Candidate tuberculosis vaccine in phase II/III trial

March 23 2018

Researchers hope VPM1002 will reduce the infection risk of newborns of HIV-infected mothers. Credit: Leander Grode, VPM (with consent of study participants

Tuberculosis remains the most deadly infectious diseases in the world. In particular, the growing number of multiresistant microbes is a cause of great concern to doctors and healthcare policymakers. At least a dozen candidate vaccines are currently undergoing clinical testing. One of them, VPM1002, has now been approved for use in a clinical efficacy trial. The trial is designed to test the vaccine's efficacy and safety in patients in whom tuberculosis resurfaces following successful drug therapy. In addition, a phase II trial on newborns exposed to HIV has been completed with promising results.

Despite the fact that tuberculosis affects two billion people in the world with over ten million new cases every year, it sometimes seems like it is a forgotten disease. In any case, it rarely makes headlines like Ebola and Zika, despite claiming more lives in the past 200 years than smallpox, malaria, plague, influenza, cholera and AIDS put together. Yet experts have been warning of the increasing threat posed by tuberculosis for years, especially in view of rapidly spreading resistance. In response to this situation, the United Nations is holding a high-level meeting devoted to tuberculosis at its General Assembly meeting in New York at the end of September – only the fifth meeting to be dedicated to a health-related topic.

Scientists are also urgently working on new diagnostic agents, drugs and vaccines. Researchers at the Max Planck Institute for Infection Biology laid the scientific foundations for the clinical development of the candidate vaccine VPM1002. In 2015, the Max Planck Society licensed VPM1002 to the Serum Institute of India, one of the biggest vaccine manufacturers in the world. Since then, the company has been refining the vaccine together with Vakzine Projekt Management GmbH (VPM).

VPM1002 is currently being tested in a trial with some 2000 subjects in India. The trial was launched in early 2018 and is slated to end in mid-2020. In order to minimize the number of trial subjects and the trial

duration while still obtaining meaningful results, the researchers are testing the vaccine in patients who have already been successfully treated for tuberculosis in the past. For unknown reasons, around ten percent of such patients experience a resurgence of tuberculosis within a year.

Some of the subjects will be immunized with VPM1002 a few weeks after being cured. "If VPM1002 is able to reduce the relapse rate in this particularly difficult group with recurrent tuberculosis, and if it proves to be well tolerated, it will have cleared a key hurdle on the path towards marketing authorization," explains Stefan Kaufmann of the Max Planck Institute for Infection Biology, who was instrumental in developing the scientific concept for VPM1002.

Clinical study on newborns completed

A clinical phase II trial on over 400 newborns of HIV-infected or uninfected mothers, which began in mid-2015, has meanwhile been completed without any untoward results. It is hoped that the trial results will be validated after the final data analysis of a phase III trial on at least 5000 newborns. "This large-scale trial in southern Africa is designed to determine whether the vaccine is safe for HIV-exposed and unexposed newborns and whether it confers protection. The European and Developing Countries Clinical Trials Partnership (EDCTP) has approved the trial, meaning that funding has been secured," Kaufmann says.

Tuberculosis research has made very little progress over the past century. Only since the early 21st century has this gradually begun to change. More than a dozen candidates are currently undergoing clinical testing. Of all the candidates, VPM1002 has proved to be the most successful and effective in clinical trials. It was developed on the basis of a tuberculosis vaccine called BCG – short for Bacillus Calmette–Guérin.

Every year millions of infants are immunized with the BCG vaccine in regions where tuberculosis is endemic. The vaccine protects newborns against severe forms of tuberculosis. However, it does not protect adults and newborns against pulmonary tuberculosis, a widespread form of the disease. Scientists at the Max Planck Institute in Berlin genetically modified VPM1002 so that it primes the immune system more strongly against the tuberculosis bacterium. Consequently, it confers protection against tuberculosis more effectively than the BCG vaccine and some day may be used as a replacement for the BCG vaccine in newborns as well as for boosting BCG vaccinations in adults.

Provided by Max Planck Society