Qdenga™ ▼
Dengue Tetravalent Vaccine (Live, Attenuated)

TIDES
Takeda's Pivotal Phase 3 Dengue Clinical Trial

Initiated and funded by Takeda UK Ltd for Healthcare Professionals in the UK and Ireland.
Prescribing information can be found on the next page.

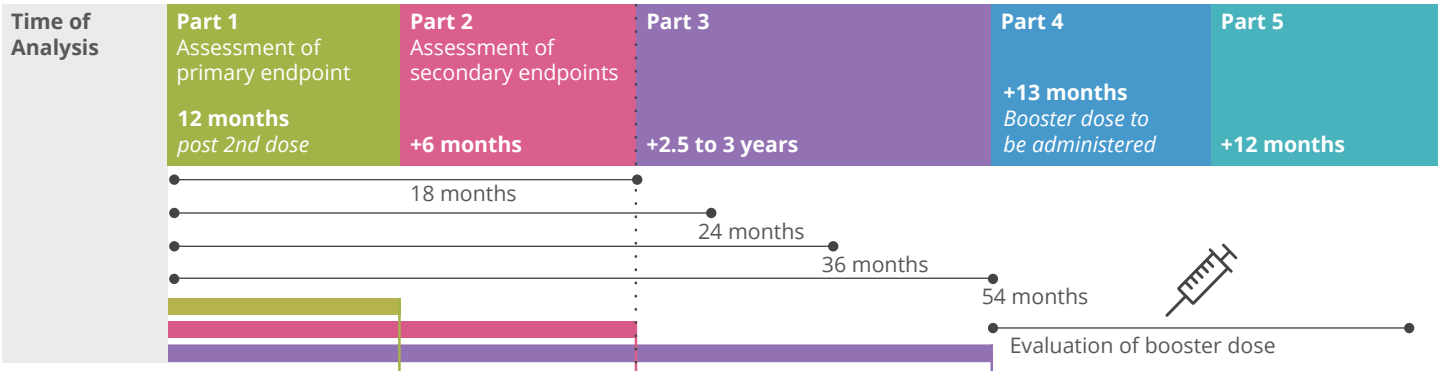
This fact sheet provides an overview of primary and secondary endpoints and long-term follow up exploratory results at 54 months from the Tetravalent Immunisation against Dengue Efficacy Study (TIDES) trial. This trial evaluates TAK-003, also known as Qdenga™▼ (dengue tetravalent vaccine (live attenuated)). The trial includes several exploratory analyses.

Trial Overview

The TIDES trial is a Phase 3, double-blind, randomised, 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/Qdenga™) in healthy children (n=20,099).[1]

The TIDES trial is Takeda Vaccines' largest interventional clinical trial to date. The trial enrolled over 20,000 healthy children and adolescents ages 4 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 fever) 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% (TAK-003: 61/12,700, Placebo: 149/6,316; 95% confidence interval [CI]: 73.3% to 85.3%; p<0.001)
- Incidence of VCD fever 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 hospitalised dengue (TAK-003: 13/12,700, Placebo: 66/6,316; 95% CI: 82.6% to 94.7%; p<0.001)
- 76.1% VE in seropositive individuals (TAK-003: 75/9,167, Placebo: 150/4,589; 95% CI: 68.5% to 81.9%) and 66.2% VE in seronegative individuals (TAK-003: 39/3,531, Placebo: 56/1,726; 95% CI: 49.1% to 77.5%)
- 85.9% VE against dengue haemorrhagic fever (TAK-003: 2/12,700, Placebo: 7/6,316; 95% CI: 31.9% to 97.1%)
- Varying VE by individual serotype:
  - 69.8% for dengue serotype 1 (TAK-003: 38/12,700, Placebo: 62/6,31; 95% CI: 54.8% to 79.9%)
  - 95.1% for dengue serotype 2 (TAK-003: 8/12,700, Placebo: 80/6,316; 95% CI: 89.9% to 97.6%)
  - 48.9% for dengue serotype 3 (TAK-003: 63/12,700, Placebo: 60/6,316; 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 fever (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 (TAK-003: 442/13,380, Placebo: 547/6,687; 95% CI: 56.0% to 65.8%)
- 84.1% VE against hospitalised dengue (TAK-003: 46/13,380, Placebo: 142/6,687; 95% CI: 77.8% to 88.6%)
- 64.2% VE in seropositive individuals (TAK-003: 295/9,663, Placebo: 394/4,854; 95% CI: 58.4% to 69.2%) and 53.5% VE in seronegative individuals (TAK-003: 147/3,714, Placebo: 153/1,832; 95% CI: 41.6% to 62.9%)

These data were published in The Lancet in February 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

In Part 1, the most commonly reported unsolicited adverse events within 4 weeks after any dose were nasopharyngitis, upper respiratory tract infection and viral infection. One vaccine recipient and four placebo recipients reported serious adverse events. No additional cases of related serious adverse events were observed during Part 2.[2,3]

The cumulative rates of serious adverse events (Parts 1 and 2) were similar in the vaccine group and the placebo group (4.0% vs 4.8%).[3]

Serious adverse event rates during Part 3 of the study were similar in the placebo and vaccine groups regardless of baseline serostatus.[4] TAK-003 has been generally well tolerated, and no important safety risks have been observed in the TIDES trial to date.[4]

In clinical studies, the most frequently reported reactions in subjects 4 to 60 years of age were injection site pain (50%), headache (35%), myalgia (31%), injection site erythema (27%), malaise (24%), asthenia (20%) and fever (11%).[5]

These adverse reactions usually occurred within 2 days after the injection, were mild to moderate in severity, had a short duration (1 to 3 days) and were less frequent after the second injection of Qdenga™ than after the first injection.[5]

▼ This medicinal product is subject to additional monitoring.

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Scan the QR code or click here to visit the Qdenga™ Prescribing Information for the **UK** and for details of how to report an Adverse Event.

Qdenga▼: this medicinal product is subject to additional monitoring. Adverse events should be reported. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Takeda at: AE.GBR-IRL@takeda.com

PRESCRIBING INFORMATION - Republic of Ireland

Qdenga▼ (Dengue tetravalent vaccine - live, attenuated) powder and solvent for solution for injection in pre-filled syringe.
PRESCRIBING INFORMATION FOR REPUBLIC OF IRELAND
Refer to Summary of Product Characteristics (SmPC) before prescribing

