Vaccine 34 (2016) 4205–4212

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

A phase III clinical study to compare the immunogenicity and safety of the 9-valent and quadrivalent HPV vaccines in men

Pierre Van Damme [a], Chris J.L.M. Meijer [b], Dorothee Kieninger [c], Anne Schuyleman [d], Stephane Thomas [d], Alain Luxembourg [e,*], Martine Baudin [d]

[a] Centre for the Evaluation of Vaccination, Vaccine and Infectious Disease Institute, University of Antwerp, Antwerp, Universiteitsplein 1, 2610 Wilrijk, Belgium
[b] VU University Medical Centre, De Boelelaan 1117, 1084HV Amsterdam, The Netherlands
[c] Centre for Clinical Trials, Children's Hospital, Universitätsmedizin, Mainz, Germany
[d] Sanofi Pasteur MSD, Lyon, France
[e] Merck & Co. Inc., 2000 Galloping Hill Road, Kenilworth, NJ 07033, USA

ARTICLE INFO

Article history:
Received 14 April 2016
Received in revised form 13 June 2016
Accepted 17 June 2016
Available online 25 June 2016

Keywords:
Human papilloma virus
Anogenital cancers
Anogenital warts
Immunogenicity
Safety
Nine-valent human papilloma virus vaccine

ABSTRACT

Background: A nine-valent human papilloma virus (9vHPV) vaccine has been developed to prevent infections and diseases related to HPV 6/11/16/18 (as per the licensed quadrivalent HPV (qHPV) vaccine) as well as to five additional oncogenic HPV types (HPV 31/33/45/52/58). The 9vHPV vaccine has the potential to prevent 90% of cervical cancers, HPV-related anal, vaginal and vulval cancers and anogenital warts. We compared the immunogenicity and safety of the 9vHPV vaccine versus the qHPV vaccine in 16–26-year-old men.

Methods: Participants ($N = 500$) were randomised to receive 9vHPV or qHPV vaccines on day 1, month 2 and month 6. Serology testing was performed on day 1 and month 7. HPV type-specific antibody titres (anti-HPV 6/11/16/18/31/33/45/52/58) were determined by competitive Luminex immunoassay and expressed as geometric mean titres and seroconversion rates. Vaccine safety was also assessed.

Results: The HPV 6/11/16/18 immune responses elicited by the 9vHPV vaccine were comparable with those elicited by the qHPV vaccine. All participants receiving the 9vHPV vaccine seroconverted for HPV 31/33/45/52/58. The 9vHPV and qHPV vaccines showed comparable safety profiles.

Conclusions: In addition to immune responses to HPV 31/33/45/52/58, a three-dose regimen of the 9vHPV vaccine elicited a similar immune response to HPV 6/11/16/18 when compared with the qHPV vaccine in men aged 16–26 years. The safety profile was also similar for the two vaccines. The results from this study support extending the efficacy findings with qHPV vaccine to 9vHPV vaccine in men aged 16–26 years.

NCT02114385

© 2016 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

1. Introduction

A nine-valent human papilloma virus (types 6/11/16/18/31/33/45/52/58) (9vHPV) vaccine (Gardasil 9, Merck & Co. Inc., Kenilworth, NJ, USA) was developed to provide protection against the HPV types already covered by the quadrivalent HPV (types 6/11/16/18) (qHPV) vaccine and the next five most common oncogenic types associated with cervical cancer worldwide (types 31/33/45/52/58) [1]. The 9vHPV vaccine could potentially prevent approximately 90% of cervical cancers, 90% of HPV-related vulval, vaginal and anal cancers and 90% of genital warts worldwide [2–7]. The 9vHPV vaccine was licensed in 2014 in the USA, and in 2015 in Canada, the EU and Australia.

In clinical trials in women aged 16–26 years, the qHPV vaccine prevented infection and cervical/vaginal/vulval dysplasia caused by HPV 6/11/16/18 as well as HPV 6/11-related condyloma. In a clinical trial in men aged 16–26 years, the qHPV vaccine prevented genital and anal infection and anal dysplasia caused by HPV

Abbreviations: 9vHPV vaccine, 9-valent HPV vaccine; AE, adverse event; ANOVA, analysis of variance; CI, confidence interval; cLIA, competitive Luminex immunoassay; EU, European Union; GMTs, geometric mean titres; HPV, human papilloma virus; qHPV vaccine, quadrivalent HPV vaccine; SAE, serious adverse event; USA, United States of America; VLP, virus-like particle; VRC, vaccination report card.

* Corresponding author.
E-mail addresses: pierre.vandamme@uantwerpen.be (P. Van Damme), CJLM.Meijer@vumc.nl (C.J.L.M. Meijer), Dorothee.kieninger@unimedizin-mainz.de (D. Kieninger), ASchuyleman@spmsd.com (A. Schuyleman), SThomas@spmsd.com (S. Thomas), alain_luxembourg@merck.com (A. Luxembourg), baudinmartine@yahoo.fr (M. Baudin).

http://dx.doi.org/10.1016/j.vaccine.2016.06.056
0264-410X/© 2016 The Authors. Published by Elsevier Ltd.
This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

6/11/16/18 as well as HPV 6/11-related condyloma [8,9]. Based on these results, the qHPV vaccine has been widely licensed for use in both genders.

In a clinical trial conducted in women aged 16–26 years, the 9vHPV vaccine prevented infection and disease caused by HPV 31/33/45/52/58. It also induced anti-HPV 6/11/16/18 antibody responses that were non-inferior to responses induced by the qHPV vaccine; efficacy of the 9vHPV vaccine against infection and disease caused by HPV 6/11/16/18 in women aged 16–26 years was inferred based on these results [10].

