



NEWS RELEASE

Six-year Efficacy Data for GARDASIL® 9 Presented at EUROGIN 2017 Congress

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Merck's 20-year commitment to HPV research highlighted in oral session

Merck (NYSE:MRK), known as MSD outside of the United States and Canada, announced results from final analyses of the pivotal Phase III efficacy, immunogenicity, and safety clinical trial for GARDASIL® 9 (Human Papillomavirus 9-valent Vaccine, Recombinant). The data, which showed sustained efficacy for up to six years in the per protocol population, were presented during an oral session at the European Research Organization on Genital Infection and Neoplasia (EUROGIN) congress in Amsterdam, Netherlands.

GARDASIL 9 is a vaccine indicated for use in girls and women 9 through 26 years of age for the prevention of cervical, vulvar, vaginal, and anal cancers caused by HPV types 16, 18, 31, 33, 45, 52, and 58; pre-cancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58; and genital warts caused by HPV types 6 and 11. GARDASIL 9 is also indicated for use in boys and men 9 through 26 years of age for the prevention of anal cancer caused by HPV types 16, 18, 31, 33, 45, 52, and 58; precancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58; and genital warts caused by HPV types 6 and 11. GARDASIL 9 is contraindicated in individuals with hypersensitivity, including severe allergic reactions to yeast, or after a previous dose of GARDASIL 9 or GARDASIL® [Human Papillomavirus Quadrivalent (types 6, 11, 16, and 18) Vaccine, Recombinant].

These final analyses evaluated study outcomes, including efficacy for up to six years following receipt of first vaccine dose, and antibody responses over five years. Vaccination impact on cervical cytology abnormalities and related therapeutic procedures were also reported. These final analyses are from the base study; a study extension is ongoing to evaluate long term follow-up for an additional 10 years following the end of the base study.



In these analyses at six years, efficacy for GARDASIL 9 against HPV31/33/45/52/58-related cervical pre-cancers (cervical intraepithelial neoplasia Grade 3 (CIN 3) was 100 percent (95% CI: 39.4, 100) in the per-protocol population. Efficacy against HPV type 31/33/45/52/58-related cervical, vulvar, and vaginal disease, persistent infection, cervical cytological abnormalities; cervical biopsy; and cervical definitive therapy ranged from 90-98 percent. Incidence of HPV6/11/16/18-related persistent infection, disease, cytological abnormalities, and procedures was similar in recipients of GARDASIL 9 (Human Papillomavirus 9-valent Vaccine, Recombinant) and GARDASIL [Human Papillomavirus Quadrivalent (Types 6, 11, 16 and 18) Vaccine, Recombinant].

GARDASIL 9 produced similar antibody protection against the four HPV types in GARDASIL. Antibodies to the HPV types targeted by GARDASIL 9 persisted through five years following vaccination. Geometric mean titer ratios (GARDASIL 9/GARDASIL) for HPV6/11/16/18 varied minimally over time. The two vaccines had similar adverse event profiles; injection-site adverse events were more common with GARDASIL 9; most were mild-to-moderate in intensity. A paper detailing these results was also published online on September 5 in The Lancet.

“These new analyses show that efficacy of GARDASIL 9 in preventing certain HPV-related cancers and diseases was sustained for up to six years,” said Elmar A. Joura, M.D., Associate Professor of Gynecology and Obstetrics at the Medical University of Vienna, General Hospital (AKH), and Comprehensive Cancer Center Vienna, Austria, who presented these data at EUROGIN. “Despite the progress we’ve made with HPV vaccination over the past 11 years, HPV-related cancers and diseases are still a significant public health issue and continued efforts are needed to increase uptake of the vaccine.”

About the study

The clinical trial program for GARDASIL 9 was designed to build upon the efficacy established in clinical trials with GARDASIL. In this Phase III active comparator-controlled, double-blind, randomized clinical trial (Protocol 001), 14,215 females 16-26 years of age were randomized to receive a three-dose series of GARDASIL 9 (n=7,106) or GARDASIL (n=7,109). The primary comparison between GARDASIL 9 and GARDASIL was clinical efficacy for the five additional HPV types. Efficacy of GARDASIL 9 against persistent infection and disease related to the original four HPV types (6, 11, 16, or 18) was inferred based on immunogenicity comparisons. The primary efficacy analysis was conducted in those who received all three doses of vaccine within one year of enrollment, did not have deviations from the study protocol that could affect the evaluation of vaccine efficacy, were negative (PCR negative and seronegative) to the relevant HPV type(s) prior to dose 1, and who remained PCR negative to the relevant HPV type(s) through Month 7 (per-protocol efficacy, or PPE, population).

