Vaccines and Related Biological Products Advisory Committee Meeting

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Safety Surveillance of COVID-19 Vaccines in Children and Adolescents

Vaccines and Related Biological Products Advisory Committee
June 14, 2022

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Outline

• Evaluation of Evidence for Myocarditis/Pericarditis Risk in Young Males following Second Dose of Moderna vs. Pfizer-BioNTech COVID-19 Vaccines

• FDA Biologics Effectiveness and Safety (BEST) Initiative Results: Comparative Risk of Myocarditis/Pericarditis between Moderna (mRNA-1273) versus Pfizer-BioNTech (BNT162b2) COVID-19 Vaccines in Males 18-25 Years of Age

• Safety Surveillance in Vaccine Recipients 5-17 Years of Age in FDA BEST
Evaluation of Myocarditis/Pericarditis Risk in Young Males following Second Dose of Moderna vs. Pfizer-BioNTech COVID-19 Vaccines
Comparison of myocarditis/pericarditis risk for Moderna vs Pfizer-BioNTech COVID-19 vaccines in young males post dose 2
Data through October 2021

<table>
<thead>
<tr>
<th>Reports concluding lack of evidence for significant differential risk</th>
<th>Reports concluding higher myocarditis/pericarditis rates in Moderna COVID-19 vaccine</th>
</tr>
</thead>
</table>
| **Passive Surveillance: 1.3x higher**  
• US VAERS\(^a\) (18-24 years) | **Passive Surveillance: 1.7x – 6.6x higher**  
• Medicines and Healthcare products Regulatory Agency (18-29 years)  
• European Medicines Agency (18-24 years)  
• Public Health Agency of Canada (18-29 years)  
• Public Health Ontario, Canada (18-24 years) |
| **Active Surveillance: 1.2x higher**  
• US FDA BEST\(^b\) (18-25 years) | **Active Surveillance: 2.3x – 3.1x higher**  
• US CDC VSD\(^c\) (18-39 years)  
• Denmark/Norway/Finland/Sweden (16-24 years) |

Based on the available evidence, FDA did not take regulatory action on the EUA amendment for use of Moderna COVID-19 vaccine in adolescents

Sources: Results either shared with FDA under confidentiality agreements or FDA studies
\(^a\) US Vaccine Adverse Event Reporting System; \(^b\) Food and Drug Administration Biologics Effectiveness and Safety System; \(^c\) Centers for Disease Control and Prevention (CDC) Vaccine Safety Datalink
Note: Risk windows were within 7 days for all reports/publications except for European Medicines Agency (0-14 days)
Comparison of myocarditis/pericarditis risk for Moderna vs Pfizer-BioNTech COVID-19 vaccines in young males post dose 2
Data through May 2022

<table>
<thead>
<tr>
<th>Reports concluding lack of evidence for significant differential risk</th>
<th>Reports concluding higher myocarditis/pericarditis rates in the Moderna COVID-19 vaccine</th>
</tr>
</thead>
</table>
| Passive Surveillance: 1.1x higher  
- US VAERS\(^a\) (18-24 years) | Passive Surveillance: 1.7x – 6.6x higher  
- Medicines and Healthcare products Regulatory Agency (18-29 years)  
- European Medicines Agency (18-24 years)  
- Public Health Agency of Canada (18-29 years)  
- Public Health Ontario, Canada (18-24 years) |
| Active Surveillance: 1.3x – 1.5x higher  
- US FDA BEST\(^b\) (18-25 years)  
- US CDC VSD\(^c\) (18-39 years) | Active Surveillance: 3.1x – 7.3x higher  
- Denmark/Norway/Finland/Sweden (16-24 years)  
- Denmark (12-39 years)  
- United Kingdom (13-39 years)  
- France (12-29 years)  
- Italy (12-39 years) |

As of May 2022, US surveillance data do not support a statistically significant higher myocarditis/pericarditis risk of Moderna COVID-19 vaccine relative to Pfizer-BioNTech COVID-19 vaccine

Sources: Per Appendix
\(^a\) US Vaccine Adverse Event Reporting System; \(^b\) Food and Drug Administration Biologics Effectiveness and Safety System; \(^c\) Centers for Disease Control and Prevention Vaccine Safety Datalink
Note: Risk windows were within 7 days for all reports/publications except for European Medicines Agency (0-14 days), Husby 2021 (0-28 days) and Patone 2021 (1-28 days)
Summary

• International passive and active surveillance data sources suggest a higher myocarditis/pericarditis risk following vaccination with Moderna COVID-19 vaccine relative to Pfizer-BioNTech COVID-19 vaccine

