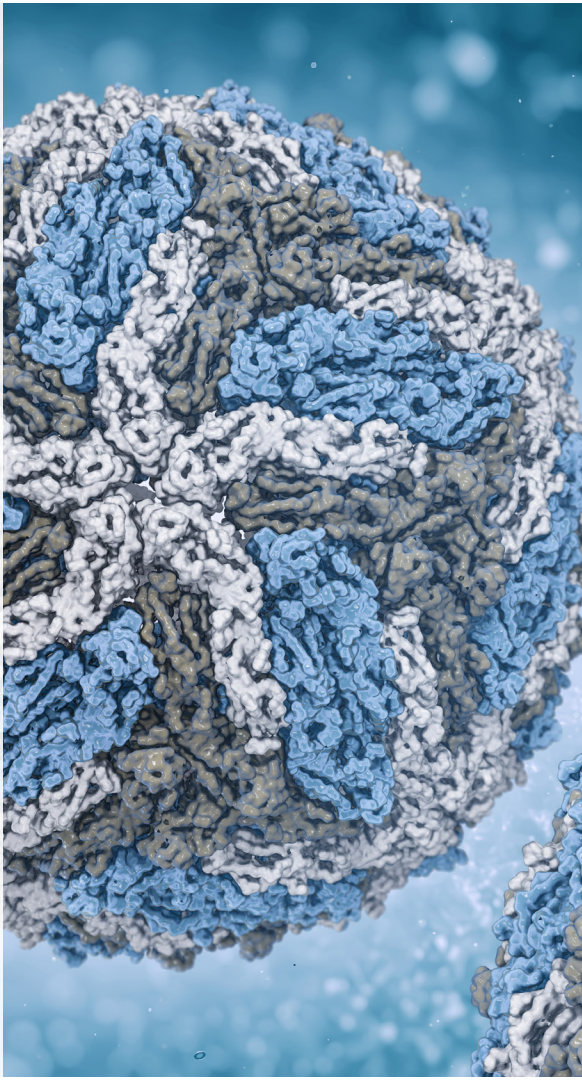
Takeda

Better Health, Brighter Future

ABOUT DENGUE AND TAKEDA'S DENGUE VACCINE CANDIDATE (TAK-003)



Dengue is caused by four distinct, but closely related, dengue virus serotypes (DENV-1, 2, 3 and 4).[1]

Each serotype can cause debilitating dengue fever, also called "breakbone fever," or more severe, life-threatening disease forms.[1]

Infection with one dengue serotype confers life-long protection against re-infection with the same serotype, but only short-term protection against the other three serotypes.

Sequential infections with different serotypes can potentially increase the risk of developing severe dengue disease.[1] However, less than 5% of secondary infections lead to severe dengue.

Dengue virus can infect people of all ages and is a leading cause of serious illness among children in some countries in Latin America and Asia.[1]

Approximately 3.9 billion people around the globe – half of the world's population – are at risk of dengue.[1] Dengue is now endemic in more than 100 countries and causes an approximately 390 million infections and more than 20,000 deaths globally each year.[1,2]

Dengue has expanded in recent years due to urbanization, air travel, population growth and climate change.[3]

Successful control of vector-borne diseases, such as dengue, requires a comprehensive set of interventions, including vector control, public education and, ideally, safe and effective vaccines.

Takeda is developing a live-attenuated tetravalent dengue vaccine candidate (TAK-003) to help address unmet needs in dengue prevention. We are committed to developing a dengue vaccine that is safe for and protects those at risk of symptomatic dengue caused by any of the four virus types, regardless of whether they have previously been exposed to dengue.

Takeda's dengue vaccine candidate is designed to protect against all four types of the dengue virus, and activate multiple arms of the immune system, including antibodies and immune cells. This is because TAK-003 is based on a live-attenuated dengue serotype 2 virus (DENV-2), which provides the genetic 'backbone' for all four vaccine viruses.[4,5]

Because TAK-003 is based on an attenuated form of the dengue virus itself, it exposes the individual to a number of components of the virus that could be important in protection against future infection with dengue virus. Data from ongoing Phase 3 trials will determine vaccine efficacy and safety against all four virus serotypes, in both seronegative and seropositive individuals.

In clinical trials to date, Takeda's dengue vaccine candidate (TAK-003) has been shown to be generally well-tolerated, with no significant safety risks observed.[6,7,8]

The Phase 1 and Phase 2 clinical trial program for TAK-003 is comprised of eight studies in children and/or adults.[6,7,8]

The data generated from these studies supported progression into a Phase 3 study (Tetravalent Immunization against Dengue Efficacy Study ([TIDES]) based on the overall safety and reactogenicity profile, as well as the induction of neutralizing antibody responses against any of the four dengue virus serotypes across age groups and in both seropositive and seronegative individuals.[6,7,8]

Safety data from an 18-month interim analysis of the ongoing Phase 2 DEN-204 trial also showed that TAK-003 was associated with reduced incidence of dengue in children and adolescents, supporting the decision to continue the Phase 3 study.[9]

The TIDES trial, Takeda's largest interventional clinical trial to date, enrolled over 20,000 healthy children and adolescents ages four to 16 years living in dengue-endemic areas. The study was designed to evaluate the efficacy, safety and immunogenicity of two doses of TAK-003, in both dengue exposed and naïve individuals.

The pivotal Phase 3 TIDES trial met the primary endpoint of overall vaccine efficacy irrespective of dengue serotype, serostatus, or severity (based on 12-month follow-up data after the second dose). TAK-003 was generally well tolerated, and no important safety risks have been observed to date.[10]

The second part of the study continued for an additional six months (18 months after the second dose, which was administered three months after the first dose) to complete assessment of secondary efficacy endpoints by serotype, baseline serostatus and disease severity. Overall vaccine efficacy (VE) and safety results from the second part of the study were generally consistent with the data reported in the primary endpoint analysis.

The 18-month data demonstrated VE against hospitalized dengue and dengue hemorrhagic fever. VE was similar in baseline seropositive and seronegative individuals, and varied by individual serotype. Efficacy against severe virologically-confirmed dengue could not be determined due to insufficient number of cases.

The TIDES trial is ongoing, and longer-term data will be important in determining the efficacy and safety profile of Takeda's dengue vaccine candidate. Safety and efficacy will be assessed over a total of four and a half years.[11]

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