The primary efficacy evaluation was based on a composite clinical endpoint of HPV 31-, 33-, 45-, 52-, and 58-related cervical, vulvar, and vaginal cancer, and high-grade cervical/vulvar/vaginal disease [CIN 2/3 (cervical intraepithelial

neoplasia 2/3) or AIS (adenocarcinoma in situ), VIN 2/3 (vulvar intraepithelial neoplasia 2/3), and VaIN 2/3 (vaginal intraepithelial neoplasia 2/3)]. Additional secondary endpoints related to HPV 31, 33, 45, 52, and 58 were also evaluated. Efficacy for all endpoints was measured starting after the Month 7 visit.

Efficacy of GARDASIL 9 against persistent infection and disease related to HPV types 6, 11, 16, or 18 was inferred from non-inferiority comparisons of geometric mean titers (GMTs) in 16- through 26-year-old girls and women following vaccination with GARDASIL 9 with those following vaccination with GARDASIL [Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant]. Antibody responses for HPV 6, 11, 16, and 18 (measured by GMTs and seroconversion rates at Month 7) for GARDASIL 9 among young women 16 to 26 years of age were non-inferior to those who received GARDASIL.

Important Information about GARDASIL 9 (Human Papillomavirus 9-valent Vaccine, Recombinant)

GARDASIL 9 does not eliminate the necessity for women to continue to undergo recommended cervical cancer screening. Recipients of GARDASIL 9 should not discontinue anal cancer screening if it has been recommended by a health care professional.

GARDASIL 9 has not been demonstrated to provide protection against diseases from vaccine HPV types to which a person has previously been exposed through sexual activity.

GARDASIL 9 is not a treatment for external genital lesions; cervical, vulvar, vaginal, and anal cancers; or CIN; VIN; VaIN; or AIN.

Not all vulvar, vaginal, and anal cancers are caused by HPV, and GARDASIL 9 protects only against those vulvar, vaginal, and anal cancers caused by HPV 16, 18, 31, 33, 45, 52, and 58.

Vaccination with GARDASIL 9 may not result in protection in all vaccine recipients.

Select Safety Information for GARDASIL 9

GARDASIL 9 is contraindicated in individuals with hypersensitivity, including severe allergic reactions to yeast, or after a previous dose of GARDASIL 9 or GARDASIL.

Because vaccinees may develop syncope, sometimes resulting in falling with injury, observation for 15 minutes after administration is recommended. Syncope, sometimes associated with tonic-clonic movements and other seizure-like activity, has been reported following HPV vaccination. When syncope is associated with tonic-clonic

movements, the activity is usually transient and typically responds to restoring cerebral perfusion.

Safety and effectiveness of GARDASIL 9 have not been established in pregnant women.

The most common ($\geq 10\%$) local and systemic adverse reactions in females were injection-site pain, swelling, erythema, and headache. The most common ($\geq 10\%$) local and systemic reactions in males were injection-site pain, swelling, and erythema.

The duration of immunity with GARDASIL 9 has not been established.

About GARDASIL® 9 (Human Papillomavirus 9-valent Vaccine, Recombinant)

GARDASIL 9 includes the greatest number of HPV types in any available HPV vaccine. After HPV types 16 and 18, the five additional HPV types in GARDASIL 9 are the most common cervical cancer-causing types worldwide. Seven HPV types in GARDASIL 9 (HPV 16, 18, 31, 33, 45, 52 and 58) cause approximately 90 percent of cervical cancer cases and approximately 80 percent of high-grade cervical lesions (cervical precancers, defined as CIN 2, CIN 3 and AIS) worldwide. These seven HPV types also cause 85-90 percent of HPV-related vulvar cancers, 80-85 percent of HPV-related vaginal cancers, and 90-95 percent of HPV-related anal cancers. HPV types 6 and 11 cause approximately 90 percent of genital warts cases. In addition, approximately 50 percent of cases of low-grade cervical lesions (CIN 1) are caused by the nine HPV types included in the vaccine.

GARDASIL 9 is approved for use in more than 60 countries, and since 2015 more than 26 million doses have been distributed worldwide, although the exact number of doses that have been administered is unknown. GARDASIL [Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant] is no longer available in the United States.

