture-derived influenza vaccine	Biological/Vaccine: Cell-derived influenza vaccine 1 dose of 0.5 mL in the deltoid region of the non-dominant arm
Active Comparator: TIV Subjects received one vaccination of egg-derived influenza vaccine	Biological/Vaccine: Egg-derived influenza vaccine 1 dose of 0.5 mL in the deltoid region of the non-dominant arm

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	Yes
Criteria:	Inclusion Criteria:

1. Subjects 18 years of age and above, mentally competent, willing and able to give informed consent prior to study entry;
2. Able to comply with all study procedures and requirements.

Exclusion Criteria:

1. History of any anaphylaxis, serious vaccine reactions, or hypersensitivity to any vaccine component;
2. Fatal prognosis of an underlying medical condition (<12 months life expectancy);
3. History of Guillain-Barre syndrome;
4. Bleeding diathesis or receiving anticoagulants of the coumarin type;
5. Hospitalization or residence in a nursing care facility;
6. Planned to receive seasonal influenza vaccine outside of this study;

7. Receipt of another vaccine within 2 weeks (for inactivated vaccines) or 4 weeks (for live vaccines) prior to enrollment in this study;
8. Fever (defined as axillary temperature ≥38.0°C) or any acute illness within 3 days prior to study vaccination;
9. Receipt of another investigational agent within 30 days prior to enrollment in the study or before completion of the safety follow-up period in another study, whichever is longer, and unwilling to refuse participation in another clinical study through the end safety follow up period of the study;
10. Any condition, which, in the opinion of the investigator, might prevent the subject from participation or interfere with the evaluation of the study objectives;
11. Females who were pregnant or nursing (breastfeeding) mothers, or females of childbearing potential who were sexually active and had not used or did not plan to use acceptable birth control measures during the first 3 weeks after vaccination. Oral, injected or implanted hormonal contraceptive, diaphragm or condom with spermicidal agent or intrauterine device were considered acceptable forms of birth control.

Contacts/Locations

Study Officials: Novartis Vaccines
Study Chair
Novartis Vaccines

Locations: Germany
Duisberg, Germany

Potsdam, Germany

Kiel, Germany

Unterschleißheim, Germany

Marburg, Germany

Garmisch-Partenkirchen, Germany

Regensburg, Germany

Illingen, Germany

Midlum, Germany

Balve, Germany

Laufach, Germany

Olpe, Germany

Wiesbaden, Germany

Hannover, Germany

Herborn, Germany

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	Subjects were enrolled at 17 centres in Germany.
Pre-Assignment Details	All enrolled subjects were included in the trial.

Reporting Groups

	Description
Egg-derived Vaccine (TIV)	Subjects received one vaccination of a egg-derived trivalent influenza virus vaccine.
Cell Culture-derived Vaccine (cTIV)	Subjects received one vaccination of a cell-derived trivalent influenza virus vaccine.

Overall Study

	Egg-derived Vaccine (TIV)	Cell Culture-derived Vaccine (cTIV)
Started	396	1002
Completed	390	980
Not Completed	6	22
Death	2	1
Withdrawal by Subject	0	3
Lost to Follow-up	4	10
Protocol Violation	0	1

	Egg-derived Vaccine (TIV)	Cell Culture-derived Vaccine (cTIV)
Administrative reason	0	5
Missing primary reason	0	2

Baseline Characteristics

Reporting Groups

	Description
Egg-derived Vaccine (TIV)	Subjects received one vaccination of a egg-derived trivalent influenza virus vaccine
Cell Culture-derived Vaccine (cTIV)	Subjects received one vaccination of a cell-derived trivalent influenza virus vaccine

Baseline Measures

	Egg-derived Vaccine (TIV)	Cell Culture-derived Vaccine (cTIV)	Total
Number of Participants	396	1002	1398
Age, Continuous [units: years] Mean (Standard Deviation)	47.6 (17.3)	48.7 (16.3)	48.3 (16.6)
Gender, Male/Female [units: participants]			
Female	206	533	739
Male	190	469	659

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Subjects Who Reported At Least One Reactogenicity Sign After One Vaccination of TIV or cTIV
Measure Description	Safety was assessed as the number of all subjects who reported at least one sign of reactogenicity after one vaccination of egg-derived (TIV) or cell culture-derived (cTIV) influenza virus vaccine from Day 1 through Day 7 post-vaccination.
Time Frame	From Day 1 up to and including Day 7 post-vaccination
Safety Issue?	Yes

Analysis Population Description

Analysis was performed on the safety dataset, i.e. all subjects in the exposed set who provided post-baseline safety data.

