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About Qdenga®

Help protect your patients against dengue with Qdenga® [1-4]

Qdenga® is supported by a robust clinical development program which spanned Phase 1, 2 and 3 clinical trials, including 28,175 participants, 88 study sites and 13 countries [5-22]



Qdenga® is indicated for the prevention of dengue diseases in individuals from 4 years of age. The use of Qdenga should be in accordance with official recommendations

Study Design

TIDES: Study design

TIDES: Tetravalent Immunization against Dengue Efficacy Study in Healthy Children [2,3]

- TIDES is a pivotal, ongoing, multinational, double-blind, randomized, placebo-controlled, Phase 3 study evaluating the efficacy, safety, and immunogenicity of Qdenga® against dengue fever [1-3]
- Overall, 20,099 healthy participants aged 4–16 years from 8 dengue-endemic countries were given at least one dose of the vaccine or placebo [2,3]
 - Brazil, Colombia, Dominican Republic, Nicaragua, Panama, Philippines, Sri Lanka, and Thailand
 - Balanced enrollment between Asia-Pacific (46.5%) and Latin America (53.5%)
- TIDES had a 91% subject retention rate with weekly follow-up throughout its initial 4.5-year trial duration [1,4]
- Both dengue-naïve and previously exposed individuals were included in TIDES [2,3]
 - At baseline, 27.7% of trial participants were seronegative for all four dengue serotypes
- Exclusion criteria included baseline febrile illness, impaired/ altered immune function, hypersensitivity to any vaccine component, pregnancy/breastfeeding, previous receipt of dengue vaccine, and other protocol violations as per trial criteria [2,3]



* One 0.5 mL dose of Qdenga® contained approximately 36, 416, 416, and 511 i.u. plaque-forming units of DENV-1, DENV-2, DENV-3, and DENV-4 strains, respectively, while the placebo was 0.5 mL of saline. Four participants received both vaccine and placebo because of administrative error; these participants are not included in the total [2]. Adapted from Bissel et al. 2020; Bissel S, et al. 2022[2]

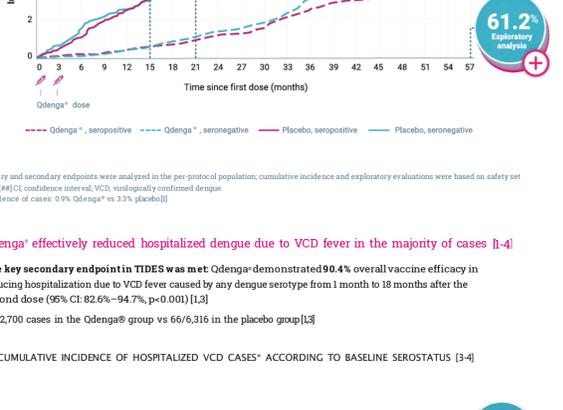
Efficacy

TIDES: Efficacy data

Qdenga® effectively prevented virologically confirmed dengue (VCD) in the majority of cases [1-4]

The primary endpoint in TIDES was met: Qdenga® demonstrated 80.2% overall vaccine efficacy in preventing VCD induced by any dengue serotype from 1 month to 12 months after the second dose (95% CI: 73.3%–85.3%, p<0.001) [2] 61/12,700 VCD cases in the Qdenga® group vs 149/6,316 cases in the placebo group [2]

CUMULATIVE INCIDENCE OF VCD CASES ACCORDING TO BASELINE SEROSTATUS [2-4]



Primary and secondary endpoints were analyzed in the per-protocol population; cumulative incidence and exploratory evaluations were based on safety set data. [4] CI, confidence interval; VCD, virologically confirmed dengue. *Incidence of cases: 0.9% Qdenga® vs 3.3% placebo [2]

Qdenga® effectively reduced hospitalized dengue due to VCD fever in the majority of cases [1-4]

The key secondary endpoint in TIDES was met: Qdenga® demonstrated 90.4% overall vaccine efficacy in reducing hospitalization due to VCD fever caused by any dengue serotype from 1 month to 18 months after the second dose (95% CI: 82.2%–94.7%, p<0.001) [1,3] 13/12,700 cases in the Qdenga® group vs 66/6,316 cases in the placebo group [1,3]

CUMULATIVE INCIDENCE OF HOSPITALIZED VCD CASES* ACCORDING TO BASELINE SEROSTATUS [3-4]



*Specific criteria for hospitalization were not defined in the study protocol; participants were hospitalized according to the judgement of individual investigators [3]

90.1% reduced hospitalizations in Latin America
(95% CI: 15.3%–98.8%) [3]

1/6,806 hospitalized cases in the Qdenga® group vs 57/3,374 in the placebo group from 1 month to 18 months after the second dose [3]

90.4% reduced hospitalizations in Asia Pacific
(95% CI: 82.2%–94.8%) [3]

12/5,894 hospitalized cases in the Qdenga® group vs 60/2,942 in the placebo group from 1 month to 18 months after the second dose [3]

