Post-licensure safety surveillance of 20-valent pneumococcal conjugate vaccine (PCV20) among U.S. adults in the Vaccine Adverse Event Reporting System (VAERS)

Advisory Committee on Immunization Practices (ACIP)
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Pedro L. Moro, MD, MPH
Immunization Safety Office
Division of Healthcare Quality Promotion
Centers for Disease Control and Prevention (CDC)

Disclaimer

- The findings and conclusions in this presentation are those of the author and do not necessarily represent the official position of the CDC
- The use of product trade names is for identification purposes only

Topics

- Background on pre-licensure safety of 20-valent pneumococcal conjugate vaccine (PCV20)
- Adverse events following PCV20 reported to the Vaccine Adverse Event Reporting System (VAERS)
- Adverse events of special interest: Guillain-Barré Syndrome (GBS)
- Summary

Background: Pre-licensure clinical trials PCV20

- Pre-licensure clinical trial data of PCV20 in adults has been reassuring
  - Six randomized controlled trials in adults aged ≥ 18 years, which included more than 6,000 participants[1,2]
  - Most common adverse reactions were injection site pain, muscle pain, fatigue, headache, and joint pain[2,3]
  - Serious adverse events (SAEs) balanced among vaccinees and controls[2]
  - No SAEs or deaths considered to be related to study vaccines[3]
  - No cases of Guillain-Barré Syndrome (GBS) identified in prelicensure studies[2,3]

[1] Pfizer's Adult and Pediatric Clinical Trial Programs for 20-Valent Pneumococcal Conjugate Vaccine Presented at IDWeek 2020. October 21, 2020.

[2] Kobayashi M, Farrar JL, Gierke R, et al. Use of 15-Valent Pneumococcal Conjugate Vaccine and 20-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2022. MMWR Morb Mortal Wkly Rep 2022;71:109–117. DOI: http://dx.doi.org/10.15585/mmwr.mm7104a1

[3] Prevnar20 vaccine insert https://www.fda.gov/vaccines-blood-biologics/vaccines/prevnar-20

Introduction

- June 8, 2021 – PCV20 approved for adults aged ≥ 18 years by the FDA
- October 20, 2021 – ACIP recommendation
  - PCV20 for adults aged ≥65
  - PCV20 for adults aged 19–64 years with underlying medical conditions

FDA: Food and Drug Administration
ACIP: Advisory Committee on Immunization Practices

Objectives

- Describe the safety profile of reports submitted to the Vaccine Adverse Event Reporting System (VAERS) following PCV20 in
  - Adults aged ≥65 years
  - Adults aged 19–64 years

VAERS

Strengths

- National data
- Accepts reports from anyone
- Rapidly detects safety signals
- Can detect rare adverse events
- Data available to public

Limitations

- Reporting bias
- Inconsistent data quality and completeness
- Lack of unvaccinated comparison group or denominator
- Generally cannot assess causality

- VAERS accepts all reports from all reporters without making judgments on causality or judging clinical seriousness of the event
- As a hypothesis generating system, VAERS identifies potential vaccine safety concerns that can be studied in more robust data systems

Methods – 1: PCV20

- Searched VAERS database for U.S. PCV20 reports during:
  - October 21, 2021 through December 31, 2023 for adults aged ≥ 19 years (19–64 years and ≥ 65 years)
- Signs and symptoms of AEs coded using Medical Dictionary for Regulatory Activities (MedDRA)[1] Preferred Terms (PTs)
  - PTs are not mutually exclusive
  - A single report may be assigned more than one PT
- Review of serious[2] reports and medical records; categorized main diagnosis in a MedDRA system organ class
- Case definitions for AESIs: Guillain-Barré Syndrome[3]

[1] https://www.meddra.org/ ; [2] Based on the Code of Federal Regulations 21 CFR 600.80 ; [3]Sejvar JJ, et al. Brighton Collaboration GBS Working Group. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine. 2011 Jan 10;29(3):599-612. doi: 10.1016/j.vaccine.2010.06.003. Epub 2010 Jun 18. PMID: 20600491

Methods – 2: PCV20

- Reporting rates
  - Use of doses distributed of PCV20 in the United States during 2022 and 2023 (20,579,720 doses)
- Empirical Bayesian data mining (FDA)*
  - Used to detect disproportional reporting for the entire post marketing period for each product
  - Identifies adverse events reported more frequently than expected after vaccine of interest compared with other vaccines in the VAERS database
  - Analysis by age groups and serious reports.**

*The presence of disproportionality may not suggest a safety signal. Conversely, the absence of disproportionality does not confirm the absence of a safety signal nor negate a signal detected by other methods.

