

Tuberculosis vaccine candidate VPM1002 safe in HIV- and non-HIV-exposed newborns as study shows

No other infectious disease has killed more people than tuberculosis. Currently, only one vaccine is available to prevent severe courses: *Bacillus Calmette Guérin* (BCG). However, it is not equally effective against all types of tuberculosis. Especially infants and immunocompromised patients are therefore in urgent need for more effective tuberculosis vaccines. A clinical trial in South Africa has now shown that the new vaccine candidate VPM1002, developed by Max Planck researcher Stefan H.E. Kaufmann and his team, is equally safe for newborns with and without HIV exposure and has fewer side effects compared to BCG.

At least 20 million people worldwide suffer from tuberculosis, according to World Health Organization (WHO), with 10 million new cases every year and about 1.5 million deaths annually. The disease is caused by mycobacteria, which predominantly affect the lungs, but can also infect any other organ. Tuberculosis is particularly common in low income countries. Here, the WHO recommends that newborns be immunized against it as soon as possible.

First used 100 years ago, the BCG vaccine against the disease contains attenuated pathogens of cattle tuberculosis. “We know that BCG can prevent so-called tuberculous meningitis and miliary tuberculosis in infants with a 75 to 86 percent effectiveness rate. But this is not the case for the most common form of the disease, pulmonary tuberculosis, in all age groups. Here, BCG is only insufficiently effective,” explains Kaufmann, Emeritus Director at the Max Planck Institute (MPI) for Multidisciplinary Sciences in Göttingen and the MPI for Infection Biology in Berlin.

Since the 1990s, the infection biologist and his team have been working on an improved next-generation vaccine, called VPM1002. To achieve this, the researchers genetically modified the attenuated BCG vaccine strain so that immune cells can better recognize the pathogens. “We developed VPM1002 in no small part to combine increased safety with improved efficacy for immunocompromised children,” the Max Planck researcher reports.

The group of immunocompromised children includes, for example, HIV-exposed infants born to HIV-positive mothers. In a clinical trial in South Africa, an international research consortium including Kaufmann has now compared VPM1002 with BCG in HIV-exposed and non-HIV-exposed newborns. The study examined both the safety and the immune response induced – called immunogenicity – associated with the formation of immune cells and immunostimulatory proteins. The results of this study are published in the current issue of the medical journal *The Lancet Infectious Diseases*. The conclusion: VPM1002 is safe in both HIV-exposed and non-HIV-exposed newborns, has fewer side effects than BCG, and elicits a similar immune response.

In the randomized phase II double-blind study in South Africa, 416 eligible newborns were randomly selected and vaccinated before day 12 of life. 312 of them received VPM1002, and 104 received the BCG vaccine. As the study showed, VPM1002 triggered fewer vaccine-

related adverse reactions than BCG. This was true for reactions occurring at the injection site, such as scarring and abscess formation, as well as enlargement of lymph nodes. This finding is important because local and regional reactions after vaccination are among the limitations of the BCG vaccine, Kaufmann points out.

Newborns with or without HIV exposure showed similar immunogenicity with both vaccines. However, starting at six weeks of age, the BCG-triggered immune response was greater than in even younger infants.

“Studies such as those described here examine a vaccine’s immunogenicity, but not its protection. For the latter, we have already developed a larger phase III clinical trial and have successfully enrolled mothers with their newborns to participate. Now the clock is ticking,” Kaufmann said. The infectious biologist expects initial results showing whether VPM1002 can provide comparable or better protection than existing BCG vaccines in about three years. In addition, the VPM1002 vaccine is currently evaluated in adults in two other phase III clinical trials in India for protection against tuberculosis. These trials are expected to be completed in 2023 and 2024, respectively.

The Max Planck Society licensed the VPM1002 vaccine to the company *Vakzine Projekt Management* (VPM) in 2004. Starting in 2012, the company continued to develop the vaccine in collaboration with the Serum Institute of India, one of the world’s largest vaccine manufacturers. “Serum Institute of India is giving access to a unique solution for tuberculosis elimination by detect-treat-prevent strategy. VPM1002 is a unique component of this strategy, and it will help in preventing infection and disease. The ongoing phase III trial is one of the key trials in order to strengthen our scientific rationale. Pleased to see that we have completed recruitment of all infants in such an important trial,” said Umesh Shaligram, Executive Director R&D of Serum Institute of India. (cr)

Original Publication

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