### **Monthly Public Health Webinar**

#### Nirsevimab (Beyfortus™) RSV Vaccines

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Benjamin Chan Elizabeth Talbot Anne Marie Mercuri Erik Shessler



# PPT Slides Will Be Posted to a New Healthcare Provider Resources Website

 https://www.dhhs.nh.gov/programs-services/disease-prevention/infectiousdisease-control/bidc-resources-healthcare-providers





#### **RSV Background**

#### **Symptoms**

People infected with RSV usually show symptoms within 4 to 6 days after getting infected. Symptoms of RSV infection usually include

- Runny nose
- Decrease in appetite
- Coughing
- Sneezing
- Fever
- Wheezing



#### Severe RSV

Virtually all children get an RSV infection by the time they are 2 years old. Most of the time RSV will cause a mild, cold-like illness, but it can also cause severe illness such as

- Bronchiolitis (inflammation of the small airways in the lung)
- Pneumonia (infection of the lungs)

Some children are at increased risk of severe RSV disease, including those who were born prematurely, or who have chronic lung or heart disease or a weakened immune system.



#### **RSV Burden Estimates**



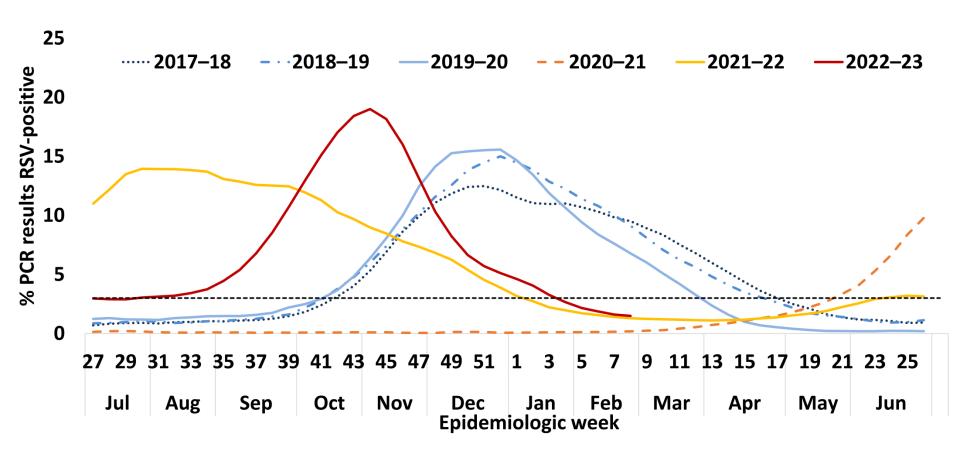
#### **RSV Burden Estimates**

Each year in the United States, RSV leads to approximately:

- 2.1 million outpatient (non-hospitalization) visits among children younger than 5 years old.(1)
- 58,000-80,000 hospitalizations among children younger than 5 years old. (1,2,3)
- 60,000-160,000 hospitalizations among adults 65 years and older. (4-8)
- 6,000-10,000 deaths among adults 65 years and older. (9-11)
- 100–300 deaths in children younger than 5 years old. (11)



#### Seasonal RSV Activity, 2017-2023





#### **RSV Treatment and Prevention**

- RSV infections in most persons are mild and symptoms resolve in 1-2 weeks
- People with severe disease may need to be hospitalized for supportive care (oxygen, IV fluids, etc.) until symptoms improve
- Monoclonal antibody products are available for prevention in infants and young children
  - Nirsevimab: see today's discussion
  - Palivizumab: for infants at highest risk of serious RSV disease, administered as monthly injections (up to 5 doses) during RSV season
- RSV vaccines for older adults 60+ years of age

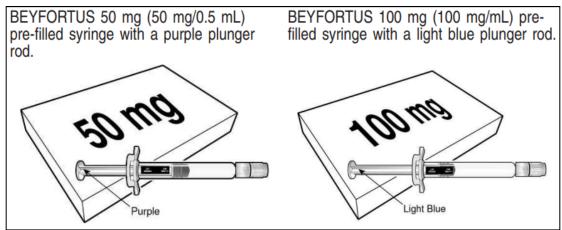


## Nirsevimab



#### Background

- Nirsevimab is a long-acting (half-life is ~71 days) recombinant human monoclonal antibody (immunoglobulin) that targets and binds the RSV Fprotein inhibiting viral fusion and host cell entry
- Prevents RSV lower respiratory tract infection/disease (LRTI/LRTD) through passive immunity
- Produced in hamster ovary cells by recombinant DNA technology
- Supplied as 50 mg (purple plunger rod) and 100 mg (light blue plunger rod) pre-filled syringes (50 mg and 100 mg syringes are the same cost)





