

Therapeutic HPV vaccine for cervical intraepithelial neoplasia



Tipapkinogen sovacivec (TS), a therapeutic human papillomavirus (HPV) vaccine, provides histological resolution of cervical intraepithelial neoplasia (CIN) grades 2 and 3 in a third of patients, irrespective of HPV type, according to a new study.

In a randomised phase 2 trial, Diane M Harper (University of Michigan, Ann Arbor, MI, USA) and colleagues recruited women aged 18 years and older, with grade 2–3 CIN associated with single or multiple infections by any of the 13 high-risk HPV types. Women were randomly assigned (2:1) to receive three subcutaneous doses of the TS vaccine (n=129) or placebo (n=63). The primary endpoint was histological resolution assessed 6 months after treatment in patients with HPV16 monoinfection (55 in the vaccine group and 27 in the placebo group).

Among the women with HPV16 monoinfection, histological resolution of grade 2–3 CIN was 18% (95% CI 8–28) in the vaccine group and 4% (0–11) in the placebo group. Histological resolution in all randomised women, irrespective of HPV types, was significantly higher in the vaccine group than in the placebo group (24% [95% CI 17–31] vs 10% [2–17]; $p<0.05$). Among women with grade 3 CIN lesions at baseline, histological resolution was also significantly higher in the vaccine group (21% [95% CI 12 to 30] vs 0% [–2 to 2]; $p<0.01$). Viral DNA clearance of all HPV types was significantly higher in vaccine-treated patients than in the placebo group ($p<0.01$). Nearly all recipients in the vaccine group had an injection-site reaction compared with 37% who received placebo.

"This is the first time that we have seen such a high level of

HPV and grade 2–3 CIN clearance with a therapeutic vaccine," notes Harper. Peter Sasieni (King's College London, London, UK) welcomed the findings. "The results are scientifically important," he said. "They open up the possibility of exploring whether the vaccine can be applied to other HPV-associated cancers and anal or vulvar lesions, which are much harder to treat." But he suspects that the clearance rate for grade 2–3 CIN is not high enough to warrant further investigation, given the availability of effective surgery.

"For women hoping to preserve their cervix, even a 24% clearance of both HPV and abnormal cells is promising, especially since surgery does not clear the causative agent," responds Harper. A decision is yet to be made on whether to advance the vaccine to phase 3 trials.

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Published Online
April 12, 2019
[http://dx.doi.org/10.1016/S1470-2045\(19\)30224-4](http://dx.doi.org/10.1016/S1470-2045(19)30224-4)

For the study by Harper and colleagues see *Gynecol Oncol* 2019; published online April 4. DOI:10.1016/j.ygyno.2019.03.250