

Five-Year Antibody Persistence Following A Booster Dose of Live-Attenuated Japanese Encephalitis Vaccine (IMOJEV[®]) in Children

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Disclosure

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- Danaya Chansinghakul, Emmanuel Feroldi, Thelma Laot, Celine Monfredo, and Alain Bouckenoghe are Sanofi Pasteur employees.
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JE-CV in Pediatric Populations

Indications

- Prophylaxis of Japanese encephalitis caused by the Japanese encephalitis virus, in individuals from 9 months of age and over
 - Single-dose vaccine for primary immunization
 - Booster dose should be given after the first vaccination, preferably 1 year after the first vaccination and up to 2 years after the first vaccination

Immunogenicity

- JE-CV Primary immunization in JE vaccine-naïve toddlers
 - Seroprotection in more than 95% of subjects 28 days after JE-CV single dose for primary immunization^{1, 2, 3}
 - More than 80% seroprotection 2 years after a JE-CV single dose for primary immunization⁴
- JE-CV Booster vaccination in JE vaccine (inactivated or LAV) primed children
 - All were seroprotected 28 days after JE-CV booster vaccination^{1, 4}
 - GMT increased by 60-fold on 28 days then decreased up to Year 1 to a plateau far above the threshold for protection
 - Seroprotection rates over time remain very high (more than 97% of subjects)⁵













The accepted threshold for seroprotection is defined as having antibody (Ab) titers against JE greater than or equal to 10 / dilution units⁶

1. Chokephaibulkit et al. *Pediatr Infect Dis J* 2010
2. Feroldi et al. *Hum Vaccin Immunother* 2012
3. Chokephaibulkit et al. *Expert Review of Vaccines* 2015

4. Feroldi et al. *Hum Vaccin Immunother* 2013
5. Chokephaibulkit et al. *Vaccine* 2016
6. Hombach et al. *Vaccine* 2005











Study Designs

- Study 1 – **JEC01** (Clinicaltrials.gov: NCT00621764)¹

Phase II study (Thailand) JE-CV in MBDV primed*	N	Screening	D0	D28	D56	M6	Y1-Y5
JE-CV (D0) / Hep A (D28)	50			 			
Hep A (D0) / JE-CV (D28)	50						

* Primary immunization: MBDV (2 doses) according to immunization schedule in Thailand

- Study 2 – **JEC15** (Clinicaltrials.gov: NCT01190228)⁴

Phase III study (The Philippines)	N	D0	D7	D28	Y1-Y5
JE-CV in JE-CV primed*	400	 			
JE-CV in JE-vaccine naive	45	 			
Varicella vaccine (safety control group)	60				

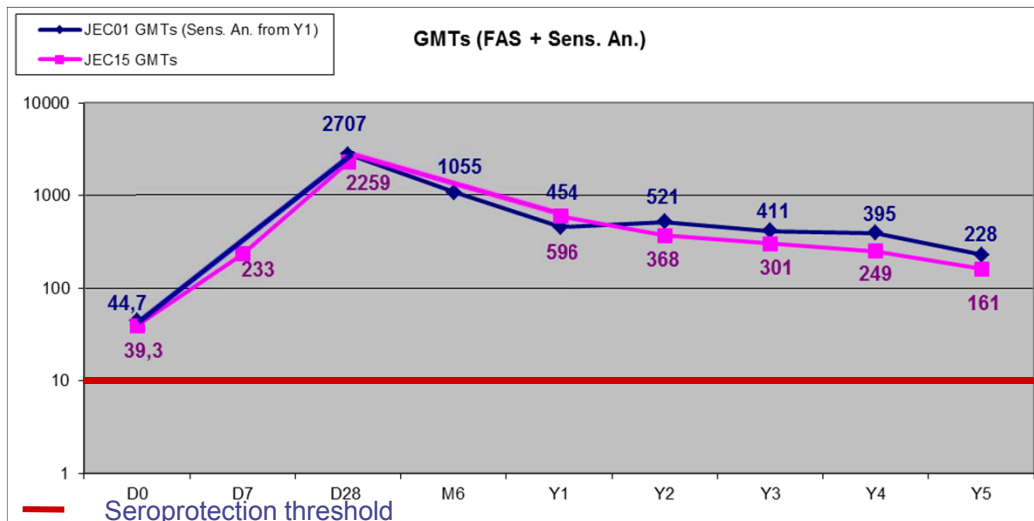
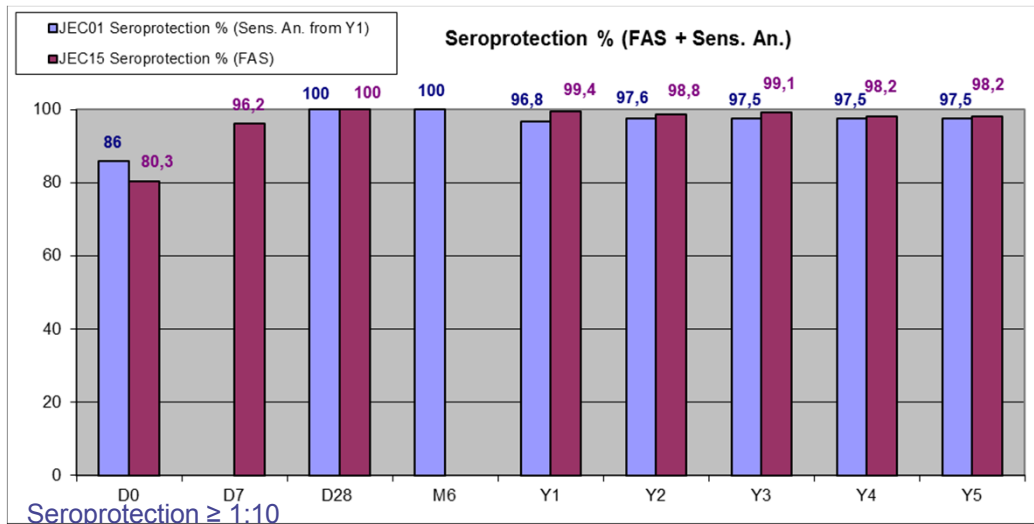
* JE-CV booster 2 years after primary immunization (JE-CV single dose)