**A Serious Adverse Event (SAE) is defined as any untoward medical occurrence that meets any of the following criteria: 1. Results in death; 2. Is life-threatening; 3. Requires inpatient hospitalization or prolongation of existing hospitalization; 4. Results in persistent or significant disability/incapacity; 5. Is a congenital anomaly/birth defect. [FDA regulatory definition; U.S. Code of Federal Regulations, 21 CFR 600.80. Postmarketing reporting of adverse experiences (2014). Available at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=600.80]

PCV20 reports to VAERS, October 2021–December 2023

	19 – 64 years	≥ 65 years	≥ 19 years	All[2]
Characteristics[1]	N (%)	N (%)	N (%)	N (%)
Total reports	798	1,178	1,976	2,393
Female	582 (72.9)	846 (71.8)	1,428 (72.3)	1,598 (66.7)
Male	212 (26.6)	330 (28.0)	542 (27.4)	680 (28.4)
Unknown sex	4 (0.5)	1 (0.1)	5 (0.3)	115 (4.8)
Serious reports[3]	49 (6.1)	70 (5.9)	119 (6)	149 (6.2)
Deaths	2 (0.3)	9 (0.8)	11 (0.6)	20 (0.8)
Median age [IQR] in years	54 [45,60]	69 [66,75]		65 [56,70]
Median onset interval [IQR] in days	1 [0,2]	1 [0,2]	1 [0,2]	1 [0,1]
Received PCV20 alone	438 (54.9)	711 (60.4)	1,149 (58.1)	1,412 (59.0)

[1] U.S. primary reports (foreign reports excluded) ; [2]Includes reports in adults aged ≥19 years and 176 reports in persons aged 0-18 years and 241 reports of unknown age

[3] Based on the Code of Federal Regulations if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization or permanent disability

Most common signs and symptoms[1] in reports to VAERS following PCV20 in adults aged 19–64 years, October 2021–December 2023

PCV20 Non-serious (N=749)	N (%)
Injection site reaction	227 (30)
Pain	129 (17)
Erythema	117 (16)
Fever	103 (14)
Pain in extremity	90 (12)
Peripheral swelling	77 (10)
Headache	59 (8)
Skin warm	59 (8)
Fatigue	56 (7)
Arthralgia	52 (7)

PCV20 Serious (N=49)	N (%)
Fever	14 (29)
Dyspnea	12 (25)
Condition aggravated	10 (20)
Cough	10 (20)
Pain	10 (20)
Nausea	9 (18)
Pain in extremity	8 (16)
Dizziness	7 (14)
Fatigue	7 (14)
Headache	7 (14)

[1] Coded using the MedDRA Preferred Terms; more than one MedDRA Preferred Term may be assigned to a single report (i.e., not mutually exclusive)

Most common signs and symptoms[1] in reports to VAERS following PCV20 in adults aged ≥65 years, October 2021–December 2023

PCV20 non-serious (N=1,108)	N (%)
Injection site reaction	417 (35)
Pain	180 (15)
Pain in extremity	162 (14)
Erythema	158 (13)
Fever	135 (12)
Peripheral swelling	103 (9)
Rash	99 (8)
Fatigue	96 (8)
Headache	88 (7)
Pruritus	78 (7)

PCV20 Serious (N=70)	N (%)
Pain	14 (20)
Asthenia	13 (19)
Gait disturbance	11 (16)
Guillain Barre Syndrome	11 (16)
Dyspnea	8 (11)
Fatigue	8 (11)
Fever	8 (11)
Chest pain	7 (10)
Death	7 (10)
Dysphagia	7 (10)

[1] Coded using the MedDRA Preferred Terms; more than one MedDRA Preferred Term may be assigned to a single report (i.e., not mutually exclusive)

