Surveillance for adverse events following use of live attenuated chikungunya vaccine and its use among travelers

Dr. Susan Hills
CDC Lead, Chikungunya Vaccines Work Group
Arboviral Diseases Branch
Division of Vector-Borne Diseases
Fort Collins, Colorado

Advisory Committee on Immunization Practices meeting
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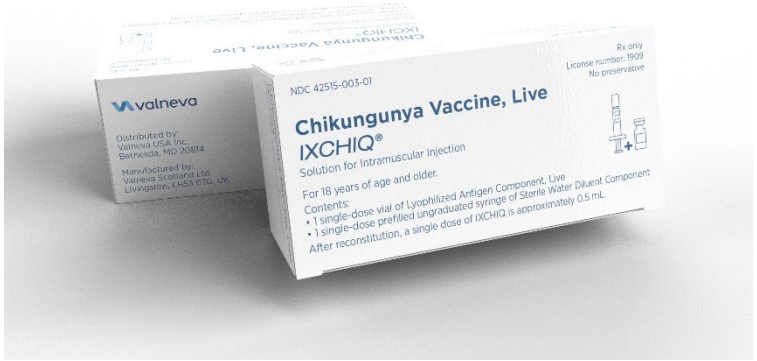
Background on live attenuated chikungunya vaccine

Live attenuated chikungunya vaccine (CHIK-LA)

- Manufactured by Valneva and called IXCHIQ
- Licensed in United States in November 2023 for individuals aged ≥18 years
- Single dose primary schedule
- Licensed based on immunogenicity and safety data in ~3,500 adults



Local and systemic adverse events in pivotal Phase 3 trial

- Safety data from 3,082 subjects
- Solicited local reactions within 10 days after vaccination
  - 15% in vaccinees vs 11% in placebo recipients
- Solicited systemic adverse events (AE) within 10 days after vaccination
  - 50% in vaccinees vs 27% in placebo recipients
  - Most common were headache, fatigue and myalgia in ~25%–30% of vaccinees

Schneider M et al. Safety and immunogenicity of a single-shot live-attenuated chikungunya vaccine: a double-blind, multicentre, randomised, placebo-controlled, phase 3 trial. Lancet 2023; 401: 2138–2147.

Comparison of adverse events in 18–64 years and ≥65 years*

	18–64 years				≥65 years			
	Vaccine (n=2,736)	(95% CI)	Placebo (n=916)	(95% CI)	Vaccine (n=346)	(95% CI)	Placebo (n=117)	(95% CI)
Any related AE	52%	(50%–54%)	32%	(29%–35%)	46%	(41%–52%)	26%	(18%–35%)
Any related severe AE	2%	(2%–3%)	0.1%	(0%–0.6%)	1%	(0.3%–3%)	0	(0%–3%)

*Data from pivotal Phase 3 trial

Comparison of adverse events in 18–64 years and ≥65 years*

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Any related severe AE	**2%**	**(2%–3%)**	0.1%	(0%–0.6%)	**1%**	**(0.3%–3%)**	0	(0%–3%)

*Data from pivotal Phase 3 trial

Chikungunya-like adverse reactions (1)

- Fever ≥100.4°F (38°C) **and** ≥1 of:
  - Arthralgia or arthritis
  - Myalgia
  - Headache
  - Back pain
  - Rash
  - Lymphadenopathy
  - Certain neurologic, cardiac, or ocular symptoms
- Symptom onset within 30 days of vaccination

Package insert – IXCHIQ (https://www.fda.gov/vaccines-blood-biologics/ixchiq)

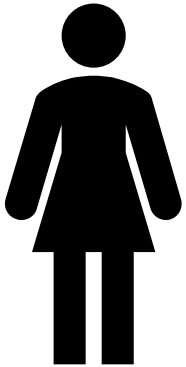
Chikungunya-like adverse reactions (2)

- **Chikungunya-like adverse reactions**
  - **11.7%** of vaccine recipients and 0.6% of placebo recipients
- **Severe reactions** preventing daily activity or requiring medical intervention
  - **1.6%** vaccine recipients vs 0% of placebo recipients
- **Prolonged reactions** with duration ≥30 days
  - **0.5%** vaccine recipients vs 0% of placebo recipients

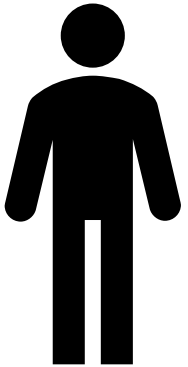
----------**WARNINGS AND PRECAUTIONS**----------

- IXCHIQ may cause severe or prolonged chikungunya-like adverse reactions. (5.2)

Two serious adverse events considered related to vaccination



- 58-year-old female, history of fibromyalgia and hypertension
- Severe myalgia
- Hospitalized for 6 days for pain management and diagnostic procedures



- 66-year-old male, history of hypertension
- Myalgia, high fever, atrial fibrillation, and hypovolemic hyponatremia
- Hospitalized for 4 days

FDA Clinical Review Memo (https://www.fda.gov/vaccines-blood-biologics/ixchiq)

ACIP Work Group summary of CHIK-LA safety in Evidence to Recommendations, February 2024

- Reactogenic vaccine but similar adverse event rates to some other vaccines
- Important to monitor for rare adverse events post-licensure as sample size of ~3,500 vaccinated subjects too small to detect rare events

Post-marketing studies

- FDA-required post-marketing studies
  - Vaccine effectiveness study in persons aged ≥12 years with safety component (Brazil)
  - Pragmatic randomized controlled trial in ≥10,000 individuals to assess effectiveness and safety

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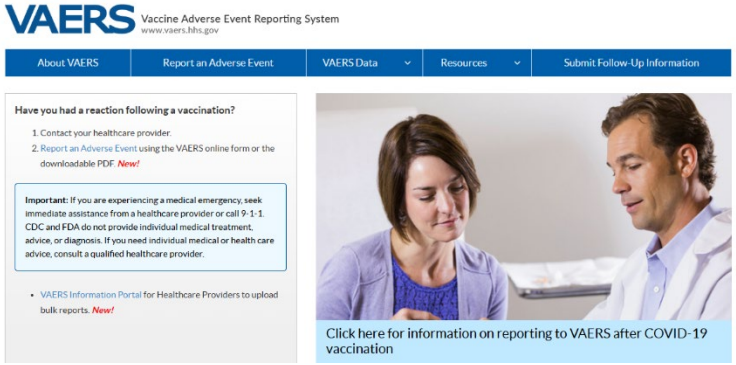
  - Vaccine effectiveness study in persons aged ≥12 years with safety component (Brazil)
  - Pragmatic randomized controlled trial in ≥10,000 individuals to assess effectiveness and safety
- Additional safety data collection
  - Valneva conducting safety study of 5,000 U.S. travelers for medically attended adverse events of special interest
  - Observational registry study of pregnant women in Brazil

Post-licensure surveillance for adverse events following use of CHIK-LA

Vaccine Adverse Event Reporting System (VAERS)

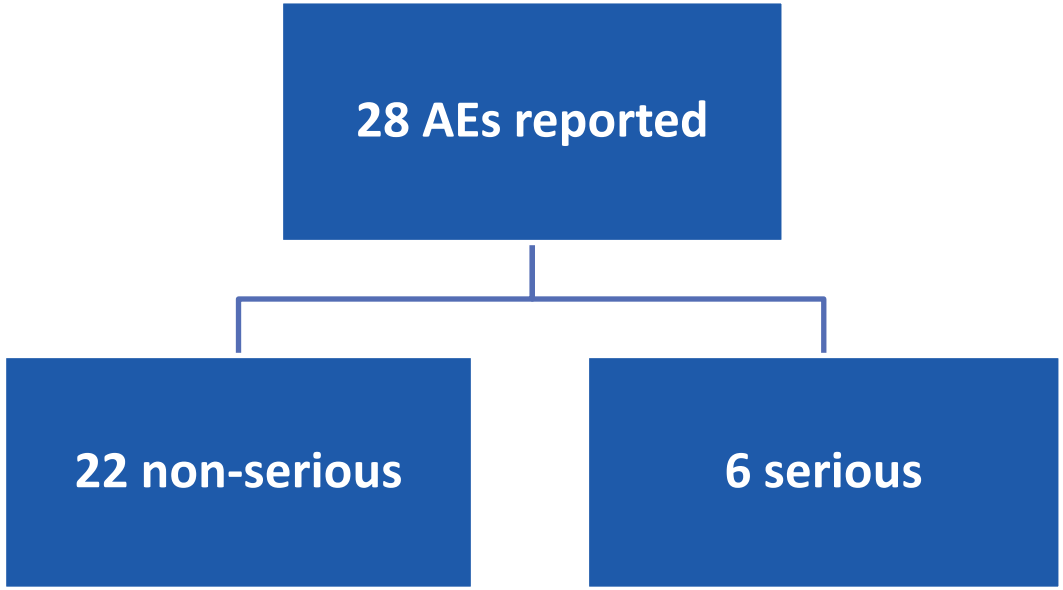
- National reporting system for adverse events (AE) following vaccination co-managed by CDC and FDA
- Designed to detect rare or previously unreported AE or changes in reporting patterns that might signal a potential safety concern that warrants further investigation
- Anyone (e.g., healthcare providers, patients, vaccine manufacturers) can submit reports
- Effective in intended role as early warning system but limitations include
  - Under-and over-reporting, variable report quality and accuracy, lack of data on vaccine doses administered, and lack of unvaccinated comparator group
- Generally cannot determine if AEs caused by vaccine



