COVID-19 Vaccine Safety Technical (VaST) Work Group

Assessment

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Advisory Committee on Immunization Practices
August 30, 2021
COVID-19 Vaccine Safety Technical (VaST) Work Group

Objectives

- Review, evaluate, and interpret post-authorization/approval COVID-19 vaccine safety data
- Serve as the central hub for technical subject matter expertise from federal agencies conducting post-authorization/approval safety monitoring
- Advise on analyses, interpretation, and data presentation
- Provide updates to the ACIP COVID-19 Vaccines Work Group and the ACIP on COVID-19 vaccine safety
**VaST Activities**

**Dec 21, 2020 – present**
32 independent meetings to review vaccine safety data
8 joint meetings with COVID-19 Vaccines Work Group focused on safety

- ACIP votes following EUA
  - Dec 12 Pfizer (16+)
  - Dec 19 Moderna (18+)
  - Feb 28 Janssen (18+)
  - May 12 Pfizer (12-15)
  - Aug 13 Additional mRNA vaccine doses

- VaST assessments at ACIP meetings or website
  - Jan 27 Anaphylaxis following mRNA vaccines
  - Mar 1 Anaphylaxis updates; Pregnancy vaccine safety data
  - Apr 14 CVST following Janssen
  - Apr 23 TTS updates; Janssen resumed
  - May 12 TTS updates
  - May 12 Myocarditis updates
  - May 17 & 24 Myocarditis
  - Jun 23 Myocarditis updates
  - July 22 GBS following Janssen

CVST, cerebral venous sinus thrombosis; TTS, thrombosis with thrombocytopenia syndrome; GBS, Guillain-Barré syndrome
U.S. Vaccine Safety Monitoring Systems and Timelines

**active surveillance**

- va-safe™: after vaccination health checker
- CDC + FDA

**passive surveillance**

- VA EHR & data warehouse
- VSD (Vaccine Safety Datalink)

**individual case consults**

- FDA Vaccine Surveillance Program
  - Federal Partners
    - CMS, VA
  - BEST Initiative
    - Acumen, IBM, IQVIA/OHDSI

**large-linked database monitoring**

- DoD DMSS (Defense Medical Surveillance System)
Monitoring and Responding to Safety Data

Safety monitoring
- mRNA COVID-19 vaccines
  - Anaphylaxis
  - Myocarditis
- Janssen COVID-19 vaccine
  - TTS
  - GBS
- Pre-specified AESI
- Maternal immunization

Incorporating safety data into decision-making
- Dynamic benefit-risk balance
- Risk mitigation strategies
  - Support informed discussions about benefits and risks of available vaccines
  - Clinical guidance to support early detection and appropriate management
- Guidance for use of post-approval safety data in GRADE

TTS, thrombosis with thrombocytopenia syndrome; GBS, Guillain-Barré syndrome
VaST continues to review data on myocarditis, GBS and TTS from passive and active surveillance systems

- Data from
  - U.S. systems including VAERS, VSD
    - Most updated data on myocarditis presented today
  - U.S. data from VA, DoD, FDA, and IHS
  - Israel, Canada, Global Advisory Committee on Vaccine Safety
Anaphylaxis following mRNA COVID-19 vaccination

- Anaphylaxis following mRNA COVID-19 vaccination identified Dec 2020
- Safety data and VaST assessment presented at January and March 2021 ACIP meetings*
- CDC and FDA recommended risk mitigation strategies, including:
  - Screening for risk prior to vaccination
  - Monitoring for symptoms post-vaccination
  - Early recognition and management of anaphylaxis on-site
  - Provider and patient education by CDC and partners


As of January 20, 2021, the CDC received 13 reports of anaphylaxis and five deaths reportedly associated with the Moderna COVID-19 vaccine. These reports were related to the first dose of the vaccine. Anaphylaxis is a severe, potentially life-threatening allergic reaction. The CDC will continue to monitor for adverse events related to the Moderna COVID-19 vaccine.

On December 11, 2020, the U.S. Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the Pfizer-BioNTech COVID-19 vaccine. The Advisory Committee on Immunization Practices (ACIP) issued interim recommendations for its use. Following implementation of vaccination, reports of anaphylaxis after the first dose of the Pfizer-BioNTech COVID-19 vaccine emerged. Anaphylaxis is a life-threatening allergic reaction that occurs rarely after vaccination, with onset typically within minutes to hours. Notifications and reports of suspected severe allergic reactions and anaphylaxis following vaccination were captured in the Vaccine Adverse Event Reporting System (VAERS), the national
Prevaccination Checklist for COVID-19 Vaccines

For vaccine recipients:
The following questions will help us determine if there is any reason you should not get the COVID-19 vaccine. If you answer “yes” to any question, it does not mean you should not be vaccinated. It just means additional evaluation needed. If a question is not clear, please ask your healthcare provider.

