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

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Background: An ongoing long-term efficacy trial in eight dengue-endemic countries is evaluating a recombinant tetravalent dengue vaccine based on a DENV-2 backbone (TAK-003). Here we present an additional 18 months of follow-up data for a total of 4.5 years of follow-up.

Materials and methods: From September 2016 to March 2017, healthy 4–16-years-old children (n=20,099) were randomized 2:1 to receive two doses of TAK-003 or placebo three 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.

Results: 20,071 children received ≥1 dose 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 first dose until 4.5 years after the second dose is summarized in the

Table. Efficacy continued beyond 3 years of vaccination regardless of baseline serostatus with sustained robust protection against hospitalized virologically-confirmed dengue (VCD). Rates of SAEs were similar between the vaccine and placebo groups and no important safety risks were identified.

Conclusion: 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. Efficacy was higher, and sustained against dengue leading to hospitalization.

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Table: Cumulative VE from Dose 1 to 4.5 years post-Dose 2

	VE %	**95% CI**
Cumulative VE from Dose 1 to 4.5 years post-Dose 2		
Against VCD	61.2	56.0–65.8
Against hospitalized VCD	84.1	77.8–88.6
VE in baseline seronegative participants		
Against VCD	53.5	41.6–62.9
Against hospitalized VCD	79.3	63.5–88.2
VE in baseline seropositive participants		
Against VCD	64.2	58.4–69.2
Against hospitalized VCD	85.9	78.7–90.7

VCD = virologically confirmed dengue; VE = vaccine efficacy.