TIDES
Takeda's Pivotal Phase 3 Dengue Clinical Trial

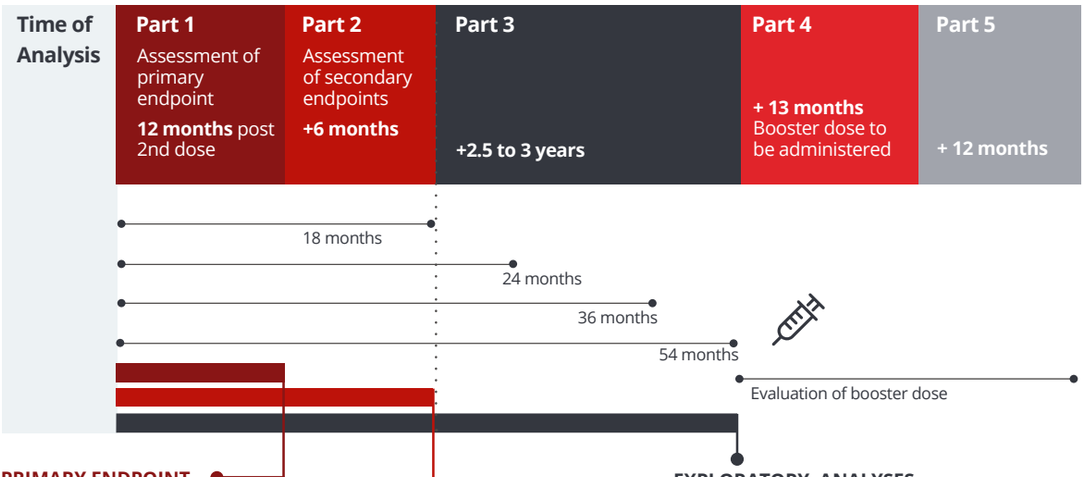
This fact sheet provides an overview of primary and secondary endpoints and long-term follow up exploratory results at 54 months from the Tetravalent Immunization against Dengue Efficacy Study (TIDES) trial. The trial is ongoing and includes several exploratory analyses.

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.[1]

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.[1]

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.[2]

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.[3]

EXPLORATORY ANALYSES

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

- 61.2% overall VE (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.[4]

Takeda has extended the 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, with no evidence of disease enhancement in vaccine recipients, and no important safety risks have been observed in the TIDES trial to date.[4] Most frequently reported reactions were injection site pain, headache, myalgia, injection site erythema, malaise, asthenia and fever. [1]

References

1. ClinicalTrials.gov. Efficacy, Safety and Immunogenicity of Takeda's Tetravalent Dengue Vaccine (TDV) in Healthy Children (TIDES). 2019. Retrieved May 2022.
2. Biswal S, et al. Efficacy of a tetravalent dengue vaccine in healthy children and adolescents. N Engl J Med. 2019; 2019;381:2009-2019.
3. 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.
4. Tricou V, et al. Long-term efficacy and safety of a tetravalent dengue vaccine (TAK-003): 4·5-year results from a phase 3, randomised, double-blind, placebo-controlled trial. Lancet Glob Health. 2024; 12: e257-e270.