Timeline

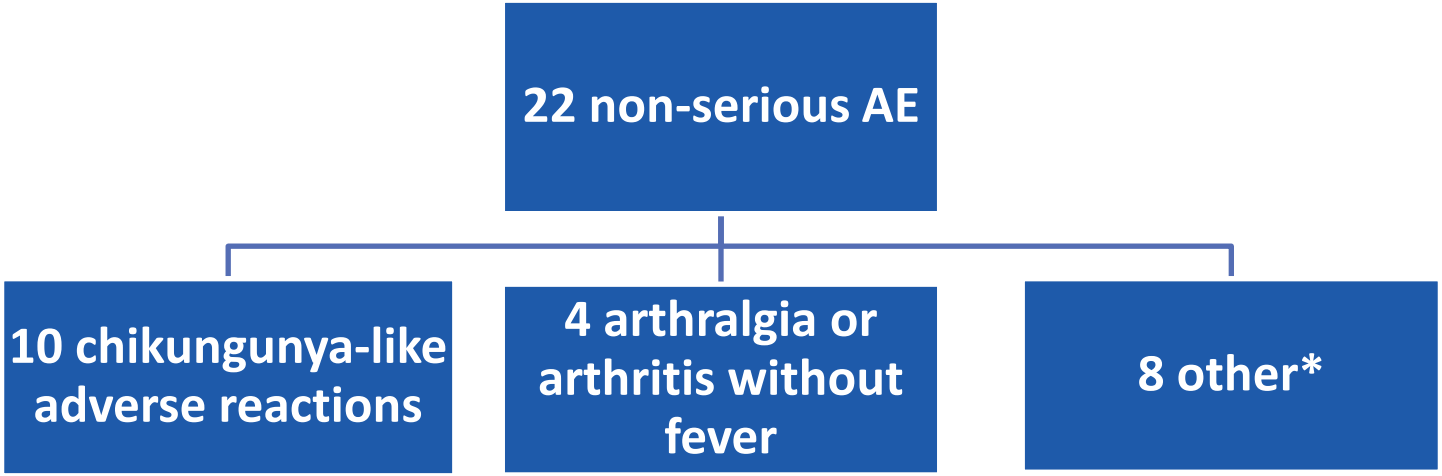
*First report (non-serious event) to VAERS received May 6, 2024

28 AEs reported to VAERS after CHIK-LA vaccine administered in May-Dec 2024*



*Excludes 1 foreign report (non-serious)

22 non-serious AEs



*Syncope (n=1), flushing (n=1), rash/headache (n=1), musculoskeletal pain (n=1), low grade fever/headache (n=2), respiratory tract symptoms (n=2)

Serious adverse events (SAEs)

FDA definition of SAE per federal law

Any adverse event associated with use of biological product, whether or not considered product-related, that results in:

- Death
- Life-threatening adverse experience
- **Inpatient hospitalization** or prolongation of existing hospitalization
- Persistent or significant disability/incapacity
- Congenital anomaly/birth defect
- **Other medically important event** that may jeopardize patient and may require intervention to prevent one of the outcomes listed

Code of Federal Regulations Title 21 (https://www.ecfr.gov/current/title-21/chapter-I/subchapter-F/part-600/subpart-D/section-600.80)

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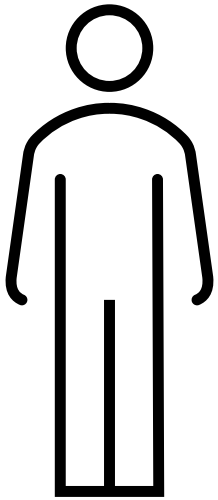
When SAEs reported to VAERS, attempts made to collect additional information (e.g., medical records)

Code of Federal Regulations Title 21 (https://www.ecfr.gov/current/title-21/chapter-I/subchapter-F/part-600/subpart-D/section-600.80)

Case 1: 83-year-old male

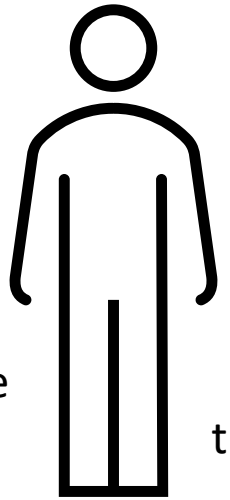


Case 1: 83-year-old male

Coronary artery disease

Chronic heart failure

Chronic kidney disease



Hypertension

Hyperlipidemia

Chronic thrombocytopenia

Multiple medications to treat comorbidities

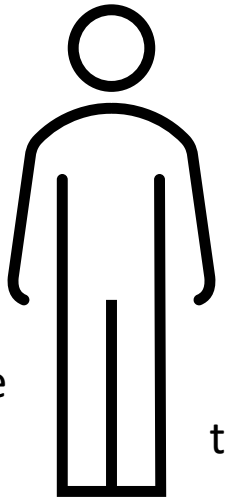
Active at baseline

Case 1: 83-year-old male

Coronary artery disease

Chronic heart failure

Chronic kidney disease



Hypertension

Hyperlipidemia

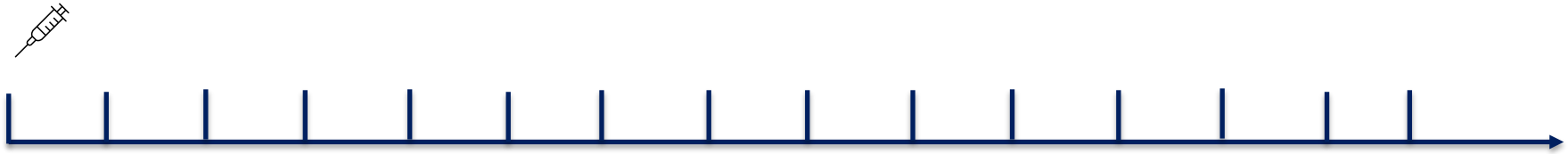
Chronic thrombocytopenia

Multiple medications to treat comorbidities
Active at baseline

- **Received CHIK-LA vaccine for travel to South America and Africa**

Case 1. 83-year-old male

Day 0:
Received
CHIK-LA
(only)



Case 1. 83-year-old male

Day 0:
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Day 3:
Initial
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Case 1. 83-year-old male

Day 0: Received CHIK-LA (only)

Day 3: Initial symptoms

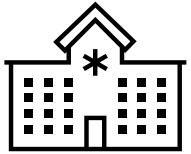
Myalgia, arthralgia, mild fever, chills, headache, generalized weakness, brain fog, anorexia, severe fatigue, unsteady gait

Case 1. 83-year-old male

Day 0: Received CHIK-LA (only)

Day 3: Initial symptoms

Day 7: Presents to ED with ongoing generalized weakness



Case 1. 83-year-old male

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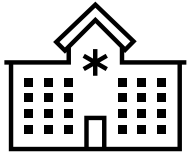
Day 7: Presents to ED with ongoing generalized weakness



Determined to have acute kidney injury likely from dehydration; brain MRI and head CT - no acute changes; discharged home

Case 1. 83-year-old male

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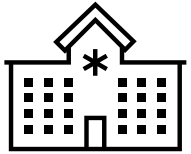
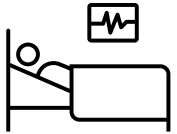
Day 3: Initial symptoms

Day 7: Presents to ED with ongoing generalized weakness



Day 11: Returned to hospital with persistent weakness; admitted



Left lower extremity (hip flexor) weakness, myalgia, fatigue

Case 1. 83-year-old male

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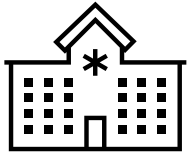

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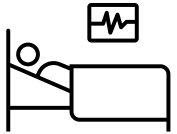

Left lower extremity (hip flexor) weakness, myalgia, fatigue

Leukopenia, acute on chronic thrombocytopenia, elevated liver function tests; declined lumbar puncture

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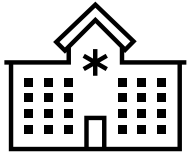

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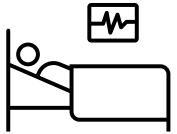

Left lower extremity (hip flexor) weakness, myalgia, fatigue

Leukopenia, acute on chronic thrombocytopenia, elevated liver function tests; declined lumbar puncture

COVID, influenza A/B, RSV PCR: negative

Blood cultures: no growth

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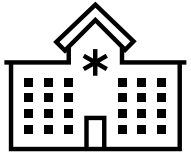
Day 3: Initial symptoms

Day 7: Presents to ED with ongoing generalized weakness



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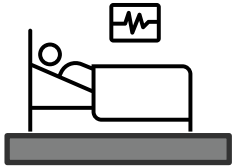


Case 1. Encephalopathy in 83-year-old male

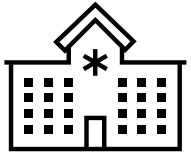
- Discharge diagnosis: **Encephalopathy and generalized weakness - suspected association with chikungunya vaccination**
- Completely resolved after 3.5 weeks

Case 1. Encephalopathy in 83-year-old male

Day 0: Received CHIK-LA (only)

