

## LETTER TO THE EDITOR

### Could the human papillomavirus recombinant vaccine be a new valid approach in the management of ano-genital warts?

*Il vaccino ricombinante per il Papilloma Virus umano può rappresentare un nuovo valido approccio terapeutico nella gestione delle lesioni condilomatose ano-genitali?*

#### Abstract

*In line with previous case-reports, the study conducted by Hoom Choi ascertained the effectiveness of the HPV vaccine as a promising approach in the therapeutic management of ano-genital warts. The uncertain length of time and the varying effectiveness of traditional treatments encourage a reduction in the use of them and the development of a therapeutic use of HPV-vaccination. While the efficacy, safety profile and effects of the HPV vaccination in preventing ano-genital warts is well-known, therapeutic HPV vaccination has not been evaluated in a Randomized Prospective Trial, to date, and has not received a formal approval and an off-label indication for the treatment of those lesions. For these reasons, RCTs or cohort studies are warranted.*

To the Editor:

We read with interest the article by Hoom Choi (1) discussing the effectiveness of the human papillomavirus (HPV) vaccine towards HPV-associated genital warts, compared to surgical excision. Although this retrospective observational study presents some limitations and weaknesses that must be taken into account (e.g., the small size of the population involved and the study design), the utilization of HPV quadrivalent human papillomavirus prophylactic vaccine seems to represent a new valid and promising approach in the therapeutic management of genital and/or anal warts. Those findings confirm previous case-reports. Specifically, Hee Jung Lee et al. (2) showed a significant regression of a condyloma acuminatum in the perianal area after a single course of recombinant quadrivalent HPV vaccine in a 46-year-old man, who, not responding to imiquimod alone, had to stop this treatment because of an adverse reaction (cutaneous irritation). Similarly, Venugopal (3) presented a clinical case showing a complete resolution of recalcitrant multiple cutaneous warts after three injections of HPV vaccine.

HPV, a DNA virus from the papillomavirus group that resides in the basal cells of the stratified squamous epithelium and squamocolumnar junction of skin, is described in literature as the causative agent of genital and anal warts (4). The uncertain length of time and the varying effectiveness of the treatments

might have a significant impact on patients that experienced high levels of emotional distress, anxiety and depression.

Among treatments for HPV-associated lesions, we can list salicylic acid, trichloroacetic acid, bichloroacetic acid, cryotherapy, podophyllin resin, podophyllotoxin, imiquimod, carbon dioxide laser, and – finally - surgical excision.

Reducing the use of those traditional treatments could profoundly impact the healthcare system, entailing clinical and epidemiological implications in public health policies, including costs.

In order to achieve this goal, the identification, promotion and development of personalized therapeutic use of HPV vaccination is warranted in order to limit risk of complications, access to health services and morbidity, improving the quality of life of people diagnosed with HPV ano – genital lesions.

According to a vast body of literature, the efficacy, safety profile and effects of the HPV vaccination in preventing anal or genital warts is well-known. Indeed, in line with current guidelines, the nonovalent recombinant vaccine is normally injected in order to induce the production of neutralizing antibodies and thereby to prevent the spread of the viral infection. Several systematic reviews (5) have ascertained the role of prophylactic quadrivalent (4vHPV, against types 6, 11, 16, and 18) and nonavalent (9vHPV, against types 6, 11, 16, 18, 31, 45, 52 and 58) HPV vaccines in the prevention of HPV-associated precancerous and cancerous lesions, showing a significant protective effect. Thus, it is routinely recommended for female and male patients aged between 9 and 45 years.

Nevertheless, there is a limited evidence on the effectiveness and safety of HPV vaccination as an alternative approach for the therapeutic management of genital and anal warts. Therapeutic HPV vaccination has not been evaluated in a randomized prospective trial, to date. For these reasons, it has not received a formal approval and an off label indication for the treatment of genital and anal warts. The aforementioned studies demonstrated and ascertained a promising potential effect in determining a cell-mediated immune response. The regression of HPV-associated lesions after the therapeutic use of HPV vaccination could be potentially explained by the activation of the immune system, including T cells and macrophages.

With this letter, we want to highlight and put in evidence the potential use of the HPV vaccine for the treatment of genital and anal warts, especially in combination with immunomodulators and/or surgical techniques. Furthermore, the recourse to this vaccination might limit the side effects of some traditional treatments, such as excision.

Due to the small number of experimental studies conducted to date to assess the effectiveness of HPV vaccination in the therapeutic management of anal and genital warts, RCTs or cohort studies with a better methodological quality and larger sample sizes are needed to determine the beneficial effects of HPV vaccination, together with cost-benefit assessments in public healthcare system.

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