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Use of 9-valent HPV vaccine. A review

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Abstract

Since 2006, vaccination against human papillomavirus (HPV) has been implemented in most developed countries. Two vaccines have been successfully used: a bivalent vaccine targeting (bHPV)- related cancers and a quadrivalent (qHPV) vaccine targeting both HPV-related cancers and genital warts. By 2015, a new nonavalent HPV (9vHPV) vaccine was granted by marketing authorization, first in the USA in 2014 and subsequently in Europe. The efficiency and/or immunogenicity of the 9vHPV has been assessed in the clinical studies which have been conducted so far and rendered positive results. The real impact of the 9vHPV wide use in comparison with the bHPV or qHPV cannot be specifically anticipated as it depends on different variables. However, the 5 further types in 9vHPV (HPV types 31, 33, 45, 52, and 58) increase the protection against cervical cancer to almost 90%. While, as mentioned above it is rather difficult to precisely assess the impact of this additional aim, it is nonetheless its significance in which the clinical studies conducted so far reported a successful rate of the 9vHPV vaccine use. Thus it can be argued that substituting the qHPV with the 9vHPV may justify a significantly higher impact on HPV-related cancers both in females and males.
Keywords: *human papillomavirus vaccine, quadrivalent vaccine, nonavalent vaccine, clinical studies, cervical cancer*

Introduction

Since 2006, vaccination against human papillomavirus (HPV) has been implemented in most developed countries. Until present, two vaccines have been successfully used: a bivalent vaccine targeting HPV- related cancers. In 2007 this vaccine received a positive view from the European Medicine Agency[1]. Later on, in 2009, it was approved by the Food and Drug Administration (FDA). A quadrivalent vaccine, was later developed and called qHPV or 4vHPV, targeting both HPV-related cancers and genital warts. The latter gained approval from the FDA in 2006 and also received a positive view from the European Medicine Agency[2-4].

Later on, in 2014 and 2015, a new nonavalent HPV vaccine (9vHPV) was granted marketing authorization in the USA and Europe. The 9vHPV was developed from the qHPV and includes five additional HPV types that should increase the level of protection toward HPV-related cancers[1,5].

The 9vHPV vaccine (also known as Gardasil 9) has been approved for use in several countries (USA, Canada and subsequently in the European Union). This vaccine includes high-risk HPV 16, 18, 31, 33, 45, 52 and 58 types, along with low-risk HPV 6 and 11 types[1,2,3,4,5].

What is 9Vhpv vaccine?

Up to present, the International Agency for Research on Cancer, under the World Health Organization, has classified 12 HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59) among the "Group 1 carcinogens"[6].

According to the European public assessment report for Gardasil 9, the Gardasil9 is administered for: condylomata acuminata, Papillomavirus infections, uterine cervical dysplasia and immunization. It is a vaccine used in males and females, from the age of nine years, to protect against precancerous lesions and cancers in the cervix, vulva/vagina, anus and genital warts caused by HPV 6, 11, 16, 18, 31, 33, 45, 52 and 58 types[7-9].

The vaccine contains purified proteins from the above-mentioned nine types of HPV and it is usually given in line with a 2 or 3-dose schedule for subjects between 9 to 14 years old and a 3 dose schedule for subjects 15 years old and over[9]. For a 2-dose schedule, the second dose should be administered 5 to 13 months after the first dose. For a three-dose schedule, the second dose should be administered 2 months after the first dose and the third after another 4 months[9].

As mentioned above, this new vaccine comes in addition to the two HPV vaccines already commercially available in a large number of countries, namely Cervarix - a bivalent vaccine, targeting HPV 16 and 18 types, two HPV types that cause cervical cancer and Gardasil - a quadrivalent vaccine targeting the same oncogenic types and also HPV 6 and 11 types, which cause external genital warts[5,10].

So far, millions of women and a smaller number of men have been immunized with these two HPV vaccines. Both vaccines protect against HPV 16/18 types related genital diseases, primarily against 50% of cervical intraepithelial neoplasia (CIN) 2/3 and 70% of cervical cancer[7].

The 5 further types in 9vHPV (HPV 31, 33, 45, 52, and 58 types) increase the protection against cervical cancer to almost 90%. For CIN1, CIN2 and CIN3 lesions, the increases are 20%, 30% and 30% respectively[8] (Figure 1).