Day 3: Initial symptoms

Day 7: Presents to ED with ongoing generalized weakness



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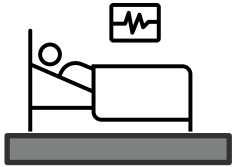


Myalgia, arthralgia, mild fever, chills, headache, generalized weakness, brain fog, anorexia, severe fatigue, unsteady gait

Determined to have acute kidney injury likely from dehydration

Brain MRI and head CT - no acute changes

Discharged home

Left lower extremity (hip flexor) weakness, myalgia, fatigue

Leukopenia, acute on chronic thrombocytopenia, elevated liver function tests; declined lumbar puncture

COVID–19, influenza A/B, RSV PCR: negative

Blood cultures: no growth

Case 2. 77-year-old male

Coronary artery disease

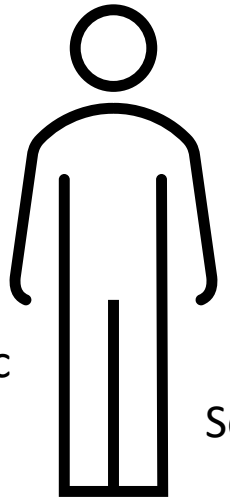
Hyperlipidemia

Hypothyroidism

Hypertension

Benign prostatic hyperplasia

Selective IgA deficiency



Several medications to treat comorbidities

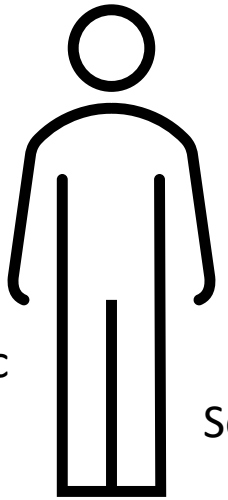
Active at baseline

Case 2. 77-year-old male

Coronary artery disease

Hypothyroidism

Benign prostatic hyperplasia



Hyperlipidemia

Hypertension

Selective IgA deficiency

- **Received CHIK-LA vaccine for travel to Southeast Asia**

Several medications to treat comorbidities
Active at baseline

Case 2. 77-year-old male

Day 0:
Received
CHIK-LA &
JE-VC*

*JE-VC: Inactivated Vero cell culture-derived JE vaccine

Case 2. 77-year-old male

Day 0:
Received
CHIK-LA &
JE-VC

Day 4:
Initial
symptoms

Case 2. 77-year-old male

Day 0: Received CHIK-LA & JE-VC

Day 4: Initial symptoms

Severe fatigue, fever, diarrhea, myalgia, urinary urgency

Case 2. 77-year-old male

Day 0: Received CHIK-LA & JE-VC

Day 4: Initial symptoms

Day 6: Presented to Urgent Care

Diagnosed with viral illness

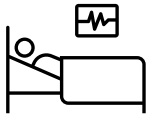
Case 2. 77-year-old male

Day 0: Received CHIK-LA & JE-VC

Day 4: Initial symptoms

Day 6: Presented to Urgent Care

Day 8: Presented to hospital with worsening symptoms; admitted

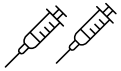


Profound weakness with inability to stand and intermittent confusion; no dysuria or macroscopic hematuria

Admission diagnosis of fever of unknown origin, diarrhea, dehydration, hyponatremia, hypochloremia, and suspected urinary tract infection

Case 2. 77-year-old male

Day 0: Received CHIK-LA & JE-VC



Day 4: Initial symptoms

Day 6: Presented to Urgent Care

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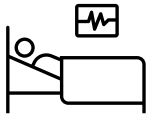

Urinalysis: Negative

Case 2. 77-year-old male

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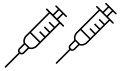

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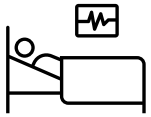


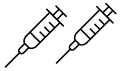
Urinalysis: Negative

COVID PCR, influenza A/B antigen: negative

Blood cultures: no growth

Case 2. 77-year-old male

Day 0: Received CHIK-LA & JE-VC



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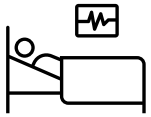

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Blood cultures: no growth

Brain MRI: no acute intracranial abnormalities

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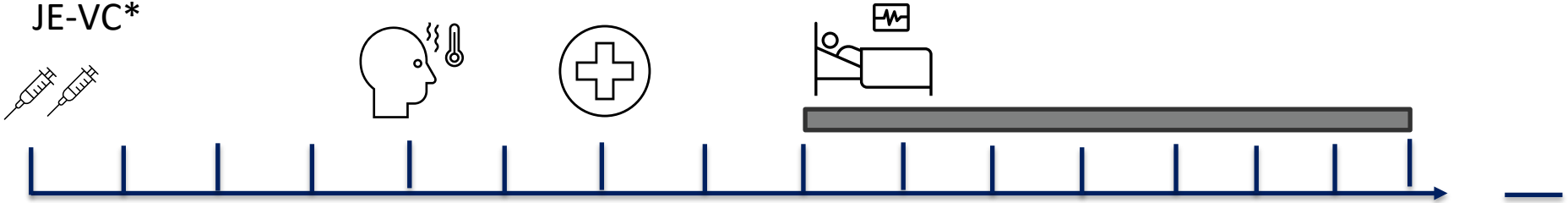


Urinalysis: Negative

COVID PCR, influenza A/B antigen: negative

Blood cultures: no growth

Brain MRI: no acute intracranial abnormalities

Case 2. Encephalopathy in 77-year-old male

- Discharge diagnosis: **Acute metabolic encephalopathy – possible association with vaccination – and fever of unknown origin (resolved)**

Case 2. Encephalopathy in 77-year-old male

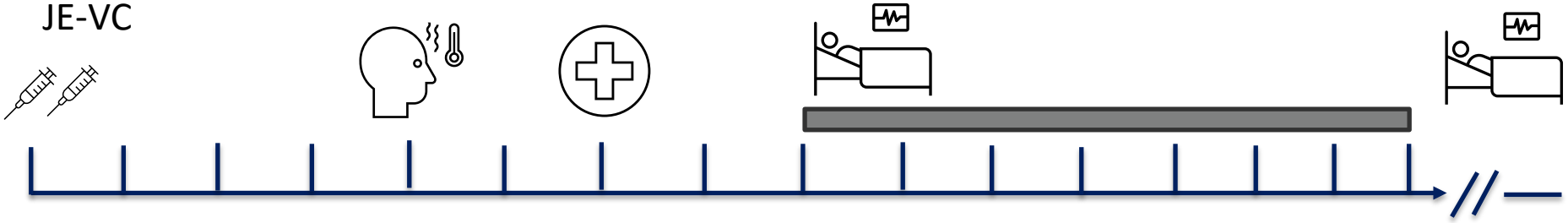
Day 0: Received CHIK-LA & JE-VC

Day 4: Initial symptoms

Day 6: Presented to Urgent Care

Day 8: Presented to hospital with worsening symptoms; admitted

Day 19: Readmitted with urinary retention for ~24 hours



Case 2. Encephalopathy in 77-year-old male: outcome

- At ~4 months after onset: Still recovering with ongoing weakness

Case 2. Encephalopathy in 77-year-old male

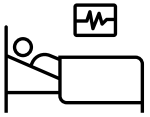
Day 0: Received CHIK-LA & JE-VC*

Day 4: Initial symptoms

Day 6: Presented to Urgent Care

Day 8: Presented to hospital with worsening symptoms; admitted

Day 19: Readmitted for ~24 hours with urinary retention



Severe fatigue, fever, diarrhea, myalgia, urinary urgency

Diagnosed with viral illness

Profound weakness with inability to stand and intermittent confusion; no dysuria or macroscopic hematuria

Admission diagnosis of fever of unknown origin, diarrhea, dehydration, hyponatremia, hypochloremia, and suspected urinary tract infection

Urinalysis: Negative

COVID PCR, influenza A/B antigen: negative

Blood cultures: no growth

Brain MRI: no acute intracranial abnormalities

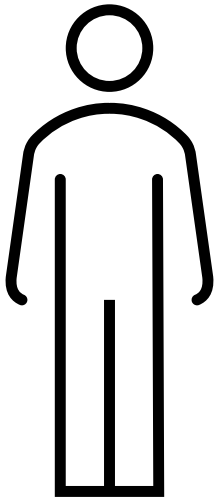
*JE-VC: Inactivated Vero cell culture-derived JE vaccine

