A Phase 3, Open-label Trial to Evaluate the Safety, Tolerability, and Immunogenicity of 13-valent Pneumococcal Conjugate Vaccine Followed by 23-valent Pneumococcal Polysaccharide Vaccine in Recipients of Allogeneic Hematopoietic Stem Cell Transplant Aged 2 Years and Older

Published: 15-03-2010
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Primary Objective: *To evaluate the immune responses 1 month after 3 doses of 13vPnC as measured by fold rises of serotype-specific immunoglobulin G (IgG) geometric mean concentrations (GMCs) in subjects *2 years of age. Secondary Objectives: *To...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON36335

Source
ToetsingOnline

Brief title
13vPnC - Stem Cell study

Condition

- Bacterial infectious disorders

Synonym
pneumococcal infection, streptococcus pneumonia

Research involving
Human

Sponsors and support

Primary sponsor: Pfizer
Source(s) of monetary or material Support: Wyeth pharmaceuticals

Intervention

Keyword: 13-valent Pneumococcal Conjugate Vaccine, 23-valent Pneumococcal Polysaccharide Vaccine, pneumococcal disease, Stem cell transplant

Outcome measures

Primary outcome

Primary Objective: *To evaluate the immune responses 1 month after 3 doses of 13vPnC as measured by fold rises of serotype-specific immunoglobulin G (IgG) geometric mean concentrations (GMCs) in subjects *2 years of age.

Secondary outcome

Secondary Objectives: *To evaluate the immune responses 1 month after 3 doses of 13vPnC as measured by serotype-specific IgG GMCs in subjects *2 years of age. *To evaluate the immune responses 1 month after 4 doses of 13vPnC as measured by serotype-specific IgG GMCs and fold rises of IgG GMCs in subjects *2 years of age. *To evaluate the immune responses 1 month after 3 doses and 1 month after 4 doses of 13vPnC as measured by IgG GMCs and fold rise IgG GMCs in the pediatric subgroup (*2 to <18 years) and by serotype-specific IgG GMCs and fold rise IgG GMCs in the adult subgroup (*18 years). Exploratory Objectives: *To evaluate the immune responses measured by serotype-specific IgG GMCs and fold rise IgG GMCs in subjects *2 years of age, in the pediatric subgroup (*2

to <18 years) and in the adult subgroup (*18 years). -1 month after dose 1 and 1 month after dose 2 of 13vPnC. (Fold rise IgG GMCs: 1 month after dose 1 and 1 month after dose 2 relative to before dose 1). -Before and 1 month after dose 4 of 13vPnC. (Fold rise IgG GMCs: 1 month after dose 4 relative to before dose 4). -1 month after dose 4 of 13vPnC compared with 1 month after dose 3 of 13vPnC. (Fold rise IgG GMCs: 1 month after dose 4 relative to 1 month after dose 3). -1 month after 23vPS for the 12 common serotypes and 6A. (Fold rise IgG GMCs: 1 month after 23vPS relative to before 23vPS, 1 month after 23vPS relative to before dose 1 of 13vPnC). *To evaluate the immune response 1 month after 3 and 1 month after 4 doses of 13vPnC as measured by proportion of subjects achieving a serotype-specific IgG GMC *0.35 *g/mL in subjects *2 years of age, in the pediatric subgroup (*2 to <18 years) and in the adult subgroup (*18 years). Safety Objective: *To evaluate the acceptability of the safety profile of 13vPnC as measured by the incidence rates of local reactions, systemic events, and adverse events (AEs).

Study description

Background summary

Streptococcus pneumoniae is a significant cause of morbidity after hematopoietic stem cell transplantation (HSCT), especially after allogeneic HSCT, and particularly when complicated by graft-versus-host disease (GVHD). Current guidelines from the United States Centers for Disease Control and Prevention (CDC) and the Infectious Diseases Working Party of the European Group for Blood and Marrow Transplantation (EBMT) recommend vaccinating HSCT recipients with 23-valent pneumococcal polysaccharide vaccine (23vPS) as a single dose at 12 months (EBMT) or as sequential doses at 12 months and 24 months (CDC) after HSCT, because antibody responses to these vaccines are impaired after HSCT. Current EBMT recommendations have been further updated to

include 3 doses of 7-valent pneumococcal conjugate vaccine (7vPnC) starting as early as 3 to 6 months, to protect against pneumococcal disease caused by the serotypes in 7vPnC during the first year after HSCT. Based on current knowledge it is anticipated that future recommendations for vaccination against pneumococcal disease will include 3 doses of 7vPnC, starting as early as 3 to 6 months after HSCT and followed later by a fourth dose of 7vPnC or 1 dose of 23vPS in the second year after HSCT. Three (3) doses of 13vPnC will be administered at intervals of 1 month, starting at approximately 3 months after HSCT, followed by a fourth dose of 13vPnC at approximately 6 months after the third dose. Some patients receive immunoglobulins after HSCT; thus, the proposed start of vaccination in this study is 3 to 6 months (91 to 203 days) after HSCT, provided that the immunoglobulin administration has been stopped for at least 60 days to avoid confounding the immunogenicity results. 23vPS will be administered approximately 1 month after the fourth dose of 13vPnC because of the extended serotype coverage of 23vPS.