#### ACIP Unanimously Voted to Recommend:

- Infants aged <8 months born during or entering their first RSV season receive one dose of nirsevimab (50 mg for infants <5 kg and 100 mg for infants ≥5 kg)
  - Based on Phase 2/3 clinical trial data showing safety and efficacy
- Children aged 8-19 months who are at increased risk of severe RSV disease and entering their second RSV season receive one dose of nirsevimab (200 mg)
  - Based on safety data and limited pharmacokinetic data comparing nirsevimab serum concentrations (as a surrogate for efficacy data)



## The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

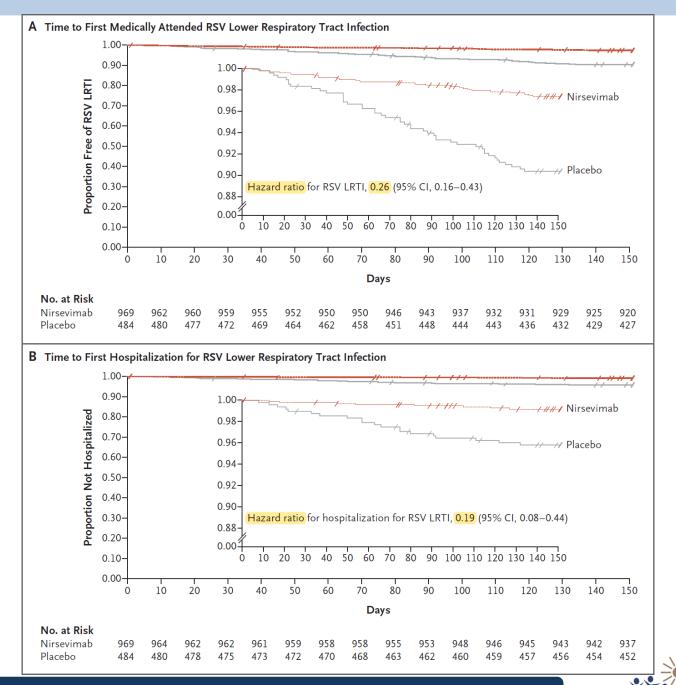
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#### Single-Dose Nirsevimab for Prevention of RSV in Preterm Infants

- Randomized placebo controlled clinical trial with 150 days of follow-up
- Included preterm healthy infants born at 29–34 weeks gestational age entering their first RSV season (N=1,453)
- Participants given a single 50 mg IM injection of nirsevimab or normal saline
- Adverse events were similar between treatment and placebo groups; no serious adverse events occurred that were related to nirsevimab
- Efficacy at preventing medically-attended RSV-associated LRTI: **70% lower in nirsevimab group** (2.6% in nirsevimab vs. 9.5% in placebo group)
- Efficacy at preventing hospitalization due to RSV-associated LRTI: 78% lower in nirsevimab group (0.8% in nirsevimab vs. 4.1% in placebo group)





Public Health Services

#### ORIGINAL ARTICLE

#### Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants

- Randomized placebo controlled clinical trial with 150 days of follow-up
- Included healthy infants born at 35+ weeks gestational age entering their first RSV season (N=1,490)
- Participants given a single 50 mg or 100 mg (based on weight) IM injection of nirsevimab or normal saline
- Adverse events were similar between treatment and placebo groups; no serious adverse events occurred that were related to nirsevimab
- Efficacy at preventing medically-attended RSV-associated LRTI: **74.5%** (1.2% in nirsevimab vs. 5.0% in placebo group)
- Efficacy at preventing hospitalization due to RSV-associated LRTI: 62% (0.6% in nirsevimab vs. 1.6% in placebo group); p=0.07
  - Pre-specific pooled analysis including preterm infants from earlier study showed an efficacy at preventing RSV-associated hospitalization of 77%