Case 3. 86-year-old male

Diabetes mellitus

Heart failure

Anemia



Hypertension

Hypothyroidism

Hyperlipidemia

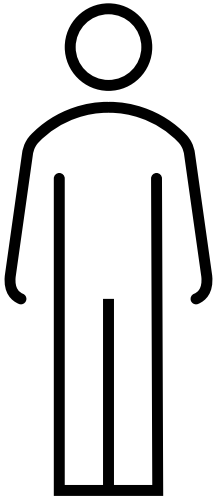
Medications to manage comorbidities

Case 3. 86-year-old male

Diabetes mellitus

Heart failure

Anemia



Hypertension

Hypothyroidism

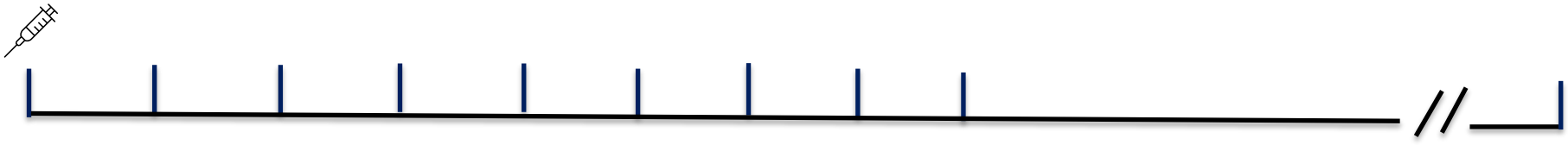
Hyperlipidemia

Medications to manage comorbidities

- **Received CHIK-LA vaccine for travel to South Asia**

Case 3. 86-year-old male

Day 0:
Received
CHIK-LA



Case 3. 86-year-old male

Day 0:
Received
CHIK-LA

Day 3:
Initial
symptoms

Lethargy,
drowsiness,
fever

Case 3. 86-year-old male

Day 0: Received CHIK-LA

Day 3: Initial symptoms

Lethargy, drowsiness, fever

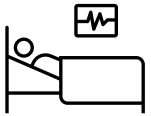
Deterioration in mental status, shortness of breath

Case 3. 86-year-old male

Day 0:
Received
CHIK-LA

Day 3:
Initial
symptoms

Day 8:
Hospitalized,
admitted to ICU



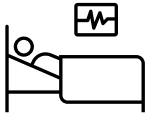
Altered mental
status, acute
encephalopathy
secondary to
hyponatremia
(118 mmol/L),
shortness of
breath

Case 3. 86-year-old male

Day 0:
Received
CHIK-LA

Day 3:
Initial
symptoms

Day 8:
Hospitalized,
admitted to ICU



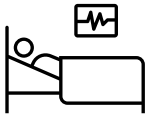
Hypokalemia, hypochloremia,
hypocalcemia, hypomagnesemia
Elevated liver function tests

Case 3. 86-year-old male

Day 0:
Received
CHIK-LA

Day 3:
Initial
symptoms

Day 8:
Hospitalized,
admitted to ICU



Hypokalemia, hypochloremia, hypocalcemia, hypomagnesemia
Elevated liver function tests

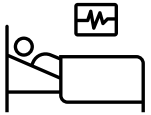
CT head: No acute abnormalities
Chest X-ray: bilateral infiltrates
Echocardiogram: Small pericardial effusion

Case 3. 86-year-old male

Day 0:
Received
CHIK-LA

Day 3:
Initial
symptoms

Day 8:
Hospitalized,
admitted to ICU



Hypokalemia, hypochloremia, hypocalcemia, hypomagnesemia
Elevated liver function tests

CT head: No acute abnormalities
Chest X-ray: bilateral infiltrates
Echocardiogram: Small pericardial effusion

Day 13 post-vaccination serum sample: chikungunya virus RNA

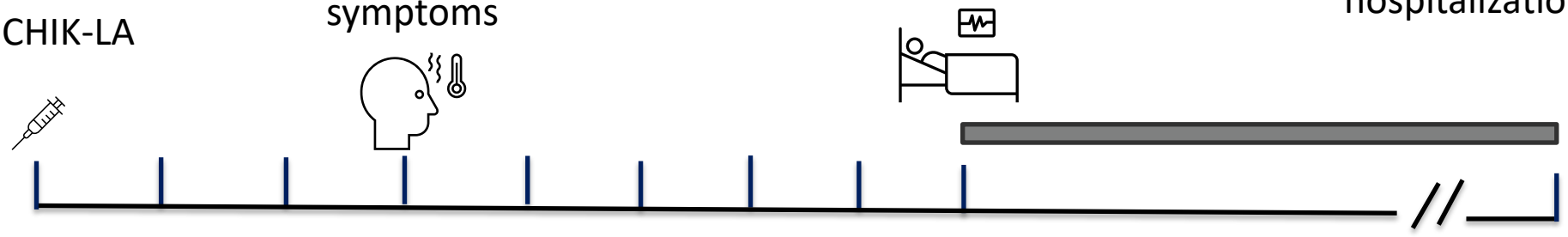
Case 3. 86-year-old male

Day 0:
Received
CHIK-LA

Day 3:
Initial
symptoms

Day 8:
Hospitalized,
admitted to ICU

Day 31:
Discharged
after 23-day
hospitalization



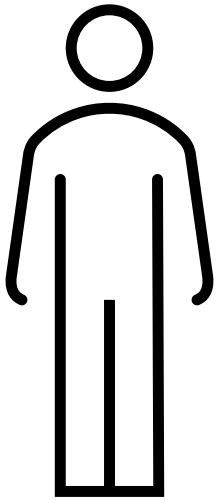
Case 3. Metabolic encephalopathy in 83-year-old male

- Discharge diagnosis:
  - **Toxic metabolic encephalopathy**
  - **Fever possibly related to a post-vaccination inflammatory response with possible superadded bacterial pneumonia**
- Mostly recovered at 1 month after discharge from hospital

Case 4. 68-year-old male

Prostate cancer*

Hypertension



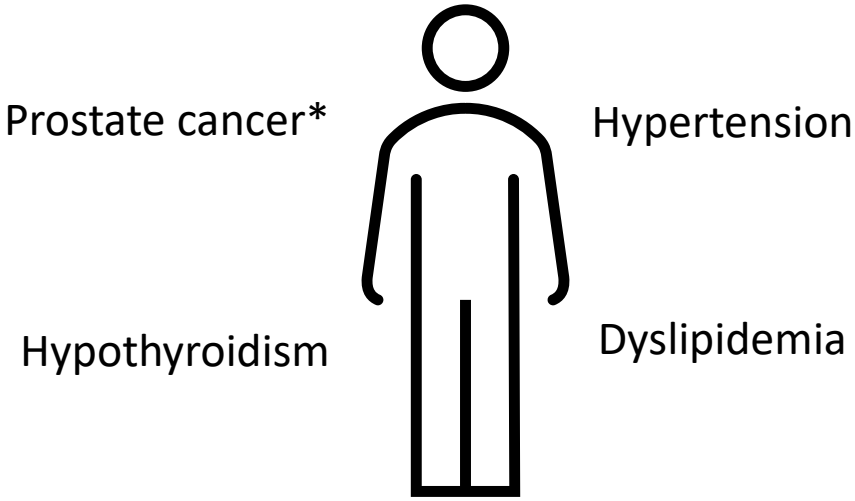
Hypothyroidism

Dyslipidemia

Medications to manage comorbidities

*Radiation therapy pending

Case 4. 68-year-old male



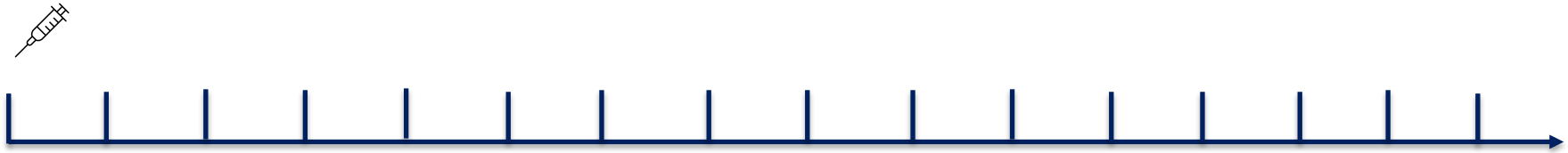
Medications to manage comorbidities

- **Received CHIK-LA vaccine for trip to Southeast Asia**

*Radiation therapy pending

Case 4. 68-year-old male

Day 0:
Received
CHIK-LA*



*At intervals 8–15 days earlier, received six inactivated vaccines: Tdap, influenza, polio, typhoid, Japanese encephalitis, hepatitis A

Case 4. 68-year-old male

Day 0:
Received
CHIK-LA

Day 5:
Initial symptoms

Fever, headache, fatigue, body aches

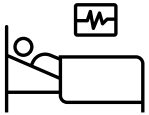
Photophobia and neck stiffness

Case 4. 68-year-old male

Day 0:
Received
CHIK-LA

Day 5:
Initial symptoms

Day 12: Hospitalized
with meningitis

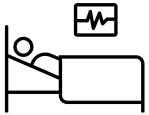


Case 4. 68-year-old male

Day 0:
Received
CHIK-LA

Day 5:
Initial symptoms

Day 12: Hospitalized
with meningitis



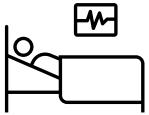
CSF pleocytosis (109 WBC/µL with
mononuclear predominance; 157 RBC/µL)

Case 4. 68-year-old male

Day 0:
Received
CHIK-LA

Day 5:
Initial symptoms

Day 12: Hospitalized
with meningitis



CSF pleocytosis (109 WBC/µL with mononuclear predominance; 157 RBC/µL)

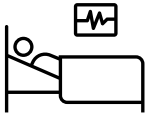
Meningoencephalitis and respiratory PCR panels negative, CSF culture no growth

Case 4. 68-year-old male

Day 0:
Received
CHIK-LA

Day 5:
Initial symptoms

Day 12: Hospitalized
with meningitis



CSF pleocytosis (109 WBC/µL with mononuclear predominance; 157 RBC/µL)

