Title: Efficacy and Safety of Takeda's Tetravalent Dengue Vaccine Candidate (TAK-003) After 4.5 Years of Follow-up

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Summary: There remains an urgent need for a dengue vaccine which can be used broadly without any pre-screening to confirm prior dengue infection. Takeda's dengue vaccine candidate (TAK-003), a recombinant tetravalent dengue vaccine based on a DENV-2 backbone, is under evaluation in an ongoing long-term efficacy clinical trial in 8 dengue endemic countries. Previously, we have reported data on primary and secondary efficacy endpoints obtained 12 and 18 months after vaccination, respectively, and exploratory data after 2 years. Here, we present exploratory data after 4.5 years of follow up.

Methods–Results: From September 2016 to March 2017, healthy 4–16 years-old children (n=20,099) were randomized 2:1 to receive 2 doses of TAK-003 or placebo 3 months apart and were under active febrile illness surveillance to detect symptomatic dengue (both outpatient and hospitalized) using a serotype-specific RT-PCR. Serious adverse events (SAEs) were collected throughout the trial. 20,071 children received ≥1dose of TAK-003 or placebo; 27.6% (5547 / 20,063) were seronegative at baseline. 18,260 (91.0%) completed up to 4.5 years post vaccination follow-up and 27,684 febrile illnesses were reported. These led to detection of 1007 RT-PCR confirmed dengue cases, 188 of which required hospitalization. The cumulative vaccine efficacy (VE) from 1st dose until 4.5 years after the 2nd dose was 61.2% (95% CI: 56.0–65.8) against virologically-confirmed dengue (VCD) and 84.1% (77.8–88.6) against hospitalized VCD. In baseline seronegative participants, VE was 53.5% (41.6–62.9) against VCD and 79.3% (63.5–88.2) against hospitalized VCD. In baseline seropositive participants, VE was 64.2% (58.4–69.2) against VCD and 85.9% (78.7–90.7) against hospitalized VCD. Efficacy varied by serotype and some decline in efficacy was noted in a year-to-year comparison but remained robust against hospitalized VCD. Rates of SAEs were similar between the vaccine and placebo groups and no important safety risk was identified.

Conclusions: Two doses of TAK-003 three months apart were well tolerated and protected against symptomatic dengue through 4.5 years after vaccination in both dengue-naïve and pre-exposed children in dengue endemic countries. VE was higher against hospitalized VCD.

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