Reporting Groups

	Description
Egg-derived Vaccine (TIV)	Subjects received one vaccination of a egg-derived trivalent influenza virus vaccine
Cell Culture-derived Vaccine (cTIV)	Subjects received one vaccination of a cell-derived trivalent influenza virus vaccine

Measured Values

	Egg-derived Vaccine (TIV)	Cell Culture-derived Vaccine (cTIV)
Number of Participants Analyzed	396	1001
Number of Subjects Who Reported At Least One Reactogenicity Sign After One Vaccination of TIV or cTIV [units: Subjects]		
Any reaction - Missing	1	2
Any reaction - None	204	488
Any reaction - Other than severe	186	495
Any reaction - Severe	5	16
Local reaction - Missing	5	17
Local reaction - None	274	654
Local reaction - Other than severe	117	325
Local reaction - Severe	0	5
Systemic reaction - Missing	1	2
Systemic reaction - None	250	616
Systemic reaction - Other than severe	140	369
Systemic reaction - Severe	5	14

2. Secondary Outcome Measure:

Measure Title	Number of Healthy Adults and Elderly Who Reported Solicited Local and Systemic Adverse Events (AEs) After One Vaccination of TIV or cTIV
Measure Description	Analysis was performed on a subset of safety population which included the healthy adults (≥18 to ≤60 years) and elderly (≥61 years).

Time Frame	From Day 1 through Day 7 post-vaccination
Safety Issue?	Yes

Analysis Population Description

Analysis was done on a subset of safety population (i.e. all subjects in the exposed population who provide postvaccination safety data) which included the healthy adults and elderly.

Reporting Groups

	Description
TIV (Adults)	Subjects ≥18 to ≤60 years years-old received one vaccination of egg-derived influenza virus vaccine
cTIV (Adults)	Subjects ≥18 to ≤60 years-old received one vaccination of cell-derived influenza virus vaccine
TIV (Elderly)	Subjects ≥61 years-old received one vaccination of egg-derived influenza virus vaccine
cTIV (Elderly)	Subjects ≥61 years-old received one vaccination of cell-derived influenza virus vaccine

Measured Values

	TIV (Adults)	cTIV (Adults)	TIV (Elderly)	cTIV (Elderly)
Number of Participants Analyzed	70	235	7	11
Number of Healthy Adults and Elderly Who Reported Solicited Local and Systemic Adverse Events (AEs) After One Vaccination of TIV or cTIV [units: Subjects]				
Pain (N=66,226,7,11)	24	107	1	2
Chills (N=66,226,7,11)	1	10	0	0
Malaise (N=66,226,7,11)	7	25	0	0
Myalgia (N=66,226,7,11)	10	46	0	0
Arthralgia (N=66,226,7,11)	2	13	0	1
Headache (N=66,226,7,11)	14	47	0	2
Sweating (N=66,226,7,11)	1	13	2	0
Fatigue (N=66,226,7,11)	11	49	1	1
Fever (≥38 °C)	0	2	0	0

3. Secondary Outcome Measure:

Measure Title	Number of Adults and Elderly With Underlying Medical Conditions Who Reported Solicited Local and Systemic Adverse Events After One Vaccination of TIV or cTIV
Measure Description	Analysis was performed on a subset of safety population which included the adults (≥18 to ≤60 years) and elderly (≥61 years) with underlying medical conditions.
Time Frame	From Day 1 through Day 7 post-vaccination
Safety Issue?	Yes

Analysis Population Description

Analysis was done on the subset of safety population which included the adults and elderly with underlying medical conditions.