Meningoencephalitis and respiratory PCR panels negative, CSF culture no growth

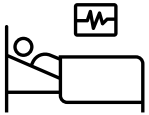
Brain MRI, CT: no acute abnormalities

Case 4. 68-year-old male

Day 0:
Received
CHIK-LA

Day 5:
Initial symptoms

Day 12: Hospitalized
with meningitis



CSF pleocytosis (109 WBC/µL with mononuclear predominance; 157 RBC/µL)

Meningoencephalitis and respiratory PCR panels negative, CSF culture no growth

Brain MRI, CT: no acute abnormalities

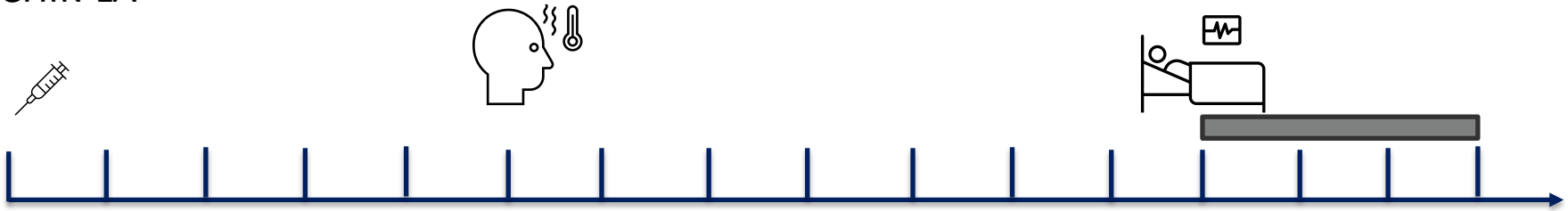
CSF chikungunya testing: IgM and neutralizing antibodies detected

Case 4. 68-year-old male

Day 0:
Received
CHIK-LA

Day 5:
Initial symptoms

Day 12: Hospitalized
with meningitis



Case 4. Meningitis in 68-year-old male

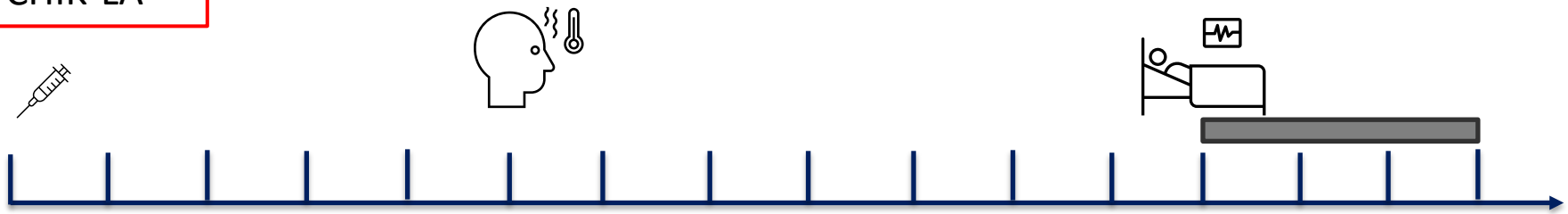
- Discharge diagnoses: **Meningismus/aseptic meningitis likely secondary to recent vaccination**
- Status**:** Headache and fatigue initially persisted but fully recovered by ~1 month

Case 4. Meningitis in 68-year-old male

Day 0: Received CHIK-LA*

Day 5: Initial symptoms

Day 12: Hospitalized with meningitis



Fever, headache, fatigue, body aches

Photophobia and neck stiffness

CSF pleocytosis (109 WBC/µL with mononuclear predominance; 157 RBC/µL)

Meningoencephalitis and respiratory PCR panels negative, CSF culture no growth

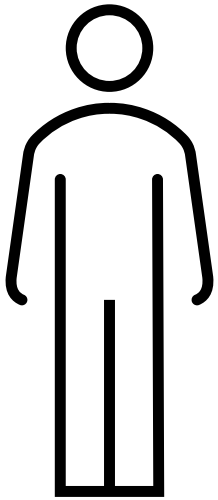
Brain MRI, CT: no acute abnormalities

CSF chikungunya testing: IgM and neutralizing antibodies detected

*At intervals 8–15 days earlier, received six inactivated vaccines: Tdap, influenza, polio, typhoid, Japanese encephalitis, hepatitis A

Case 5. 67-year-old male

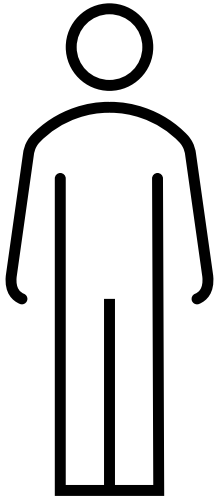
Hyperlipidemia



Medication to manage condition

Case 5. 67-year-old male

Hyperlipidemia



Medication to manage condition

- **Received CHIK-LA vaccine for trip to central America**

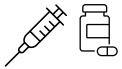
Case 5. 67-year-old male

Day 0:
Received
CHIK-LA & oral
typhoid vaccine*

*19 days prior: COVID-19 and inactivated influenza vaccines

Case 5. 67-year-old male

Day 0:
Received
CHIK-LA & oral
typhoid vaccine

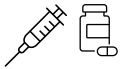


Day 4:
Initial
symptoms

Myalgia, fever

Case 5. 67-year-old male

Day 0:
Received
CHIK-LA & oral
typhoid vaccine

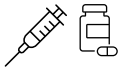


Day 4:
Initial
symptoms

Day 6:
Palpitations

Case 5. 67-year-old male

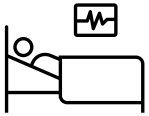
Day 0: Received CHIK-LA & oral typhoid vaccine



Day 4: Initial symptoms

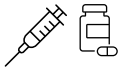
Day 6: Palpitations

Day 8: Presented to hospital with atrial flutter with rapid ventricular response



Case 5. 67-year-old male

Day 0:
Received
CHIK-LA & oral
typhoid vaccine



Day 4:
Initial
symptoms

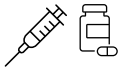
Day 6:
Palpitations

Day 8: Presented to
hospital with atrial
flutter with rapid
ventricular response

Elevated troponin, proBNP
Nuclear stress test: suspicious for small infarct

Case 5. 67-year-old male

Day 0:
Received CHIK-LA & oral typhoid vaccine



Day 4:
Initial symptoms

Day 6:
Palpitations

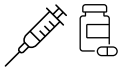
Day 8: Presented to hospital with atrial flutter with rapid ventricular response

Elevated troponin, proBNP
Nuclear stress test: suspicious for small infarct

No evidence of pulmonary embolism, normal thyroid-stimulating hormone

Case 5. 67-year-old male

Day 0:
Received CHIK-LA & oral typhoid vaccine



Day 4:
Initial symptoms

Day 6:
Palpitations

Day 8: Presented to hospital with atrial flutter with rapid ventricular response

Elevated troponin, proBNP

Nuclear stress test: suspicious for small infarct

No evidence of pulmonary embolism, normal thyroid-stimulating hormone

COVID, influenza, RSV PCR: negative

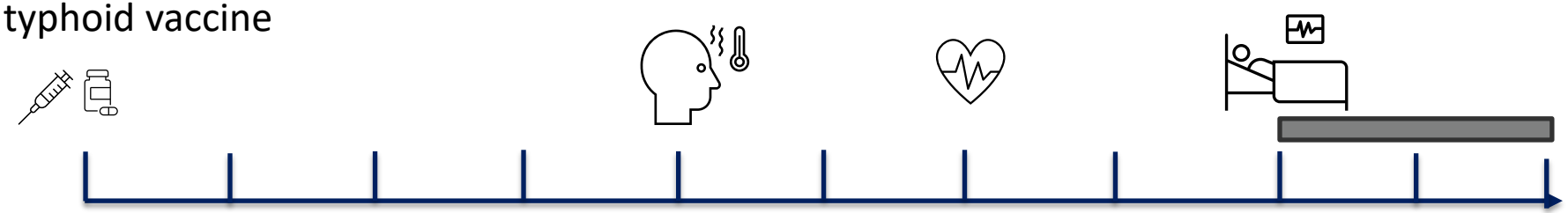
Case 5. 67-year-old male

Day 0: Received CHIK-LA & oral typhoid vaccine

Day 4: Initial symptoms

Day 6: Palpitations

Day 8: Presented to hospital with atrial flutter with rapid ventricular response

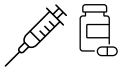


Case 5. Atrial flutter and non-ST segment elevation myocardial infarction in 67-year-old male

- Discharge diagnoses: **atrial flutter with rapid ventricular response, suspected small non-ST segment elevation myocardial infarction**
- Status**:** Fully recovered on discharge, medication ongoing 3 months later

Case 5. Atrial flutter and non-ST segment elevation myocardial infarction in 67-year-old male with

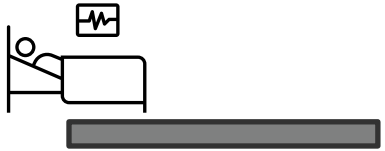
Day 0: Received CHIK-LA & oral typhoid vaccine*



