COVID-19 Vaccine Safety Technical (VaST) Work Group

Safety Assessments

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Advisory Committee on Immunization Practices
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Topics

- VaST objectives and activities
- Brief overview of selected Moderna and Janssen COVID-19 vaccination safety data
- VaST assessments
  - Moderna COVID-19 vaccination
  - Janssen COVID-19 vaccination
  - Heterologous boosting
- VaST future plans

COVID-19 Vaccine Safety Technical (VaST) Work Group

Objectives

- Review, evaluate, and interpret post-authorization/approval COVID-19 vaccination 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 continues to review COVID-19 vaccination safety data from passive and active surveillance systems

- U.S. safety monitoring systems including Vaccine Adverse Events Reporting System (VAERS), Vaccine Safety Datalink (VSD), FDA BEST System,[1] VA, IHS, DoD
- Israel, Canada, Global Advisory Committee on Vaccine Safety
- Special evaluations underway, such as follow-up studies of myocarditis cases

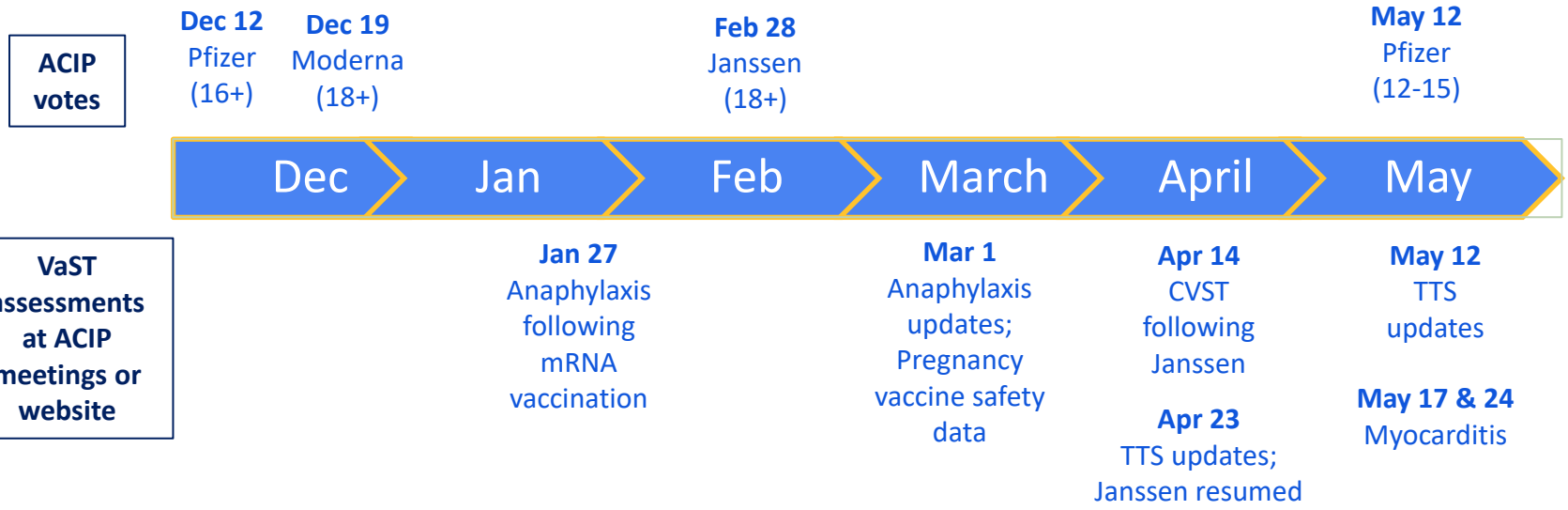
[1]https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/cber-biologics-effectiveness-and-safety-best-system
VA, Veterans Affairs; IHS, Indian Health Service; DoD, Department of Defense

VaST activities

December 21, 2020 – present

38 independent meetings to review vaccine safety data

10 joint meetings with COVID-19 Vaccines Work Group focused on safety



CVST, cerebral venous sinus thrombosis; TTS, thrombosis with thrombocytopenia syndrome; GBS, Guillain-Barré syndrome

VaST activities

December 21, 2020 – present (continued)
38 independent meetings to review vaccine safety data
10 joint meetings with COVID-19 Vaccines Work Group focused on safety

ACIP votes

Aug 13
Additional mRNA vaccine doses for immunocompromised

Aug 30
Pfizer BLA (16+)

Sept 22
Pfizer 3rd dose

Oct 21
Moderna 3rd dose
Janssen 2nd dose

VaST assessments at ACIP meetings or website

Jun 23
Myocarditis updates

July 22
GBS following Janssen

Aug 30
Safety overview

Sept 23
3rd dose Pfizer

Oct 21
3rd dose Pfizer
2nd dose Janssen

CVST, cerebral venous sinus thrombosis; TTS, thrombosis with thrombocytopenia syndrome; GBS, Guillain-Barré syndrome

Moderna COVID-19 vaccination: Overview of post-authorization safety – myocarditis/pericarditis

