COVID-19 Vaccine Safety Technical (VaST) Work Group

Assessment of 3rd dose safety data

H. Keipp Talbot, MD MPH (VaST Chair)

Robert H. Hopkins, Jr., MD (NVAC Chair)

Advisory Committee on Immunization Practices

September 22, 2021

COVID-19 Vaccine Safety Technical (VaST) Work Group

Objectives

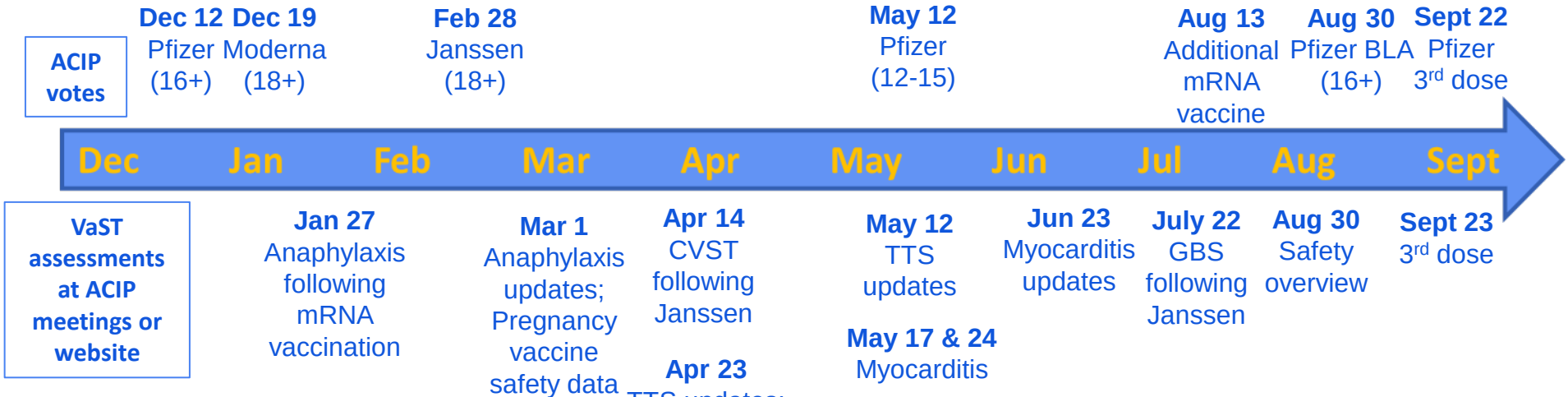
- Review, evaluate, and interpret post-authorization/approval COVID-19 vaccine safety data
- Serve as the central hub for technical subject matter expertise from federal agencies conducting post-authorization/approval safety monitoring
- Advise on analyses, interpretation, and data presentation
- Provide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

VaST Activities

Dec 21, 2020 – present

35 independent meetings to review vaccine safety data

8 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 continues to review data on myocarditis, GBS, anaphylaxis, and TTS following COVID-19 vaccination from passive and active surveillance systems

- U.S. safety monitoring systems including VAERS, VSD, CMS, VA, IHS, DoD
- Israel, Canada, Global Advisory Committee on Vaccine Safety
- Special evaluations underway, such as follow-up studies of myocarditis cases in VAERS, VSD, and DoD

VSD, Vaccine Safety Datalink; CMS, Centers for Medicare & Medicaid Services; VA, Veterans Affairs; IHS, Indian Health Service; DoD, Department of Defense

Safety data regarding 3rd dose COVID-19 vaccination reviewed by VaST

- Israel – data from spontaneous reporting system*
- United States – data from v-safe

*Also presented at VRBPAC meeting, September 17, 2021

Safety data regarding 3rd dose Pfizer-BioNTech COVID-19 vaccination, Israel

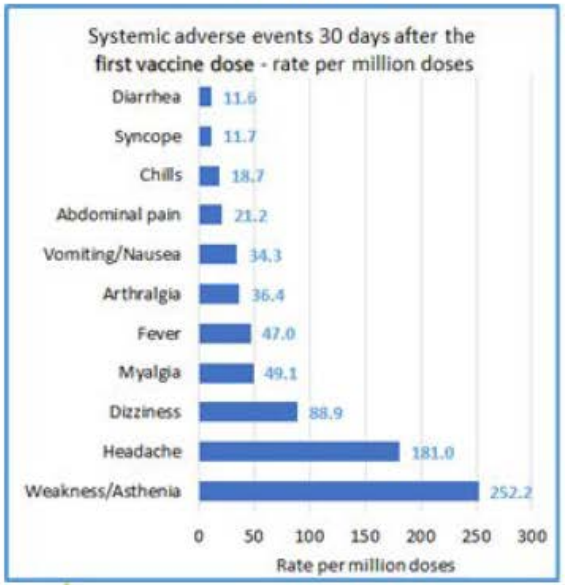
- 3rd doses were phased in, first for persons ≥60 years; since the end of August everyone ≥12 years has been eligible for 3rd dose
- ~2.8 M 3rd doses administered to persons ≥12 years (through September 13)
  - Most to persons ≥60 years
- Rates of reported systemic, local, neurologic, allergic, and other reactions were substantially lower after dose 3 than after dose 1 or 2
  - Suspected under-reporting
- 1328 non serious and 19 serious adverse events (SAE)
  - All hospitalized patients and deaths investigated by a work group
  - Among serious cases, 7 possibly associated with vaccination