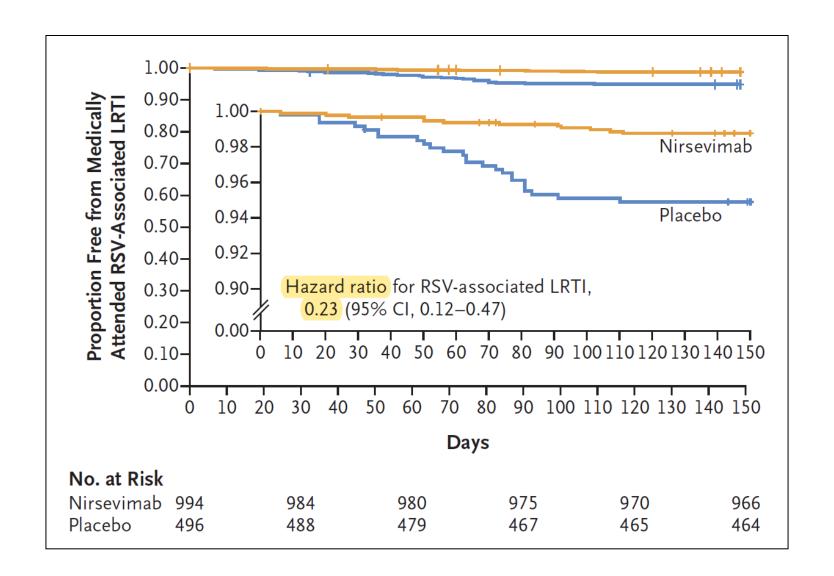


Table 3. Outcomes through 150 Days after the Injection.\* **Cases Averted** per 1000 Infants **Number Needed** Efficacy Nirsevimab Placebo Treated to Treat (N = 686)(N = 342)(95% CI)† (95% CI)± (95% CI) ( Outcome no. (%) 77.0 (59.8 to 86.8) 83.4 (62.0 to 105.0) 12 (10 to 17) Medically attended RSV-associated 17 (2.5) 37 (10.8) lower respiratory tract infection on any test result¶ Medically attended RSV-associated 77.2 (58.7 to 87.5) 74.7 (53.0 to 95.0) 14 (11 to 19) 15 (2.2) 33 (9.6) lower respiratory tract infection on central test result¶ Medically attended lower respiratory 60 (8.7) 93.6 (63.0 to 124.0) 11 (9 to 16) 62 (18.1) 51.5 (32.6 to 65.2) tract infection of any cause¶ Hospitalization for any respiratory ill-9 (1.3) 11 (3.2) 59.0 (2.1 to 82.9) 19.0 (5.5 to 32.0) 53 (32 to 182) ness due to RSV on any test result 62 (36 to 223) Hospitalization for any respiratory 7 (1.0) 9 (2.6) 61.1 (-3.7 to 85.4) 16.1 (4.5 to 28.0) illness due to RSV on central test

14 (4.1)

42.8 (-15.8 to 71.7) 17.7 (2.0 to 33.0)



57 (31 to 500)

16 (2.3)

result

Hospitalization for any respiratory ill-

ness of any cause

<sup>¶</sup> Included are medically attended lower respiratory tract infections, regardless of whether they met the criteria for the definition used for the primary end point.

# CDC/ACIP Updated Efficacy of Nirsevimab in Infants Entering Their 1st RSV Season

Outcome	Efficacy estimate*	Concerns in certainty of assessment
Benefits		
Medically attended RSV LRTI	79.0% (95% CI: 68.5%–86.1%)	None
RSV LRTI with hospitalization	80.6% (95% CI: 62.3%–90.1%)	None
RSV LRTI with ICU admission	90.0% (95% CI: 16.4%–98.8%)	Serious (imprecision): Too few events
Death due to RSV respiratory illness	None recorded	N/A
All-cause medically attended- LRTI	34.8% (95% CI: 23.0-44.7%)	None
All-cause LRTI-associated hospitalization	44.9% (95% CI:24.9%–59.6%)	None

<sup>\*</sup>Pooled phase 2b (excluding underdosed) and phase 3 trial estimate comparing nirsevimab arm to placebo arm



