ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 01/18/2013

Safety and Immunogenicity of Trivalent Subunit Influenza Vaccine Produced in Mammalian Cell Culture Using the Strain Composition 2007/2008

This study has been completed.

Sponsor:	Novartis Vaccines
Collaborators:	Novartis Vaccines
Information provided by (Responsible Party):	Novartis (Novartis Vaccines)
ClinicalTrials.gov Identifier:	NCT00511914

Purpose

Annual trial for registration of sub-unit influenza vaccine produced in mammalian cell culture, using the strain composition 2007/2008, when administered to adult and elderly subjects

Condition	Intervention	Phase
Seasonal Influenza Vaccine	Biological/Vaccine: cTIV	Phase 3

Study Type: Interventional
Study Design: Prevention, Single Group Assignment, Open Label, N/A, Safety/Efficacy Study
Official Title: A Phase III, Multicenter, Uncontrolled, Open-label Study to Evaluate Safety and Immunogenicity of a Single Intramuscular Dose of a Trivalent Subunit Influenza Vaccine Produced in Mammalian Cell Culture, Using the Strain Composition 2007/2008, When Administered to Adult and Elderly Subjects

Further study details as provided by Novartis (Novartis Vaccines):

Primary Outcome Measure:

- Geometric Mean Titers (GMT) After 1 Dose of Cell Culture Derived Vaccine (cTIV). [Time Frame: 3 weeks postvaccination (Day 22)] [Designated as safety issue: No]

  Pre and postvaccination geometric mean titers against all 3 strains were assessed by hemagglutination inhibition (HI) assay using egg derived antigen in adults and elderly subjects.

- Geometric Mean Ratio After 1 Dose of the Cell Culture Derived Vaccine (cTIV) [Time Frame: 3 weeks postvaccination (Day 22)] [Designated as safety issue: No]
  Geometric mean ratio (GMR) of Day 22 / Day 1 geometric mean antibody titers was assessed by hemagglutination inhibition (HI)assay using egg derived antigen in adults and elderly subjects. The criterion is met according to European (CHMP) guideline if the mean geometric increase GMR (Day22 / Day1) in HI antibody titer is >2.5 for adults and >2.0 for elderly subjects.
- Percentages of Subjects With HI Titer ≥40 After 1 Dose of Cell Culture Derived Vaccine (cTIV). [Time Frame: 3 weeks postvaccination (Day 22)] [Designated as safety issue: No]
  HI titer as assessed by hemagglutination inhibition (HI) assay using egg derived antigen in adults and elderly subjects. This criterion is met according to European (CHMP) guideline if the percentages of subjects achieving HI titers ≥40 is >70% for adults and >60% for elderly subjects.
- Percentages of Subjects With Seroconversion or Significant Increase After 1 Dose of Cell Culture Derived Vaccine (cTIV). [Time Frame: 3 weeks postvaccination (Day 22)] [Designated as safety issue: No]
  Proportion of subjects with either seroconversion (antibody increase from < 10 pre vaccination to ≥40 post vaccination) or significant increase (antibody titer of ≥10 pre vaccination and 4-fold antibody increase post vaccination). According to the CHMP criteria, the percentages of subjects achieving seroconversion or significant increase should be >40% for adults and >30% for elderly subjects.

Secondary Outcome Measures:
- Number of Subjects Reporting Local and Systemic Reactions [Time Frame: 3 days postvaccination] [Designated as safety issue: Yes]
  To evaluate the safety and tolerability of cell culture derived vaccine (cTIV) in adults and elderly subjects in terms of number of subjects reporting local and systemic reactions after 1 vaccine dose.

Enrollment: 135
Study Start Date: July 2007
Primary Completion Date: August 2007
Study Completion Date: August 2007

Arms	Assigned Interventions
Experimental: cTIV (Adults) Received one dose of cell-culture derived trivalent influenza vaccine (cTIV).	Biological/Vaccine: cTIV One dose (0.5 mL) of cell culture-derived influenza vaccine, administered in the deltoid muscle
Experimental: cTIV (Elderly) Received one dose of cell-culture derived trivalent influenza vaccine (cTIV).	Biological/Vaccine: cTIV One dose (0.5 mL) of cell culture-derived influenza vaccine, administered in the deltoid muscle

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: Yes

Criteria

Inclusion Criteria:

Subjects eligible for enrollment into this study are male and female adults who were:

1. ≥ 18 years of age, mentally competent, willing and able to give informed consent prior to study entry
2. available for all the visits scheduled in the study and able to comply with all study requirements
3. in good health as determined by:

    - medical history
    - physical examination
    - clinical judgment of the investigator Written informed consent had to be obtained from all the subjects before enrollment in the study after the nature of the study had been explained.

