A phase III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the prophylactic efficacy, safety, and immunogenicity of GSK Biologicals* herpes zoster gE/AS01B candidate vaccine when administered intramuscularly on a twodose schedule to adult autologous haematopoietic stem cell transplant (HCT) recipients.

Published: 07-03-2013
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The purpose of this study is to test how well a new vaccine works to protect against shingles in people after they have received a transplant with their own blood stem cells.

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

Summary

ID

NL-OMON41283

Source
ToetsingOnline

Brief title
ZOSTER-002

Condition

- Viral infectious disorders

Synonym
shingles

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline Biologicals
Source(s) of monetary or material Support: GSK Biologicals

Intervention

Keyword: -autologous haematopoietic stem cell transplant (HCT), -herpes zoster, -placebo controlled, -randomized

Outcome measures

Primary outcome

Primary

* Occurrence of confirmed HZ cases

* Incidence of confirmed HZ cases from Month 0 until study end.

Secondary outcome

Secondary

* Duration of *worst* HZ-associated pain

* Duration of HZ-associated pain rated as 3 or greater on the *worst pain*

Zoster Brief Pain Inventory (ZBPI) question, following the onset of a confirmed

HZ rash over the entire pain reporting period in subjects with confirmed HZ;

* Occurrence of confirmed HZ-associated complications

* Incidence of confirmed HZ complications following the onset of HZ from Month

0 until study end;

* Occurrence of PHN

* Incidence of PHN from Month 0 until study end;

* Antigen-specific Ab concentrations in a sub-cohort of subjects

* Anti- gE Ab concentrations as determined by ELISA in a sub-cohort of subjects at Month 0, Month 1, Month 2, Month 13 and Month 25;

* Occurrence of solicited local and general symptoms

* Occurrence and intensity of each solicited local symptom within 7 days (Days 0-6) after each vaccination in all subjects;

* Occurrence, intensity and relationship to vaccination of each solicited general symptom within 7 days (Days 0-6) after each vaccination, in all subjects;

* Occurrence of unsolicited adverse events (AEs)

* Occurrence, intensity and relationship to vaccination of unsolicited AEs during 30 days (Days 0*29) after each vaccination, according to the Medical Dictionary for Regulatory Activities (MedDRA) classification in all subjects;

* Occurrence of Serious Adverse Events (SAEs)

* Occurrence and relationship to vaccination of all SAEs from Month 0 until Month 13 in all subjects;

* Occurrence of SAEs related to the GSK study vaccine/placebo from Month 0 until study end in all subjects;

* Occurrence of SAEs related to study participation or to a concurrent GSK medication/vaccine from the Pre- vaccination visit until study end in all subjects;

* Occurrence of any fatal SAEs from the Pre-vaccination visit until study end in all subjects;

* Occurrence of AEs of specific interest

* Occurrence and relationship to vaccination of any potential Immune Mediated Diseases (pIMDs) from Month 0 until Month 13 in all subjects;

* Occurrence of relapse cases4 from Month 0 until study end in all subjects.

Tertiary

* Occurrence of confirmed HZ cases in subjects having at least 1 year post-HCT

* Incidence of confirmed HZ cases in subjects having at least 1 year post-HCT

* Occurrence of PHN in subjects with confirmed HZ

* Incidence of PHN from Month 0 until study end in subjects with confirmed HZ;

* Acute HZ severity

* Acute HZ severity as determined by the mean Area Under Curve (AUC) of the severity-by-duration of HZassociated pain as measured by the ZBPI during a 4-week period following the onset of confirmed HZ in subjects with confirmed HZ;

* Interference of HZ with QoL

* Interference of HZ with QoL as measured by ZBPI in subjects with confirmed HZ;

* Interference of HZ with QoL as measured by EQ-5D in subjects with confirmed HZ;

* Interference of HZ with QoL as measured by SF-36 in subjects with confirmed HZ;

* Occurrence of overall mortality

* Incidence of overall mortality from Month 0 until study end;

* Occurrence of HZ-related mortality

* Incidence of HZ-related mortality from Month 0 until study end;

* Occurrence of overall hospitalisations

* Incidence of overall hospitalisations from Month 0 until study end;

* Occurrence of HZ-related hospitalisations

* Incidence of HZ-related hospitalisations from Month 0 until study end;

* Duration of pain medication administered for HZ

* Duration of pain medication administered for HZ from Month 0 until study end in subjects with confirmed HZ;

* Cell-mediated Immunity (CMI) in terms of frequencies of antigen-specific CD4 T cells in a sub-cohort of subjects

* Frequencies of CD4 T cells following induction with gE antigens, as determined by in vitro ICS, expressing at least 2 activation markers (from among IFN-*, IL-2, TNF-* and CD40L) in a sub-cohort of subjects at Month 0, Month 1, Month 2, Month 13 and Month 25;

* Frequencies of CD4 T cells following induction with gE antigens, as determined by in vitro ICS, expressing each individual activation marker in addition to one other marker (from among IFN-*, IL-2, TNF-* and CD40L) in a sub-cohort of subjects at Month 0, Month 1, Month 2, Month 13 and Month 25;

* Antigen-specific Ab concentrations at Month 0 and at Month 2 in subjects with confirmed HZ

* Anti-gE Ab concentrations as determined by ELISA at Month 0 and at Month 2, in all subjects with confirmed HZ compared to matched controls.

Study description

Background summary

The study medication that GlaxoSmithKline Biologicals is testing is a new vaccine against shingles. It is not yet approved for doctors to prescribe to the public. It is being studied first. Therefore we call it a study vaccine.
One part of the study vaccine is recognised by the immune system. It is hoped that the defense responses of the body to the study vaccine will protect against shingles, in particular during the period after a transplant with your own blood stem cells, but that has not yet been shown. The vaccine also contains a substance, called an adjuvant that helps the body make stronger defenses.
Shingles is an infection that is caused by the same virus that causes chickenpox. After getting chickenpox during childhood, the virus remains in the body. Shingles occurs when the virus becomes active again. In people with decreased immunity due to disease or medical interventions such as after a transplant with your own blood stem cells, the risk of developing shingles increases.
Shingles most often occurs on the chest or back, but it can occur anywhere on the body including the face or on an arm or leg. The first sign of shingles is often pain, tingling, itching or burning, usually on only one side of your body. This can also include pain triggered by air blowing on the skin, by clothing rubbing against the skin, or by hot or cold temperatures. Within a few days, a rash appears in the same area. The rash may begin as red spots, but blisters soon form. This typical rash is usually painful and may also be itchy. Some people with shingles also have fever, muscle aches and headaches. After the rash has healed, sometimes people can still feel pain in the same area. The pain tends to improve over time, but it can last for months or even years.

Study objective

The purpose of this study is to test how well a new vaccine works to protect against shingles in people after they have received a transplant with their own blood stem cells.

Study design

About 1474 people from different countries will take part in this study. There will be two groups in the study. One group will receive 2 injections of the active study vaccine and the other group will receive 2 injections of a solution without active ingredients called placebo. A computer will be used to put you into one of the 2 groups (study vaccine or placebo). You have an equal chance of being placed in either group. Neither you nor the study doctor can choose a group. During the study, neither you nor the study doctor, or other

study staff who are looking at how the vaccine affects you, will know which group you are in. We will be able to tell you what you were given after the whole study is finished or in case of a medical emergency.

The effects seen in the group of people who received the study vaccine, both good and bad, will be compared to the group of people who receive the placebo. In this way, we make sure that the effects we see during the study have not occurred by chance, but occurred because of the study vaccine.