Day 4: Initial symptoms

Day 6: Palpitations

Day 8: Presented to hospital with atrial flutter with rapid ventricular response



Myalgia, fever 1 day later

Elevated troponin, proBNP

Nuclear stress test: suspicious for small infarct

No evidence of pulmonary embolism, normal thyroid-stimulating hormone

COVID, influenza, RSV PCR: negative

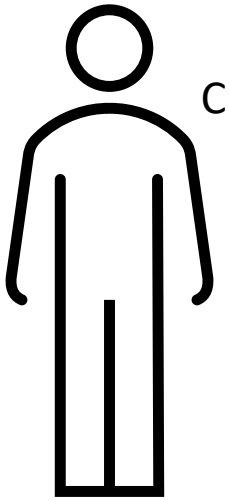
*19 days prior: COVID-19 and inactivated influenza vaccines

Case 6. 74-year-old male

Ischemic cardiomyopathy

Hypotension

Coronary artery disease



Chronic leukopenia

Chronic thrombocytopenia

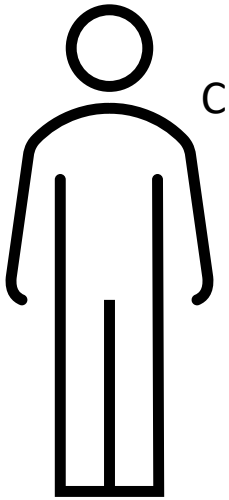
Medications to manage comorbidities

Case 6. 74-year-old male

Ischemic cardiomyopathy

Hypotension

Coronary artery disease



Chronic leukopenia

Chronic thrombocytopenia

Medications to manage comorbidities

- **Received CHIK-LA vaccine for planned travel to Southeast Asia**

Case 6. 74-year-old male

Day 0:
Received
CHIK-LA
& JE-VC*

*JE-VC: Inactivated Vero cell culture-derived JE vaccine

Case 6. 74-year-old male

Day 0:
Received
CHIK-LA
& JE-VC

Day 3:
Initial
symptoms

Fatigue, weakness, lightheadedness, mild shortness of breath, noted hypotension

Case 6. 74-year-old male

Day 0:
Received
CHIK-LA
& JE-VC

Day 3:
Initial
symptoms

Day 8:
Presented
to internist

Severe
hypotension
No evidence
of heart
failure

Case 6. 74-year-old male

Day 0: Received CHIK-LA & JE-VC

Day 3: Initial symptoms

Day 8: Presented to internist

Day 10: Blood collection

Leukopenia, thrombocytopenia

Case 6. 74-year-old male

Day 0: Received CHIK-LA & JE-VC

Day 3: Initial symptoms

Day 8: Presented to internist

Day 10: Blood collection

Day 15: Follow-up visit to internist

Some improvement in blood pressure

Case 6. 74-year-old male[#]

Day 0: Received CHIK-LA & JE-VC

Day 3: Initial symptoms

Day 8: Presented to internist

Day 10: Blood collection

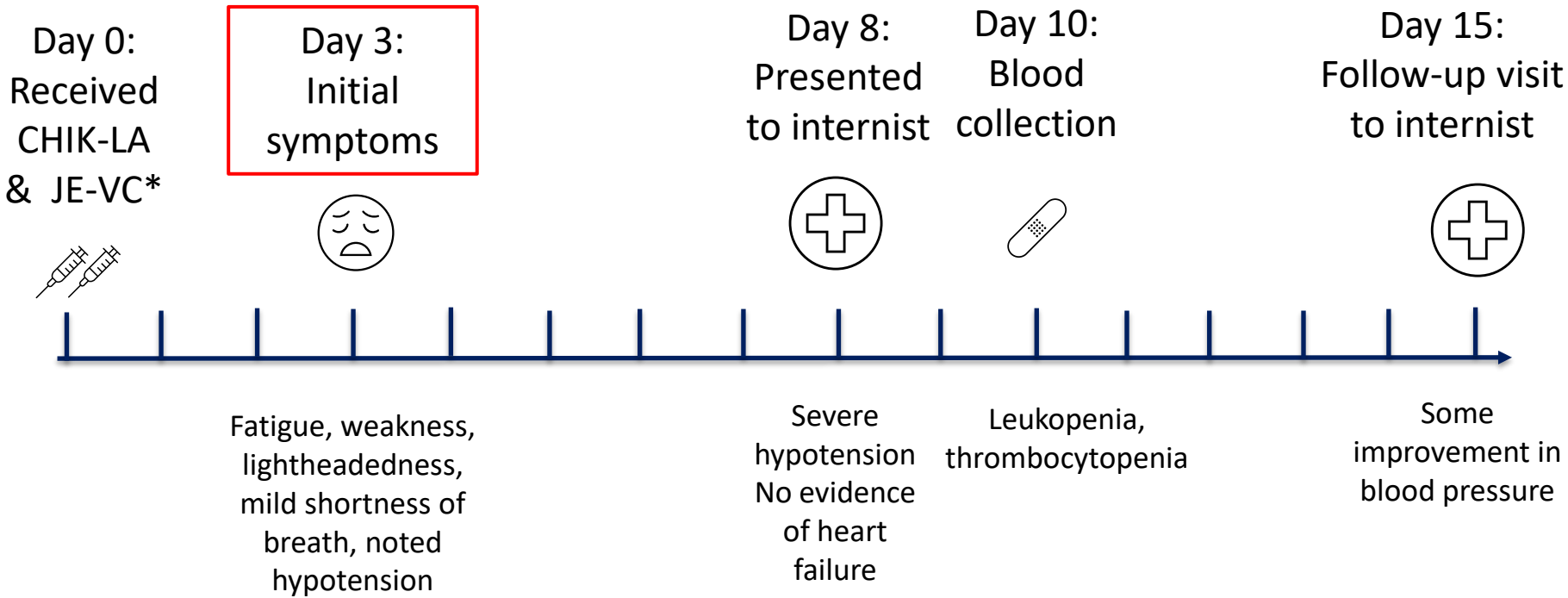
Day 15: Follow-up visit to internist

[#]SAE as “Other medically important event”

Case 6. Worsened and prolonged hypotension in 74-year-old male

- Final diagnosis: **Episode of worsened and prolonged hypotension on the background of pre-existing cardiomyopathy and hypotension - likely related to CHIK-LA vaccination**
- Resolved within ~2 weeks

Case 6. 74-year-old male[#]



*JE-VC: Inactivated Vero cell culture-derived JE vaccine

[#]SAE as "Other medically important event"

Summary of case characteristics (N=6)

Age (yrs)	Sex	Key comorbidities	Co-administered vaccines	Symptom onset (days)	Discharge diagnosis(es)	Chikungunya testing
83	Male	Coronary artery disease, chronic heart failure, chronic kidney disease, hypertension, hyperlipidemia, chronic thrombocytopenia	–	3	Encephalopathy Generalized weakness	N/A
77	Male	Coronary artery disease, hypothyroidism, benign prostatic hyperplasia, hyperlipidemia, hypertension, IgA deficiency	Japanese encephalitis (inactivated)	4	Acute metabolic encephalopathy Fever of unknown origin	N/A
86	Male	Diabetes mellitus, heart failure, anemia, hypertension, hypothyroidism, hyperlipidemia	–	3	Metabolic encephalopathy Fever possibly related to post-vaccination inflammatory response	RT-PCR on serum on day 13: positive
68	Male	Prostate cancer, hypothyroidism, hypertension, dyslipidemia	–[†]	5	Aseptic meningitis	IgM & neutralizing antibodies in CSF
67	Male	Hyperlipidemia	Typhoid (oral, live)*	4	Atrial flutter Non-ST segment elevation myocardial infarction (NSTEMI)	N/A
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*19 days prior: COVID-19 & influenza (inactivated); [†]8–15 days prior: Tdap, influenza, polio, typhoid, Japanese encephalitis, hepatitis A; N/A: Not available

Summary of case characteristics (N=6)

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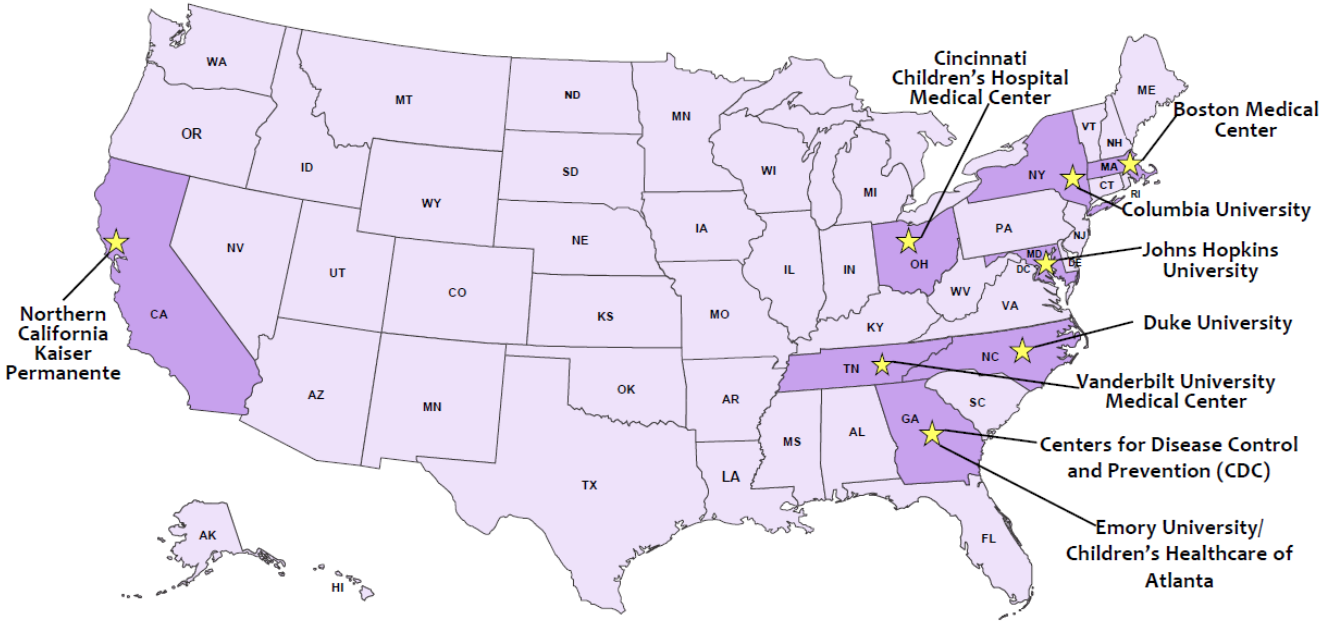
U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION

