Sponsor: Novartis Vaccines and Diagnostics, Srl

Investigational Product: Trivalent influenza virus vaccine (surface antigen, inactivated, egg derived: Agrippal S)

Indication: Prophylaxis for seasonal flu

Protocol Number: V71_21

Protocol Title: Evaluating the safeness of the trivalent influenza virus vaccine (surface antigen, inactivated, egg derived) in preventing flu on Vietnamese volunteers

Phase of Development: Bridge Study

Study Period: Overall Study

Date of first enrolment: 29 JAN 10

Date of last visit: 04 MAR 10

Methodology:

This open label, uncontrolled, clinical trial was performed in healthy Vietnamese volunteers. A single 0.5mL dose of trivalent influenza virus vaccine (surface antigen, inactivated, egg derived) was administered intramuscularly into the deltoid muscle.

Information on Adverse Events (AEs) after vaccination including local, systemic reactions were followed up and recorded into standard case report forms within 30 minutes after vaccination and for 7 days after vaccination, and the safety follow up including AE and Serious Adverse Events (SAEs) was of approximately 30 days for each individual subject.

Number of Subjects (planned and analyzed):

A total of 30 subjects were planned to be enrolled in the study. Overall, 33 subjects were actually enrolled in the study.

Study Center:

One center in Vietnam.

Publication (reference) and/or ClinicalTrials.gov National Clinical Trial (NCT) Number:

NCT Number: NCT01123954.

Objectives:

The study was designed to evaluate the safety of a single 0.5mL dose of the trivalent influenza virus vaccine (surface antigen, inactivated, egg derived: Agrippal S) administered to Vietnamese volunteers.

Test Product, Dose, Mode of Administration, Lot Number:

A 0.5 mL dose of the trivalent inactivated subunit influenza vaccine (Lot number: 095601B) contains the purified viral envelope-glycoproteins neuraminidase (NA) and hemagglutinin (HA), including HA of the A/H1N1, A/H3N2 and B antigens recommended for the influenza season 2009/2010 in the Northern Hemisphere.

The vaccination course consisted of a single IM injection, administered in the deltoid muscle, preferably of the non-dominant arm.

Duration of Study:

Date of first enrollment: 29 JAN 10

Date of last visit: 04 MAR 10

Reference Therapy, Dose, Mode of Administration, Lot Number:

None.

Statistical Methods:

The analysis of the safety data was performed descriptively.

Diagnosis and Main Criteria for Inclusion and Exclusion:

Inclusion Criteria:
1. Healthy volunteers aged 1 to 45 years with no previous history of influenza vaccination;
2. Able to understand, consent to study participation and comply with all study procedures.

Exclusion Criteria:
1. Subjects who had the suspected symptoms of influenza: cough, sore throat, stuffy or running nose, headache, malaise, myalgia and arthralgia, weakness, chilly or sweat;
2. Subjects with prior history of allergy to any components of candidate vaccine;
3. Subjects with hypersensitivity to eggs or chicken protein, kanamycin, neomycin sulphate, formaldehyde, cetyltrimethylammonium bromide (CTAB) and polysorbate 80.

4. 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;
5. Subjects immunodeficient due to treatment;

Criteria for Evaluation:

Criteria For Assessing Safety Objectives**:**
The safety of the study vaccine was assessed in terms of number of subjects with reported local and systemic reactions, as well as the number of subjects with reported adverse events, including serious adverse events.

Results:

Summary of Study Terminations – Enrolled Population

Study Terminations	N=33
None	0

Overview of Subject Populations

Vaccine Group	Vaccine Name N=33
Enrolled	33 (100%)
Safety Population	33 (100%)

Demographic and Other Baseline Characteristics

	Enrolled and Evaluable for Safety N=33
Age (Yrs):	26.48±9.34
Gender:	
Male	21 (63.6%)
Female	12 (36.4%)

Overview of Solicited Reactions (Number and Percentage of Subjects With any Solicited Reaction)

Solicited Reaction	N=33
Any Reaction	13 (39.4%)
Any Local Reaction	11 (33.3%)
Any Systemic Reaction	7 (21.3%)
Any Severe Reaction	0
Any Severe Local Reaction	0
Any Severe Systemic Reaction	0

Number (and Percentage) of Subjects with Local Reactions Reported between Day 0 to Study Termination