There are a total of 6 hospital visits planned. One visit some time before the day of the first vaccination (called the pre-vaccination visit).Visits 1, 2 and 3 take place in the following 2-3 months. For visit 4 you return approximately 1 year after the vaccination and visit 5 is the last visit 2 years after your vaccination. After Visit 3, the study staff will contact you monthly by phone except in the months that you visit the hospital. You will be in the study for at least 13 months.

Intervention

Twice an injection of study medication (either active vaccine or placebo), twice blood sampling

Study burden and risks

The most common side effects are side effects at the site of the injection such as pain, redness and swelling
* Tiredness
* Muscle pain
* Headache
* Fever
* Pain
* Gastrointestinal symptoms (nausea, vomiting, diarrhea and/or abdominal pain)
* Shivering

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Subjects who the investigator believes can and will comply with the requirements (e.g. completion of the diary cards, return for follow-up visits, have
regular contact to allow evaluation during the study);
* Written informed consent obtained from the subject;
* A male or female aged 18 years or older at the time of study entry.
* Has undergone or will undergo autologous HCT within 50-70 days prior to the first vaccination with the study vaccine/placebo, and there are no plans for additional HCTs (tandem autologous HCT recipients may participate following their final HCT);
* Female subjects of non-childbearing potential may be enrolled in the study;
For this study population, non-childbearing potential is defined as current tubal ligation, hysterectomy, ovariectomy or post-menopause.
Female subjects of childbearing potential may be enrolled in the study, if the subject has practiced adequate contraception for 30 days prior to vaccination with the study vaccine/placebo, and has a negative pregnancy test on the day of vaccination, and has agreed to continue adequate contraception during the entire treatment period and for 12 months after completion of the vaccination series (i.e., until Month 13).

Exclusion criteria

* Use of any investigational or non-registered product (drug or vaccine) other than the study vaccine within 30 days preceding the first dose of study vaccine/placebo, or planned use during the study period. However, the investigational use of a registered

or non-registered product to treat the subject*s underlying disease for which the HCT was undertaken, or a complication of the underlying disease, is allowed;
* Previous vaccination against HZ or varicella within the 12 months preceding the first dose of study vaccine/placebo;
* Planned administration during the study of a HZ vaccine (including an investigational or non-registered vaccine) other than the study vaccine;
* Occurrence of a varicella or HZ episode by clinical history within the 12 months preceding the first dose of study vaccine/placebo;
* History of allergic disease or reactions likely to be exacerbated by any component of the vaccine or study material and equipment;
* Prophylactic antiviral therapy (1) with activity against VZV expected to last more than 6 months after transplantation;
(1) Prophylactic antiviral therapy with activity against VZV (e.g. Acyclovir, Valacyclovir, Famciclovir, Penciclovir, Brivudin, Ganciclovir, Valganciclovir) following HCT to be administered according to local standard of care based on the Investigator*s judgment (duration, choice of antiviral agent and dose of antiviral agent). Subjects for whom prophylactic antiviral therapy is expected to be given for 6 months or less following HCT may be enrolled.
* Administration and/or planned administration of a vaccine not foreseen by the study protocol between HCT and 30 days after the last dose of study vaccine/placebo. However, licensed non-replicating vaccines (e.g., inactivated and subunit vaccines, including inactivated and subunit influenza vaccines and pneumococcal conjugate vaccines) may be administered up to 8 days prior to dose 1and/or 2, and/or at least 14 days after any dose of study vaccine/placebo;
* HIV infection by clinical history;
* Pregnant or lactating female;
* Female planning to become pregnant or planning to discontinue contraceptive precautions (if of childbearing potential) before Month 13 (i.e., one year after the last dose of study vaccine/placebo).

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-12-2013
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GSK1437173A

Ethics review

Approved WMO Date:	07-03-2013
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-03-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-10-2013
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-07-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-08-2014
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-03-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-04-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-09-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-12-2015
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	EUCTR2012-000138-20-NL
ClinicalTrials.gov	NCT01610414
CCMO	NL43345.000.13