CISA

Clinical Immunization Safety Assessment (CISA) Project



- clinical consult services†
- support enhanced surveillance
- clinical research

8 participating medical research centers with vaccine safety experts

†More information about clinical consults available at https://www.cdc.gov/vaccine-safety-systems/hcp/cisa/index.html

Summary of CISA review of SAEs following CHIK-LA reported to VAERS

- Available medical records for each of neurologic (n=4) and cardiac (n=2) reports reviewed with experts in vaccine safety, infectious diseases, cardiology and neurology
- For each report, at least one CISA expert considered association of CHIK-LA with SAE plausible
- However, experts noted difficulty differentiating between general reactogenicity in older patients with comorbidities leading to SAE versus chikungunya vaccine causing SAE

Generally cannot determine causality from VAERS data

- Temporal association ≠ causal association
- Sometimes concomitant or recent administration of other vaccines
- Comprehensive investigations of possible etiologies not always conducted or available
- Unlike in controlled clinical trials, no unvaccinated comparator group

Shimabukuro TT, et al. Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS). Vaccine 2015;33:4398-4405.

Factors supporting possible causality of CHIK-LA for SAEs

All events began within 3–5 days of vaccination

For 3 patients with co-administration of other vaccines (i.e., JE, typhoid), association with other vaccines less likely[1-3]

Investigations did not indicate clear alternate etiologies for any patient and most (n=5) discharge summaries noted potential association with vaccination

For 2 cases with chikungunya laboratory testing, results suggested an association with CHIK-LA

1. Rabe IB et al, Vaccine 2015; 2. Walker WL et al, Vaccine 2018; 3. Begier EM et al. Clin Infect Dis 2004.

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CHIK-LA and SAEs in persons ≥65 years

- Immunosenescence affects older person's ability to adequately control replication of live attenuated vaccine virus
  - Example: With live attenuated yellow fever vaccine, SAEs more frequent in older persons, and age ≥60 years is precaution for use
- Wild-type chikungunya virus infections more likely to result in severe disease in older adults

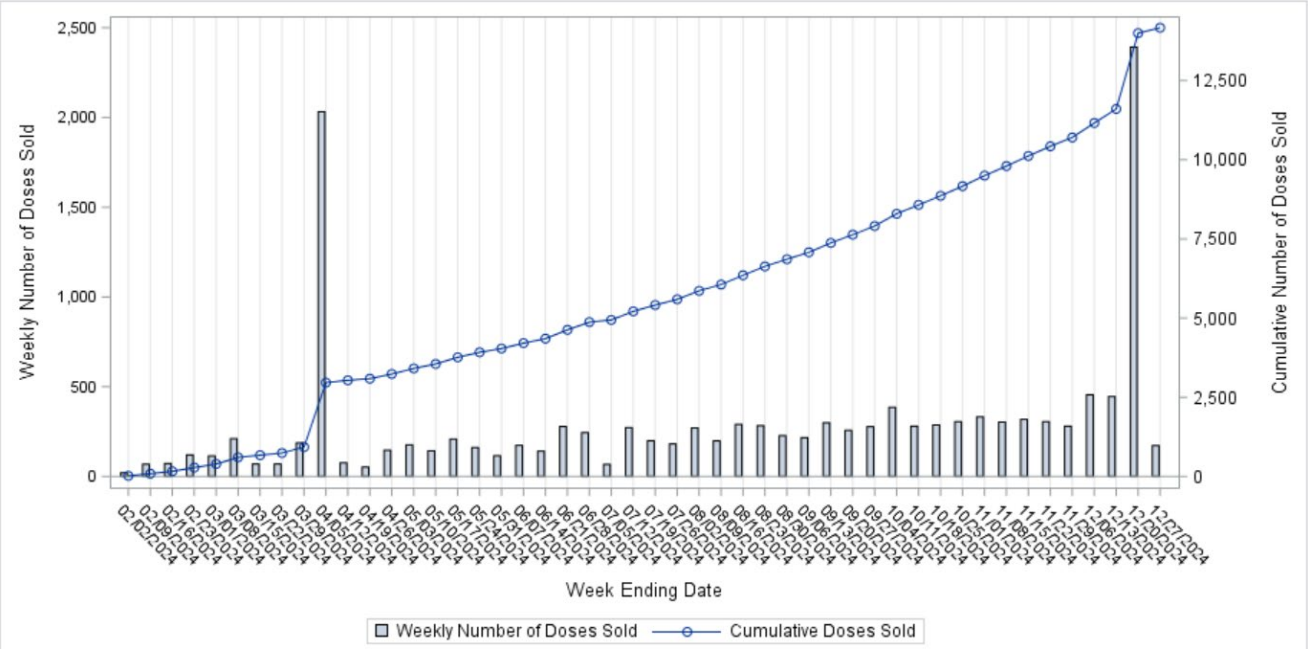
Estimating incidence of SAEs after CHIK-LA

- Difficult as limited data on vaccine doses **distributed** and very limited data on doses **administered**
- Obtained data from commercial source (IQVIA; private-sector company that provides healthcare data)
  - **Sales data**: Weekly Sales Perspectives (WSP) data are **unprojected** (i.e., actual) sales for prescription products (vaccinations) **sold to retail, non-retail, and mail channels** and capture about ~90% of total sales*
  - **Administration data**: National Prescription Audit (NPA) data represent **projected estimates** of vaccinations **administered** in retail and long-term care **pharmacies**

*Information from IQVIA

CHIK-LA (IXCHIQ) weekly and cumulative sales as of week ending December 27, 2024
IQVIA SMART Weekly Sales Perspective (WSP)

IQVIA data cannot be shared further due to data use and clearance requirements set by IQVIA.

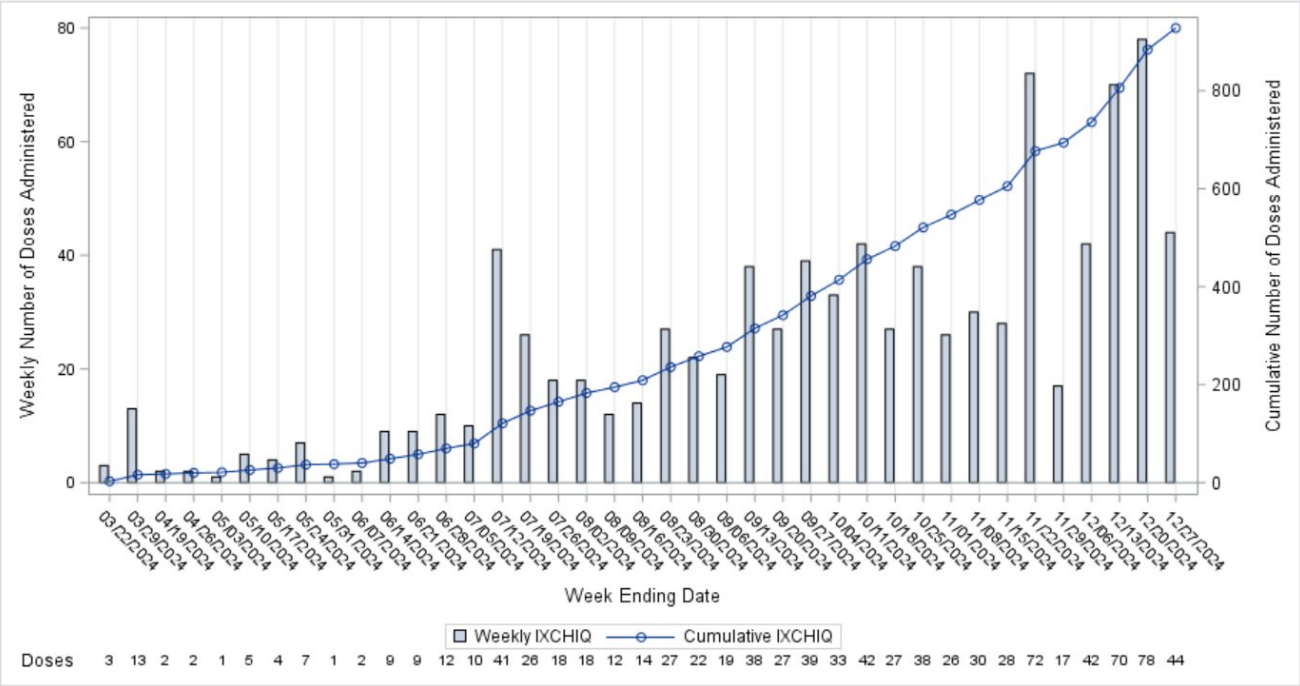


13,891 total doses distributed

Pharmacy total = 1,275 (9%) Medical office total = 12,616 (91%)

CHIK-LA (IXCHIQ) weekly and cumulative vaccinations administered in pharmacies, as of week ending December 27, 2024. IQVIA SMART NPA Weekly Extended Insights

IQVIA data cannot be shared further due to data use and clearance requirements set by IQVIA.



