HPV vaccination and risk of miscarriage

26 Mar 2010

Wacholder A et al. – March 2010 – BMJ 2010; 340:c712

Risk of miscarriage with bivalent vaccine against human papillomavirus (HPV) types 16 and 18: Pooled analysis of two randomised controlled trials

Description: The interim analysis of one RCT (PATRICIA) performed to evaluate the efficacy of the two-valent HPV vaccine for prevention of cervical cancer precursors and persistent HPV infection showed an imbalance in the miscarriage rates between the two study arms. Because of this signal and the fact that the main target group for HPV vaccination is women of reproductive age, the decision was taken to use the data from two double blinded randomised controlled efficacy trials (CVT and PATRICIA) to assess whether vaccination with HPV vaccine increases the risk of miscarriage. In total 26 130 women aged 15-25 at enrolment participated in both efficacy studies. Participants were randomly assigned to receive three doses of bivalent HPV 16/18 VLP vaccine with AS04 adjuvant (n=13 075) or hepatitis A vaccine as control (n=13 055) over six months. Participants agreed to use birth control starting one month before the first and lasting until two months after the last vaccination. All participants underwent a pregnancy test before each vaccination. 3599 pregnancies during the follow up period were eligible for the present analysis. Miscarriage was defined as loss of pregnancy within 20 weeks after the last period. Women were instructed to report any adverse event related to pregnancy at any time during follow-up, and they were contacted after their expected delivery date to learn the pregnancy outcome. Overall, the rates of pregnancies and live births were similar in both arms and there was no significant increase in miscarriage among women assigned to the HPV vaccine arm. Among the subgroup analyses, there was a statistically non-significant imbalance for estimated miscarriage rates for pregnancies conceived within three months after the nearest vaccination.
The full text article is available free of charge here.

Disclosure statement: The CVT trial in Costa Rica is sponsored and funded by the National Cancer Institute (N01-CP-11005) with support from the NIH Office for Research on Women's Health and conducted in agreement with the Ministry of Health of Costa Rica. PATRICIA is funded by GSK Biologicals. GSK Biologicals contributed data from PATRICIA to the here presented analysis, and commented on aspects of the trial at the design stage and after the results were shared with investigators of both trials, with the permission of the Data Safety Monitoring Board of CVT. GSK Biologicals had no role in study design and the collection, analysis, and interpretation of data from CVT in this paper, or in the writing of the article.

ECDC comment: Although the study provides some reassurance that there is no significant increased risk of miscarriage associated with HPV vaccination, the results also clearly show the need for further close monitoring of vaccine safety using post-marketing surveillance if possible combined or complemented by independently done pooled analyses of all data available from efficacy studies, as shown in the here presented paper.