Local Reaction		Day 0 to Day 6 N=33	Day 7 to Study End N=33
Redness	Any	3 (9.1%)	0
	Size <10 mm	3 (9.1%)	0
	Size 11 to 25 mm	0	0
	Size 26 to 50 mm	0	0
	Size >50 mm	0	0
Swelling	Any	1 (3%)	0
	Size <10 mm	0	0
	Size 11 to 25 mm	1 (3%)	0
	Size 26 to 50 mm	0	0
	Size >50 mm	0	0
Injection site Pain	1: Pain when exposure	8 (24.2%)	0
	2: Pain that impacts the normal	3 (9.1%)	0
	3: Pain that set obstacles to the normal activities.	0	0
Other local symptoms	Pustules located only on arm and there was no involvement of face, chest, abdomen and leg	0	1 (3%)

Number (and Percentage) of Subjects with Systemic Reactions Reported Between Day 0 to Study Termination

Systemic Reaction		Day 0 to Day 6 N=33	Day 7 to Day N=33
Fever	≤ 38.5°C - < 39 °C	0	1 (3%)
	≤ 39 - <39.5°C	0	0
	≥ 39.5 °C	0	0
Myalgia	1: Withstandable myalgia	4 (12.1%)	0
	2: Myalgia that impacts the normal activities	2 (6.1%)	0
	3: Myalgia that set obstacles to the normal activities.	0	0
Arthralgia	1: Withstandable arthralgia	1 (3%)	0
	2: Arthralgia that impacts the normal activities	0	0
	3: Arthralgia that set obstacles to the normal activities.	0	0
Malaise	1: Withstandable malaise	0	1 (3%)
	2: Malaise that impacts the normal activities	0	0
	3: Malaise that set obstacles to the normal activities.	0	0
Headache	1: Withstandable headache	4 (12.1%)	0
	2: Headache that impacts the normal activities	0	0
	3: Headache that set obstacles to the normal activities.	0	0
Nausea	1: Withstandable nausea	0	0
	2: Nausea that impacts the normal activities	0	0
	3: Nausea that set obstacles to the normal activities.	0	0
Vomiting	1: Withstandable vomiting	0	0
	2: Vomiting that impacts the normal activities	0	0
	3: Vomiting that set obstacles to the normal activities.	0	0
Diarrhea	1: Withstandable diarrhea	0	0
	2: Diarrhea that impacts the normal activities	0	1 (3%)
	3: Diarrhea that set obstacles to the normal activities.	0	0
Stomachache	1: Withstandable stomachache	0	0
	2: Stomachache that impacts the normal activities	0	1 (3%)
	3: Stomachache that set obstacles to the normal activities.	0	0
Rash	1: Withstandable rash	0	1 (3%)
	2: Rash that impacts the normal activities	0	0
	3: Rash that set obstacles to the normal activities.	0	0
Urticaria	1: In 01 specific area	0	0
	2: In 02 or 03 areas but not over 03	0	0
	3: In at least 04 areas	0	0

Overview of Unsolicited Reactions (Number and Percentage of Subjects With any Unsolicited Reaction)

Unsolicited Reaction	N=33
None	0

Summary of Subjects with Serious Adverse Events Sorted by System Organ Class and Preferred Term

System Organ Class	Preferred Term	N=33
None	N/A	

Summary of Subjects with Unsolicited Non-Serious Adverse Events Reported by >5% of Subjects, Sorted by System Organ Class and Preferred Term

System Organ Class	Preferred Term	N=33
None	N/A	0

Conclusion:

This study was designed, according to local regulations, to evaluate the safety of a trivalent influenza virus vaccine (surface antigen, inactivated, egg derived) in Vietnamese volunteers and to support the licensure of the trivalent influenza virus vaccine (surface antigen, inactivated, egg derived) in Vietnam.
Trivalent influenza virus vaccine (surface antigen, inactivated, egg derived) was well tolerated and safe influenza vaccine with no SAEs, deaths or premature withdrawal reported. These safety data collected in this study are in line with those reported in subjects from other ethnic origins, and confirm trivalent influenza virus vaccine (surface antigen, inactivated, egg derived) a well-tolerated and safe seasonal influenza vaccine, fully supporting trivalent influenza virus vaccine (surface antigen, inactivated, egg derived) licensure in Vietnam.

Date of Clinical Trial Report: 27 APR 10

Date Inclusion on Novartis Clinical Trial Results Database: 09 JAN 12

Date of Latest Update: 09 JAN 12

Reason for Update: Releasing data on EudraCT.