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SHORT REPORT

TAK-003 dengue vaccine – a new hope for safe travel to endemic areas: efficacy, safety and future perspectives

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Abstract

Background: Dengue fever remains a major health risk, with 100 to 400 million clinical cases occurring each year. TAK-003 a tetravalent live-attenuated vaccine, offers potential protection against all four dengue virus (DENV) serotypes (DENV-1, DENV-2, DENV-3, DENV-4), providing a new option for travelers to dengue-endemic areas.
Material and methods: This paper examines the efficacy and safety of the TAK-003 dengue vaccine, with a focus on its potential to protect seronegative travelers visiting regions endemic to dengue. The analysis includes data from clinical trials assessing its performance in both seropositive and seronegative individuals, and its ability to prevent severe disease and hospitalizations.
Results: TAK-003 dengue vaccine has shown high efficacy against DENV-1 and DENV-2, while efficacy against DENV-3 was comparatively lower, particularly in seronegative individuals. The vaccine is generally well-tolerated, with mild side effects such as injection site pain and headaches. Importantly, it offers strong protection against severe dengue cases and hospitalizations, making it a valuable tool for travelers.
Conclusions: TAK-003 dengue vaccine provides high protection in dengue-endemic regions, particularly against DENV-1 and DENV-2. Protection is higher in seropositive individuals, likely due to prior infection. Vaccination is not recommended for travelers with no history of dengue fever. A booster dose study is under consideration.
Keywords: safety, vaccine, dengue fever, efficacy, TAK-003

Introduction

Global travel increases exposure to health risks, including dengue fever in endemic regions. The new TAK-003 vaccine offers travellers added protection against this mosquito-borne disease. TAK-003, a tetravalent live-attenuated vaccine, offers potential protection against all four dengue virus (DENV) serotypes (DENV-1, DENV-2, DENV-3, DENV-4) [2].

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Traditional prevention has relied on mosquito control and personal protection, although effectiveness is limited. The existing Dengvaxia® vaccine is limited to seropositive individuals, as seronegative vaccination may worsen dengue due to antibody-dependent enhancement, leading to more severe reinfection outcomes. During a mass Dengvaxia® campaign in the Philippines, 51 deaths were reported, primarily among seronegative children, most between 9 and 13 years of age, with 15 cases confirmed as dengue-related [3].

This report evaluates the TAK-003 dengue vaccine's potential as a standard health measure for tourists in endemic zones, assessing its efficacy and prospects for safer travel and protection against dengue fever.

Vaccine efficacy

Clinical trials were conducted in endemic countries (Brazil, Colombia, Nicaragua, Panama, the Philippines, Sri Lanka, the Dominican Republic, Thailand) in the 4–16 age group and non-endemic countries (the United States) in the 18–60 age group. The first dose of the vaccine was administered on day 0, and then the second dose after 90 days [4–6].

During the vaccine immunogenicity study, seropositivity rates in baseline seronegative individuals increased from 0% at the start of the study to between 94.6% and 100% on day 120 after vaccine injection. Seropositivity declined slightly by day 270 post-injection, but still remained at substantially high levels, ensuring efficacy. Clinical immunogenicity trials have confirmed that the TAK-003 vaccine is highly immunogenic against all four dengue serotypes in both adults and children, regardless of whether they have been previously exposed to the virus [4,5].

In people who are baseline seronegative (i.e., no previous contact with the dengue virus), the TAK-003 dengue vaccine provides protection primarily against serotypes DENV-1 and DENV-2, which are responsible for the most severe cases of dengue fever. In particular, DENV-2 often leads to hemorrhagic fever (HF). However, it is worth mentioning that the vaccine does not provide high protection against less common serotypes, such as DENV-3 and DENV-4.

In the long-term study, three years after two doses of TAK-003, the efficacy of the vaccine against hospitalized virologically confirmed dengue (VCD) remains high, providing solid protection against a severe clinical course and possible hospitalization. However the decline in efficacy against VCD observed in the long-term clinical studies suggests some reduction in protection against milder courses of infection (Figure 1).

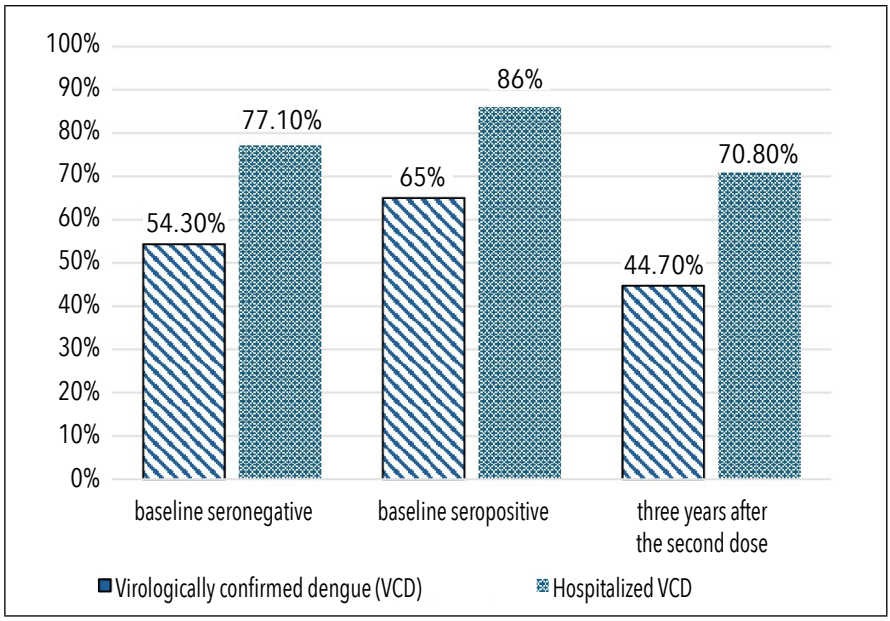

Figure 1. Efficacy of the TAK-003 dengue vaccine over time

Source: Figure created by the author, based on data from [5].