Reporting Groups

	Description
TIV (Adults)	Subjects ≥18 to ≤60 years-old received one vaccination of egg-derived influenza virus vaccine
cTIV (Adults)	Subjects ≥18 to ≤60 years-old received one vaccination of cell-derived influenza virus vaccine
TIV (Elderly)	Subjects ≥61 years-old received one vaccination of egg-derived influenza virus vaccine
cTIV (Elderly)	Subjects ≥61 years-old received one vaccination of cell-derived influenza virus vaccine

Measured Values

	TIV (Adults)	cTIV (Adults)	TIV (Elderly)	cTIV (Elderly)
Number of Participants Analyzed	220	490	99	265
Number of Adults and Elderly With Underlying Medical Conditions Who Reported Solicited Local and Systemic Adverse Events After One Vaccination of TIV or cTIV [units: Subjects]				
Pain (N=220,484,98,263)	77	189	15	32
Chills (N=220,484,98,263)	5	15	3	9
Malaise (N=220,484,98,263)	27	51	5	13
Myalgia (N=220,484,98,263)	32	80	15	23
Arthralgia (N=220,484,98,263)	10	35	8	14
Headache (N=220,484,98,263)	40	94	15	40
Sweating (N=220,484,98,263)	12	33	6	10
Fatigue (N=220,484,98,263)	37	102	14	33

	TIV (Adults)	cTIV (Adults)	TIV (Elderly)	cTIV (Elderly)
Fever (≥38 °C)	1	5	2	1

4. Secondary Outcome Measure:

Measure Title	Percentages Of Subjects With Underlying Medical Conditions Who Achieved Hemagglutination Inhibition (HI) Titer ≥40 After One Vaccination of TIV or cTIV
Measure Description	Immunogenicity was measured as the percentage of adults (≥18 to ≤60 years) and elderly (≥61 years) achieving HI titers ≥40 at baseline (Day 1) and three weeks (Day 22) after one vaccination of TIV or cTIV for each of three vaccine strains, evaluated using hemagglutination inhibition (HI) egg-derived antigen assay. This criterion is met according to European (CHMP) guideline if the percentage of subjects achieving HI titers ≥40 is >70% (≥18 to ≤60 years), or >60% (≥61 years).
Time Frame	Before vaccination (Day 1) and three weeks after vaccination (Day 22)
Safety Issue?	No

Analysis Population Description

Analysis was performed on the immunogenicity subset of adults and elderly with underlying medical conditions (full analysis set [FAS]: all enrolled subjects who received a study vaccine and provided one evaluable serum sample before and after baseline)

Reporting Groups

	Description
TIV (Adults)	Subjects ≥18 to ≤60 years-old received one vaccination of egg-derived influenza virus vaccine
cTIV (Adults)	Subjects ≥18 to ≤60 years-old received one vaccination of cell-derived influenza virus vaccine
TIV (Elderly)	Subjects ≥61 years-old received one vaccination of egg-derived influenza virus vaccine
cTIV (Elderly)	Subjects ≥61 years-old received one vaccination of cell-derived influenza virus vaccine

Measured Values

	TIV (Adults)	cTIV (Adults)	TIV (Elderly)	cTIV (Elderly)
Number of Participants Analyzed	118	118	25	25
Percentages Of Subjects With Underlying Medical Conditions Who Achieved Hemagglutination Inhibition (HI) Titer ≥40 After One Vaccination of TIV or cTIV [units: Percentages of Subjects] Number (95% Confidence Interval)				
A/H1N1 (Day 1)	56 (46 to 65)	53 (43 to 62)	40 (21 to 61)	56 (35 to 76)

	TIV (Adults)	cTIV (Adults)	TIV (Elderly)	cTIV (Elderly)
A/H1N1 (Day 22)	98 (94 to 100)	95 (89 to 98)	96 (80 to 100)	100 (86 to 100)
A/H3N2 (Day 1)	53 (44 to 63)	46 (37 to 55)	80 (59 to 93)	64 (43 to 82)
A/H3N2 (Day 22)	97 (92 to 99)	87 (80 to 93)	100 (86 to 100)	88 (69 to 97)
B (Day 1)	14 (8 to 21)	16 (10 to 24)	40 (21 to 61)	28 (12 to 49)
B (Day 22)	77 (68 to 84)	63 (53 to 71)	68 (46 to 85)	48 (28 to 69)