#### ACIP Unanimously Voted to Recommend:

- Infants aged <8 months born during or entering their first RSV season receive one dose of nirsevimab (50 mg for infants <5 kg and 100 mg for infants ≥5 kg)
- Children aged 8-19 months who are at increased risk of severe RSV disease and entering their second RSV season receive one dose of nirsevimab (200 mg)
  - Includes those recommended to receive palivizumab by the American Academy of Pediatrics (AAP), and American Indian and Alaska Native Children
  - See the AAP Red Book and their <u>Guidance for Palivizumab</u>



#### **Dosing and Administration**

- Intramuscular (IM) administration
- Neonates and infants born during or entering their 1<sup>st</sup> RSV season:
  - If body weight <5 kg: 50 mg IM in a single dose</li>
  - If body weight ≥5 kg: 100 mg IM in a single dose
- High-risk children entering their 2<sup>nd</sup> RSV season:
  - 200 mg IM once (2 x 100 mg injections)



#### **Most Common Side Effects**

- Rash (0.9%)
- Injection site reactions (0.3%)

#### Contraindications

- Do not give nirsevimab to infants and children with a history of serious hypersensitivity reactions (e.g., anaphylaxis) to nirsevimab or any of the ingredients (excipients), which include:
  - Nirsevimab-alip (monoclonal antibody)
  - Arginine hydrochloride
  - Histidine
  - L-histidine hydrochloride monohydrate
  - Polysorbate 80
  - Sucrose
  - Water



#### CDC's Preliminary Clinical Considerations

#### **Timing of nirsevimab**

- Providers should target administration¹:
  - In the first week of life for infants born shortly before and during the season
  - Shortly before the start of the RSV season for infants aged <8 months</li>
  - Shortly before the start of the RSV season for children aged 8–19 months who are at increased risk of severe RSV disease
- Based on pre-pandemic patterns, this means nirsevimab could be administered in most of the continental United States from October through the end of March
- Because timing of the onset, peak, and decline of RSV activity may vary, providers can adjust administration schedules based on local epidemiology



<sup>&</sup>lt;sup>1</sup> While optimal timing for nirsevimab administration is shortly before the season, nirsevimab may be given at any time during the RSV season for ageeligible infants and children who have not yet received a dose

#### CDC's Preliminary Clinical Considerations

## Timing of nirsevimab for infants born shortly before or during RSV season

- Nirsevimab should be administered within 1 week of birth.
  - Administration can be during the birth hospitalization or in the outpatient setting
- Infants with prolonged birth hospitalizations due to prematurity or other causes should receive nirsevimab shortly before or promptly after discharge

#### CDC's Preliminary Clinical Considerations

#### Coadministration with routine childhood vaccines

- In accordance with CDC's general best practices for immunizations, simultaneous administration of nirsevimab with age-appropriate vaccines is recommended
- In clinical trials, when nirsevimab was given concomitantly with routine childhood vaccines, the safety and reactogenicity profile of the coadministered regimen was similar to the childhood vaccines given alone<sup>1</sup>
- When coadministered, nirsevimab is not expected to interfere with the immune response to vaccines<sup>2</sup>

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<sup>1</sup>FDA label for nirsevimab; <sup>2</sup>Espocito Front Immunol. 2021 Aug 11;12:708939.



#### Reporting Adverse Events and Reactions

## Consumers and health care providers reporting suspected adverse reactions for nirsevimab

- Report suspect adverse reactions following the administration of nirsevimab without coadministration with any vaccine to MedWatch
  - Reports can be submitted to MedWatch online at www.fda.gov/medwatch or by phone at 1-800-FDA-1088
- Report suspect adverse reactions following co-administration of nirsevimab with any vaccine to the Vaccine Adverse Event Reporting System (VAERS)
  - Please specify that the patient received nirsevimab on the VAERS form, specifically, in Section 9: 'Prescriptions, over-the-counter medications, dietary supplements, or herbal remedies being taken at the time of vaccination'



