TIDES
Takeda's Pivotal Phase 3 Dengue Clinical Trial

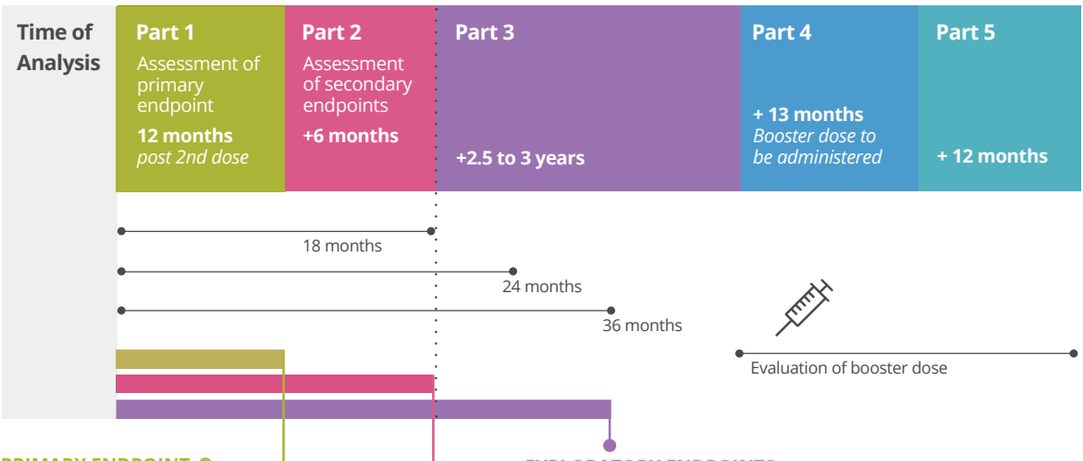
This fact sheet provides an overview of primary and secondary endpoints and long-term follow up results up to 36 months from the Tetravalent Immunization against Dengue Efficacy Study (TIDES) trial. The trial includes several exploratory analyses.

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 Vaccines' 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 five parts:



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.[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:

- 90.4% VE against hospitalized dengue (95% CI: 82.6% to 94.7%; p<0.001)
- 76.1% VE 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.[iii]

EXPLORATORY ENDPOINTS

36-month follow-up data showed[iv]:

- 62.0% overall VE (95% CI: 56.6% to 66.7%)
- 83.6% VE against hospitalized dengue (95% CI: 76.8% to 88.4%)
- 65.0% VE in seropositive individuals (95% CI: 58.9% to 70.1%) and 54.3% VE in seronegative individuals (95% CI: 41.9% to 64.1%)
- 65.4% VE against dengue hemorrhagic fever (95% CI: 19.0% to 85.2%)
- Varying VE by individual serotype:
  - 51.8% for dengue serotype 1 (95% CI: 41.1% to 60.5%)
  - 86.0% for dengue serotype 2 (95% CI: 80.9% to 89.9%)
  - 41.9% for dengue serotype 3 (95% CI: 25.2% to 55.0%)
  - 41.5% for dengue serotype 4 (95% CI: -11.7% to 69.4%)

Results show waning efficacy over time.

Takeda has initiated an extension of the TIDES trial to evaluate a booster dose of TAK-003. Part 4 of the trial will evaluate safety and efficacy for 13 months following one dose of booster vaccination and Part 5 will evaluate long-term safety for one year after completion of Part 4.

SAFETY

TAK-003 has been generally well tolerated, and no important safety risks have been observed in the TIDES trial to date.[iv] Most frequently reported reactions were injection site pain, headache, myalgia, malaise and asthenia.[i]

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. Three Years Efficacy of Takeda's Tetravalent Dengue Vaccine Candidate. Presented at 17th Conference of the International Society of Travel Medicine; May 2021.