5. Secondary Outcome Measure:

Measure Title	Percentages Of Subjects Who Achieved Seroconversion Or Significant Increase In HI Titers After One Vaccination of TIV or cTIV
Measure Description	Seroconversion or significant increase in HI titer as per CHMP criteria for each of the three strains is defined as the percentage of subjects with a prevaccination HI titer <10 to a postvaccination titer ≥40; or in subjects with prevaccination HI titer ≥10, a ≥4-fold increase in postvaccination HI antibody titer. According to the CHMP criteria, the percentage of subjects achieving seroconversion/significant increase should be >40% (≥18 to ≤60 years) or >30% (≥61 years).
Time Frame	Three weeks post-vaccination (Day 22)
Safety Issue?	No

Analysis Population Description

Analysis was performed on the immunogenicity subset of adults and elderly with underlying medical conditions.

Reporting Groups

	Description
TIV (Adults)	Subjects ≥18 to ≤60 years-old received one vaccination of egg-derived influenza virus vaccine
cTIV (Adults)	Subjects ≥18 to ≤60 years-old received one vaccination of cell-derived influenza virus vaccine
TIV (Elderly)	Subjects ≥61 years-old received one vaccination of egg-derived influenza virus vaccine
cTIV (Elderly)	Subjects ≥61 years-old received one vaccination of cell-derived influenza virus vaccine

Measured Values

	TIV (Adults)	cTIV (Adults)	TIV (Elderly)	cTIV (Elderly)
Number of Participants Analyzed	118	118	25	25

	TIV (Adults)	cTIV (Adults)	TIV (Elderly)	cTIV (Elderly)
Percentages Of Subjects Who Achieved Seroconversion Or Significant Increase In HI Titers After One Vaccination of TIV or cTIV [units: Percentages of Subjects] Number (95% Confidence Interval)				
A/H1N1	64 (54 to 72)	65 (56 to 74)	72 (51 to 88)	60 (39 to 79)
A/H3N2	62 (52 to 71)	56 (46 to 65)	40 (21 to 61)	40 (21 to 61)
B	55 (46 to 64)	41 (32 to 50)	24 (9 to 45)	20 (7 to 41)

6. Secondary Outcome Measure:

Measure Title	Geometric Mean Titers of Subjects With Underlying Medical Conditions After One Vaccination of TIV or cTIV
Measure Description	Immunogenicity was measured as HI geometric mean titers (GMTs) of subjects with underlying conditions, directed against each of three vaccine strains at baseline (Day 1) and three weeks after vaccination (Day 22) in adults (≥18 to ≤60 years) and elderly (≥61 years).
Time Frame	Before vaccination (Day 1) and three weeks after vaccination (Day 22)
Safety Issue?	No

Analysis Population Description

Analysis was performed on the immunogenicity subset of adults and elderly with underlying medical conditions.

Reporting Groups

	Description
TIV (Adults)	Subjects ≥18 to ≤60 years-old received one vaccination of egg-derived influenza virus vaccine
cTIV (Adults)	Subjects ≥18 to ≤60 years-old received one vaccination of cell-derived influenza virus vaccine
TIV (Elderly)	Subjects ≥61 years-old received one vaccination of egg-derived influenza virus vaccine
cTIV (Elderly)	Subjects ≥61 years-old received one vaccination of cell-derived influenza virus vaccine

Measured Values

	TIV (Adults)	cTIV (Adults)	TIV (Elderly)	cTIV (Elderly)
Number of Participants Analyzed	118	118	25	25

	TIV (Adults)	cTIV (Adults)	TIV (Elderly)	cTIV (Elderly)
Geometric Mean Titers of Subjects With Underlying Medical Conditions After One Vaccination of TIV or cTIV [units: Titers] Geometric Mean (95% Confidence Interval)				
A/H1N1 (Day 1)	37 (27 to 49)	34 (25 to 46)	19 (11 to 33)	29 (17 to 51)
A/H1N1 (Day 22)	354 (282 to 443)	308 (246 to 386)	132 (87 to 199)	158 (104 to 238)
A/H3N2 (Day 1)	31 (23 to 40)	29 (22 to 38)	56 (32 to 97)	41 (23 to 71)
A/H3N2 (Day 22)	224 (179 to 281)	156 (125 to 196)	174 (112 to 271)	145 (93 to 226)
B (Day 1)	9.35 (7.96 to 11)	11 (9.24 to 13)	20 (13 to 31)	14 (8.86 to 21)
B (Day 22)	55 (46 to 66)	39 (32 to 47)	43 (26 to 72)	26 (16 to 44)