Study objective

Primary Objective: *To evaluate the immune responses 1 month after 3 doses of 13vPnC as measured by fold rises of serotype-specific immunoglobulin G (IgG) geometric mean concentrations (GMCs) in subjects *2 years of age. Secondary Objectives: *To evaluate the immune responses 1 month after 3 doses of 13vPnC as measured by serotype-specific IgG GMCs in subjects *2 years of age. *To evaluate the immune responses 1 month after 4 doses of 13vPnC as measured by serotype-specific IgG GMCs and fold rises of IgG GMCs in subjects *2 years of age. *To evaluate the immune responses 1 month after 3 doses and 1 month after 4 doses of 13vPnC as measured by IgG GMCs and fold rise IgG GMCs in the pediatric subgroup (*2 to <18 years) and by serotype-specific IgG GMCs and fold rise IgG GMCs in the adult subgroup (*18 years). Exploratory Objectives: *To evaluate the immune responses measured by serotype-specific IgG GMCs and fold rise IgG GMCs in subjects *2 years of age, in the pediatric subgroup (*2 to <18 years) and in the adult subgroup (*18 years). -1 month after dose 1 and 1 month after dose 2 of 13vPnC. (Fold rise IgG GMCs: 1 month after dose 1 and 1 month after dose 2 relative to before dose 1). -Before and 1 month after dose 4 of 13vPnC. (Fold rise IgG GMCs: 1 month after dose 4 relative to before dose 4). -1 month after dose 4 of 13vPnC compared with 1 month after dose 3 of 13vPnC. (Fold rise IgG GMCs: 1 month after dose 4 relative to 1 month after dose 3). -1 month after 23vPS for the 12 common serotypes and 6A. (Fold rise IgG GMCs: 1 month after 23vPS relative to before 23vPS, 1 month after 23vPS relative to before dose 1 of 13vPnC). *To evaluate the immune response 1 month after 3 and 1 month after 4 doses of 13vPnC as measured by proportion of subjects achieving a serotype-specific IgG GMC *0.35 *g/mL in subjects *2 years of age, in the pediatric subgroup (*2 to <18 years) and in the adult subgroup (*18 years). Safety Objective: *To evaluate the acceptability of the safety profile of 13vPnC as measured by the incidence rates of local reactions, systemic events, and adverse events (AEs).

Study design

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Intervention

The subjects should/ will come to the hospital 7 times. There are 2 types of requests, a vaccination visit and an inspection visit. At each visit blood samples will be taken. About 4 months after the last visit, the study doctor or nurse will call the subjects to ask how she / he feel. For 14 days after each 13vPnC vaccination the subject will answer some questions in an electronic diary. The subjects given a digital thermometer and a measurement device to take home to measure the redness or swelling that may occur at the spot where the vaccine was 13vPnC was given. Visit 1, 2, 3 and 5 are 13vPnC vaccination visits. Visit 6 is a 23vPS vaccination visit. Visit 4 and 7 are check up visits. During this visit the physical examination and vital signs will be determined.

Study burden and risks

The risk associated with the participation is not different from the standard therapy.

Contacts

Public
Pfizer

Rivium Westlaan 142
2909 LD Capelle aan den IJssel
NL
Scientific
Pfizer

Rivium Westlaan 142
2909 LD Capelle aan den IJssel
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

*Male or female subject *2 years of age. *Allogeneic HSCT for hematologic disorder. *Allogeneic HSCT with full myeloablative conditioning or reduced intensity conditioning. *Allogeneic HSCT approximately 3 to 6 months (91 days to 203 days) before enrollment. *Stable engraftment (absolute neutrophil count (ANC) >1000/µl; platelet count >50,000/µl). *Complete hematologic remission of underlying disease. *Subject or parent/legal guardian expected to be available for the entire study and can be contacted by telephone. *Subject or parent/legal guardian must be able to complete an electronic diary (e-diary) and complete all relevant study procedures during study participation. * All female and male subjects who are biologically capable of having children must agree to abstinence or commit to the use of a reliable method of birth control for 3 months after the last vaccination. * Negative urine pregnancy test for all female subjects of child bearing potential.

Exclusion criteria

*Autologous HSCT. *Receipt of donor lymphocyte infusions during the 28 days preceding enrollment. *Uncontrolled GVHD that in the opinion of the investigator would prevent the subject from participating in the study. *Lansky/Karnofsky Score *60%. *Receipt of plasma products or immunoglobulins during the 60 days preceding enrollment. *Receipt of rituximab since HSCT. *Receipt of chemotherapy since HSCT. *Human immunodeficiency virus (HIV) infection. *Lymphoproliferative disorder since HSCT. *Chronic illnesses with cardiac, pulmonary, renal, or liver failure that in the opinion of the investigator would prevent the subject participating in the study. *Vaccination with any licensed or experimental pneumococcal vaccine since HSCT. *Previous anaphylactic reaction to any vaccine or vaccine-related component. *Bleeding diathesis or condition associated with prolonged

bleeding time that would in the opinion of the investigator contraindicate intramuscular injection. *Participation in another study with ongoing use of an unlicensed investigational product from 28 days before study enrollment until the end of the study. *Participation in another study with ongoing use of a licensed investigational product that in the opinion of the investigator would interfere with the evaluation of the study objectives. *Permanent residence in a nursing home or other residential care facility. *Pregnant or breastfeeding female subject. *Subject who is a direct relative (child, grandchild, parent, or grandparent) of study personnel, or is a member of the study personnel.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-11-2011
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Pneumo 23
Product type:	Medicine
Brand name:	Prevenar 13

Ethics review

Approved WMO

Date:	15-03-2010
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-10-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-11-2010
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-07-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-08-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-10-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-04-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-06-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	26-06-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-10-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-01-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2009-012087-13-NL
ClinicalTrials.gov	NCT00980655
CCMO	NL30456.000.09