Adverse events following JE-VC reported to the Vaccine Adverse Events Reporting System (VAERS) 2012–2016

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JE vaccine and VAERS report review

- May 2009: JE-VC distribution began for adults aged ≥17 years
- 2013: JE-VC distribution for persons 2 months to <17 years
- 2015: review of VAERS reports for adults who received JE-VC from May 2009 through April 2012*
- Current: review VAERS reports from May 2012 through April 2016

*Rabe IB et al. Adverse events following vaccination with an inactivated, Vero cell culture-derived Japanese encephalitis vaccine in the United States, 2009-2012. Vaccine 2015; 33:708-12

VAERS

- Passive reporting system
- Manufacturers, healthcare providers, or vaccine recipients can submit reports
- Standard form: demographics, vaccination, adverse event (AE)
- Events coded with Medical Dictionary for Regulatory Activities (MedDRA) terms
- Causal relationship between vaccination and reported events usually cannot be determined

Serious AE definitions*

- Life-threatening
- Death
- Persistent or significant disability
- Congenital anomaly
- Hospitalization or prolongation of hospitalization
- Require medical or surgical intervention to prevent one of the outcomes

*FDA regulatory definition (21 CFR 600.80)

Data review

- Exclusions
  - >60 days after vaccination
  - Local reactions contralateral to the site of JE-VC administration
  - Administered inappropriately with no AE
  - Symptoms clearly related and unique to another co-administered vaccine
- High percentage of doses distributed to U.S. military

Case definitions

- Hypersensitivity reactions
  - Anaphylaxis: Brighton definition*
  - Non-anaphylaxis - modified Brighton definition¥
    - Immediate: < 2 hours after vaccination
    - Delayed: 2 hours–14 days after vaccination
- Neurologic events
  - Central
  - Peripheral

*Ruggeberg JU et al. Vaccine 2007;25:5675–84.
¥ Rabe IB et al. Vaccine 2015; 33:708-12.

Denominator data for rate calculations

- Valneva provided total doses distributed by month
- No data on doses administered by age and sex

AEs following vaccination with JE-VC

	N (%)	Incidence per 100,000 doses distributed*
Total	119 (100)	14.8
Serious	9 (8)	1.1
Non-serious	110 (92)	13.7

* 802,229 doses distributed in the U.S. from May 1, 2012 –April 30, 2016

AEs following JE-VC by sex and age (N=119)

	N	(%)
Sex		
Male	73	(61)
Female	46	(39)
Age group (years)		
<17	11	(9)
17–39	79	(66)
40–59	21	(18)
≥60	8	(7)

AEs following JE-VC by dose number (N=119)

	N (%)
First	63 (53)
Second	26 (22)
> 2 doses	10 (8)
Unknown	20 (17)

AEs following JE-VC administered alone or concurrently by seriousness (N=119)

	Serious N (%)	Non-serious N (%)	Total N (%)
JE-VC alone	1 (1)	38 (32)	39 (33)
Concurrent vaccines	8 (7)	72 (61)	80 (67)

AEs following JE-VC administered alone or concurrently by seriousness (N=119)

	Serious N (%)	Non-serious N (%)	Total N (%)
JE-VC alone	1 (1)	38 (32)	39 (33)
Concurrent vaccines	8 (7)	72 (61)	80 (67)

Serious and non-serious AEs following JE-VC by event type (N=119)

	Serious N (%)	Non-serious N (%)	Total N (%)
Hypersensitivity	2 (2)	22 (18)	24 (20)
Neurologic	1 (1)	10 (8)	11 (9)
Other	6 (5)	78 (66)	84 (71)

Serious and non-serious hypersensitivity AEs following JE-VC (N=23)*

	Serious N (%)	Non-serious N (%)	Total N (%)
Anaphylaxis	1 (4)	0 (0)	1 (4)
Immediate	1 (4)	6 (26)	7 (30)
Delayed	0 (0)	15 (65)	15 (65)

*Timing for one event not specified

Serious hypersensitivity events following JE-VC

Type	Age/Sex	Time post vaccination	Concurrent vaccines
Anaphylaxis	19/F	25 min	Anthrax, typhoid, yellow fever
Immediate hypersensitivity	23/M	15 min	Anthrax, typhoid

Serious and non-serious neurologic AEs following JE-VC (N=11)

	Serious N (%)	Non-serious N (%)	Total N (%)
Central*	1 (9)	1 (9)	2 (18)
Peripheral¥	0 (0)	9 (82)	9 (82)

*Seizures (N=2)

¥Paresthesias (N=6), Somatosensory events (N=2), Sensorineural hearing loss (N=1)

Serious central neurologic event following JE-VC

Type	Age/Sex	Time post vaccination	Concurrent vaccines
Seizures	15/M	7 days	Rabies

Serious and non-serious other AEs following JE-VC (N=84)

	Serious N (%)	Non-serious N (%)	Total N (%)
Local	0 (0)	23 (27)	23 (27)
Non-local	6 (7)	55 (65)	61 (73)

Serious other events following JE-VC

Age/Sex	Description	Time post vaccination	Concurrent vaccines
42/M	Sudden cardiac death	8 days	None
42/M	Cardiomyopathy	22 days	Anthrax, meningococcal, smallpox, typhoid
21/M	Myocardial infarct, acute myocarditis	12 days	Smallpox
19/F	Angina pectoris	24 days	Anthrax, smallpox, typhoid, varicella
35/M	Systemic febrile reaction and acute vaccinia syndrome	2 days	Anthrax, smallpox
75/F	Acute kidney injury, myopathy	7 days	Pneumococcal, typhoid

Comparison of reporting rates of AEs following JE-VC per 100,000 doses distributed

	2009–2012[1]	2012–2016
All AEs	15.2	14.8
Hypersensitivity	4.4	3.0
Neurologic	2.2	1.4

1. Rabe IB et al. Adverse events following vaccination with an inactivated, Vero cell culture-derived Japanese encephalitis vaccine in the United States, 2009-2012. Vaccine 2015; 33:708-12

Conclusions

- Rates of adverse events have not increased compared with the previous VAERS analysis
- Few adverse events reported in persons aged <17 years, but administration data by age group not available to calculate rates
- Hypersensitivity and neurologic adverse events occur but uncommon; with >800,000 doses distributed during period, data support good overall JE-VC safety profile

Thank you