7. Secondary Outcome Measure:

Measure Title	Geometric Mean Ratio of Subjects With Underlying Medical Conditions After One Vaccination of TIV or cTIV
Measure Description	Immunogenicity was measured as the geometric mean ratio (GMR), calculated as the ratio of postvaccination to prevaccination HI GMTs for each of the three strains, three weeks after one vaccination (Day 22) of TIV or cTIV. CHMP criteria is considered fulfilled for each of the three strains if the geometric mean increase GMR (Day 22/Day 1) in HI antibody titer is >2.5 (≥18 to ≤60 years) or >2.0 (≥61 Years).
Time Frame	Three weeks post-vaccination (Day 22)
Safety Issue?	No

Analysis Population Description

Analysis was performed on the immunogenicity subset of adults and elderly with underlying medical conditions.

Reporting Groups

	Description
TIV (Adults)	Subjects ≥18 to ≤60 years-old received one vaccination of egg-derived influenza virus vaccine
cTIV (Adults)	Subjects ≥18 to ≤60 years-old received one vaccination of cell-derived influenza virus vaccine
TIV (Elderly)	Subjects ≥61 years-old received one vaccination of egg-derived influenza virus vaccine
cTIV (Elderly)	Subjects ≥61 years-old received one vaccination of cell-derived influenza virus vaccine

Measured Values

	TIV (Adults)	cTIV (Adults)	TIV (Elderly)	cTIV (Elderly)
Number of Participants Analyzed	118	118	25	25
Geometric Mean Ratio of Subjects With Underlying Medical Conditions After One Vaccination of TIV or cTIV [units: Ratio] Geometric Mean (95% Confidence Interval)				
A/H1N1	9.65 (7.03 to 13)	9 (6.55 to 12)	6.96 (3.98 to 12)	5.35 (3.06 to 9.37)
A/H3N2	7.35 (5.62 to 9.61)	5.32 (4.07 to 6.95)	3.12 (1.76 to 5.51)	3.58 (2.02 to 6.33)
B	5.88 (4.62 to 7.49)	3.57 (2.8 to 4.54)	2.17 (1.3 to 3.64)	1.92 (1.15 to 3.21)

Reported Adverse Events

Time Frame	Throughout the study period (day 1 to day 181).
Additional Description	All enrolled subjects met entry criteria with one exception. One subject was enrolled and randomized to the CTIV group but did not receive the study vaccine due to a protocol deviation. This subject was excluded from both the safety and immunogenicity analyses.

Reporting Groups

	Description
Egg-derived Vaccine (TIV)	Subjects received one vaccination of a egg-derived trivalent influenza virus vaccine
Cell Culture-derived Vaccine (cTIV)	Subjects received one vaccination of a cell-derived trivalent influenza virus vaccine

Serious Adverse Events

	Egg-derived Vaccine (TIV)	Cell Culture-derived Vaccine (cTIV)
	Affected/At Risk (%)	Affected/At Risk (%)
Total	10/396 (2.53%)	20/1001 (2%)
Blood and lymphatic system disorders		
Acute Chest Syndrome *	0/396 (0%)	1/1001 (0.1%)
Cardiac disorders		