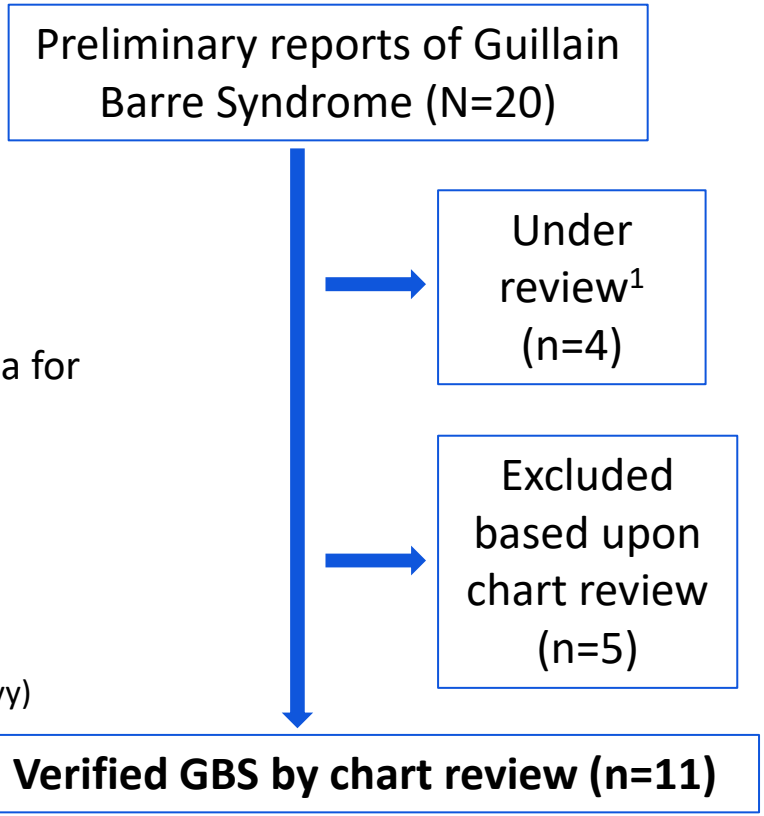
Empirical Bayesian data mining (as of January 26, 2024)

- Disproportional reporting observed for:
  - PT for “Guillain-Barré Syndrome” when limited to serious reports (EB05=3.6)[1]
    - When not limited to serious reports EB05=1.87

[1] EB05 = Empirical Bayesian data mining threshold for statistical alert; alert considered if EB05 >2.0

Reports to VAERS of Guillain Barre Syndrome after PCV20 vaccination among adults aged ≥19 years (as of December 31, 2023)

- 11 verified reports of Guillain Barré Syndrome[2]
  - Median age (range), years: 66 years (46-79 years)[3]
  - Median time to onset (range), days: 14 days (0-23)
  - 4 males, 7 females
  - All verified reports met Brighton Collaboration criteria for GBS:
    - 2 were Brighton level 1, 6 were level 2 and 3 were level 3
  - Other vaccines during same visit (5 of 11):
    - Two RZV (Shingrix)
    - One Fluad quadrivalent
    - One bivalent mRNA COVID-19 (Pfizer), HD-IIV4, RSV (Arexvy)
    - One Tdap (Boostrix)



[1] Awaiting medical records

[2] One patient had a norovirus infection 1-2 days before neurological symptoms

[3] No GBS reports in persons aged <19 years

Reporting rate for GBS after PCV20, 2022–2023

- Reporting rate: 0.5 cases per million doses distributed or 0.9 cases per 100,000 person-years (background rate 1.72 cases per 100,000 persons-years) [1]

[1]Gubernot D, et al. U.S. Population-Based background incidence rates of medical conditions for use in safety assessment of COVID-19 vaccines. Vaccine. 2021;39:3666–3677.

Summary

- VAERS received 1,976 reports after PCV20 in adults during October 2021–December 2023
  - 798 in adults aged 19–64 years; 93.9% non-serious
  - 1,178 in adults aged ≥65 years; 94.1% non-serious

- Most commonly reported adverse events were injection site (e.g. injection site erythema) and systemic reactions (e.g. fever, headache); consistent with findings from pre-licensure studies

Summary (continued)

- Disproportionate reporting for Guillain-Barré Syndrome (GBS) identified in VAERS after PCV20 vaccine (11 verified GBS cases in adults)
- Potential safety signals detected in VAERS need to be evaluated in more robust population-based active systems such as the Vaccine Safety Datalink (VSD) or Center for Medicaid Services (CMS)
- Separate studies currently in progress in the VSD (CDC) and CMS (FDA) to assess PCV20 vaccine safety
- CDC and FDA will continue to closely monitor the safety of PCV20

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

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