https://www.fda.gov/media/152205/download

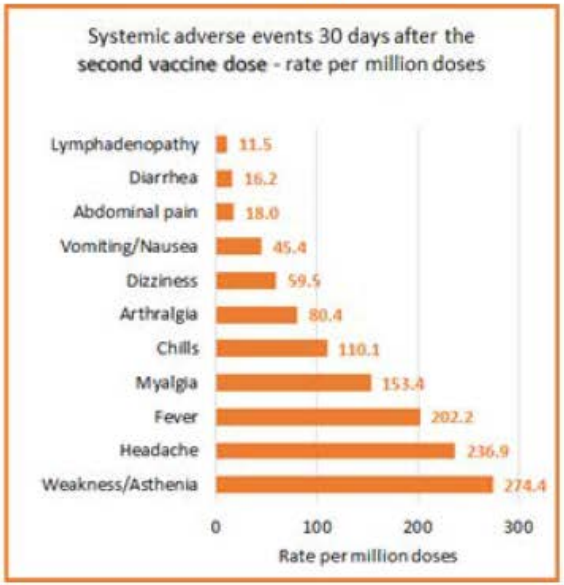
Data from Israeli Ministry of Health

Rate of systemic adverse events by dose
(under-reporting expected in all cases)

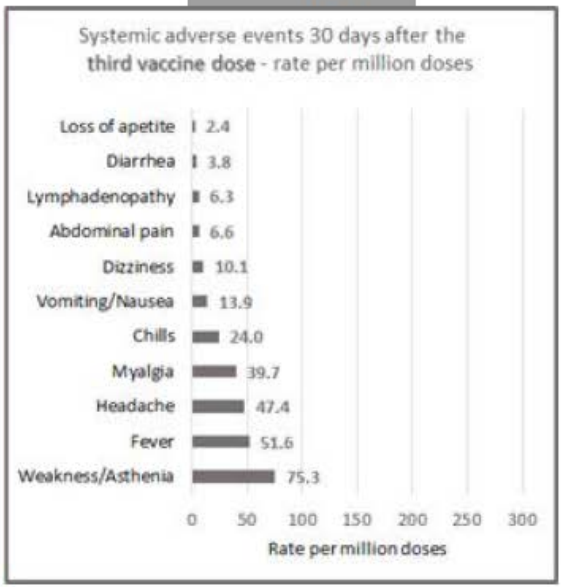
1st dose



2nd dose



3rd dose



MINISTRY OF HEALTH

https://www.fda.gov/media/152205/download

Data from Israeli Ministry of Health

Myocarditis cases and number of vaccinees by age group and sex

Gender	Age group	1st dose (0-21 days after vac.)		2nd dose (0-30 days after vac.)		3rd dose (0-30 days after vac. but in many vaccinees less days so far)	
		Number of vaccinees	Myocarditis cases	Number of vaccinees	Myocarditis cases	Number of vaccinees	Myocarditis cases
Female	12-15	186,655	0	134,637	1	163	No cases observed
	16-19	242,497	0	215,725	2	55,107	
	20-24	260,693	1	239,427	6	79,174	
	25-29	244,705	0	226,471	1	74,222	
	30+	2,116,016	3	2,013,329	8	1,273,773	
Male	12-15	174,597	1	126,723	9	142	
	16-19	248,673	3	217,006	33	57,195	
	20-24	272,641	6	248,747	26	85,961	
	25-29	255,426	3	236,913	20	77,325	
	30+	1,973,238	10	1,882,588	32	1,211,543	1

* All cases reported in Israel Dec. 2020 - Sep 13. 2021

Most young vaccinees received booster only in last two weeks

https://www.fda.gov/media/152205/download

Safety data after 3rd dose COVID-19 vaccination, v-safe

- As of September 11, 3rd doses were recorded by 24,165 participants
- While 3rd doses are currently only recommended for persons with immunocompromising conditions in the United States, there are no data in v-safe to indicate underlying conditions
- Compared with dose 2
  - Larger proportion of participants report local reactions following mRNA vaccination dose 3
  - Smaller proportion of participants report systemic reactions following mRNA vaccination dose 3

VaST assessment of 3rd dose Pfizer-BioNTech COVID-19 vaccination safety data

- **Safety data from Israel**
  - Assessment limited by likely underreporting of local, systemic, and SAEs.
  - The few SAEs potentially associated with vaccination need further follow-up.
  - VaST noted single case of myocarditis reported in male aged 30-34 years.
- **Safety data from v-safe**
  - Systemic reactions following dose 3 slightly less than following dose 2.
  - Assessment limited by lack of data on underlying conditions or whether recipients are individuals with immunocompromise.
  - v-safe data significance unclear given that local and systemic reactogenicity does not predict more severe adverse events.