In both studies

- Blood samples tested by plaque reduction neutralization test (PRNT₅₀) against JE-CV virus
- Children with titers ≥ 10 (1/dil) are considered seroprotected against JE⁶
- Protocol approved by the Ethics Committee of each center before beginning of the study and conducted according to Good Clinical Practice guidelines
 - Study 1: Siriraj Ethics Committee, Faculty of Medicine Siriraj Hospital, Mahidol University; the Institutional Review Board, Faculty of Medicine, Chulalongkorn University; and the Ethics Committee of the Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
 - Study 2: The Institutional and Ethical Review Board of the Research Institute for Tropical Medicine (RITM), Manila, the Philippines
- The child's parent or guardian provided signed informed consent to the study before exposure to any study procedures

6. Hombach et al. Vaccine 2005

JE-CV booster response is independent of the JE vaccine used for primary immunization (*Full Analysis*)



Strong memory response to JE-CV booster irrespective of priming vaccination (JE-CV or inactivated JE vaccine)

- Seroprotection
 - In all subjects (Day 28)
 - Almost all from Year 1 onwards
- GMTs
 - Increased by 57-fold 28 days after JE-CV booster
 - Decreased from Day 28 to Year 1
 - Then slightly decreased and remained stable over time, far above the threshold for protection

2-5yrs olds on D0 (N= 100)

1. Chokephaibulkit et al. *Pediatr Infect Dis J* 2010

5. Chokephaibulkit et al. *Vaccine* 2016

• JE-CV Primary (The Philippines):

36-42mos olds on D0 (N= 345)

4. Feroldi et al. *Hum Vaccin Immunother* 2013

Study 1 (JEC01) – JE-CV virus PRNT₅₀; Sensitivity Analysis – Clinicaltrials.gov: NCT00621764

Study 2 (JEC15) – JE-CV virus PRNT₅₀; FAS – Clinicaltrials.gov: NCT01190228

Main findings

- Immune responses persist and remain consistent over time up to at least 5 years after a JE-CV booster vaccination in JE primed subjects.
 - High JE neutralizing antibody titers 28 days after a JE-CV booster dose indicative of a memory response in children previously immunized with a JE vaccine.
 - Titers decrease between 28 days and 1 year after vaccination, then slightly decreased and tend to remain stable for the following 5 years.
- The seroprotection rate 5 years after a JE-CV booster vaccination in primed subjects remains very high (more than 97%).
- Similar immune responses (seroprotection rates, GMT values) after JE-CV booster vaccination in JE-CV primed subjects and in inactivated JE primed subjects.
- Results suggest that JE-CV booster vaccination in primed subjects confers long-term protection.
- No case of JE was reported and there were no vaccine related SAEs during the long-term follow-up (data not shown).
- JE-CV (IMOJEV®) can be used as a booster dose following primary immunization with either JE-CV or inactivated JE vaccines.
- Long-term immune responses after a JE-CV booster dose in toddlers are able to neutralize WT viruses from various genotypes circulating in Southeast Asia and India⁷

Conclusion

- JE-CV (IMOJEV[®]) can be used as a booster dose following primary immunization with either JE-CV or inactivated JE vaccines.
 - More than 97% of subjects primed with inactivated JE vaccines remain protected 5 years after the administration of a JE-CV booster dose.
- IMOJEV[®] single-dose primary and booster vaccination induces long-lasting protection in children.

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Thank You