

SESSION 5

Prevention of Female and Male Genital Cancer

S14. Cervical Cancer: HPV-Screening and Vaccination

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Cervical cancer and precancerous lesions of the genital tract are major threats to the health of women worldwide. The introduction of screening tests to detect cervical cancer precursor lesions has reduced cervical cancer rates in the developed world, but not in developing countries. Human papillomavirus (HPV) is the primary etiologic agent of cervical cancer and dysplasia. Thus, cervical cancer and other HPV-associated malignancies might be prevented or treated by HPV vaccines. Two vaccine strategies have been developed. First, prevention of HPV infection through induction of capsid-specific neutralizing antibodies has been studied in clinical trials. However, because the capsid proteins are not expressed at detectable levels by infected basal keratinocytes or in HPV-transformed cells, a second approach of developing therapeutic vaccines by targeting nonstructural early viral antigens has also been devel-

oped. Because two HPV oncogenic proteins, E6 and E7, are critical to the induction and maintenance of cellular transformation and are coexpressed in the majority of HPV-containing carcinomas, most therapeutic vaccines target one or both of these gene products. A variety of approaches is being tested in therapeutic vaccine clinical trials, whereby E6 and/or E7 are administered in live vectors, as peptides or protein, in nucleic acid form, or in cell-based vaccines. The paradigm of preventing HPV infection through vaccination has been tested, and two vaccines are currently in phase III clinical trials. However, current therapeutic vaccine trials are less mature with respect to disease clearance. A number of approaches have shown significant therapeutic benefit in preclinical papillomavirus models and await testing in patient populations to determine the most effective curative strategy.