Guillain-Barré Syndrome (GBS) after Janssen COVID-19 Vaccine: Vaccine Adverse Event Reporting System (VAERS)

Meeting of the Advisory Committee on Immunization Practices (ACIP)
July 22, 2021

Office of Biostatistics and Epidemiology (OBE)
FDA - Center for Biologics Evaluation and Research (CBER)

Outline

- Vaccine Adverse Event Reporting System (VAERS)
- Preliminary reports of GBS after Janssen COVID-19 Vaccine
- Updated Janssen COVID-19 Vaccine EUA Fact Sheets
- Summary and Next Steps

VAERS Vaccine Adverse Event Reporting System
www.vaers.hhs.gov

FDA

Vaccine Adverse Event Reporting System

- Passive surveillance of vaccines
- Nation's early warning system for vaccine safety
- VAERS accepts all reports regardless of the plausibility of the vaccine causing the event or the clinical seriousness of the event

Strengths

- Rapidly detects potential safety problems
- Potential detection of rare adverse events
- Open-ended for hypothesis generation
- Geographic diversity
- Capability to monitor production lots

Limitations

- Missing and/or inaccurate data
- Reported diagnoses are not verified
- Under-reporting
- Reporting bias (stimulated reporting)
- Absence of unvaccinated control group
- Inability to assess causation
- Not likely to detect long latency events

Identifying preliminary VAERS reports of GBS after Janssen COVID-19 Vaccine

- Preliminary reports of GBS identified via:
  - FDA medical officers daily review of incoming serious reports and/or
  - Automated query of VAERS for adverse event terms for GBS*
- Data Lock Point: June 30, 2021
- Further analysis is pending follow-up by VAERS program contractors for medical records, confirmation of diagnosis, and adjudication of each case using the Brighton case definition for GBS

*MedDRA PTs for query: acute polyneuropathy, autoimmune polyneuropathy, axonal and demyelinating polyneuropathy, demyelinating polyneuropathy, Guillain Barré syndrome, Miller Fisher syndrome.

Preliminary reports of GBS after Janssen COVID-19 Vaccine

COVID-19 Vaccine	Total	Serious	Deaths
Janssen	100	95	1

Data Lock Point: June 30, 2021

Serious adverse events include death, life-threatening events, hospitalization, prolongation of hospitalization, congenital anomaly, significant disability, or otherwise medically important conditions.

Overview of GBS reports after Janssen COVID-19 Vaccine

Characteristics	n = 100
Sex [a]	
Male	61 (61%)
Female	38 (38%)
Seriousness [b]	
Serious	95 (95%)
Hospitalized	95 (95%)
Died	1 (1%)
Non-serious	5 (5%)

[a] One report had missing age, sex, and onset information.

[b] Serious adverse events include death, life-threatening events, hospitalization, prolongation of hospitalization, congenital anomaly, significant disability, or otherwise medically important conditions.

Overview of GBS reports after Janssen COVID-19 Vaccine

Characteristics	
Age [a]	
Median	57 years
Mean (standard deviation)	53.6 (12.46) years
Range	24 – 76 years
Number of reports with age 18 – 64 years	83 (83%)
Number of reports in with age ≥ 65 years	16 (16%)
Time to onset [a]	
Median	13 days
Mean (standard deviation)	13.8 (9.80) days
Range	0 – 75 days
Number of cases in 21-day risk window	84 (84%)
Number of cases in 42-day risk window	98 (98%)

[a] One report had missing age, sex, and onset information.

Reports of GBS after Janssen COVID-19 vaccine: Selected Case Details

- 95 (95%) patients were hospitalized
  - 10 patients were intubated and/or required mechanical ventilation
- 1 death
  - 57-year-old man with past medical history of heart failure, stroke, hypertension, and diabetes mellitus presented with weakness 5 days post vaccination and was later hospitalized and died 25 days post vaccination

Reports of GBS after Janssen COVID-19 Vaccine: Selected Case Details

- 24 reports described bilateral facial paresis
- 12 reports described unilateral Bell's palsy
- 6 reports mentioned a recent illness: generalized rash, upper respiratory infection, or flu-like symptoms 1-2 weeks before GBS
- No reports listed concomitant vaccines

Observed-to-expected (O/E) analysis assuming 42-day risk window

Age (years)	Cases	Vaccine doses administered*	Person-years (PY)**	Background Rate per 100,000 PY***	Expected Cases	Rate Ratio, 95% CI
All Ages (18+)	98	12,235,978	1295623	1.51	19.56	5.010 (4.07; 6.11)
18 - <65	82	10,302,966	1090944	1.22	13.31	6.16 (4.90; 7.65)
65+	16	1,933,012	204679.6	2.34	4.79	3.34 (1.91; 5.43)

* From CDC data as of 06/28/2021

** Person-Years was based on number of vaccine doses administered within the age group; see slides 19 – 20 for statistical methods.