Exclusion Criteria:

Subjects were not to be enrolled into the study if at least one of the following criteria was fulfilled:

1. Any serious chronic or acute disease such as:

    a. Cancer (leukemia, lymphomas, neoplasm), except for benign or localized skin cancer and non-metastatic prostate cancer not presently treated with chemotherapy
    b. Congestive heart failure
    c. Advanced arteriosclerotic disease
    d. Chronic obstructive pulmonary disease (COPD) requiring oxygen therapy and/or acute exacerbation of a COPD within the last 14 days.
    e. Autoimmune disease (including rheumatoid arthritis), if under immunosuppressive therapy (see below)
    f. Insulin dependent diabetes mellitus
    g. Acute or progressive hepatic disease
    h. Acute or progressive renal disease
    i. Severe neurological or psychiatric disorder
2. History of any anaphylactic reaction and/or serious allergic reaction following a vaccination, a proven hypersensitivity to any component of the study vaccine or chemically related substances
3. Known or suspected (or have a high risk of developing) impairment/alteration of immune function (excluding that normally associated with advanced age) resulting for example from:

    a. Receipt of immunosuppressive therapy (chronic therapy with immunosuppressive drugs, any parenteral or oral corticosteroid (substitution dose in case of absence of suprarenal function allowed) or cancer chemotherapy/radiotherapy) within the last 2 months and for the full length of the study,
    b. Receipt of immunostimulants,
    c. Receipt of parenteral immunoglobulin preparation, blood products, and/or plasma derivatives within the past 3 months and for the full length of the study,
    d. Suspected or known HIV infection or HIV-related disease.
4. Known or suspected history of drug or alcohol abuse
5. Bleeding diathesis or receive anticoagulants of the coumarin type
6. Women who are pregnant or woman of childbearing potential unwilling to practice acceptable contraception for the duration of the study (21 days)
7. Influenza immunization or laboratory confirmed influenza within the last 6 months and more than one influenza immunization within the past 12 months
8. Immunization with any other vaccine and/or any investigational vaccine four weeks prior to study start
9. Any significant acute or chronic infections requiring systemic antibiotic treatment or antiviral therapy within the last 7 days
10. Fever (i.e. body temperature ≥ 38.0°C) within the past 3 days prior to study entry
11. Simultaneous participation in another clinical study
12. Any condition, which, in the opinion of the investigator, might prevent the subject from participation or interfere with the evaluation of the study objectives.

Contacts and Locations

Locations

Germany

Z29, Blutspendezentrale, Gebaude Z29, Behringwerke
Emil-von-Behring-Str. 76, Marburg, Germany, 35041

Betriebsaerztlicher Dienst, Standort Marburg
Baldingerstrasse, Marburg Hessen, Germany, 35033

Investigators

Study Chair:	Novartis Vaccines	Novartis Vaccines

More Information

Responsible Party:	Novartis Vaccines
Study ID Numbers:	V58P1S 2007-001404-20
Health Authority:	Germany: Paul-Ehrlich-Institute

Study Results

Participant Flow

Reporting Groups

	Description
cTIV (Adults)	Adults 18-60 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).
cTIV (Elderly)	Elderly subjects >= 61 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).

Overall Study

	cTIV (Adults)	cTIV (Elderly)
Started	68	67
Completed	68	67
Not Completed	0	0

Baseline Characteristics

Reporting Groups

	Description
cTIV (Adults)	Adults 18-60 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).
cTIV (Elderly)	Elderly subjects >= 61 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).