Vaccines & Immunizations

Interim Considerations: Preparing for the Potential Management of Anaphylaxis After COVID-19 Vaccination

Anaphylaxis, an acute and potentially life-threatening allergic reaction, has been reported following COVID-19 vaccination. Detailed information on CDC recommendations for vaccination, including contraindications and precautions to vaccination, can be found in the Clinical Considerations for Use of mRNA COVID-19 Vaccines Currently Authorized in the United States.

These interim considerations provide information on preparing for the initial assessment and management of anaphylaxis following COVID-19 vaccination. Institutional practices and site-specific factors may also be considered. In all cases, appropriate medical treatment for severe allergic reactions must be immediately available in the event that an acute anaphylactic reaction occurs following administration of a COVID-19 vaccine.

Appropriate medical treatment for severe allergic reactions must be immediately available in the event that an acute anaphylactic reaction occurs following administration of an mRNA COVID-19 vaccine.
Anaphylaxis: VaST Discussion and Interpretation

- Initial data from VAERS
  - Rate for Pfizer-BioNTech: 11.1 per million doses admin (Dec 14-Dec 23)
    https://www.cdc.gov/mmwr/volumes/70/wr/mm7002e1.htm
  - Rate for Moderna vaccine: 2.5 per million doses admin (Dec 21-Jan 10)
    https://www.cdc.gov/mmwr/volumes/70/wr/mm7004e1.htm

- Most recent data from VSD among persons aged 12 and older*
  - 5.0 (95% CI 3.5, 6.9) (Pfizer-BioNTech) and 4.9 (95% CI 3.2, 7.2) (Moderna) per million doses administered
  - Most in females after first dose

- No substantial change in benefit-risk balance with risk mitigation strategies in place

*1-day risk interval
Myocarditis following mRNA COVID-19 vaccination

- Myocarditis following mRNA COVID-19 vaccination identified in May 2021\(^1\)
- CDC issued clinical guidance for myocarditis/pericarditis following mRNA vaccines, May 2021
- Data presented at the Vaccines and Related Biologics Products Advisory Committee (VRBPAC), June 10
- Data and VaST assessment presented at ACIP meeting on June 23\(^2\) and MMWR published
- EUA fact sheets revised with warning added, June 25
- FDA approval of Pfizer BioNTech COVID-19 vaccine on August 23
  - Information on myocarditis/pericarditis in package insert\(^3\)

\(^1\)https://www.cdc.gov/vaccines/acip/work-groups-vast/index.html; \(^2\)https://www.cdc.gov/vaccines/acip/meetings/slides-2021-06.htm; \(^3\)https://www.fda.gov/media/151707/download
Clinical Considerations: Myocarditis and Pericarditis after Receipt of mRNA COVID-19 Vaccines Among Adolescents and Young Adults

Summary
Since April 2021, increased cases of myocarditis and pericarditis have been reported in the United States after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna), particularly in adolescents and young adults. There has not been a similar reporting pattern observed after receipt of the Janssen COVID-19 Vaccine (Johnson & Johnson).

In most cases, patients who presented for medical care have responded well to medications and rest and had prompt improvement of symptoms. Reported cases have occurred predominantly in male adolescents and young adults 16 years of age or older, and most cases occurred soon after receipt of the second dose of mRNA COVID-19 vaccine. The timing of reported cases suggests a possible association with receipt of the second dose of mRNA COVID-19 vaccine. The Advisory Committee on Immunization Practices (ACIP) does not recommend withholding the second dose of mRNA COVID-19 vaccine for healthy individuals who initially experienced myocarditis or pericarditis following receipt of the first dose of an mRNA COVID-19 vaccine. Additional information and resources can be found on the CDC website.