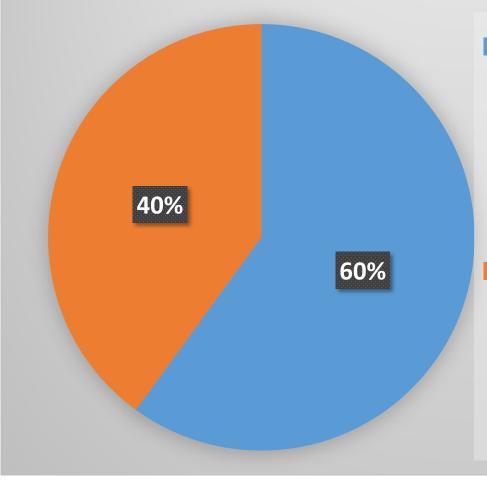
# Nirsevimab Added to the Vaccines For Children (VFC) Program





### NH Immunization Program

#### NH Universal Vaccine Purchasing, Children Birth Through 18 Years of Age



- NH Vaccine Association (NHVA) Reimbursement: Covers commercially insured children through Insurance Assessments
- Federal VFC Program: Covers VFC eligible children who are Medicaid, Uninsured, American Indian/Alaska Native, or Underinsured



## NH Immunization Program

Since Nirsevimab is a mAb and <u>not</u> a vaccine, it is not likely to be included in the RSA <u>Chapter 126-Q</u> definition of vaccines and NHVA insurance assessment for vaccine purchases.

If Nirsevimab can not be covered by the NHVA, then NH providers will need to privately purchase it for commercially insured children and will need to manage public and private inventories separately.





### Implementation Assumptions

## There is still much that is yet to be determined/confirmed...

- Timing/Availability:
  - Private Purchasing: Early to mid-September (pre-order possibly earlier)
  - NHIP VFC: Date available is TBD (Late fall?)
- Cost:
  - Public VFC \$395/dose
  - Private \$495/dose





#### Other TBD Considerations

- Inventory Management, Separate Private/Public stock
  - Borrowing between Private/Public inventory is not allowable
- Administration: outside MA Scope of Practice:
- Coding Challenges: NHIIS, EMR, Billing systems
- Reimbursement Mechanisms
- Provider/Patient Education & Resource Materials
  - Immunization Information
  - Reporting Adverse Events: FAERS (FDA) and VAERS (HHS) systems





#### Poll Question #1

How soon would your office be able to offer privately purchased nirsevimab for insured children?

- 0-2 months
- 2-4 months
- 4-6 months
- More than 6 months
- We do not immunize children of this age
- We do immunize children of this age, but will NOT offer privately purchased nirsevimab for insured children



#### **Poll Question #2**

How easy will it be for your office to privately purchase & manage separate nirsevimab inventories (private vs. VFC supplied)?

- Very easy
- Easy
- Neutral
- Difficult
- Very difficult
- I do not know (another team member handles this responsibility)
- N/A, my office will not be offering nirsevimab

Please enter barriers in the comments tab



## **Q&A** and Discussion



#### **RSV Vaccine for Adults 60+ Years Old**



#### **ACIP** Recommendations

 ACIP recommends that adults aged 60+ years of age may receive a single dose of an RSV vaccine using shared clinical decisionmaking (based on a discussion between the healthcare provider and patient) taking into account the patient's risk for severe RSV disease



# Medical Conditions and Factors Associated with Increased Risk for Severe RSV Disease

#### Chronic underlying medical conditions associated with increased risk

- Lung disease (such as chronic obstructive pulmonary disease and asthma)
- Cardiovascular diseases (such as congestive heart failure and coronary artery disease)
- Moderate or severe immune compromise\*
- Diabetes mellitus
- Neurologic or neuromuscular conditions
- Kidney disorders
- Liver disorders
- Hematologic disorders
- Other underlying conditions that a health care provider determines might increase the risk for severe respiratory disease

#### Other factors associated with increased risk

- Frailty<sup>†</sup>
- Advanced age<sup>§</sup>
- Residence in a nursing home or other long-term care facility
- Other underlying factors that a health care provider determines might increase the risk for severe respiratory disease



#### **ACIP** Recommendations

- ACIP recommends that adults aged 60+ years of age may receive a single dose of an RSV vaccine using shared clinical decisionmaking (based on a discussion between the healthcare provider and patient) taking into account the patient's risk for severe RSV disease
- Offer vaccination to adults aged ≥60 years as early as vaccine supply becomes available and continue to offer vaccination to eligible adults who remain unvaccinated
- Coadministration of RSV vaccines with other adult vaccines during the same visit is acceptable



## Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023

- GSK: 1-dose adjuvanted recombinant prefusion F-protein vaccine
- Pfizer: 1-dose (non-adjuvanted) recombinant prefusion F-protein vaccine
- GSK and Pfizer studies were not powered to estimate efficacy against hospitalization, severe RSV illness requiring respiratory support, or death

TABLE 1. Efficacy of 1 dose of GSK respiratory syncytial virus RSVpreF3 vaccine against respiratory syncytial virus—associated disease among adults aged ≥60 years — multiple countries, 2021–2023

	Vaccine efficacy against outcome*			
Efficacy evaluation period	RSV-associated LRTD <sup>†</sup>	RSV-associated medically attended LRTD§		
Season 1 <sup>¶</sup>	82.6 (57.9–94.1)**	87.5 (58.9–97.6)††		
Season 2 <sup>§§</sup>	56.1 (28.2-74.4) <sup>††</sup>	¶		
Combined seasons 1 and 2 (interim)***	74.5 (60.0–84.5)†††	77.5 (57.9–89.0)††		

**Abbreviations:** LRTD = lower respiratory tract disease; RSV = respiratory syncytial virus.

TABLE 3. Efficacy of 1 dose of Pfizer respiratory syncytial virus RSV preF vaccine against respiratory syncytial virus – associated disease among adults aged ≥60 years — multiple countries, 2021–2023

	Vaccine efficacy again	gainst outcome, % (95% CI)	
Efficacy evaluation period	RSV-associated LRTD <sup>†</sup>	RSV-associated medically attended LRTD <sup>§</sup>	
Season 1 <sup>¶</sup>	88.9 (53.6–98.7)	84.6 (32.0-98.3)	
Season 2 (interim)**	78.6 (23.2–96.1)	††	
Combined seasons 1 and 2 (interim) <sup>§§</sup>	84.4 (59.6–95.2)	81.0 (43.5–95.2)	

**Abbreviations:** LRTD = lower respiratory tract disease; LRTI = lower respiratory tract illness; RSV = respiratory syncytial virus.



TABLE 2. Safety\* of 1 dose of GSK respiratory syncytial virus RSVPreF3 vaccine in adults aged ≥60 years — multiple countries, 2021–2023

	Risk for event			
Safety event	RSVPreF3 recipients no./No. (%) <sup>†</sup>	Placebo recipients no./No. (%)§	Relative risk (95% CI)¶	
Serious AE**	549/12,570 (4.4)	540/12,604 (4.3)	1.02 (0.91–1.15)	
Severe reactogenicity events <sup>††</sup>	37/979 ( <mark>3.8</mark> )	9/976 ( <mark>0.9</mark> )	4.10 (1.99–8.45)	
Inflammatory neurologic events <sup>§§</sup>	<mark>3 events</mark> in trials without placebo recipients <sup>¶¶</sup>	¶	111	
<b>Abbreviations:</b> AE = adverse event; GBS = Guillain-Barré syndrome.				

TABLE 4. Safety\* of 1 dose of Pfizer respiratory syncytial virus RSVpreF vaccine in adults aged ≥60 years — multiple countries, 2021–2023

1		Risk for event			
Safety event	RSVpreF recipients no./No. (%) <sup>†</sup>	Placebo recipients no./No. (%) <sup>§</sup>	Relative risk (95% CI)¶		
Serious AE**	792/18619 (4.3%)	749/18334 (4.1%)	1.04 (0.94–1.15)		
Severe reactogenicity events <sup>††</sup>	36/3673 (1.0%)	24/3491 (0.7%)	1.43 (0.85–2.39)		
Inflammatory neurologic events <sup>§§</sup>	<mark>3</mark> /18622 (—) <sup>¶¶</sup>	0/18335 (—)	¶¶		

