TIDES
Takeda's Pivotal Phase 3 Dengue Clinical Trial

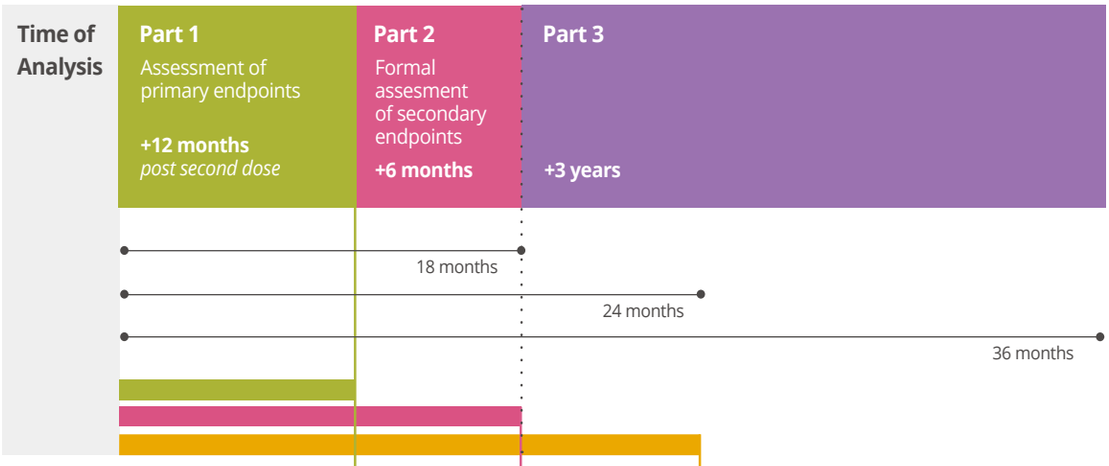
This fact sheet provides an overview of primary and secondary endpoint results of the Tetravalent Immunization against Dengue Efficacy Study (TIDES) trial through 24 months. The trial includes several exploratory endpoints, and those results are available in scientific journals as noted below.

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, of Takeda's dengue vaccine candidate (TAK-003) in healthy children.[i]

The TIDES trial is Takeda's largest interventional clinical trial to date. The trial enrolled over 20,000 healthy children and adolescents ages four to 16 years living in dengue-endemic areas.[i]

The study is comprised of three parts:



PRIMARY ENDPOINT

The trial met the primary endpoint, demonstrating protection against virologically-confirmed dengue (VCD) irrespective of dengue serotype, serostatus or severity (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).

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

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:

- Similar VE in seropositive and seronegative individuals (VE: 76.1% [95% CI: 68.5% to 81.9%] vs. VE: 66.2% [95% CI: 49.1% to 77.5%], respectively)
- 90.4% VE against hospitalized dengue (95% CI: 82.6% to 94.7%; p<0.001)
- 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.[iii]

UPDATE ON PRIMARY AND SECONDARY ENDPOINTS THROUGH EXPLORATORY ANALYSIS

24-month follow-up data showed that TAK-003 demonstrated:

- 72.7% overall VE (95% CI: 67.1% to 77.3%)
- Similar VE in seropositive and seronegative individuals (VE: 74.8% [95% CI: 68.6% to 79.8%] vs. VE: 67.0% [95% CI: 53.6% to 76.5%], respectively)
- 89.2% VE against hospitalized dengue (95% CI: 82.4% to 93.3%)
- 81.2% VE against dengue hemorrhagic fever (95% CI: 29.3% to 95.0%)
- Varying VE by individual serotype:
  - 69.0% for dengue serotype 1 (95% CI: 57.1% to 77.5%)
  - 90.8% for dengue serotype 2 (95% CI: 85.6% to 94.1%)
  - 51.4% for dengue serotype 3 (95% CI: 34.0% to 64.2%)
  - Efficacy against dengue serotype 4 could not be determined given the small number of cases.

The results show a decline in efficacy between Year 1 and Year 2.

Exploratory results of efficacy by serotype and serostatus varied, consistent with the 18-month analysis. Detailed data including an update on exploratory endpoints will be published in a scientific journal.

SAFETY

TAK-003 has been generally well tolerated, and no important safety risks have been observed in the TIDES trial to date.[iv]

References

i. ClinicalTrials.gov. Efficacy, Safety and Immunogenicity of Takeda's Tetravalent Dengue Vaccine (TDV) in Healthy Children (TIDES). 2019. Retrieved October 2020.
ii. Biswal S, et al. Efficacy of a tetravalent dengue vaccine in healthy children and adolescents. *N Engl J Med*. 2019; 2019;381:2009-2019.
iii. Biswal S, et al. Efficacy of a tetravalent dengue vaccine in healthy children aged 4-16 years: a randomized, placebo-controlled, phase 3 trial. *Lancet*. 2020. 2020;395:1423-1433.
iv. Biswal S. Takeda's Tetravalent Dengue Vaccine – Two Years Efficacy Surveillance. Presented at 69th Annual Meeting, American Society of Tropical Medicine and Hygiene; November 2020.