*** Sejvar JJ, Baughman AL, Wise M, Morgan OW. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. Neuroepidemiology. 2011;36(2):123-33.

O/E analysis assuming 42-day risk window

Age (years)	Cases	Vaccine doses administered*	Person-years (PY)**	Background Rate per 100,000 PY***	Expected Cases	Rate Ratio, 95% CI
18 – 29	4	2,138,259	226412.5	0.88	1.99	2.01 (0.55; 5.14)
30 – 39	10	2,071,932	219389.4	1.07	2.348	4.26 (2.04; 7.83)
40 – 49	21	2,174,362	230235.3	1.29	2.97	7.07 (4.38; 10.81)
50 – 64	47	3,918,413	414906.6	1.63	6.76	6.95 (5.11; 9.24)
65+	16	1,933,012	204679.6	2.34	4.79	3.34 (1.91; 5.43)

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Updated Janssen COVID-19 Vaccine EUA Fact Sheets

- July 12, 2021: Authorized EUA Fact Sheets were updated to include new information about GBS

EUA Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers)

5 WARNINGS AND PRECAUTIONS

Subsection '5.3 Guillain-Barré Syndrome' including the following information was added: Reports of adverse events following use of the Janssen COVID-19 Vaccine under emergency use authorization suggest an increased risk of Guillain-Barré syndrome during the 42 days following vaccination.

Section 6 OVERALL SAFETY SUMMARY and *subsection 6.2 Post Authorization Experience* were also updated with information about GBS.

EUA Fact Sheet for Recipients and Caregivers

Section on "WHAT ARE THE RISKS OF THE JANSSEN COVID-19 VACCINE?" was updated to include information under a new subsection entitled "Guillain Barré syndrome"

Crude comparison with mRNA vaccines

COVID-19 Vaccine	VAERS reports with GBS screening*	Doses administered	Crude** VAERS GBS reporting rate per million doses administered
Janssen	100	12,235,978	8.1
Moderna	162	134,076,668	1.21
Pfizer-BioNTech	190	181,347,436	1.05

VAERS reports processed through June 30, 2021

Notes:
Doses administered data per CDC Vaccination Report as of 7/1/2021
*GBS screening definition is any one of the following encoded MedDRA preferred terms: DEMYELINATING POLYNEUROPATHY;GUILLAIN-BARRE SYNDROME; MILLER FISHER SYNDROME. Include reports processed through 7/1/2021.
**Counts of VAERS reports meeting GBS screening definition divided by doses administered; counts are based on encoded terms

Reports of GBS after AstraZeneca COVID-19 Vaccine

- A total of 227 cases of GBS had been reported to EudraVigilance as of 27 June 2021, while around 51.4 million doses administered as of 20 June 2021
- EMA Pharmacovigilance Risk Assessment Committee (PRAC) 5 - 8 July 2021 meeting:
  - Recommended an update to the product information to include a warning for Guillain-Barre syndrome (GBS) reported following vaccination with AstraZeneca COVID-19 Vaccine

References:

06 Public Safety Update_VAXZEVRIA_14 July 2021 (europa.eu)
Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 5-8 July 2021 | European Medicines Agency (europa.eu)

Summary

- 100 preliminary reports of GBS after Janssen identified in VAERS as of June 30, 2021
  - Observed reports > expected across multiple age groups, without respect to Brighton Collaboration criteria
  - Reporting rate for GBS is higher for Janssen than for mRNA vaccines
- July 12, 2021: Authorized EUA Fact Sheets were updated to include new information about GBS

- Next Steps
  - Obtain additional follow-up/medical records for Janssen reports
  - Evaluate Janssen reports to determine whether they meet the Brighton Collaboration case definition of GBS
  - Based on the number of confirmed cases, re-assess the observed-to-expected analysis for GBS after Janssen
  - Follow up on updates from FDA Biologics Effectiveness and Safety System, the Center for Medicare and Medicaid Services databases, and the CDC Vaccine Safety Datalink active surveillance

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