Efficacy of Qdenga® by serostatus, dengue serotype and severity

EFFICACY OF QDENGATM IN PREVENTING VCD FEVER FROM 1 MONTH TO 18 MONTHS AFTER THE SECOND DOSE (SECONDARY ENDPOINTS) [3]



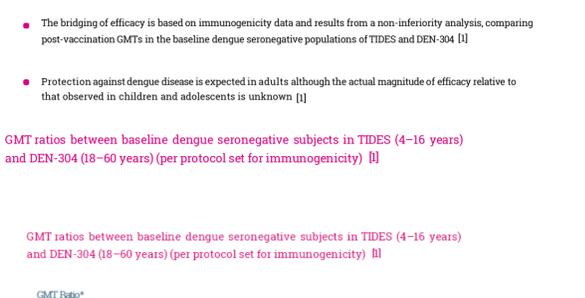
Two secondary endpoints were not met, largely due to the small number of cases: [3]

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

Data currently suggests a lack of efficacy against DENV-3 infection in baseline seronegative participants, but there is no evidence of disease enhancement [1,3]

Clinical Program > Efficacy > Serostatus Alternate State

EFFICACY OF QDENGATM IN PREVENTING VCD FEVER FROM 1 MONTH TO 18 MONTHS AFTER THE SECOND DOSE (SECONDARY ENDPOINTS) [3]



Efficacy of Qdenga® in people over 17 years of age

The clinical efficacy of Qdenga® in individuals from 17 years of age is based on bridging of immunogenicity data [1]

- Immunogenicity of Qdenga® in adults aged 18 to 60 years was assessed in DEN-304, a double-blind, randomized, placebo-controlled Phase 3 study in a non-endemic country (US) [1]
- The bridging of efficacy is based on immunogenicity data and results from a non-inferiority analysis, comparing post-vaccination GMTs in the baseline dengue seronegative populations of TIDES and DEN-304 [1]
- Protection against dengue disease is expected in adults although the actual magnitude of efficacy relative to that observed in children and adolescents is unknown [1]

GMT ratios between baseline dengue seronegative subjects in TIDES (4–16 years) and DEN-304 (18–60 years) (per protocol set for immunogenicity) [1]

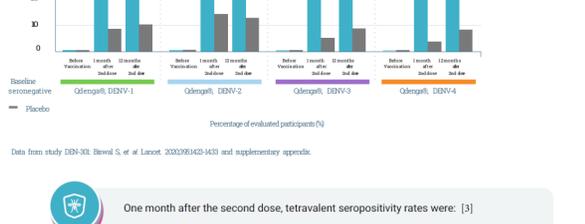
GMT ratios between baseline dengue seronegative subjects in TIDES (4–16 years) and DEN-304 (18–60 years) (per protocol set for immunogenicity) [1]

GMT Ratio* (95% CI)	DENV-1	DENV-2	DENV-3	DENV-4
1 month post-2 nd dose	0.69 (0.58, 0.82)	0.59 (0.52, 0.66)	1.77 (1.53, 2.04)	1.05 (0.92, 1.20)
6 months post-2 nd dose	0.62 (0.51, 0.76)	0.66 (0.57, 0.76)	0.98 (0.84, 1.14)	1.01 (0.86, 1.18)

*Non-inferiority Upper bound of the 95% CI less than 2 [1]

Immunogenicity

IN TIDES, SEROPOSITIVITY RATES AGAINST ALL FOUR SEROTYPES OF DENGUE REMAINED ABOVE 90% UP TO 15 MONTHS AFTER THE SECOND DOSE OF QDENGATM [3]



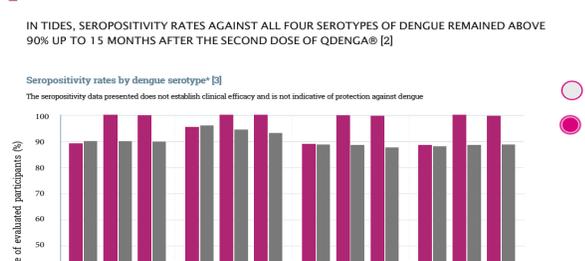
One month after the second dose, tetravalent seropositivity rates were: [3]

- 99.5% in baseline seronegative individuals (vs 3.5% placebo)

*Per-protocol set for immunogenicity data. Seropositive defined as a reciprocal neutralizing antibody titer ≥10. Baseline seronegative defined as seronegative to all four dengue serotypes. Baseline seropositive defined as seropositive to one or more serotypes [1]

Clinical Program > Immunogenicity > Seropositive Alternate State

IN TIDES, SEROPOSITIVITY RATES AGAINST ALL FOUR SEROTYPES OF DENGUE REMAINED ABOVE 90% UP TO 15 MONTHS AFTER THE SECOND DOSE OF QDENGATM [2]



Safety Profile

TIDES: Safety data

Qdenga® has been generally well-tolerated to date in TIDES [1-4]

In TIDES:

- No important safety risks have been observed up to 4.5 years after the second dose of Qdenga® [1,4]
- No similar cumulative incidences of serious AEs were observed for individuals treated with Qdenga® [1,4] and placebo [3]
 - Up to 18 months after the second dose: 4.0% vs 4.8%, respectively
 - Consistent with expected medical disorders in the study population
- No evidence to date that Qdenga® enhanced disease in seronegative individuals [1,3]
 - Serious AEs occurred at 4.3% for both seropositive (624/14,520) and seronegative individuals (238/5,547) up to 18 months after the second dose

Overview of serious adverse events in the TIDES safety set data*, between months 1 to 18 after the second dose of Qdenga® [4]

Serious Adverse Events (n, %)	Qdenga® (%) (n=13,380)	Placebo (%) (n=6,687)
Not related to vaccine/placebo	537 (4.0)	320 (4.8)
Related to vaccine/placebo	1 (<0.1)	4 (0.1)
Deaths	5 (<0.1)	1 (<0.1)

All deaths* were considered to be unrelated to Qdenga® or study procedures by the investigators, sponsor and data monitoring committee. Aseptic meningitis, arteriovenous malformation of the cerebral vessels, anaplastic erythrocytosis, gunshot wound, suffocation, and road traffic accident [1]

Overview of serious adverse events in the TIDES safety set data*, between months 19 to 54 after the second dose of Qdenga® [4]

Serious Adverse Events (n, %)	Qdenga® (%) (n=13,380)	Placebo (%) (n=6,687)
Not related to vaccine/placebo	664 (5.0)	396 (5.9)
Related to vaccine/placebo	0	0
Deaths	11 (<0.1)	6 (<0.1)

*As assessed by investigator [1]

Overall clinical safety of Qdenga®

The overall safety profile for Qdenga® is based on a stratified analysis including seronegative individuals, consisting of 14,627 participants aged 4–60 years (3,839 children and 788 adults) who have been vaccinated with Qdenga®, including a reactivity subset of 3,830 participants (3,042 children and 788 adults) [1]

- The most common adverse reactions in clinical studies were mild to moderate with a short duration (1–3 days) [1]
- The most frequently reported reactions in subjects 4 to 60 years of age were injection site pain, headache, myalgia, injection site erythema, malaise, asthenia and fever [1]
- Adverse reactions were less frequent after the second injection than after the first injection [1]
- Frequency, type, and severity of adverse reactions in children were consistent with those in adults [1]
- Qdenga® has minor influence on the ability to drive and use machines [1]
- Transient vaccine viremia was observed in one clinical study (DEN-205), associated with mild to moderate symptoms for a mean duration of 4 days, but rarely detected after the second dose of Qdenga® [1]
- Please refer to the Product Information for the full safety profile, special warnings, precautions, and contraindications to use of Qdenga®

Adverse reactions from clinical studies (age 4 to 60 years) [1]

Adverse reactions are listed according to the following frequency categories: Very common (≥1/10), common (≥1/100 to <1/100), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000) and very rare (<1/10,000) [1]

System Organ Class	Frequency	Adverse Reactions
Infections and infestations	Very common	• Upper respiratory tract infection
	Common	• Nasopharyngitis • Pharyngotonsillitis
	Uncommon	• Bronchitis • Rhinitis
Metabolism and nutrition disorders	Very common	• Decreased appetite
Psychiatric disorders	Very common	• Irritability
Nervous system disorders	Very common	• Headache • Somnolence
	Uncommon	• Dizziness
Gastrointestinal disorders	Uncommon	• Diarrhea • Nausea • Abdominal pain • Vomiting
	Uncommon	• Rash • Pruritus • Urticaria
	Very rare	• Angioedema
Musculoskeletal and connective tissue disorders	Very common	• Myalgia

	Common	• Arthralgia
General disorders and administration site conditions	Very common	<ul style="list-style-type: none"> • Injection site pain • Injection site erythema • Malaise • Asthenia • Fever
	Common	<ul style="list-style-type: none"> • Injection site swelling • Injection site bruising • Injection site pruritus • Influenza like illness
	Uncommon	<ul style="list-style-type: none"> • Injection site hemorrhage • Fatigue^a • Injection site discoloration

^a Includes upper respiratory tract infection and viral upper respiratory tract infection

^b Includes pharyngotonsillitis and tonsillitis

^c Collected in children below 6 years of age in clinical studies

^d Includes rash, viral rash, rash maculopapular, with pruritus

^e Reported in adults in clinical studies

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AE, adverse event; CI, confidence interval; DCAC, dengue case adjudication committee; DENV, dengue virus; DMF, dengue hemorrhagic fever; GMT, geometric mean titer; RT-PCR, reverse transcription polymerase chain reaction; TDV, the DENV [dengue virus] strain; VCD, virologically confirmed dengue; WHO, World Health Organization.

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