Efficiency of 9vHPV vaccine and clinical studies

Like with any other medicine on the market, the efficacy of Gardasil 9 has been assessed in several clinical studies,

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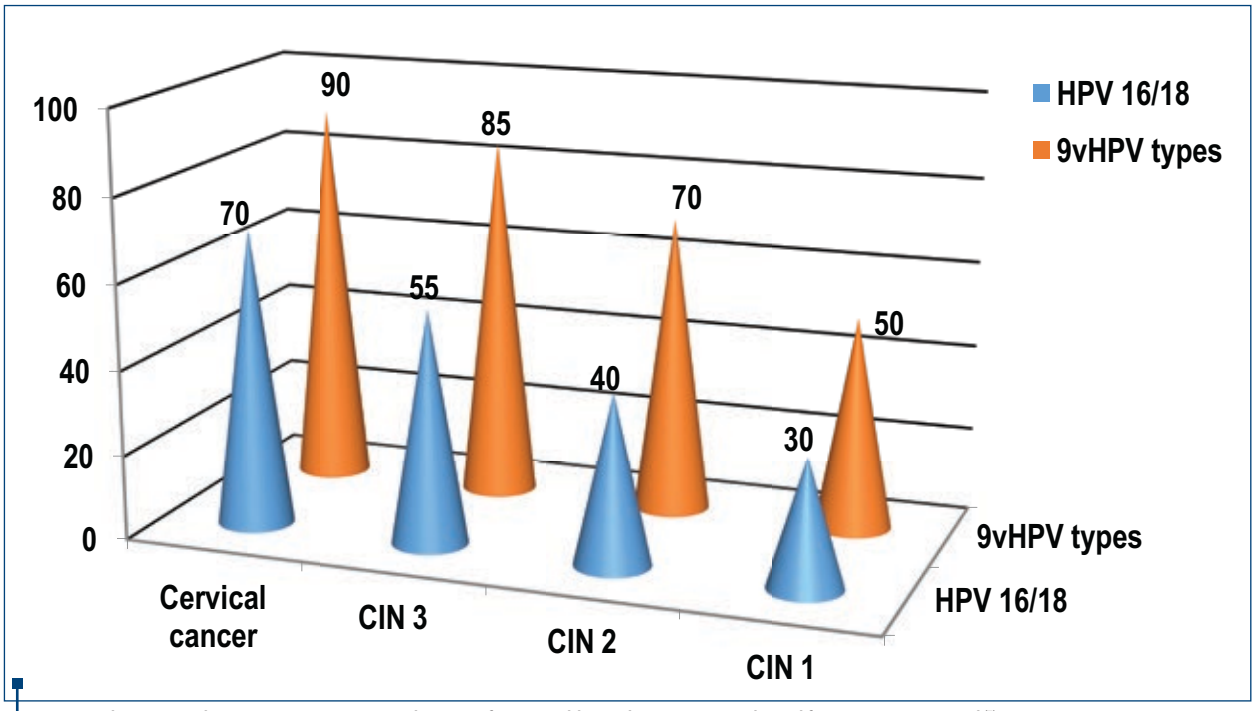

Figure 1. The increased protection against cervical cancer of 9vHPV additional types – 90% (adapted from Van Damme et al.[7])

among which there are 5 main studies that are worth mentioning in this review[8].

The first study targeted the effectiveness of Gardasil 9 in over 14.000 women (aged 16-26 years old). It focused on how many women that were given the 9vHPV vaccine developed a disease due to infection with HPV 31, 33, 45, 52 and 58 types as compared to women administered a quadrivalent vaccine which protects against types 6, 11, 16 and 18. The conclusion was that 1 of 6.016 women that were administered 3 doses of Gardasil 9 vaccine developed a disease linked to HPV 31, 33, 45, 52 and 58 types, compared to 30 women out of 6.017 who received 3 doses of Gardasil[8].

The second study involved the administration of Gardasil 9 to 3.066 subjects divided in 2 groups (i.e. boys and girls aged 9 to 15 years old and young women aged 16 to 26 years old). As regards the first group of age it resulted that the levels of antibodies against all 9 types of HPV, one month after the 3rd dose, are satisfactory. The vaccine stimulated the adequate level of antibodies, thus providing a proper protection in comparison to the second group of age (women aged 16-26 years old) whose protection rate was demonstrated in the first study mentioned above[8].

Another study conducted on 1.419 men aged between 16 and 26 years old versus 1.101 women aged between 16 and 18 years old measured the level of protection (level of antibodies against all 9 HPV types) after the administration of the third dose of Gardasil 9. It was concluded that both females and males were equally protected[8].

The final relevant study, which was already mentioned above, focused on the efficiency of a 2 dose schedule versus a 3 dose schedule of Gardasil 9. The study was conducted on 1.518 subjects and monitored the development of antibodies 1 month after the administration of the last dose of Gardasil 9. It pointed out that the subjects administered two doses of Gardasil 9 have similar levels of protection against all nine virus types as those given three doses of Gardasil 9[9]. In support of this argument, another study on the cost versus efficiency of 2 versus 3 doses of 9vHPVvaccine, conducted in the United States, pointed out that either 2 or 3 doses have the same comparable vaccine effect, thus 2-dose schedules are fairly profitable[10,11].