	Egg-derived Vaccine (TIV)	Cell Culture-derived Vaccine (cTIV)
	Affected/At Risk (%)	Affected/At Risk (%)
Angina Pectoris *	1/396 (0.25%)	0/1001 (0%)
Aortic Valve Incompetence *	0/396 (0%)	1/1001 (0.1%)
Aortic Valve Stenosis *	0/396 (0%)	1/1001 (0.1%)
Atrial Fibrillation *	1/396 (0.25%)	0/1001 (0%)
Myocardial Infarction *	0/396 (0%)	1/1001 (0.1%)
Tachycardia *	0/396 (0%)	1/1001 (0.1%)
Ear and labyrinth disorders		
Sudden Hearing Loss *	0/396 (0%)	1/1001 (0.1%)
Gastrointestinal disorders		
Haemorrhoidal Haemorrhage *	0/396 (0%)	1/1001 (0.1%)
General disorders		
Chest Pain *	1/396 (0.25%)	0/1001 (0%)
Device Occlusion *	1/396 (0.25%)	0/1001 (0%)
Hepatobiliary disorders		
Cholecystitis *	0/396 (0%)	1/1001 (0.1%)
Cholelithiasis *	1/396 (0.25%)	0/1001 (0%)
Infections and infestations		
Device Related Infection *	0/396 (0%)	1/1001 (0.1%)
Herpes Zoster *	0/396 (0%)	1/1001 (0.1%)
Otitis Media *	0/396 (0%)	1/1001 (0.1%)
Sinusitis *	0/396 (0%)	2/1001 (0.2%)
Urinary Tract Infection *	1/396 (0.25%)	1/1001 (0.1%)
Injury, poisoning and procedural complications		
Animal Bite *	0/396 (0%)	1/1001 (0.1%)
Joint Dislocation *	1/396 (0.25%)	0/1001 (0%)
Musculoskeletal and connective tissue disorders		

	Egg-derived Vaccine (TIV)	Cell Culture-derived Vaccine (cTIV)
	Affected/At Risk (%)	Affected/At Risk (%)
Intervertebral Disc Protrusion *	0/396 (0%)	1/1001 (0.1%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Ovarian Cancer *	0/396 (0%)	1/1001 (0.1%)
Pancreatic Carcinoma *	1/396 (0.25%)	0/1001 (0%)
Nervous system disorders		
Cerebrovascular Accident *	0/396 (0%)	1/1001 (0.1%)
Optic Neuritis *	1/396 (0.25%)	0/1001 (0%)
Syncope *	0/396 (0%)	1/1001 (0.1%)
Transient Ischaemic Attack *	1/396 (0.25%)	1/1001 (0.1%)
Renal and urinary disorders		
Urethral Caruncle *	0/396 (0%)	1/1001 (0.1%)
Respiratory, thoracic and mediastinal disorders		
Pulmonary Embolism *	0/396 (0%)	2/1001 (0.2%)
Vascular disorders		
Deep Vein Thrombosis *	1/396 (0.25%)	1/1001 (0.1%)
Hypertensive Crisis *	0/396 (0%)	1/1001 (0.1%)

* Indicates events were collected by non-systematic methods.

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Egg-derived Vaccine (TIV)	Cell Culture-derived Vaccine (cTIV)
	Affected/At Risk (%)	Affected/At Risk (%)
Total	204/396 (51.52%)	568/1001 (56.74%)
General disorders		
Fatigue †	63/396 (15.91%)	185/1001 (18.48%)
Injection site pain †	117/396 (29.55%)	330/1001 (32.97%)
Malaise †	39/396 (9.85%)	89/1001 (8.89%)

	Egg-derived Vaccine (TIV)	Cell Culture-derived Vaccine (cTIV)
	Affected/At Risk (%)	Affected/At Risk (%)
Infections and infestations		
Bronchitis *	14/396 (3.54%)	59/1001 (5.89%)
Nasopharyngitis *	10/396 (2.53%)	90/1001 (8.99%)
Musculoskeletal and connective tissue disorders		
Arthralgia †	22/396 (5.56%)	76/1001 (7.59%)
Myalgia †	57/396 (14.39%)	150/1001 (14.99%)
Nervous system disorders		
Headache †	73/396 (18.43%)	198/1001 (19.78%)
Skin and subcutaneous tissue disorders		
Hyperhidrosis *	21/396 (5.3%)	56/1001 (5.59%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.

Limitations and Caveats

Because cTIV was not available, the second part of the study was not performed. In addition, as deviations from protocol procedures and GCP were identified at some sites, data collected for this study were not used to support licensure of cTIV.

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There is NOT an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Results Point of Contact:

Name/Official Title: Posting Director
Organization: Novartis Vaccines and Diagnostics
Phone:
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