Safety monitoring and VaST next steps

- VaST will continue to:
  - Review safety regarding 3rd 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

VaST Members

VaST Members

Keipp Talbot (ACIP)
Robert Hopkins (NVAC)
Matt Daley
Grace Lee
Veronica McNally
Kathy Edwards
Lisa Jackson
Jennifer Nelson
Laura Riley
Robert Schechter
Patricia Whitley-Williams

CDC Co-Leads

Lauri Markowitz
Melinda Wharton

Ex Officio and Liaison Representatives

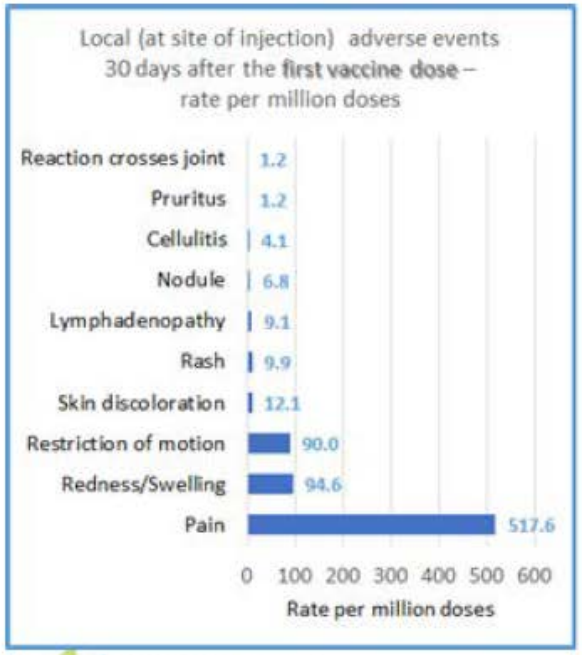
Tatiana Beresnev (NIH)
Karen Farizo; Hui Lee Wong (FDA)
Judith Steinberg (OIDP)
Jeffrey Kelman (CMS)
Matthew Clark (IHS)
Mary Rubin (HRSA)
Fran Cunningham (VA)
Limone Collins (DoD)

Administrative Support

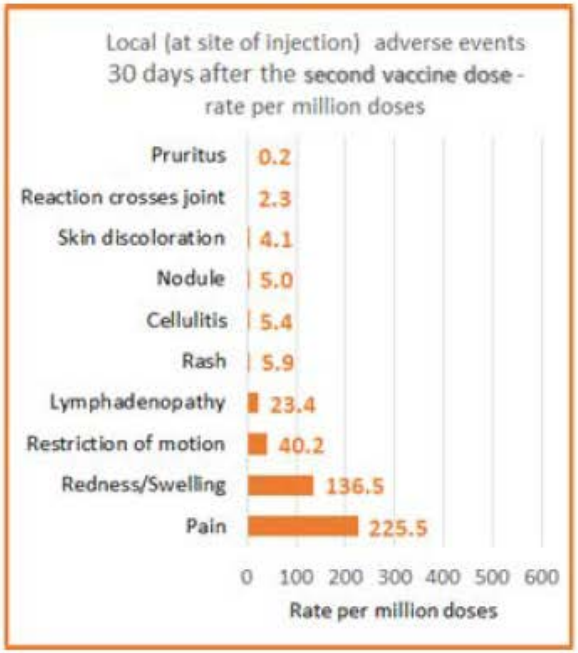
Jared Woo

Rate of local adverse events by dose
(under-reporting expected in all cases)

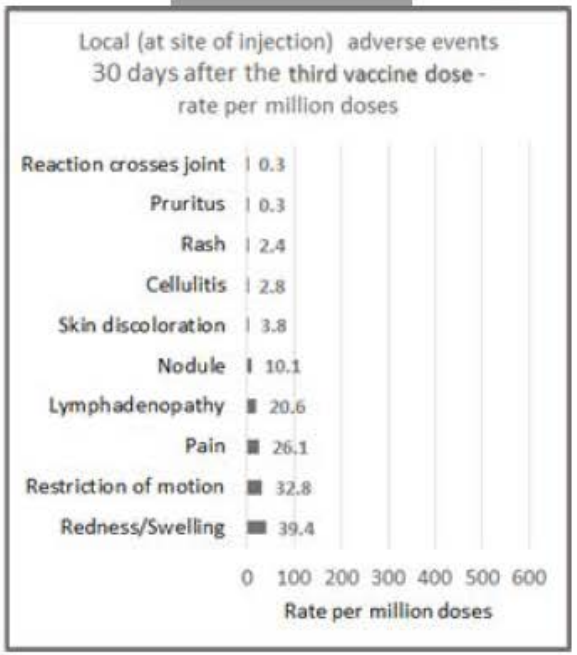
1st dose



2nd dose



3rd dose



MINISTRY OF HEALTH

https://www.fda.gov/media/152205/download

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; AESI, adverse events of special interest