



Introduction of Policy Questions for TAK-003

Alfonso Hernandez-Romieu, MD, MPH

ACIP June 22, 2023

Dengue Branch, CDC

We formulated PICO questions based on the directness of data and risk-benefit differences.

- **4–16 years:** 57-month vaccine efficacy from a phase 3 randomized controlled trial
- **17*–60 years:** Non-inferiority of antibody titer ratios post-vaccination (2 doses) compared to persons aged 4–16 years (i.e., immunobridging)

Result: Developed PICO questions by age-group

*Persons aged 17 years were considered in this category but were not included in original immunobridging (18 – 60 years) or phase 3 trials (4 – 16 years)

We formulated PICO questions based on the directness of data and risk-benefit differences.

- **No efficacy against hospitalizations for DENV-3 among seronegative vaccine recipients compared to placebo (-87.9%; 95% CI: -573.4, 47.6%).**

Hospitalization for DENV-3 and DENV-4 among seronegative* children was low.

	Placebo n=1832	Incidence density/100 person-years	TAK-003 n=3714	Incidence density/100 person-years	VE (95% CI)	
DENV-1	14	0.17	6	0.03	78.4%	(43.9, 91.7%)
DENV-2	23	0.28	0	0.0	100%	(NE, NE)
DENV-3	3	0.04	11	0.07	-87.9%	(-573.4, 47.6%)
DENV-4	1	0.01	0	0.0	100%	(NE, NE)

*Seronegative refers to no serologic evidence of previous dengue infection before vaccination.

We formulated PICO questions based on the directness of data and risk-benefit differences.

- **No efficacy against hospitalizations for DENV-3 among seronegative vaccine recipients compared to placebo (-87.9%; 95% CI: -573.4, 47.6%).**
- **Data insufficient to rule out an increased risk among seronegative vaccine recipients.**

Result: Developed PICO questions by serostatus

PICO questions include persons living in dengue endemic areas only.

- **Recommendations for travelers to dengue endemic areas** will be addressed by the work group after the October 2023 ACIP meeting.
- Travelers to endemic areas will require a **separate evidence-to-Recommendations (EtR) framework** including but not limited to:
 - public health importance
 - benefits and harms
 - resource use

PICO Questions

1. Should two doses of TAK-003 be administered routinely to **seropositive*** **persons aged 4–16 years** living in dengue-endemic areas?
2. Should two doses of TAK-003 be administered routinely to **seronegative** **persons aged 4–16 years** living in dengue-endemic areas?
3. Should two doses of TAK-003 be administered routinely to **seropositive*** **persons aged 17–60 years** living in dengue-endemic areas?
4. Should two doses of TAK-003 be administered routinely to **seronegative** **persons aged 17–60 years** living in dengue-endemic areas?

*Recommendation for seropositive individuals only will require prevaccination screening for previous dengue virus infection.

Data elements used for each policy question

	Seropositive	Seronegative
4–16 years Children/Adolescents	<ul style="list-style-type: none">• Vaccine Efficacy (VE)• Safety• Cost-effectiveness (CE)	<ul style="list-style-type: none">• VE• Safety• CE
17–60 years Adults	<ul style="list-style-type: none">• Immunobridging*• Safety• CE	<ul style="list-style-type: none">• Immunobridging• Safety• CE

*Immunogenicity in seropositive adults inferred from data in seronegative adults.