Baseline Measures

	cTIV (Adults)	cTIV (Elderly)	Total
Number of Participants	68	67	135
Age, Continuous [units: years] Mean (Standard Deviation)	37.4 (12.3)	67.4 (4.7)	52.3 (17.7)
Gender, Male/Female [units: Subjects]			
Female	39	25	64
Male	29	42	71

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Geometric Mean Titers (GMT) After 1 Dose of Cell Culture Derived Vaccine (cTIV).
Measure Description	Pre and postvaccination geometric mean titers against all 3 strains were assessed by hemagglutination inhibition (HI) assay using egg derived antigen in adults and elderly subjects.
Time Frame	3 weeks postvaccination (Day 22)
Safety Issue?	No

Analysis Population Description

Analysis was done on per protocol set

Reporting Groups

	Description
cTIV (Adults)	Adults 18-60 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).
cTIV (Elderly)	Elderly subjects >= 61 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).

Measured Values

	cTIV (Adults)	cTIV (Elderly)
Number of Participants Analyzed	68	67
Geometric Mean Titers (GMT) After 1 Dose of Cell Culture Derived Vaccine (cTIV). [units: Titer] Geometric Mean (95% Confidence Interval)		
A/H1N1 Prevaccination (Day 1)	22 (14 to 33)	23 (17 to 31)
A/H1N1 Postvaccination (Day 22)	624 (442 to 881)	199 (150 to 264)
A/H3N2 Prevaccination (Day 1)	36 (24 to 56)	80 (53 to 122)
A/H3N2 Postvaccination (Day 22)	405 (299 to 547)	283 (205 to 390)
B Prevaccination (Day 1)	8.16 (6.43 to 10)	16 (12 to 21)
B Postvaccination (Day 22)	96 (66 to 139)	40 (30 to 53)

2. Primary Outcome Measure:

Measure Title	Geometric Mean Ratio After 1 Dose of the Cell Culture Derived Vaccine (cTIV)
Measure Description	Geometric mean ratio (GMR) of Day 22 / Day 1 geometric mean antibody titers was assessed by hemagglutination inhibition (HI)assay using egg derived antigen in adults and elderly subjects. The criterion is met according to European (CHMP) guideline if the mean geometric increase GMR (Day22 / Day1) in HI antibody titer is >2.5 for adults and >2.0 for elderly subjects.
Time Frame	3 weeks postvaccination (Day 22)
Safety Issue?	No

Analysis Population Description

Analysis was done on per protocol set

Reporting Groups

	Description
cTIV (Adults)	Adults 18-60 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).
cTIV (Elderly)	Elderly subjects >= 61 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).

Measured Values

	cTIV (Adults)	cTIV (Elderly)
Number of Participants Analyzed	68	67
Geometric Mean Ratio After 1 Dose of the Cell Culture Derived Vaccine (cTIV) [units: Ratio] Geometric Mean (95% Confidence Interval)		
A/H1N1 (Day 22 / Day1)	29 (18 to 46)	8.74 (6.13 to 12)
A/H3N2 (Day 22 / Day1)	11 (7.27 to 17)	3.53 (2.47 to 5.06)
B (Day 22 / Day1)	12 (7.69 to 18)	2.51 (1.93 to 3.27)

3. Primary Outcome Measure:

Measure Title	Percentages of Subjects With HI Titer ≥40 After 1 Dose of Cell Culture Derived Vaccine (cTIV).
Measure Description	HI titer as assessed by hemagglutination inhibition (HI) assay using egg derived antigen in adults and elderly subjects. This criterion is met according to European (CHMP) guideline if the percentages of subjects achieving HI titers ≥40 is >70% for adults and >60% for elderly subjects.
Time Frame	3 weeks postvaccination (Day 22)
Safety Issue?	No

Analysis Population Description

Analysis was done on per protocol set

Reporting Groups

	Description
cTIV (Adults)	Adults 18-60 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).
cTIV (Elderly)	Elderly subjects >= 61 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).

