ACIP Dengue Vaccines Workgroup Considerations and Next Steps

Steve Waterman, MD, MPH

Dengue Branch

ACIP Meeting

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National Center for Emerging and Zoonotic Infectious Diseases

Division of Vector-Borne Diseases

Workgroup Considerations: Dengvaxia Acceptability in Puerto Rico

- **Key survey results**
  - 73% of pediatricians would use Dengvaxia given an acceptable pre-vaccination screening laboratory test
  - 84% of pediatricians who answered wanted to see a screening test specificity of at least 95%, preferably 99%
  - 76% of pediatricians supported a pilot project
  - Over 80% of pediatricians felt vaccine and lab test insurance coverage were necessary steps for implementation
  - Parents and physicians need more education about the vaccine
  - Need to explain the rationale for vaccinating in dengue endemic areas such as Puerto Rico
  - Relatively few negative perceptions about the vaccine

Dengue Vaccines Workgroup Informal Poll on Dengvaxia
December 2019

- **What information needed to make a recommendation?**
  - Acceptably specific screening laboratory test biggest concern
  - Logistics and cost of test frequently mentioned
  - Need for community engagement
  - Pilot project starting with children with previously documented dengue
  - Skepticism about shared decision making

CDC's Dengue IgG test evaluation

Literature search

- Published Landscape analysis (Robert Luo)
- CDC's analysis (publications and package instructions

October 2019

Test selection

- Based on test performance characteristics provided by vendor, independent publications, etc.
- Characteristics of clinical evaluations (E.g. sampling size and cross reactivity studies,etc…)
- Tests procured

November 2019

Evaluation

- CDC serum panel 1st evaluation for intended use in diagnosis (7-30 days after symptoms)
- Long-term sample evaluation depending on 1st evaluation

March-June, 2020

Population-level impacts of the intervention in Puerto Rico

Total numbers of symptomatic and hospitalized cases across a 10-year timeframe in Puerto Rico, as well as cases averted and additional hospitalizations among vaccinees. This represents a scenario of sensitivity = 0.80 and specificity = 0.95.

	Baseline		Averted	
Prior exposure in 9-yr-olds	Symptomatic	Hospitalizations	Symptomatic	Hospitalizations
30%	107,820	21,740	1,078	652
50%	206,130	41,590	4,122	2,080
60%	269,420	54,390	5,927	3,807

Prior exposure in 9-yr-olds	Additional hospitalizations among vaccinees
30%	225
50%	250
60%	300

- Are there specific data ACIP would like presented?
- Are there other considerations the Work Group should address?

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ACIP Dengue Vaccines Work Group Members

Thank you!
Questions?

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Original Article

Efficacy of a Tetravalent Dengue Vaccine in Healthy Children and Adolescents

Shibadas Biswal, M.D., Humberto Reynales, M.D., Ph.D., Xavier Saez-Llorens, M.D., Pio Lopez, M.D., Charissa Borja-Tabora, M.D., Pope Kosalaraksa, M.D., Chukiat Sirivichayakul, M.D., Veerachai Watanaveeradej, M.D., Luis Rivera, M.D., Felix Espinoza, M.D., LakKumar Fernando, M.D., Reynaldo Dietze, M.D., Kleber Luz, M.D., Rivaldo Venâncio da Cunha, M.D., JoséJimeno, M.D., Eduardo López-Medina, M.D., Astrid Borkowski, M.D., Ph.D., Manja Brose, M.Sc., Martina Rauscher, Ph.D., Inge LeFevre, M.D., Svetlana Bizjajeva, Ph.D., Lulu Bravo, M.D., and Derek Wallace, M.B., B.S., for the TIDES Study Group*

ABSTRACT

BACKGROUND

Dengue, a mosquito-borne viral disease, was designated a World Health Organization top 10 threat to global health in 2019.

