

News release

Sanofi Pasteur MSD seeks license extension for cervical cancer vaccine Gardasil® to include the prevention of vulvar and vaginal cancers

Clinical data showed 100% efficacy against pre-cancerous vulvar and vaginal lesions

Lyon, 4 October 2007 – Sanofi Pasteur MSD has filed for an update of the license for the cervical cancer vaccine Gardasil® to include the prevention of vulvar and vaginal cancers due to human papillomavirus types 16 and 18. The European Medicines Agency (EMA) has accepted the filing and has started its review.

In large clinical studies, Gardasil® prevented 100%^{*} of pre-cancerous vulvar lesions (VIN[†]2/3) and 100%[‡] of pre-cancerous vaginal lesions (VaIN[§]2/3) related to human papillomavirus types 16 or 18 through a mean follow up of three years after start of vaccination.^{1,a)}

"We have developed Gardasil® as a complete offer against a wide range of diseases that affect several genital organs. Starting with the prevention of cervical cancer as our first priority, we could now widen the benefits by helping protect women against vulvar and vaginal cancers." says Patrick Poirot, vice-president for Medical and Scientific Affairs at Sanofi Pasteur MSD.

Gardasil® is the only cervical cancer vaccine that directly targets the four human papillomavirus types 6, 11, 16 and 18.

It is estimated that types 6, 11, 16 and 18 cause 75% of cervical cancer in Europe,² 70% of vulvar and vaginal cancers,^{3,4} 70% of pre-cancerous^{5,6} and 35-50% of early cervical lesions,⁷ 70% of pre-cancerous vulvar and vaginal lesions^{3,4,8,9}, and 90% of genital warts.^{10,11}

It is estimated that 30,000 new cases of pre-cancerous vulvar and vaginal lesions related to human papillomavirus are diagnosed each year in Europe.^{12,13,14,15}

"Precursors of vulvar and vaginal cancers are often not recognised. Their treatment to avoid a progression to cancer is challenging, can be disfiguring and requires long-term follow-up since recurrence is common. In addition, women may suffer anxiety, depression, sexual dysfunction and poor self-image," explained Professor Elmar Joura from the University of Vienna.

Vulvar and vaginal cancers collectively account for a significant proportion of all gynaecological cancers; in the UK, for example, they represent 6% of all gynaecological cancer.¹⁶

An increasing incidence of pre-cancerous vulvar lesions and vulvar cancer has been noted over the past 30 years.^{17,18,19} The incidence of vulvar carcinoma in situ increased by 400% in the USA between 1973 and 2000; invasive vulvar cancer increased by 20% during the same period.²⁰

Whereas previously vulvar cancer was seen almost exclusively in older women, recent studies have shown that 20% of these cancers now occur in women younger than 50 years.^{17,18,21} While vulvar cancer in older women mostly occurs without association to human papillomavirus, almost all vulvar cancers among younger women are human papillomavirus-related.^{18,22}

* 95% CI [42,100]

† VIN = Vulvar Intraepithelial Neoplasia

‡ 95% CI [31,100]

§ VaIN = Vaginal Intraepithelial Neoplasia

Notes to editors

The burden of cervical cancer and other human papillomavirus diseases

Despite screening for early detection, cervical cancer remains the second most common cause of death from cancer (after breast cancer) among young women (15-44 years) in Europe^{**}.²³ Around 33,500 women are diagnosed with, and 15,000 women die from cervical cancer each year.²⁴

In addition, hundreds of thousands of women are diagnosed with other genital human papillomavirus diseases that start before the occurrence of cervical cancer and can touch other genital organs than the cervix. These diseases include pre-cancerous and early cervical lesions^{5,7,28}, vulvar and vaginal cancer^{3,4,26}, pre-cancerous vulvar and vaginal lesions^{8,9,27,28} and genital warts.²⁹

Unmatched clinical efficacy for Gardasil® against pre-cancerous and early cervical lesions and genital warts

