ESGO Prevention Committee opinion: is a single dose of HPV vaccine good enough?

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Currently licensed human papillomavirus (HPV) vaccines are very effective against cervical cancer and pre-cancer and probably also effective against five additional HPV-related cancers with no available screening strategies.[1] Antibodies triggered by the vaccine are different from antibodies subsequent to natural infection and are more effective.[2] Studies to date have shown that HPV vaccines produce a high level, high avidity, high durability, and long-lasting antibody response.

Despite the major benefits from vaccination and concerted efforts from policy makers and non-governmental organizations, effective immunization programs are yet to be established in many countries. This is largely due to limited resources for many countries and challenges in completing the recommended multi-dose vaccine regime in the target population. It is estimated that the current global coverage for fully vaccinated individuals is of the order of 15%.[3]

The emphasis of public health policies is to accelerate the impact of vaccination, to maximize vaccination coverage in the target population, to address vaccine supply shortages, and to facilitate vaccination delivery at reduced costs. The World Health Organization (WHO) 2019 recommendation emphasized that vaccinating girls by age 15 years offers the highest level of protection and public health impact on a global scale. Recently, the WHO Strategic Advisory Group of Experts (SAGE) on Immunization suggested that a single dose of the vaccine could be used in this young age group and published a recommendation for one or two doses up to the age of 20 years.[4] Interim advice from the Joint Committee on Vaccination and Immunization recommended moving to one-dose regimes for both girls and boys for routine immunization in the UK.[5] In a recent announcement, with the support of the Australian Technical Advisory Group on Immunization (ATAGI), Australia announced that it is changing its national immunization program. In line with the new program, the nonavalent vaccine, which is currently delivered free through school immunization programs to children aged 12–13, will be converted from two-dose to a single dose; young immunocompetent people under the age of 26 who have received a single dose of vaccine will be considered fully vaccinated, and free catch-up vaccine will be provided for those who have missed vaccination until the age of 26.[6]

REVIEW OF EXISTING DATA

The suggestions regarding the one-dose schedule are based on a number of observational data accumulated over the years coming from women who did not complete the vaccination schedule and recent randomized trials reporting good efficacy of a single-dose HPV vaccine.

The International Agency for Research on Cancer (IARC) study from India, a multi-center cohort study, generated effectiveness estimates of a single dose of quadrivalent vaccine compared with two and three doses in 5047 girls aged 10–18 years. The study reported that a single dose of HPV vaccine provides similar protection against persistent HPV16/18 infection as two or three doses. The follow-up was variable (interquartile range 8.2–9.6) with an average of 9 years.[7] The IARC study started as a randomized controlled trial (RCT) in 2009 (NCT00923702), aiming to compare the efficacy of two and three doses of quadrivalent vaccine in 20 000 unmarried female subjects aged 10–18 years. However, in 2010 the government of India issued a directive prohibiting any trial to recruit new participants or administer any vaccine. Therefore, the study group had girls who had completed two and three doses per protocol but also girls who were vaccinated with one dose or two doses out of protocol. An age- and site-matched control group was then recruited during 2013–2015. The sample sizes were balanced; however, the trial cannot be labeled as randomized but as a cohort study and therefore the evidence derived from the findings can be considered as moderate. In the long-term follow-up of the Costa Rica Vaccine Trial (CVT) (NCT00128661), 112 women aged 18–25 after a single dose of bivalent vaccine were assessed.[8] This cohort consists of women whose vaccine or control doses independent of trial arm were deferred mostly due to colposcopic referral and pregnancy, so that they missed the dose if the vaccination window was missed.[9] Approximately 9 and 11 years after initial HPV vaccination,