It is also worth noting that the vaccine's efficacy increases with age in children and adolescents. The results of one study suggest slightly lower cumulative vaccine efficacy in the youngest age group. In the 4–5 year age group, there was a decrease in efficacy from a result of 72.8% at one year post-vaccination to 24.5% at two years post-vaccination. In the older age groups, efficacy appeared to be higher after vaccination and showed a smaller decrease over time. In the 6–11 age group, efficacy was 80.7% after one year post-vaccination and decreased to 60.6% after two years. In the 12–16 age group, there was 83.3% efficacy after one year and 71.2% after two years post-vaccination [5,6].

Safety

Safety analyses conducted after administration of the vaccine showed no anaphylactic reactions associated with vaccination. Long-term observation after the vaccine for up to four weeks showed no serious adverse reactions or vaccine-related deaths during follow-up, which was carried out up to 36 months after the last dose [4,5,7].

No significant safety risks or concerns were identified according to gender, pre-vaccination serological status or age in the 4–60 age group.

However, local side effects, such as pain, redness and swelling at the injection site, were observed, which were mild and resolved rapidly (within one to three days). Systemic side effects mainly included headache and myalgia and resolved after three to four days. These symptoms occurred more frequently after the first dose, with a reduced number of reported cases after the second dose [8].

As it is a live vaccine, vaccination is contraindicated in pregnant or breastfeeding women, in immunosuppressed persons (including those with congenital immunodeficiencies and those undergoing immunosuppressive therapy), in people, who have received chemotherapy or high doses of systemic corticosteroids during the four weeks before vaccination, and in HIV-infected people with both symptomatic and asymptomatic impaired immune function [2].

Practical Tips for Travellers

The vaccine should be given in two doses, three months apart [2]. It is advisable to begin vaccination a few months before travel. In addition, other preventive measures, such as mosquito repellents, protective clothing and avoiding being outdoors during peak mosquito activity should be considered. In seropositive individuals only, the previous vaccine, Dengvaxia, should be explored in order to increase protection against dengue fever [1,3].

From a vaccination standpoint, there are various approaches to the issue, which depend on the committee (the UK, Germany and WHO respectively). The Joint Committee on Vaccination and Immunization (JCVI) and the Standing Committee on Vaccination (STIKO) do not recommend vaccination for those who have no history of dengue fever prior to travel. The Strategic Advisory Group of Experts on Immunization (SAGE) has highlighted the vaccine's lower efficacy in such individuals. The Swedish Society for Infectious Disease Physicians recommends that vaccination for dengue should be considered in the 4–16 age group, while above the age of 17 vaccination should only be considered for longer trips. There is no upper age restriction for the TAK-003 vaccine, and in the clinical trials there were no participants over 60 years of age [9–12].

However, the WHO has issued a recommendation regarding vaccinating children in the 6–16 age group with TAK-003 only in endemic countries with a high intensity of dengue virus transmission [1].

It is important to keep in mind that the vaccine primarily protects against severe forms of dengue and not necessarily against the infection itself, which is often asymptomatic [13] or mild. TAK-003 dengue effectively reduces the risk of hospitalization and severe cases of dengue fever [5,7,8],

which is an important concern, especially for older adults or those travelling to high-risk areas.

TAK-003 dengue vaccine can be given simultaneously with hepatitis A virus (HAV) and yellow fever vaccines. The results of the study showed that the combined administration of the vaccines does not reduce the effectiveness of any of the vaccines and has no impact on safety [14,15].

Conclusions

TAK-003 dengue vaccine provides a high level of protection to seropositive travellers in endemic countries. Studies have shown particularly high efficacy against serotypes DENV-1 and DENV-2, with lower efficacy against DENV-3. The vaccine has high efficacy that protects primarily against severe cases of dengue fever and the need for hospitalization. Vaccination of seronegative travellers should only be considered in the case of longer stays in endemic countries. The vaccine showed similarly high efficacy in every age group apart from the youngest 4–5 age group that participated in the clinical trial. However, they represented the smallest age group, making it difficult to draw firm conclusions. The vaccine demonstrates a strong safety profile, and adverse events, such as local pain at the injection site, are considered to be a natural reaction of the body to the needle injection. It is worth bearing in mind that the TAK-003 vaccine does not provide a high level of protection against serotype DENV-3 and DENV-4, and vaccine efficacy is lower in seronegative individuals. In dengue infection, antibody-dependent enhancement (ADE) may occur, increasing the risk of severe disease upon secondary infection with a different serotype. Further research is needed to investigate the possibility of a booster dose, which may increase the efficacy of the vaccine against less common serotypes and extend the duration of efficacy.

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