Gardasil® prevented 99% of pre-cancerous cervical lesions (CIN^{††}2/3) caused by human papillomavirus types 16 and 18 through a mean follow up time of three years after start of vaccination. Efficacy was demonstrated against types 16 and 18, not only together (99%^{††}) but also against each type alone (99%^{§§} for type 16 and 100%^{***} for type 18).³⁰

In addition, Gardasil® prevented 96%^{†††} of early cervical lesions (CIN1)³¹, and 99%^{†††} of genital warts due to human papillomavirus virus types 6, 11, 16 and 18.³²

Clinically proven immune memory suggests long-term protection

In a follow up study, Gardasil® prevented 100%^{§§§} of cervical lesions and genital warts caused by the four vaccine virus types up to five years after the start of vaccination.³³ Five years after vaccination, a strong and rapid immune response was observed when the immune system was exposed again to the vaccine virus types. This phenomenon called immune memory is a hallmark for long-term protection.³⁴

Gardasil® – The only cervical cancer that has shown a significant level of cross-protection against pre-cancerous cervical lesions due to virus types not directly targeted by the vaccine

First results from a supportive analysis^{****} of two large phase III studies show that Gardasil® prevented 38%^{††††} of pre-cancerous cervical lesions (CIN2/3, AIS^{††††}) caused by ten other cancer-causing human papillomavirus types, in addition to the virus types directly targeted by the vaccine.³⁵ These ten additional virus types cause around 16% of cervical cancer in Europe³⁶ and up to 22% of cervical cancer around the world.³⁷

Current EU indication of Gardasil®

Gardasil®, human papillomavirus vaccine [types 6,11,16,18] (recombinant, adsorbed), can be given to children and adolescents 9 to15 years and adult females 16 to 26 years of age and is indicated for the prevention of cervical carcinoma (cervical cancer), high grade cervical dysplasia CIN2/3 (precancerous cervical lesions), high grade vulvar dysplastic lesions VIN 2/3 (precancerous vulvar lesions) and external genital warts (condyloma acuminata) caused by human papillomavirus types 6, 11, 16 and 18.

About Sanofi Pasteur MSD

Sanofi Pasteur MSD is a joint venture between sanofi pasteur, the vaccine division of sanofi-aventis, and Merck & Co., Inc. Combining innovation and expertise, Sanofi Pasteur MSD is the only company in Europe dedicated exclusively to vaccines. Sanofi Pasteur MSD is able to draw on the research expertise of sanofi pasteur and Merck & Co., Inc., together with their teams throughout the world, to focus on the development of new vaccines for Europe, which aim to extend protection to other diseases and perfect existing vaccines in order to improve the acceptability, efficacy and tolerability of vaccination.

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** European Union member states (except Romania and Bulgaria) plus Iceland, Norway & Switzerland

†† CIN = Cervical Intraepithelial Neoplasia

†† 95% CI [93,100]

§§ 95% CI [92,100]

*** 95% CI [78,100]

††† 95% CI [89,2,98,60]

††† 95% CI [95,4,99,9]

§§§ 95% CI [12,100]

**** In a generally human papillomavirus-naïve population, through a mean follow up time of 3 years after start of vaccination.

†††† 95% CI [6,60]

†††† Adenocarcinoma In Situ

Clinical study details

- a) 18 174 women (16–26 years) from a combined analysis of 3 clinical trials were enrolled and randomised to receive either Gardasil® or placebo at day 1, and months 2 and 6. 18 150 women received at least one injection of quadrivalent vaccine or placebo. Individuals underwent detailed anogenital examination at day 1, 1 month after dose three, and at 6–12-month intervals for up to 48 months. Suspect genital lesions were biopsied and read by a panel of pathologists and vaccine Human Papillomavirus type-specific DNA testing was done. The primary endpoint was the combined incidence of VIN2/3 or VaIN2/ associated with Human Papillomavirus 16 or 18. Primary efficacy analyses were done in a per-protocol population.

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