9-Valent HPV vaccine: the new generation of vaccines

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“Live, to err, to fall, to triumph, to create life from life”

James Joyce, 1915

It is widely known that the cervical cancer is preventable through proper treatment of pre-invasive lesions. In addition, being its etiology and carcinogenesis induced by certain types of human papillomavirus (HPV), since some years ago, is preventable through immunization against viral most frequently types associated with the development of this type of neoplasia. To date, two vaccines were available: a bivalent against types 16 and 18 and a quadrivalent against 16, 18, 6 and 11. In addition to cervical cancer, prophylactic vaccines also prevent other cancers where HPV plays an important role in the initiation and development as vulva, vagina, and anus, mainly.

On December 10, 2014, the U.S. Food and Drug Administration (FDA) approved the 9-Valent vaccine, 9 Gardasil, which prevents infection with nine HPV types: in addition to types 6, 11, 16 and 18, previously included in the quadrivalent vaccine, includes 31, 33, 45, 52 and 58. This vaccine is approved for use in females ages 9 through 26 and males ages 9 through 15. It is approved for the prevention of cervical, vulvar, vaginal and anal cancers caused by HPV types 16, 18, 31, 33, 45, 52 and 58, and for the prevention of genital warts caused by HPV types 6 or 11.

According to studies of the incidence of infection by HPV types in cancer of the cervix, including a study in Venezuela, if it is attributed to types 16 and 18 at least 70% of the cases, the 9-Valent vaccine would increase coverage up to 90%, avoiding at the same time between 75% and 85% of cases of NIC2-3. This new vaccine has a design similar to quadrivalent, with the same dosage and similar profile of efficacy, safety and side effects.

Several phase III studies were conducted which are in process of publication: a first study of efficiency in 14,000 women aged 16 to 26 years to evaluate dosage, efficacy, immunogenicity and safety. Immunobridging studies where compared the immunogenicity of the vaccine among
adolescents of both sexes and in relation to adults. Studies in adolescents of concomitant use with other vaccines such as meningococcal vaccine, reinforcement of triple vaccine, and Repevax, which includes polio. Also a safety study was done in patients previously vaccinated with the quadrivalent HPV vaccine. It is important to note, that in these studies, for ethical reasons, placebo was not used as in studies with the quadrivalent vaccine, but the 9-Valent was compared with the latter. The designs were of non-inferiority with respect to the tetravalent vaccine in respect to types 6, 11, 16 and 18, and superior efficacy with respect to new types of 9-Valent vaccine. There are two other studies in phase III which have not concluded which are those of comparison of immune response between women and men and the study of two-dose vaccination.

The results of efficacy studies demonstrated non-inferiority when comparing the same types of both vaccines (6, 11, 16 and 18), greater than 97% protection against types 31, 33, 45, 52 and 58 and a not lower immunogenicity between young women and adolescents of both sexes. This means that the new vaccine could be as efficient as the previous for the prevention of the four initial types and prevents infection by recently included types properly compared with the quadrivalent vaccine. Adverse effects were similar when comparing both vaccines. There was no interference from the 9-Valent vaccine when used concomitantly with other vaccines; undesirable effects were not apparent when vaccinating patients previously vaccinated with the quadrivalent HPV vaccine.

There are several aspects to note before starting this new phase of primary prevention of cervical cancer. First, what will be the cost of the 9-Valent vaccine compared with the quadrivalent and the bivalent, which probably will be greater, and if the cost-benefit ratio is similar or greater when compared to existing vaccines, knowing that the increase of prevention would be approximately 20%. The impact on the development of genital warts and other pathologies associated with low-risk viruses theoretically will remain equal, because the new vaccine does not difference in this regard.

The other aspect to consider is if the 9-Valent vaccine would replace the vaccines available. It seems appropriate, from now onwards, vaccinating girls with the 9-Valent, because it protects against more oncogenic types of HPV, but again, it should be considered cost-benefit by comparing the three existing types of vaccine to prevent cervical cancer, because types 16 and 18, are the most prevalent and more oncogenic types. It is necessary to evaluate if a difference of 20% would justify greater investment in immunization. So far, the countries that do not have a successful implementation of available vaccines have a higher incidence of cervical cancer. Keep up this trend is unlikely to improve the programs of primary prevention, in those regions, with the advent of the new vaccine. The inequality that is evident with respect to the screening and treatment of pre-invasive cervical lesions, unfortunately adds to the lack of an efficient plan of vaccination against HPV in countries with higher incidence.

The third aspect and, perhaps most important, is to decide what to do with the millions of people already vaccinated with bivalent and quadrivalent vaccines: If they will be immunized with the
new 9-Valent vaccine, if it is justified to synthesize a complementary vaccine with five types not present in the original vaccine, which seems unlikely, and vaccinate them, or if they are simply included in a closer screening than those immunized with the 9-valent. Many of the girls who were vaccinated are women already, and most will have started their sexual activity, so they would not be considered as target population for the new vaccine, by the probability of having been in contact with some of the newly included viruses.

Another aspect to evaluate, probably in the medium term, is how it would be modified the schemes of screening in the population that has been vaccinated against the nine types of HPV, since the probability of developing cancer of the cervix or pre-invasive lesions, is much less. Probably this aspect will be changing on the fly performing selective screening of unprotected populations or identifying the types not included in any immunizations.

The introduction of the 9-Valent vaccine is definitely good news. Extending the scope of protection against HPV, the fence around the cancer of the cervix and other types of cancer associated with this virus, narrows. Probably the substantial decrease in the incidence of cervical cancer, which will be in the long run, is a tangible reality as long as organized immunization and screening programs have adequate coverage in the countries with the highest incidence of the disease. That must be the commitment of all those who advocate the eradication of the cancer of the cervix in future generations.

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