• Based on the totality of evidence available previously, FDA did not take regulatory action on the EUA amendment for use of the Moderna COVID-19 vaccine in adolescents

• More recent evidence from US surveillance did not identify a significantly higher myocarditis/pericarditis risk in the Moderna COVID-19 vaccine recipients compared to Pfizer-BioNTech COVID-19 vaccine recipients among males 18-25 years of age post-dose 2

• Results may be limited by: small case counts, lack of adjustments for confounders, self-reported data
FDA BEST Results:
Comparative Risk of Myocarditis/Pericarditis between Moderna (mRNA-1273) versus Pfizer-BioNTech (BNT162b2) COVID-19 Vaccines in Males 18-25 Years of Age
FDA CBER
Active Surveillance Program Collaborative
mRNA COVID-19 Vaccine Doses* in FDA BEST Claims Data Sources, 18-64 years

Total Doses

Pfizer-BioNTech 16,912,716

Moderna 10,631,554

*Dosage 1, Dosage 2, and other dosages. Vaccine counts for recent dates may be underestimated due to data delay.
Data cutoff date: Data Partner 1 (9/30/2021), Data Partner 2 (10/31/2021), Data Partner 3 (11/4/2021), Data Partner 4 (12/25/2021)
Direct comparisons of myocarditis/pericarditis risk within 7 days of receipt of Moderna versus Pfizer-BioNTech COVID-19 vaccines among males 18-25 years of age, by dose


Rate ratios adjusted for age, age by vaccine brand interaction, study week of vaccination, COVID-19 diagnosis prior to vaccination, urban/rural residency.
Limitations

• Chart review for events are on-going
  • Interim positive predictive values were estimated
• Partial adjustment for potential confounders
  • Cannot rule out biased estimates
• Large uncertainty incidence rate ratios
  • Small number of events, wide confidence intervals
Summary

• FDA BEST study results did not identify a significantly higher myocarditis/pericarditis risk following vaccination with dose 2 of Moderna COVID-19 vaccine compared to Pfizer-BioNTech COVID-19 vaccine among males 18-25 years of age.

• Results were compatible with a 20%-lower to 94%-higher myocarditis/pericarditis rates in Moderna COVID-19 vaccine recipients compared to Pfizer-BioNTech COVID-19 vaccine recipients.
Safety Surveillance in Vaccine Recipients 5-17 Years of Age in FDA BEST
Pediatric Data Sources in FDA BEST

• Data Sources
  • Administrative Claims Databases*
  • Immunization Information System**

• Enrollment and Vaccine Counts

<table>
<thead>
<tr>
<th>Age group, year</th>
<th>Patients covered, million</th>
<th>Total Vaccines Doses, million</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-11</td>
<td>4.7</td>
<td>2.0</td>
</tr>
<tr>
<td>12-15</td>
<td>3.1</td>
<td>2.2</td>
</tr>
<tr>
<td>16-17</td>
<td>1.6</td>
<td>1.8</td>
</tr>
<tr>
<td>Total</td>
<td>9.4</td>
<td>5.4</td>
</tr>
</tbody>
</table>

*CVS Health (data through 2/28/2022), Optum, (data through 4/30/2022), HealthCore; (data through 3/1/2022)** 23 jurisdictions
**Pre-specified Adverse Events of Interest**

These potential adverse events of special interest have not been associated with COVID-19 vaccines based on pre-authorization studies.

<table>
<thead>
<tr>
<th>Descriptive monitoring Only</th>
<th>Sequential Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Guillain-Barré syndrome</td>
<td>• Bell's Palsy</td>
</tr>
<tr>
<td>• Multisystem inflammatory syndrome in children</td>
<td>• Anaphylaxis</td>
</tr>
<tr>
<td>• Transverse myelitis</td>
<td>• Encephalitis / myelitis / encephalomyelitis</td>
</tr>
<tr>
<td>• Unusual site (cerebral and abdominal) thrombosis with thrombocytopenia</td>
<td>• Narcolepsy</td>
</tr>
<tr>
<td>• Kawasaki disease</td>
<td>• Appendicitis</td>
</tr>
<tr>
<td>• Hemorrhagic stroke</td>
<td>• Non-hemorrhagic stroke</td>
</tr>
<tr>
<td>• Acute myocardial infarction</td>
<td>• Myocarditis/pericarditis</td>
</tr>
</tbody>
</table>