In another clinical trial, the 9vHPV vaccine induced non-inferior anti-HPV antibody responses to HPV 6/11/16/18/31/33/45/52/58 in men aged 16–26 years versus women aged 16–26 years. Efficacy of the 9vHPV vaccine against infection and disease caused by the nine vaccine HPV types in men aged 16–26 years was inferred based on these results [11].

In this report, we compare the safety and immunogenicity of the 9vHPV and qHPV vaccines in men aged 16–26 years, and assess whether the 9vHPV vaccine induced non-inferior anti-HPV 6/11/16/18 antibody responses compared with the qHPV vaccine. The study aims at supporting the extension of the efficacy findings with qHPV vaccine to 9vHPV vaccine in men aged 16–26 years.

2. Materials and methods

We conducted a double-blind, randomized, controlled, with qHPV vaccine, immunogenicity and safety study of the 9vHPV vaccine in young men 16–26 years of age. Participants were enrolled from seven centres located in three countries (Belgium, Germany, and the Netherlands). The study was conducted in accordance with the principles of Good Clinical Practice, as well as the Declaration of Helsinki, the Ethical Principles for Medical Research Involving Human Subjects of the World Medical Association, the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, and national and local relevant guidelines and requirements regarding ethical committee review. This trial is registered with Clinicaltrials.gov number NCT02114385.

2.1. Population

The study was designed to enrol 500 males aged ⩾16 to <27 years who were in good physical health and had a history of no more than five lifetime female and no male sexual partners (the immunogenicity of the 9vHPV vaccine in men having sex with men (MSM) was assessed in another study [11]; see Section 4 for further information). Reasons for exclusion from the study included known allergy to any component of the vaccine, a previous history of a severe allergic reaction, thrombocytopenia, coagulation disorder, or a positive HPV test, concurrent participation in any other clinical trial of an investigational medicinal product, and previous vaccination with a marketed HPV vaccine or participation in a previous HPV vaccine clinical trial (active agent or placebo). Individuals who were immunocompromised (including those who had a splenectomy), received immunosuppressive therapy in the previous year, received immunoglobulin or a blood-derived product within the previous 6 months, or had a history of any condition that could confound study results or interfere with participation in the study were also excluded.

2.2. Randomization

An Interactive Web Response System (IWRS) was used to allocate participants to 9vHPV or qHPV vaccine in a blinded manner. The system assigned an allocation number from a randomized, age-stratified (16–17 years and 18–26 years) allocation schedule. The IWRS ensured that at least 75 participants (15%) aged 16–17 years were randomized in order to avoid underrepresentation of minor participants; whenever necessary, randomization of participants aged 18 years or older was stopped when 425 of these participants had been randomized in the study. Participants were randomized in a 1:1 ratio using blocks of randomization (size 8) within each age stratum to 9vHPV or qHPV vaccine.

2.3. Study vaccination

All participants were administered a 3-dose regimen of 9vHPV or qHPV vaccine at day 1, month 2, and month 6. Each vaccine dose was administered as a 0.5-mL intramuscular injection. Vaccination was deferred if a participant had an oral temperature ⩾37.8 °C for 24 h prior to vaccination.

2.4. Vaccine immunogenicity

Blood samples were drawn at day 1 (immediately before vaccination) and at month 7. Serum collected from all participants at day 1 and month 7 was analyzed for antibodies to the nine vaccine HPV types by competitive Luminex immunoassay (cLIA; HPV-9 cLIA Version 2.0; performed by PPD Vaccines and Biologics Lab, Wayne, PA, USA) [12]. Because antibody titres to each individual HPV type were determined using type-specific monoclonal antibodies, it is not possible to directly compare assay results across HPV types.

The primary immunogenicity objective was to show that geometric mean titres (GMTs) at month 7 for anti-HPV 6/11/16/18 in the 9vHPV vaccine group would be non-inferior to the GMTs at month 7 in the qHPV vaccine group. The secondary immunogenicity objectives were to provide a summary of GMTs and seroconversion rates at month 7 for all nine HPV types (HPV 6/11/16/18/31/33/45/52/58).

Serology results at day 1 were part of the criteria to define the per-protocol analysis populations. Participants who were seropositive to a vaccine HPV type at day 1 were excluded from the per-protocol immunogenicity analysis for the corresponding HPV type.

2.5. Vaccine safety and tolerability

Following each vaccination, participants were observed for ⩾30 min for any untoward effects, including allergic reactions. All participants received a vaccination report card (VRC) at each vaccination visit. They were asked to record their oral temperature on the VRC from day 1 to day 5 after each vaccination (starting on the evening after vaccination), and any injection-site and systemic adverse events (AEs) for a total of 15 days including the day of vaccination. The study site personnel reviewed the VRC for completeness and could not alter the original information recorded by the participants on the VRC. The investigator determined the causality of systemic AEs reported on the VRC, and classified each AE reported on the VRC as a serious or non-serious AE.

An oral temperature ⩾37.8 °C during the follow-up period was considered an elevated temperature (fever). For each AE, participants were asked to rate the symptom as mild (awareness of sign or symptom but easily tolerated), moderate (discomfort enough to cause interference with usual activities), or severe (incapacitating with inability to work or do usual activity); injection-site AEs of swelling and erythema were rated by size. Investigators were instructed to assign causality to AEs on the basis of exposure, time course, likely cause, and consistency with the vaccine's known profile.

Serious AEs (SAEs) were predefined as any AE that resulted in death, deemed by the investigator to be life-threatening, or that

Download English Version:

https://daneshyari.com/en/article/10962466

Download Persian Version:

https://daneshyari.com/article/10962466

Daneshyari.com