Vaccines available against JE

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Evaluating JE Vaccines

- Due to the rarity of JE disease, efficacy studies are impractical and vaccines are licensed based on an accepted correlate of protection.

- It is generally accepted that individuals with a serum neutralizing antibody titre of at least 1:10 are protected from JEV disease.

- **Seroconversion**: PRNT$_{50}$ titer of $< 10$ at baseline and $\geq 10$ at time of serum sampling, or a 4-fold rise from a baseline titer of $\geq 10$.

- **Most PRNT$_{50}$ titers** based on using vaccine virus and not wild-type strains.

- Different virus strains are used as vaccines and no reference reagents for standardizing PRNT titers between vaccines.
All JE vaccines are based on genotype III viruses

- Beijing-1
- Nakayama
- P3
- 821564 XZ
- SA14-14-2
  - Live SA14-14-2/PHK (CD.JEVAX)
  - JE-ChimeriVax (IMOJEV)
  - Inactivated SA14-14-2/Vero, IC51 (IXIARO, JESPECT, JEEV)
Major classes of licensed JE vaccines

Inactivated mouse brain-based JE vaccines
  • First licensed in Japan in 1954

Live attenuated JE vaccines
  • First licensed in China in 1988

Inactivated Vero cell-based JE vaccines
  • First licensed in China in 1998, Japan/US/Europe in 2009

Live attenuated chimeric JE vaccines
  • First licensed in Australia in 2010
<table>
<thead>
<tr>
<th>Class</th>
<th>Company</th>
<th>Strain (all G3)</th>
</tr>
</thead>
</table>
| Inactivated mouse brain-based| **Green Cross**, AdImmune Corp, VaBiotech  
JE VAX (Biken) – used as reference for non-inferiority for new generation vaccines | Nakayama         |
|                              | GPO                              | Beijing-1       |
| Inactivated Vero cell-based  | Biken, Kaketsuken                 | Beijing-1       |
|                              | Liaoning Chengda, Beijing Tiantan | Beijing P-3     |
|                              | **Valneva/Novartis/CSL, Biological E*** | SA 14-14-2   |
|                              | Bharat Biotech                   | Kolar strain (JEV 821564XY) |
| Live attenuated              | **Chengdu Institute of Biological Products (CDIBP)***, Wuhan Institute of Biological Products, Lanzhou Institute of Biological Products | SA 14-14-2       |
| Chimeric live attenuated     | **Sanofi Pasteur***              | SA 14-14-2       |

*Bold = internationally distributed,  
*WHO prequalified
Inactivated mouse brain-derived JE vaccines

• Manufactured by inoculating 2-week old mice intracerebrally

• Brains harvested and purified, formalin inactivated
  ➢ Possibility for variation in purification procedures and vaccine quality across manufacturers

• Excipients include gelatin and sodium glutamate

• Typically given as 2-3 dose primary series + booster(s)

• Many manufacturers no longer producing

• No mouse brain-derived vaccines are WHO prequalified
Inactivated Vero cell JE vaccines

- Vero cell derived
- Formalin-inactivated
- Two dose regimen plus boosters that vary by product (e.g., IXIARO and JESPECT are 0 and 28 days)
- Pediatric (0.25mL) and adult (0.5mL) doses
- Inactivated Vero cell products licensed in the US, Europe, Japan, China, India
- Aluminium hydroxide adjuvanted (0.1%, 250µg) (no gelatin) (Exceptions: Biken and Kaketsuken products)
- Typically licensed from 6 months – 1 year of age in endemic countries, 2 months of age in non-endemic countries
- JEEV is WHO prequalified
  - 2 doses @ 12-35 months and 18-49 years of age
Live attenuated JE vaccines

- Based on Genotype 3 SA 14-14-2 strain
- Grown on primary hamster kidney cells
- Internationally distributed product “CD.JEVAX”, manufactured by Chengdu Institute of Biological Products
- Includes gelatin, saccharose, human serum albumin, and sodium glutamate
- Often given, and prequalified, as single dose
  - In some countries a second dose is recommended at 2 years of age.
- Vaccine is licensed in China, India, South Korea, Thailand, Nepal, Sri Lanka, DPRK, Laos, Cambodia, Myanmar, Malaysia and Vietnam.
- CD.JEVAX is WHO prequalified (following construction of GMP-compliant facility)
  - One dose at ≥8 months of age
Chimeric Vaccine

- Single product “IMOJEV”- live vaccine made using recombinant DNA technology
  - Replaced prM and E coding sequences of the yellow fever live attenuated 17D vaccine virus with the SA 14-14-2 live attenuated JE vaccine virus
- Contains mannitol, lactose, glutamic acid, potassium hydroxide, histidine, human serum albumin, and sodium chloride
- Licensed in Australia, Malaysia, Brunei, Philippines, Thailand, Myanmar
- Manufacturer recommendation to give as single dose with pediatric booster
- IMOJEV is WHO prequalified
  - Single dose at ≥9 months of age + paediatric booster
ChimeriVax™ technology – YF 17D live vector

Tom Monath & Farshad Guirakhoo, Acambis / Sanofi Pasteur

Yellow fever 17D genome cloned as cDNA

5’ C prM E Non-structural genes 3’

Exchange coat protein genes of JE SA14-14-2/PHK

5’ C prM E Non-structural genes 3’

Chimeric cDNA -> transcribe to RNA

5’ C prM E Non-structural genes 3’

Envelope is heterologous virus containing SA14-14-2 antigens

RNA replicative ‘engine’ is YF 17D

Transfect mRNA

Grow virus in cell culture

Sealy Center for Vaccine Development
# Example Characteristics

<table>
<thead>
<tr>
<th>Company</th>
<th>Name</th>
<th>Technology</th>
<th>Admin/ Doses per manufacturer recommendations</th>
<th>Age</th>
<th>Presentation</th>
<th>Shelf-Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green Cross</td>
<td>JenceVac</td>
<td>Inactivated mouse brain</td>
<td>SC 3 doses + boosters</td>
<td>12-23 months for primary series</td>
<td>Liquid 1 dose vial</td>
<td>18 months</td>
</tr>
<tr>
<td>Valneva/ Novartis/ CSL</td>
<td>IXIARO/JESPECT&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Inactivated Vero cell</td>
<td>IM 2 doses + adult booster</td>
<td>≥2 months in non-endemic areas</td>
<td>Liquid 1 dose pre-filled syringe</td>
<td>24 months</td>
</tr>
<tr>
<td>CDIBP</td>
<td>CD.JEVAX&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Live attenuated PHK cell</td>
<td>SC 1 dose</td>
<td>≥8 months</td>
<td>Lyophilized 1 and 5 dose vials</td>
<td>18 months</td>
</tr>
<tr>
<td>Sanofi Pasteur/ GPO</td>
<td>Imojev&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Chimeric live attenuated Vero cell</td>
<td>SC 1 dose + paediatric booster</td>
<td>≥9 months</td>
<td>Lyophilized 1 and 4 dose vials</td>
<td>36 months</td>
</tr>
</tbody>
</table>

<sup>1</sup> “Sister” product JEEV (BioE) is WHO prequalified (12-35 months and 18-49 years)

<sup>2</sup> WHO prequalified

All products stored at 2-8°C