- Deep vein thrombosis
- Pulmonary embolism
- Disseminated intravascular coagulation
- Immune thrombocytopenia
- Common site thrombosis with thrombocytopenia
- Seizures/convulsions
## Sequential Testing Results for Primary Series & Third/Booster Doses in 5-17 years of age, FDA BEST System

<table>
<thead>
<tr>
<th>AESI</th>
<th>Ages 5-11</th>
<th>Ages 12-15</th>
<th>Ages 16-17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaphylaxis</td>
<td>No signal</td>
<td>No signal</td>
<td>No signal</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>No signal</td>
<td>No signal</td>
<td>No signal</td>
</tr>
<tr>
<td>Bell's palsy</td>
<td>No signal</td>
<td>No signal</td>
<td>No signal</td>
</tr>
<tr>
<td>Common thromboses with thrombocytopenia</td>
<td>No signal</td>
<td>No signal</td>
<td>No signal</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>No signal</td>
<td>No signal</td>
<td>No signal</td>
</tr>
<tr>
<td>Disseminated intravascular coagulation</td>
<td>No signal</td>
<td>No signal</td>
<td>No signal</td>
</tr>
<tr>
<td>Encephalitis / myelitis / encephalomyelitis</td>
<td>No signal</td>
<td>No signal</td>
<td>No signal</td>
</tr>
<tr>
<td>Immune thrombocytopenia</td>
<td>No signal</td>
<td>No signal</td>
<td>No signal</td>
</tr>
<tr>
<td>Myocarditis/Pericarditis</td>
<td>No signal</td>
<td>Primary Series Signal¹,²,³</td>
<td>Primary Series Signal¹,²,³</td>
</tr>
<tr>
<td>Narcolepsy</td>
<td>No signal</td>
<td>No signal</td>
<td>No signal</td>
</tr>
<tr>
<td>Seizures/convulsions*</td>
<td>No Signal</td>
<td>No signal</td>
<td>No signal</td>
</tr>
<tr>
<td>Non-hemorrhagic stroke</td>
<td>No signal</td>
<td>No signal</td>
<td>No signal</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>No signal</td>
<td>No signal</td>
<td>No signal</td>
</tr>
</tbody>
</table>

¹ In Optum (SAF data through 4/30)
² In HCI (data through 3/1/2022)
³ In CVS (data through 2/28/2022)

*Analyses for seizures/convulsions have not been conducted in Optum
Observed/Expected Rate Ratio of Myocarditis/Pericarditis Risk after Receipt of Pfizer-BioNTech COVID-19 vaccine in Males 12-25 years of age, by dose

Note: Observed rates adjusted for observation delay estimated from historical data. Expected rates adjusted for age and sex where background rates permit. O/E rate ratios: the rate of observed events divided by the rate of expected events. 95% exact Poisson confidence intervals are calculated.
Summary

- Myocarditis/Pericarditis was identified as a safety signal in vaccine recipients 12 – 15 years of age and 16 – 17 years of age following dose 1 and 2
- Myocarditis/pericarditis did not signal in 5 – 11 years old vaccine recipients
- No other safety signals were identified in any of the three age groups or for booster analyses
Conclusions
Conclusions

- FDA BEST study results did not identify a significantly higher myocarditis/pericarditis risk in the recipients of Moderna COVID-19 vaccine compared to Pfizer-BioNTech COVID-19 vaccine among males 18-25 years of age post-Dose 2
- Myocarditis/Pericarditis signaled for vaccine recipients 12-17 years of age, post-dose 1 and 2; no other signals were identified
- FDA continues to monitor myocarditis/pericarditis risk and the safety of COVID-19 vaccines in the pediatric population
Acknowledgements

FDA BEST Partners
Acumen
CVS Health
Optum
IQVIA/HealthCore
Blue Health Intelligence

FDA
Steven Anderson
Richard Forshee

CBER Surveillance Program
• Azadeh Shoaibi, Patricia Lloyd, Joyce Obidi, Kristin Sepúlveda, Tainya Clarke

CBER OBPV
• Xinyi Ng, Marisabel Rodriguez, Whitney Steele

www.bestinitiative.org
References for Slide 11 (in alphabetical order)


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**Denmark/Norway/Finland/Sweden.** Karlstad Ø, Hovi P, Husby A et al. SARS-CoV-2 Vaccination and Myocarditis in a Nordic Cohort Study of 23 Million Residents. JAMA Cardiol. 2022 Apr 20;e220583.

**European Medicines Agency/MHRA.** Results shared with FDA under confidentiality agreements.