Presentation: After reconstitution, 1 dose (0.5 mL) contains: live, attenuated dengue virus serotype 1: ≥ 3.3 log10 PFU [Plaque-Forming Units]/dose; live, attenuated dengue virus serotype 2: ≥ 2.7 log10 PFU/dose; live, attenuated dengue virus serotype 3: ≥ 4.0 log10 PFU/dose; and live, attenuated dengue virus serotype 4: ≥ 4.5 log10 PFU/dose. This product is produced in Vero cells and contains genetically modified organisms (GMOs). **Indication**: Qdenga is indicated for the prevention of dengue disease in individuals from 4 years of age. **Dosage and administration**: Qdenga should be administered as a 0.5 mL dose at a two-dose (0 and 3 months) schedule. The need for a booster dose has not been established. Method of administration: After complete reconstitution of the lyophilised vaccine with the solvent, Qdenga should be administered by subcutaneous injection preferably in the upper arm in the region of deltoid. Qdenga must not be injected intravascularly, intradermally or intramuscularly. The vaccine should not be mixed in the same syringe with any vaccines or other parenteral medicinal products. **Contraindications:** Hypersensitivity to the active substances or to any of the excipients or hypersensitivity to a previous dose of Qdenga. Individuals with congenital or acquired immune deficiency, including immunosuppressive therapies such as chemotherapy or high doses of systemic corticosteroids (e.g. 20 mg/day or 2 mg/kg body weight/day of prednisone for 2 weeks or more) within 4 weeks prior to vaccination, as with other live attenuated vaccines. Individuals with symptomatic HIV infection or with asymptomatic HIV infection when accompanied by evidence of impaired immune function. Pregnant women. Breast-feeding women. **Warnings and precautions**: Traceability: Name and batch number of the administered product should be clearly recorded. Anaphylaxis: Anaphylaxis has been reported in individuals who have received Qdenga. Appropriate medical treatment and supervision must be readily available in the event of a rare anaphylactic reaction. Review of medical history: vaccination should be preceded by a review of the individual's medical history (especially with regard to previous vaccination and possible hypersensitivity reactions which occurred after vaccination). Concurrent illness: Vaccination with Qdenga should be postponed in subjects suffering from an acute severe febrile illness. Limitations of vaccine effectiveness: A protective immune response with Qdenga may not be elicited in all vaccinees against all serotypes of dengue virus and may decline over time. It is currently unknown whether a lack of protection could result in an increased severity of dengue. It is recommended to continue personal protection measures against mosquito bites after vaccination. There are no data on the use of Qdenga in subjects above 60 years of age and limited data in patients with chronic medical conditions. Anxiety-related reactions: Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. Women of childbearing potential: women of childbearing potential should avoid pregnancy for at least one month following vaccination. **Interactions:** Avoid vaccination with Qdenga for at least 6 weeks, and preferably 3 months, following treatment with immunoglobulins or blood products containing immunoglobulins, such as blood or plasma. Qdenga should not be administered to subjects receiving immunosuppressive therapies within 4 weeks prior to vaccination. Use with other vaccines: Qdenga may be administered concomitantly with a hepatitis A vaccine. Co-administration has been studied in adults. Qdenga may be administered concomitantly with a yellow fever vaccine. In a clinical study involving approximately 300 adult subjects who received Qdenga concomitantly with yellow fever 17D vaccine, there was no effect on yellow fever seroprotection rate. Dengue antibody responses were decreased following concomitant administration of Qdenga and yellow fever 17D vaccine. The clinical significance of this finding is unknown. Qdenga may be administered concomitantly with a human papillomavirus (HPV) vaccine. Concomitant vaccines should be administered in separate syringes at different injection sites. **Fertility, pregnancy and lactation**: Qdenga is a live attenuated vaccine, therefore Qdenga is contraindicated during pregnancy. Qdenga is contraindicated during breast-feeding. No specific studies have been performed on fertility in humans. **Effects on ability to drive and use machines**: Qdenga has minor influence on the ability to drive and use machines. **Undesirable effects**: Very common (≥1/10): Upper respiratory tract infection, decreased appetite, irritability, headache, somnolence, myalgia, injection site pain, injection site erythema, malaise, asthenia, fever. Common (≥1/100 to <1/10): Nasopharyngitis, pharyngotonsillitis, arthralgia, injection site swelling, injection site bruising, injection site pruritus, influenza like illness. Other serious undesirable effects: (very rare), Anaphylactic reaction, including anaphylactic shock (frequency not known). **Refer to the SmPC for details on full side effect profile and interactions.** **Legal classification**: POM. **Marketing authorisation number(s)**: EU/1/22/1699/005. **Name and address of MA holder**: Takeda GmbH, Byk-Gulden-Str.2, 78467 Konstanz, Germany. **PI approval code**: pi-03389. **Date of preparation**: November 2024.

Qdenga▼: this medicinal product is subject to additional monitoring. Adverse events should be reported to the Pharmacovigilance Unit at the Health Products Regulatory Authority. Regulatory forms and information can be found at www.hpra.ie . Adverse events should also be reported to Takeda at: AE.GBR-IRL@takeda.com

References

1. Takeda. Efficacy, Safety and Immunogenicity of Takeda's Tetravalent Dengue Vaccine (TDV) in Healthy Children (TIDES). Available at: https://clinicaltrials.gov/ct2/show/NCT02747927. (Accessed January 2025).
2. Biswal S, *et al. N Engl J Med.* 2019;381(21):2009–19.
3. Biswal S, *et al. Lancet.* 2020;395:1423-33.
4. Tricou V, *et al. Lancet Global Health*. 2024;12(2):e257-e270.
5. Qdenga™ Summary of Product Characteristics.

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