Measured Values

	cTIV (Adults)	cTIV (Elderly)
Number of Participants Analyzed	68	67
Percentages of Subjects With HI Titer ≥40 After 1 Dose of Cell Culture Derived Vaccine (cTIV). [units: Percentages of Subjects]		

	cTIV (Adults)	cTIV (Elderly)
Number (95% Confidence Interval)		
A/H1N1 Prevaccination (Day 1)	35 (24 to 48)	37 (26 to 50)
A/H1N1 Postvaccination (Day 22)	96 (88 to 99)	96 (87 to 99)
A/H3N2 Prevaccination (Day 1)	51 (39 to 64)	72 (59 to 82)
A/H3N2 Postvaccination (Day 22)	97 (90 to 100)	96 (87 to 99)
B Prevaccination (Day 1)	13 (6 to 24)	28 (18 to 41)
B Postvaccination (Day 22)	79 (68 to 88)	66 (53 to 77)

4. Primary Outcome Measure:

Measure Title	Percentages of Subjects With Seroconversion or Significant Increase After 1 Dose of Cell Culture Derived Vaccine (cTIV).
Measure Description	Proportion of subjects with either seroconversion (antibody increase from < 10 pre vaccination to ≥40 post vaccination) or significant increase (antibody titer of ≥10 pre vaccination and 4-fold antibody increase post vaccination). According to the CHMP criteria, the percentages of subjects achieving seroconversion or significant increase should be >40% for adults and >30% for elderly subjects.
Time Frame	3 weeks postvaccination (Day 22)
Safety Issue?	No

Analysis Population Description

Analysis was done on per protocol set

Reporting Groups

	Description
cTIV (Adults)	Adults 18-60 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).
cTIV (Elderly)	Elderly subjects >= 61 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).

Measured Values

	cTIV (Adults)	cTIV (Elderly)
Number of Participants Analyzed	68	67

	cTIV (Adults)	cTIV (Elderly)
Percentages of Subjects With Seroconversion or Significant Increase After 1 Dose of Cell Culture Derived Vaccine (cTIV). [units: Percentages of Subjects] Number (95% Confidence Interval)		
A/H1N1	79 (68 to 88)	67 (55 to 78)
A/H3N2	72 (60 to 82)	40 (28 to 53)
B	65 (52 to 76)	25 (16 to 37)

5. Secondary Outcome Measure:

Measure Title	Number of Subjects Reporting Local and Systemic Reactions
Measure Description	To evaluate the safety and tolerability of cell culture derived vaccine (cTIV) in adults and elderly subjects in terms of number of subjects reporting local and systemic reactions after 1 vaccine dose.
Time Frame	3 days postvaccination
Safety Issue?	Yes

Analysis Population Description

Analysis was done on safety set.

Reporting Groups

	Description
cTIV (Adults)	Adults 18-60 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).
cTIV (Elderly)	Elderly subjects >= 61 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).

Measured Values

	cTIV (Adults)	cTIV (Elderly)
Number of Participants Analyzed	68	67
Number of Subjects Reporting Local and Systemic Reactions [units: Subjects]		
Redness/Erythema	0	2
Swelling	2	2

	cTIV (Adults)	cTIV (Elderly)
Pain	31	16
Ecchymosis	1	2
Induration	4	4
Fever (≥ 38°C)	0	0
Malaise	5	3
Fatigue	10	8
Headache	12	9
Sweating	2	3
Myalgia	3	2
Arthralgia	4	3
Chills	0	0

Reported Adverse Events

Time Frame	All solicited adverse reactions were collected from Day 0 - Day 3. All unsolicited adverse events and Serious adverse events were collected throughout study period (Day 0- Day 21).
Additional Description	[Not specified]

Reporting Groups

	Description
cTIV (Adults)	Adults 18-60 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).
cTIV (Elderly)	Elderly subjects >= 61 years of age received one dose of cell culture derived trivalent influenza vaccine (cTIV).

Serious Adverse Events

	cTIV (Adults)	cTIV (Elderly)
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/68 (0%)	0/67 (0%)

Other Adverse Events

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

	cTIV (Adults)	cTIV (Elderly)
	Affected/At Risk (%)	Affected/At Risk (%)
Total	40/68 (58.82%)	21/67 (31.34%)
General disorders		
Fatigue [A] †	10/68 (14.71%)	8/67 (11.94%)
Injection site induration [A] †	5/68 (7.35%)	5/67 (7.46%)
Injection site pain [A] †	31/68 (45.59%)	16/67 (23.88%)
Malaise [A] †	5/68 (7.35%)	3/67 (4.48%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	4/68 (5.88%)	3/67 (4.48%)
Nervous system disorders		
Headache [A] †	12/68 (17.65%)	9/67 (13.43%)

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA 10.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is more than 60 days but less than or equal to 180 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

Results Point of Contact:

Name/Official Title: Posting Director

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