Use of mRNA COVID-19 Vaccine After Reports of Myocarditis Among Vaccine Recipients: Update from the Advisory Committee on Immunization Practices — United States, June 2021

Weekly / July 9, 2021 / 70(27):977-982

On July 6, 2021, this report was posted online as an MMWR Early Release.
## Myocarditis/Pericarditis – 0-7 day risk interval

<table>
<thead>
<tr>
<th>Ages (yrs)</th>
<th>VAERS reporting rates per million doses administered</th>
<th>VSD excess cases per million doses based on chart confirmed data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pfizer Dose 1</td>
<td>Pfizer Dose 2</td>
</tr>
<tr>
<td>12–15</td>
<td>2.6</td>
<td>20.9</td>
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<td>16–17</td>
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</tr>
<tr>
<td>30–39</td>
<td>0.8</td>
<td>3.4</td>
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</tbody>
</table>

Data presented at Aug 30, 2021 ACIP Meeting
Myocarditis following vaccination – Clinical course

- VAERS reports for individuals <30 years of age (N=845 cases reviewed)
  - 88% of reviewed cases met CDC case definition
  - 77% were known to have recovered from symptoms at time of VAERS report

- VSD cases among individuals 12-39 years of age (N=98 cases reviewed)
  - 56% of cases met chart confirmation criteria for myocarditis within 0-21 days of vaccination
  - 100% with chest pain/pressure/discomfort
  - Elevated troponin, abnormal EKG findings, abnormal MRI common
  - 76% discharged within 0-2 days; 100% discharged to home
Myocarditis: VaST Discussion and Interpretation

- Data available to date suggest association of myocarditis with mRNA vaccination in adolescents and young adults
- Further data are being compiled to understand potential risk factors, optimal management strategies, and long-term outcomes
  - Patient survey on functional status, clinical symptoms, quality of life and ongoing need for medication or treatment
  - Provider survey on cardiac health and functional status
On August 23, 2021, the FDA approved the first COVID-19 vaccine. The vaccine has been known as the Pfizer-BioNTech COVID-19 Vaccine, and will now be marketed as Comirnaty, for the prevention of COVID-19 disease in individuals 16 years of age and older. The vaccine also continues to be available under emergency use authorization (EUA), including for individuals 12 through 15 years of age and for the administration of a third dose in certain immunocompromised individuals.
Myocarditis: FDA Post-Marketing Requirements for Pfizer-BioNTech COVID-19 mRNA vaccine

- Non-Interventional Post-Approval Safety Study to evaluate occurrence of myocarditis and pericarditis in the U.S.
- Post Conditional Approval Active Surveillance Study to evaluate occurrence of myocarditis and pericarditis in Europe
  - Sub-study to describe the natural history of myocarditis and pericarditis
- Prospective cohort study ≥5 years for potential long-term sequelae of myocarditis after vaccination (in collaboration with Pediatric Heart Network)
- Sub-studies of clinical trials to prospectively assess the incidence of subclinical myocarditis following 2nd dose in subset of participants aged 5-15 years and 16-30 years

https://www.fda.gov/media/151710/download
In a 42-day risk window for myocarditis:
- **Risk ratio 3.2** after vaccination vs. **18.3** after SARS-CoV-2 infection
- **Risk difference of 2.7** per 100,000 persons after vaccination vs. **11.0** events per 100,000 persons after SARS-CoV-2 infection
- Adverse events substantially increased after infection
- Protective effects of vaccination observed

Barda et al., NEJM 2021
Safety Monitoring and VaST Next Steps

- Continue near real-time monitoring of vaccine safety in the U.S.
  - Collaboration across U.S. federal agencies
- Continue collaboration with global vaccine safety colleagues on key issues that impact benefit-risk balance
  - Myocarditis
  - Booster doses
- Continue to provide updates to the ACIP COVID-19 Vaccines Workgroup and the ACIP at future meetings
**VaST Members**

**VaST Members**
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Robert Hopkins (NVAC)
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Matthew Clark (IHS)
Mary Rubin (HRSA)
Fran Cunningham (VA)
Limone Collins (DoD)

**Administrative Support**
Jared Woo

**CDC Co-Leads**
Lauri Markowitz
Melinda Wharton
Reporting rates of myopericarditis (per million doses administered), by manufacturer, sex, and dose number, 7-day risk period* (as of Aug 18, 2021)

<table>
<thead>
<tr>
<th>Ages‡ (yrs)</th>
<th>Pfizer (All)</th>
<th>Moderna (All)</th>
<th>Janssen (All)</th>
<th>Pfizer (Males)</th>
<th>Moderna (Males)</th>
<th>Janssen (Males)</th>
<th>Pfizer (Females)</th>
<th>Moderna (Females)</th>
<th>Janssen (Females)</th>
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<td>2.7</td>
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<td>1.1</td>
<td>6.8</td>
<td>1.6</td>
<td>8.0</td>
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* Reports with time to symptom onset within 7 days of vaccination
‡ Reports among persons 12–29 years of age were verified by provider interview of medical record review