METHODS

We present primary efficacy data from part 1 of an ongoing phase 3 randomized trial of a tetravalent dengue vaccine candidate (TAK-003) in regions of Asia and Latin America in which the disease is endemic. Healthy children and adolescents 4 to 16 years of age were randomly assigned in a 2:1 ratio (stratified according to age category and region) to receive two doses of vaccine or placebo 3 months apart. Participants presenting with febrile illness were tested for virologically confirmed dengue by serotype-specific reverse-transcriptase polymerase chain reaction. The primary end point was overall vaccine efficacy in preventing virologically confirmed dengue caused by any dengue virus serotype.

RESULTS

Of the 20,071 participants who were given at least one dose of vaccine or placebo (safety population), 19,021 (94.8%) received both injections and were included in the per-protocol analysis. The overall vaccine efficacy in the safety population was 80.9% (95% confidence interval [CI], 75.2 to 85.3; 78 cases per 13,380 [0.5 per 100 person-years] in the vaccine group vs. 199 cases per 6687 [2.5 per 100 person-years] in the placebo group). In the per-protocol analyses, vaccine efficacy was 80.2% (95% CI, 73.3 to 85.3; 61 cases of virologically confirmed dengue in the vaccine group vs. 149 cases in the placebo group), with 95.4% efficacy against dengue leading to hospitalization (95% CI, 88.4 to 98.2; 5 hospitalizations in the vaccine group vs. 53 hospitalizations in the placebo group). Planned exploratory analyses involving the 27.7% of the per-protocol population that was seronegative at baseline showed vaccine efficacy of 74.9% (95% CI, 57.0 to 85.4; 20 cases of virologically confirmed dengue in the vaccine group vs. 39 cases in the placebo group). Efficacy trends varied according to serotype. The incidence of serious adverse events was similar in the vaccine group and placebo group (3.1% and 3.8%, respectively).

CONCLUSIONS

TAK-003 was efficacious against symptomatic dengue in countries in which the disease is endemic. (Funded by Takeda Vaccines; TIDES ClinicalTrials.gov number, NCT02747927.)

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Biswal at Takeda Vaccines, 21 Biopolis Rd., Nucleos, Level 4, Singapore 138567, Singapore, or at shibadas.biswal@takeda.com.

*A list of the members of the TIDES Study Group is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Biswal and Reynales and Drs. Bravo and Wallace contributed equally to this article.

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Two CLIA Approved Dengue Diagnostic Serotests in Puerto Rico

Diagnostic Test	Internal Analysis for Prior Dengue Infection	
	Sensitivity N=200 **%** (95% CI)	**Specificity** N=332 **%** (95% CI)
SciMedx Dengue IgG Serum Microwell ELISA	**76%** (70.1, 81.9)	**100%** (98.9, 100)
Biocan RDT - Tell Me Fast Dengue IgG/IgM	**61%** (54.2, 67.8)	**99.1%** (97.4, 99.8)

Bonaparte et al. Diagnostic Microbiology and Infectious Disease 2020

For clinical dengue diagnosis based on laboratory validation under CLIA (Clinical Laboratory Improvement Amendments)

POLICY QUESTION FOR ETR

Should 3-doses of CYD-TDV be administered routinely to persons 9-16 years of age with laboratory-confirmed previous dengue infection and living in *endemic areas* to prevent virologically confirmed dengue, hospitalizations and severe dengue?

Other ACIP Dengue Vaccines Workgroup Tasks

- Workgroup has gather available information regarding safety details raised at June ACIP meeting

WHO Screening Test Target Product Profile Project

- **RDT, fingerstick whole blood, low cost**
- **Minimum sensitivity and specificity, ≥ 90%**
- **Description of minimal and optimal reference panel characteristics**
  - Optimal panel would include samples:
    - Virologically confirmed dengue at varying time points after acute infection
    - Dengue and flavivirus negatives
    - Previous flavivirus infected at varying time points
    - Dengue and previous flavivirus at varying time points
    - Variety of flavivirus vaccine recipients