Estimated 928 doses administered in pharmacies

CHIK-LA (IXCHIQ) pharmacy administrations by age, March 3–December 27, 2024
IQVIA SMART NPA Weekly Extended Insights

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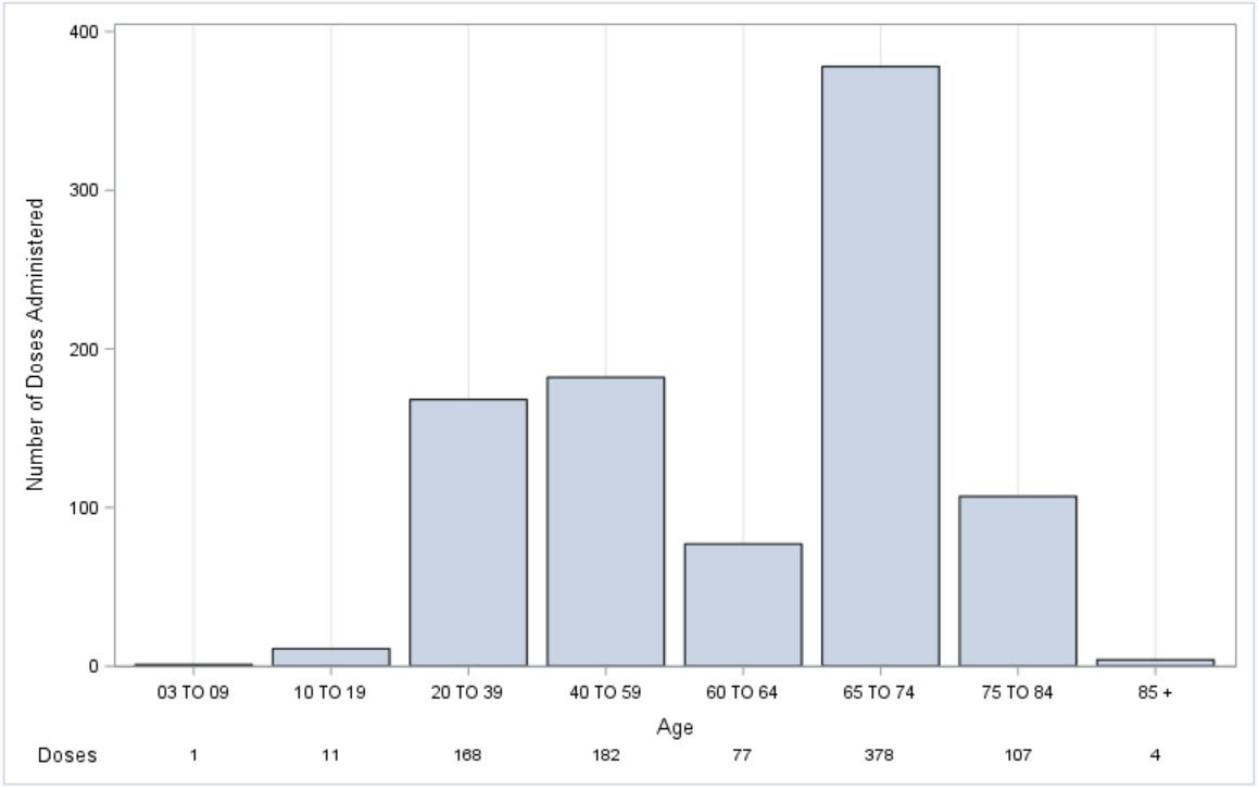

53% doses administered to individuals aged ≥65 years

N=928

Risk estimates for SAEs and hospitalizations among persons aged ≥65 years*

	No. events	Estimated rate of events per 100,000 doses administered (95% CI)	Estimated rate of doses administered resulting in 1 event (95% CI)
SAEs	**6**	82 per 100,000 (30–180)	1 SAE per 1,220 doses (1 per 3,333 doses to 1 per 556 doses)

*Based on VAERS reports, IQVIA data on doses distributed (N=13,891 doses), and IQVIA data that 52.7% (n=7,320) administered to persons aged ≥65 yrs

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SAEs	6	82 per 100,000 (30–180)	1 SAE per 1,220 doses (1 per 3,333 doses to 1 per 556 doses)
Hospitalizations	**5**	68 per 100,000 (20–160)	1 hospitalization per 1,471 doses (1 per 5,000 doses to 1 per 625 doses)

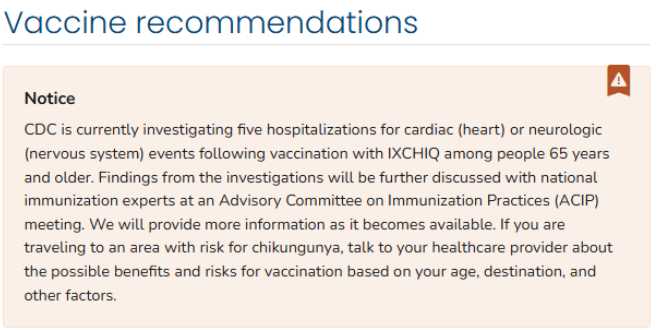
*Based on VAERS reports, IQVIA data on doses distributed (N=13,891 doses), and IQVIA data that 52.7% (n=7,320) administered to persons aged ≥65 yrs

Limitations of risk estimates

- Calculations limited by potential imprecision in numerator and denominator data
  - Unknown completeness of reporting of events to VAERS
  - Potential inaccuracies in vaccine administration data overall and by age group
- All VAERS SAE reports included in calculations but cannot confirm causal link between vaccination and all reported events
- Overall low certainty in estimates

Update: 2025 VAERS data

- Updated data as of March 21, 2025
  - **0 SAEs** and 9 non-serious AEs reported to VAERS in United States*
  - Additional ~4,250 CHIK-LA doses sold#
- Risk estimates not updated for this presentation
  - Delays in CHIK-LA reports to VAERS (median 13 days)
  - ~2,375 doses sold in last ~2 weeks of 2024 and likely not administered in 2024
  - Unknown impact of CDC alert in February 2025 about hospitalizations after CHIK-LA in ages ≥65 years
  - With updated data, risk estimates lower but within 95% confidence limits of previous estimates



https://www.cdc.gov/chikungunya/prevention/chikungunya-vaccine.html

*Excludes 6 (non-serious) reports from other countries; #IQVIA data

Work Group considerations regarding SAEs following CHIK-LA

Factors considered by Work Group

All SAEs in persons aged ≥65 years

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Association of CHIK-LA with SAEs is plausible, but causal association for each event not determined

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For individual travelers aged ≥65 years, risk-benefit assessment needed to weigh risks of disease vs risks of vaccination because vaccine use might be supported in certain higher-risk settings (e.g., outbreak) given known risks for severe disease and hospitalization in this age group

Age ≥65 years should be a precaution* for use of CHIK-LA

- In general, vaccination should be deferred
- Vaccination might be indicated if benefit from protection from vaccination outweighs risk for adverse reaction

*https://www.cdc.gov/vaccines/hcp/imz-best-practices/contraindications-precautions.html

Work Group proposes revising recommendations for use of CHIK-LA among travelers

- In accordance with updated Evidence to Recommendations for travelers presented in earlier presentation for CHIK-VLP
- In consideration of safety signal following use of vaccine in persons aged ≥65 years

Existing CHIK-LA recommendations for travelers*

Chikungunya vaccine is **recommended** for persons aged ≥18 years traveling to a country or territory where there is a chikungunya outbreak.

In addition, chikungunya vaccine **may be considered** for the following persons traveling to a country or territory without an outbreak but with evidence of chikungunya virus transmission among humans within the last 5 years

- Persons aged >65 years, particularly those with underlying medical conditions, who are likely to have at least moderate exposure to mosquitoes, OR
- Persons staying for a cumulative period of 6 months or more

*Approved in February 2024

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*Approved in February 2024

Revised draft recommendations for CHIK-LA among travelers[#]

ACIP recommends live attenuated chikungunya vaccine or persons aged ≥18 years traveling to a country or territory where there is a chikungunya outbreak.

In addition, live attenuated chikungunya vaccine may be considered for persons aged ≥18 years[#] traveling or taking up residence in a country or territory without an outbreak but with elevated risk for US travelers if planning travel for an extended period of time e.g., 6 months or more.

[#]Age ≥65 years is a precaution for use of CHIK-LA

Acknowledgements

Arboviral Diseases Branch, CDC

- Rebekah Sutter
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- Michael McNeil
- Elaine Miller

Immunization Services Division, CDC

- Seth Meador
- Suchita Patel

Clinical Immunization Safety Assessment (CISA) vaccine safety experts

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov