Updates on Dengue Vaccines

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Dengue is endemic in 6 U.S. territories and freely associated states.
Three doses of Dengvaxia are indicated for the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3, and 4 in people 9–16 years old with:

- laboratory confirmation of previous dengue virus infection
  AND
- living in endemic areas.
Takeda Dengue Vaccine (TAK-003) has been under review by the FDA since Nov 2022
Dengue Workgroup presented to ACIP 3 times

- Dengue epidemiology
- Review of Sanofi dengue vaccine and ACIP recommendation
- Takeda dengue vaccine safety and efficacy presentation
- Workgroup summary and interpretation
- Policy questions
- Cost-effective (CE) analysis (CDC/Notre Dame)
- Comparison of CE models
- Partial EtR

Plan to present draft recommendations
Overall VE
61.2% (56.0, 65.8%)

VE in Seropositives
64.2% (58.4, 69.2%)

VE in Seronegatives
53.5% (41.6–62.9%)

VE in Seropositives by Serotype
- DENV-1: 56.1% (44.6, 65.2%)
- DENV-2: 80.4% (73.1, 85.7%)
- DENV-3: 52.3% (36.7, 64.0%)
- DENV-4: 70.6% (39.9, 85.6%)

VE in Seronegatives by Serotype
- DENV-1: 45.4% (26.1, 59.7%)
- DENV-2: 88.1% (78.6, 93.3%)
- DENV-3: -15.5% (-108.2, 35.9%)
- DENV-4: -105.6% (-628.7, 42.0%)

Unpublished data presented by Takeda to ACIP and ASTMH*57 months after first dose, significant results bolded. Number for seropositive placebo participants 4,855 and vaccine 9,666; Seronegative placebo 1,832 and vaccine 3,714.
Overall VE: 84.1% (77.8, 88.6%)

VE in Seropositives: 85.9% (78.7, 90.7%)

VE in Seronegatives: 79.3% (63.5, 88.2%)

VE in Seropositives by Serotype:
- DENV-1: 66.8% (37.4, 82.3%)
- DENV-2: 95.8% (89.6, 98.3%)
- DENV-3: 74.0% (38.6, 89.0%)
- DENV-4: 100% (NE, NE)

VE in Seronegatives by Serotype:
- DENV-1: 78.4% (43.9, 91.7%)
- DENV-2: 100% (NE, NE)
- DENV-3: -87.9% (-573.4, 47.6%)
- DENV-4: 100% (NE, NE)

Hospitalization:
- DENV-4 Placebo events: 3, TAK-003 events: 0
- DENV-2 Placebo events: 23, TAK-003 events: 0
- DENV-3 Placebo events: 3, TAK-003 events: 11
- DENV-4 Placebo events: 1, TAK-003 events: 0

*57 months after first dose, significant results bolded. Number for seropositive placebo participants 4,855 and vaccine 9,666; Seronegative placebo 1,832 and vaccine 3,714.

Unpublished data presented by Takeda to ACIP and ASTMH.
European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) issued positive opinion for TAK-003

October 2023

- EU-M4all: parallel review for EU and participating dengue endemic countries globally

- TAK-003 vaccine approved in multiple countries
  - EU, UK, Brazil, Argentina, Indonesia, & Thailand
On July 11, Takeda voluntarily withdrew TAK-003 from FDA review.

Takeda Announces Voluntary Withdrawal of U.S. Biologics License Application (BLA) for Dengue Vaccine Candidate TAK-003

OSAKA, Japan and CAMBRIDGE, Massachusetts, July 11, 2023 - Takeda (TSE:4502/NYSE:TAK) today announced that the Company has voluntarily withdrawn the U.S. Biologics License Application (BLA) for its dengue vaccine candidate, TAK-003, following discussions with the U.S. Food and Drug Administration (FDA) on aspects of data collection, which cannot be addressed within the current BLA review cycle. The future plan for TAK-003 in the U.S. will be further evaluated given the need for travelers and those living in dengue-endemic areas of the U.S., such as Puerto Rico. The vaccine is approved in multiple endemic and non-endemic countries, with more approvals expected over the coming years.
WHO SAGE Recommendations for TAK-003
Sept 25, 2023

- Consider for introduction in settings with **high dengue disease burden** and **high transmission intensity**

- SAGE recommended the vaccine be introduced to children aged **6 to 16 years** of age.
  - Within that age range, the vaccine should be introduced about **1-2 years prior to the age-specific peak incidence of dengue-related hospitalizations**.
  - The vaccine should be administered in a 2-dose schedule with a 3-month interval between doses.
Future Dengue Vaccine Work

• Dengue workgroup will be paused until TAK-003 is re-submitted to FDA or a new vaccine submitted for approval
ACIP Dengue Vaccines Workgroup

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