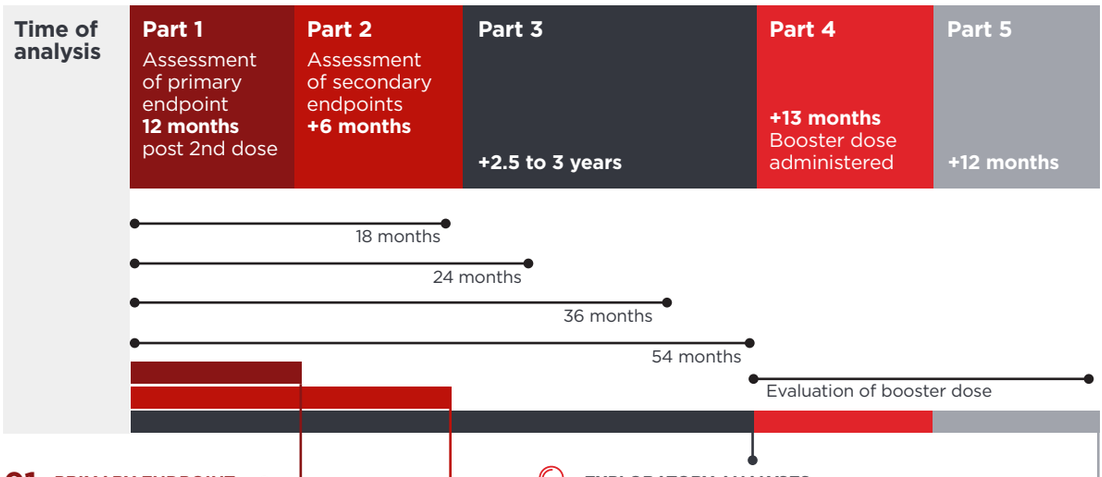
TIDES
Takeda's Pivotal Phase 3 Dengue Clinical Trial

This fact sheet provides an overview of primary and secondary endpoints and long-term follow up exploratory results through 7 years from the Tetravalent Immunization against Dengue Efficacy Study (TIDES).

Trial Overview

- The TIDES trial is a Phase 3, double-blind, randomized, placebo-controlled trial designed to evaluate the efficacy, safety and immunogenicity of a two-dose schedule, three months apart, for Takeda's dengue vaccine (TAK-003) in healthy children.[1]
- The TIDES trial is Takeda's largest interventional clinical trial to date and was designed according to the World Health Organization's dengue vaccine development guidance.[2] The trial enrolled over 20,000 healthy children and adolescents ages four to 16 years living in dengue-endemic areas.[1]

The study is comprised of five parts:



01 PRIMARY ENDPOINT

The trial met the primary endpoint, demonstrating efficacy against virologically confirmed dengue (VCD) irrespective of dengue serotype or serostatus (based on evaluation of 12-month follow-up data after the second dose).

- Overall vaccine efficacy (VE) was 80.2% (95% confidence interval [CI] 73.3% to 85.3%; p<0.001)
- Incidence of VCD in placebo recipients compared to those who received TAK 003 was 2.4% and 0.5%, respectively.

These data were published in the New England Journal of Medicine in November 2019.[3]

02 SECONDARY ENDPOINTS

The trial met all secondary endpoints for which there were a sufficient number of cases (based on evaluation of 18-month follow-up data after the second dose). TAK 003 demonstrated:

- 90.4% VE against hospitalized dengue (95% CI: 82.6% to 94.7%; p<0.001)
- 76.1% VE against VCD in seropositive individuals (95% CI: 68.5% to 81.9%) and 66.2% VE in seronegative individuals (95% CI: 49.1% to 77.5%)
- 85.9% VE against dengue hemorrhagic fever (95% CI: 31.9% to 97.1%)

Varying VE by individual serotype:

- 69.8% for dengue serotype 1 (95% CI: 54.8% to 79.9%)
- 95.1% for dengue serotype 2 (95% CI: 89.9% to 97.6%)
- 48.9% for dengue serotype 3 (95% CI: 27.2% to 64.1%)

Two secondary endpoints were not met, largely due to the small number of cases:

- Efficacy against dengue serotype 4
- Efficacy against severe VCD (Dengue Case Adjudication Committee [DCAC] criteria)

These data were published in The Lancet in March 2020.[4]

EXPLORATORY ANALYSES

54-month follow-up data showed:[4]

- 61.2% overall VE against VCD (95% CI: 56.0% to 65.8%)
- 84.1% VE against hospitalized dengue (95% CI: 77.8% to 88.6%)
- 64.2% VE in seropositive individuals (95% CI: 58.4% to 69.2%) and 53.5% VE in seronegative individuals (95% CI: 41.6% to 62.9%)

These data were published in The Lancet Global Health in January 2024.[5]

EVALUATION OF BOOSTER DOSE

7-year follow-up data showed that the two-dose regimen provided sustained protection against dengue:[5,6]

- A booster dose administered at 4.5 years marginally increased overall efficacy against VCD to 74.3% VE (95% CI: 66.7% to 80.1%) after 2 years
- VE against dengue-related hospitalizations remained consistently high at 90.6% (95% CI: 78.9% to 95.8%)

These data were presented at the World Society for Pediatric Infectious Diseases in October 2025 and Takeda plans to continue to evaluate the results in totality and publish in a peer-reviewed journal.[6]

TIDES TRIAL SAFETY RESULTS

TAK-003 has been generally well tolerated, with no evidence of disease enhancement in vaccine recipients, and no important safety risks observed in the TIDES trial.[5,6] Most frequently reported adverse reactions were injection site pain, headache, myalgia, injection site erythema, malaise, asthenia and fever.[1] There were no related serious adverse events or deaths reported. The safety profile observed in the 7-year follow-up data was largely consistent with that established up to 54-months post primary vaccination.[1,5,6]

References

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