Data used to justify Indian HPV vaccination trial questioned

A trial of human papillomavirus (HPV) vaccines in India, halted by the Indian Government in 2010, ran into fresh controversy with the publication of a study suggesting that the trial should not have been started in the first place.

The HPV vaccine trial of more than 23 000 girls from Gujarat and Andhra Pradesh, run by the Program for Appropriate Technology in Health (PATH), an international charity, was suspended by the Indian Government after reports of deaths of four girls in the trial and subsequent emergence of alleged ethical violations in the nature and conduct of the trial. The new study by researchers in the UK suggests that available scientific data on cervical cancer incidence and HPV type did not even justify starting the trial, which involved the rolling out of vaccines against HPV in the general population.

Study investigator Allyson Pollock (Queen Mary University of London, London, UK), says that, "One would not start with a trial of safety and feasibility unless the evidence is secure and the surveillance systems are in place. Our study shows the woeful neglect of public health science both in terms of ensuring the vaccine is effective, that the public health data are compelling and there are good surveillance systems".

However, Vivien Davis Tsu, (PATH, Seattle, WA, USA) claims that "PATH never called for 'the general rollout of a HPV vaccination programme either in India or in the two states' where the research was done. Our goal always was to generate evidence on which strategies for delivering the vaccines were feasible, acceptable, and affordable, should the Indian Government decide one day that such a service belonged in their cervical cancer control programme."

Roza Olyai (Federation of Obstetric and Gynecological Societies of India, Gwalior, India) feels that, "to address such research questions conclusively the need of the hour is to have a proper cancer registry which is representative of the Indian population...India is doing great work in the field of medicine but when it comes to proper documentation, registration, and other related aspects we are far behind".

Based on the findings of their study, Pollock further demands that, "The government should suspend all sales of the vaccines including those to the private market and private individuals. Marketing approvals and authorisations should be linked to public health evidence."

Tsu on the other hand feels that, "... it seems counterproductive to say that we should not save lives using new, proven medical advances until we have 'universal health care and integrated healthcare systems', as called for by the authors. That would be an example of the ideal being an enemy of the real, or possible."

Soumyadeep Bhaumik

Colin Cuthbert/Science Photo Library

Published **Online**
June 29, 2012
http://dx.doi.org/10.1016/S1470-2045(12)70299-1

For more on **the UK study questioning the Indian HPV trial data** see *J R Soc Med* 2012; **105:** 250–62

Potential therapeutic target for triple-negative breast cancer

A chromosomal rearrangement that fuses the genes *MAGI3* and *AKT3* has been identified in triple-negative breast cancer, providing a potential therapeutic target for this subtype, which has few treatment options.

The *MAGI3–AKT3* fusion gene was reported in a recent study on genomic alterations in human breast carcinomas. To identify abnormalities that drive the growth of these malignancies, whole-genome sequencing was done in untreated primary breast cancers from all major subtypes. The previously unknown fusion gene was enriched in the triple-negative subgroup—ie, those without estrogen receptors, progesterone receptors, and HER2 overexpression—of the 235 breast cancer samples screened.

Laboratory studies of the MAGI3–AKT3 fusion protein showed that the AKT3 kinase domain was hyperactivated, and in turn, activated signaling pathways that enhance tumour cell growth. A specific type of AKT inhibitor currently in clinical trials for other cancers— the type that specifically target the ATP-binding site—blocked this kinase activity. These results should therefore encourage future clinical studies of ATP-competitive AKT inhibitors in fusion-positive, triple-negative breast cancer.

Kristin Brown (Beth Israel Deaconess and Harvard Medical School, Boston, MA, USA), an investigator in this study, said that, "This study has shown that large scale breast cancer sequencing efforts can identify genetic alterations that we can target for future therapy." She added that the MAGI3–AKT3 fusion "is the first oncogenic fusion protein that has been found in the PI3-kinase pathway."

Joe Gray (Knight Cancer Institute, Oregon Health and Science University, Portland, OR, USA), added that, "We are beginning to identify recurrent and likely targetable genomic abnormalities in breast cancer. While the frequency of many of these abnormalities is disappointingly small in breast cancer, they may be tractable as targets when their prevalence in all cancer types is considered." He commented that identification of the *MAGI3–AKT3* fusion, "certainly raises the possibility that the PI3 pathway is being deregulated in a subset of triple-negative cancers. It may be possible to go after this subset using drugs already available that target this pathway."

Judith A Gilbert

Published **Online**
June 29, 2012
http://dx.doi.org/10.1016/S1470-2045(12)70298-X

For the ***MAGI3–AKT3* fusion gene study** see *Nature* 2012; **486:** 405–09