Clinical studies have showed that 9vHPV and qHPV are comparable in terms of efficacy against unremitting infection and cervical disease. The 9vHPV vaccine triggered a very strong immune response against all vaccine types, with sero-conversion rates closer to 100%. Swelling and pain, at the site of the injection, are more frequently noted after administration of 9vHPV than qHPV. It was reported to increase if the 9vHPV is co-administered with other vaccines[10].

As shown in a study of a 9vHPV vaccine administered to subjects aged between 11 and 15 years, in association with Repevax (diphtheria, tetanus, pertussis and poliomyelitis vaccines), the 9vHPV vaccine turned out to be safe and highly successful against infection and diseases related to HPV 6, 11, 16, 18, 31, 33, 45, 52 and 58 types[10].

This study concluded that concurrent administration of both 9vHPV vaccine and Repevax was on the whole well tolerated and did not interfere with the immune response to either vaccine, thus, reducing considerably the number of visits necessary to provide each vaccine individually[10].

Conclusions

The 9vHPV was authorized on the market by the FDA in 2014. It is the third vaccine that became available on the market for the purpose of preventing diseases caused by HPV.

The efficiency of the relatively new vaccine has been reviewed in many clinical studies which all rendered positive results. The real impact of the 9vHPV wide use cannot be precisely anticipated as it depends on different variables. However the impact of this new vaccine is linked to the broader coverage against five additional types of high-risk HPV. Also it is worth mentioning that the co-administration of 9vHPV with other immunization vaccines pointed out no significant interference.

In conclusion, the availability of new vaccine products on the market nowadays represents incredible breakthroughs, bringing the opportunity for implementing effective HPV vaccination programs worldwide that would lead to less prevalence of HPV related diseases. ■

References

1. FDA. FDA approves Gardasil 9 for prevention of certain cancers caused by five additional types of HPV. FDA; 2014.(Available from: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm426485.htm)
2. Health Canada. Note of compliance information Gardasil 9. Health Canada, 2015. (Available from: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/drug-med/sbd_smd_2015_gardasil9_170006-eng.php)
3. Public Health Agency of Canada Update on Human Papillomavirus (HPV) Vaccines. Canada Communicable Disease Report 2012, 38, 9. (Available from:http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/12vol38/acs-dcc-1/index-eng.php)
4. Therapeutic Goods Administration. Prescription medicines: registration of newchemical entities in Australia. Therapeutic Goods Administration, 2015. (Available from: https://www.tga.gov.au/prescription-medicines-registration-new-chemical-entities-australia-2015)
5. EMA. Gardasil 9 offers wider protection against cancers caused by human papillomavirus (HPV). EMA 2015. Available from: (http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/03/news_detail_002295.jsp&mid=WC0b01ac058004d5c1)
6. International Agency for Research on Cancer, World Health Organisation. IARC Monographs on the Evaluation of the Carcinogenic Risks to Human, 2016. (Available from: http://monographs.iarc.fr/ENG/Classification/)
7. Guan P, Howell-Jones R, Li N, Bruni L, de Sanjose S, Franceschi S. et al. Human papillomavirus types in 115,789 HPV-positive women: a meta-analysis from cervical infection to cancer. Int J Cancer 2012, 131, 2349-59.
8. Van Damme P, Bonanni P, Xavier Bosch F. et al. Use of the nonavalent HPV vaccine in individuals previously fully or partially vaccinated with bivalent or quadrivalent HPV vaccines. Vaccine 2016, Volume 34(6), 757-61.
9. European Medicines Agency Gardasil 9. Authorisation Details. [Last updated June, 2016]. (Available also from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/003852/human_med_001863.jsp&mid=WC0b01ac058001d124)
10. Kosalaraksa P, Mehlsen J, Vesikari T, et al. An open-label, randomized study of a 9-valent human papillomavirus vaccine given concomitantly with diphtheria, tetanus, pertussis, and poliomyelitis vaccines to healthy adolescents 11–15 years of age. Pediatr Infect Dis J 2015, 34(6), 627-34.
11. Laprise JF, Markowitz LE, Chesson HW, et al. Comparison of 2-Dose and 3-Dose 9-Valent Human Papillomavirus Vaccine Schedules in the United States: A Cost-effectiveness Analysis.(Available also from:https://www.ncbi.nlm.nih.gov/pubmed/27234416)