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

VRBPAC, Vaccines and Related Biologics Products Advisory Committee

[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

Moderna COVID-19 vaccination: Overview of post-authorization safety – myocarditis/pericarditis

- Data available to date show association of myocarditis with both mRNA vaccines in adolescents and young adults, males > females
  - Some systems show greater risk after Moderna than Pfizer vaccination
    - United States (VSD and DoD), Canada, Scandinavian countries
  - Other U.S. safety monitoring systems do not show a difference between the two mRNA vaccines
    - VAERS, FDA BEST Systems, VA
- Further data are being compiled to understand
  - Differences between safety systems
  - Optimal management strategies
  - Long-term outcomes

Moderna COVID-19 vaccination safety data, dose 3

- Clinical trial data – 50 µg dose in 171 participants*
  - No evidence of increased reactogenicity following a booster dose relative to dose 2, with exception of increased axillary swelling/tenderness of the vaccination arm[1]
- Post-authorization safety data for Moderna dose 3, original 100 µg dose[2]
  - v-safe: ~14,000 persons who reported dose 3
    - Local reactions were reported slightly more frequently and systemic reactions slightly less frequently following dose 3 than dose 2
  - VAERS: 1,440 reports after dose 3
    - Over 92% of reports were non-serious

[1]https://www.fda.gov/media/153087/download [2]Hause A, ACIP October 21, 2021

*participants who received 100 µg primary series; total 344 received 50 µg booster

Janssen COVID-19 vaccination: Overview of post-authorization safety, TTS and GBS

- TTS[1]
  - Surveillance in VAERS identified reports of CVST and TTS
  - Use of vaccine in the United States was paused April 13
  - EUA fact sheets updated with warning about TTS, pause was lifted April 23
  - Through October 13, 47 cases of TTS confirmed (15.3 M doses administered)
    - Most cases in women, aged 18-49 years; evaluation ongoing
- GBS[2]
  - Surveillance in VAERS identified reports of GBS
  - Higher than expected reporting, males > females; EUA fact sheets updated with information about observed risk, July 12
  - Through July 24, 130 reports of GBS identified
    - Observed reports > expected across multiple age groups

CVST: cerebral venous sinus thrombosis; TTS; thrombosis with thrombocytopenia syndrome; GBS, Guillain Barre Syndrome;
[1] Shimabukuro T, ACIP October 21, 2021; [2]https://www.fda.gov/media/153132/download

Janssen COVID-19 vaccination safety data – dose 2

- Clinical trial data[1]
  - Approximately 9,000 participants received 2 doses at least 2 months apart; approximately 2,700 have had at least 2 months of safety follow-up
  - No new safety signals identified following a second dose.
  - Interpretation of the data is limited by small sample size, particularly for 6-month interval post dose 1
- Post-authorization safety data[2]
  - v-safe
    - 83 participants recorded dose 2
  - VAERS
    - 39 reports after dose 2
    - All reports were non-serious

[1]https://www.fda.gov/media/153130/download and https://www.fda.gov/media/153129/download ; [2]Hause A, ACIP October 21, 2021

VaST assessment summary – primary series

- Moderna COVID-19 vaccination
  - There appears to be a slightly increased risk of myocarditis among 18–39 year-olds after Moderna compared with Pfizer vaccination
  - Preliminary data from follow-up study, based on data from patients/parents, suggest that cases are generally mild, with prompt resolution of symptoms [1]
- Janssen COVID-19 vaccination
  - Risks for TTS and GBS appear to be unchanged from earlier assessments – serious but rare
- Important to communicate to public and patients the balance of benefits and risks

[1] Follow-up being conducted for confirmed myocarditis cases after COVID-19 vaccination reported to VAERS

VaST assessment summary – booster doses

- Moderna COVID-19 vaccination
  - Limited data on risk of myocarditis after dose 3 (original 100 µg dose) from safety monitoring systems
  - Data on safety of the reduced 50 µg booster dose only available from small clinical trial
  - Risk of myocarditis observed following the reduced dose Moderna booster might be lower than risk following the original dose vaccination
- Janssen COVID-19 vaccination
  - Limited trial data and data from safety monitoring systems for dose 2
  - Risks after booster dose are unlikely to be greater than with primary vaccination
- Important to communicate to public and patients the balance of benefits and risks

VaST assessment summary – heterologous booster

- Preliminary data from NIH mix and match study[1] and limited data from post authorization safety data suggest that boosting of Janssen COVID-19 vaccine recipients with an mRNA vaccine, or of mRNA COVID-19 vaccine recipients with Janssen COVID-19 vaccine poses no additional safety risk compared with homologous boosting
- No evidence to date of safety concerns with respect to any of the prespecified VSD surveillance outcomes for Janssen COVID-19 vaccine recipients who received an additional dose of an mRNA COVID-19 vaccine

[1] Atmar R, ACIP October 21, 2021

Safety monitoring and VaST next steps

- VaST will continue to:
  - Review safety regarding additional and booster doses as data become available
  - Collaborate with global vaccine safety colleagues on key issues that impact benefit-risk balance
  - Provide updates to the ACIP COVID-19 Vaccines Work Group and the ACIP at future meetings

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