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 Bouckenooghe 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
  - More than 80% seroprotection 2 years after a JE-CV single dose for primary immunization
- JE-CV Booster vaccination in JE vaccine (inactivated or LAV) primed children
  - All were seroprotected 28 days after JE-CV booster vaccination
  - 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)

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

2. Feroldi et al. Hum Vaccin Immunother 2012
4. Feroldi et al. Hum Vaccin Immunother 2013
6. Hombach et al. Vaccine 2005
Study Designs

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

<table>
<thead>
<tr>
<th>Phase II study (Thailand)</th>
<th>N</th>
<th>Screening</th>
<th>D0</th>
<th>D28</th>
<th>D56</th>
<th>M6</th>
<th>Y1-Y5</th>
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</thead>
<tbody>
<tr>
<td>JE-CV in MBDV primed*</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>JE-CV (D0) / Hep A (D28)</td>
<td>50</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Hep A (D0) / JE-CV (D28)</td>
<td>50</td>
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</table>

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

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

<table>
<thead>
<tr>
<th>Phase III study (The Philippines)</th>
<th>N</th>
<th>D0</th>
<th>D7</th>
<th>D28</th>
<th>Y1-Y5</th>
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</thead>
<tbody>
<tr>
<td>JE-CV in JE-CV primed*</td>
<td>400</td>
<td></td>
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<tr>
<td>JE-CV in JE-vaccine naive</td>
<td>45</td>
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<tr>
<td>Varicella vaccine (safety control group)</td>
<td>60</td>
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</table>

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

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4. Feroldi et al. Hum Vaccin Immunother 2013
In both studies

- Blood samples tested by plaque reduction neutralization test (PRNT$_{50}$) against JE-CV virus

- Children with titers $\geq 10$ (1/dil) are considered seroprotected against JE$^6$

- 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

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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)

36-42mos olds on D0 (N= 345)
4. Feroldi et al. Hum Vaccin Immunother 2013

Study 1 (JEC01) – JE-CV virus PRNT\textsubscript{50}; Sensitivity Analysis – Clinicaltrials.gov: NCT00621764
Study 2 (JEC15) – JE-CV virus PRNT\textsubscript{50}; 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 India

7. Feroldi et al. *Journal of Infectious Diseases (JID)* 2016
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.
References


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- Research Institute for Tropical Medicine (RITM), Muntinlupa City and the Health Centers in Alabang, Buli, and Cupang

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ขอบคุณค่ะ

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Thank You