Dosage and administration for GARDASIL 9

GARDASIL 9 should be administered intramuscularly in the deltoid region of the upper arm or in the higher anterolateral area of the thigh.

- For individuals 9 through 14 years of age, GARDASIL 9 can be administered using a 2-dose or 3-dose schedule. For the 2-dose schedule, the second dose should be administered 6-12 months after the first dose. If the second dose is administered less than 5 months after the first dose, a third dose should be given at least 4 months after the second dose. For the 3-dose schedule, GARDASIL 9 should be administered at 0, 2 months, and 6 months.
- For individuals 15 through 26 years of age, GARDASIL 9 is administered using a

3-dose schedule at 0, 2 months, and 6 months.

20-year commitment to HPV vaccine research

Prof. Anna Giuliano of Moffitt Cancer Center in Tampa, Fla. presented a review of Merck's 20-year history of HPV vaccine research during an oral session at EUROGIN. Merck's proof-of-principle studies with monovalent HPV vaccines in 1997 were followed in 2000 with the start of clinical studies for the quadrivalent HPV vaccine, GARDASIL [Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant]. First regulatory approvals of GARDASIL were received in 2006. Studies have continued to evaluate duration of protection as well as safety.

HPV types 16 and 18 cause approximately 70 percent of cervical cancer cases. In 2004, HPV types 31, 33, 45, 52, and 58 were classified as the next most frequent HPV types associated with cervical cancer, causing an additional 20 percent of cases. Merck started a Phase II study in 2005 to evaluate a HPV vaccine candidate that could protect against more HPV types. Ultimately this led to the development of the 9-valent HPV vaccine, GARDASIL 9 (Human Papillomavirus 9-valent Vaccine, Recombinant), which helps to protect against certain cancers and diseases caused by these five HPV types in addition to the four original HPV types covered by GARDASIL. Phase III clinical studies for GARDASIL 9, which evaluated more than 20,000 individuals who received the vaccine, began in 2007, just one year after GARDASIL was licensed.

"Merck has had a sustained and unwavering commitment to HPV vaccine research for 20 years," said Eliav Barr, MD, senior vice president, Global Clinical Development – Infectious Disease & Vaccines, Merck Research Laboratories. "With HPV vaccination, screening, treatment, and education, it is our aspiration that one day the number of women and men affected by HPV-related cancers and diseases will be significantly reduced. There is obviously much work ahead of us, but we look forward to continuing our efforts in collaboration with the many stakeholders around the world who share our commitment."

About HPV and related cancers and diseases

In the United States, human papillomavirus (HPV) will infect most sexually active males and females in their lifetime. According to the CDC, there are approximately 14 million new genital HPV infections in the United States each year, half of which occur in people 15 through 24 years of age. For most people, HPV clears on its own, but for others who don't clear the virus it could lead to certain cancers and other diseases in males as well as females. There is no way to predict who will or won't clear the virus.

HPV causes virtually all cervical cancer cases. Each day, about 35 women are diagnosed with cervical cancer in the United States -- about 12,900 women per year. HPV also causes approximately 70-75 percent of vaginal cancer cases and approximately 30 percent of vulvar cancer cases in females, and approximately 85-90 percent of anal

cancers and 90 percent of genital warts in both females and males. Additionally, there are an estimated 3 million abnormal Pap results, many of which are caused by HPV, that require follow-up each year in the United States.

Anal cancer and genital warts affect both men and women. According to the American Cancer Society, an estimated 2,920 men and 5,160 women in the United States will be diagnosed with anal cancer in 2016, and overall rates have been increasing. There is no routine screening recommended for the general population to reduce the risk of anal cancer. Approximately 355,000 cases of genital warts occur each year in the United States. Treatment of genital warts can be painful, and they may recur after treatment, especially in the first three months. Approximately 3 out of 4 people get them after having genital contact with someone who has genital warts.

About Merck

For more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. For more information, visit www.merck.com and connect with us on [Twitter](#), [Facebook](#), [Instagram](#), [YouTube](#) and [LinkedIn](#).

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for

innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2016 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

Please see Prescribing Information for GARDASIL ® 9 (Human Papillomavirus 9-valent Vaccine, Recombinant) at

http://www.merck.com/product/usa/pi_circulars/g/gardasil_9/gardasil_9_pi.pdf and Patient Product Information for GARDASIL ® 9 at

http://www.merck.com/product/usa/pi_circulars/g/gardasil_9/gardasil_9_ppi.pdf .

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