**Abbreviations:** AE = adverse events; GBS = Guillain-Barré syndrome.



#### Rare Adverse Events Requiring Further Study

- Inflammatory neurological events
  - GSK clinical trial 3 episodes in vaccine group (without a control/placebo comparator group), including 1 case of GBS and 2 cases of ADEM
  - Pfizer clinical trial 3 events in vaccine group, including 1 case of GBS, 1 case of Miller Fisher syndrome (GBS variant), and 1 case of a worsening undifferentiated motor-sensory axonal polyneuropathy
- Atrial fibrillation (within 30 days):
  - GSK clinical trial 10 events (0.1%) in vaccine group vs. 4 events (<0.1%) in control group (not all events were new-onset A-fib)
  - Pfizer clinical trial 10 events (<0.1%) in vaccine group vs. 4 events (<0.1%) in control group (not all events were new-onset A-fib)</li>



#### Follow-up Study Planned

- Both GSK and Pfizer planning on conducting post-marketing study evaluating the risk for inflammatory neurologic conditions (e.g. GBS) and atrial fibrillation
  - 6 cases of inflammatory neurological events reported after RSV vaccination in clinical trials (out of 30,000+ vaccine recipients) – unclear if these occurred by chance, or if RSV vaccination might increase the risk for inflammatory neurologic events
  - A small number of episodes of Atrial Fibrillation occurred after vaccination, many of which were NOT new-onset



#### ORIGINAL ARTICLE

#### Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults

- Phase 3 randomized placebo-controlled clinical trial for the GSK adjuvanted RSV prefusion F-protein vaccine in adults 60+ years of age
- Report safety and vaccine efficacy (VE) for 1<sup>st</sup> RSV season;
   following for 3 consecutive seasons (N=24,966 participants)
- VE at preventing RSV-related:
  - Lower respiratory tract disease (LRTD): 83% (7 vs. 40 cases)
  - Severe LRTD: **94%** (1 vs. 17 cases)
  - Acute respiratory infection: 72% (27 vs. 95 cases)



#### Local and Systemic Side Effects

Event	RSVPreF3 OA Group		Placebo Group	
	Participants	Incidence (95% CI)	Participants	Incidence (95% CI)
	no.	%	no.	%
Solicited safety population	879		878	
Solicited reactions				
Any solicited reaction	632	71.9 (68.8–74.9)	245	27.9 (25.0–31.0)
Any grade 3 solicited reaction	36	4.1 (2.9–5.6)	8	0.9 (0.4–1.8)
Solicited injection-site reactions				
Pain	535	60.9 (57.5–64.1)	81†	9.3 (7.4–11.4)
Erythema	66	7.5 (5.9–9.5)	7†	0.8 (0.3–1.6)
Swelling	48	5.5 (4.1–7.2)	5†	0.6 (0.2–1.3)
Solicited systemic reactions				
Fever‡	18	2.0 (1.2–3.2)	3	0.3 (0.1–1.0)
Headache	239	27.2 (24.3–30.3)	111	12.6 (10.5–15.0)
Fatigue	295	33.6 (30.4–36.8)	141	16.1 (13.7–18.7)
Myalgia	254	28.9 (25.9–32.0)	72	8.2 (6.5–10.2)
Arthralgia	159	18.1 (15.6–20.8)	56	6.4 (4.9–8.2)



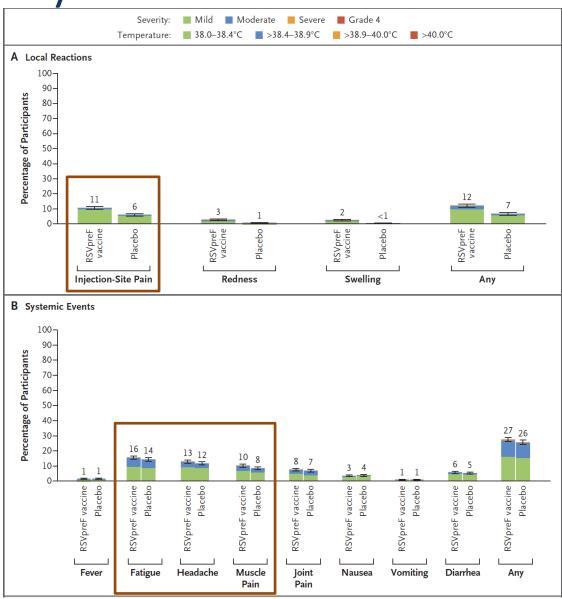
#### ORIGINAL ARTICLE

## Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults

- Phase 3 randomized placebo-controlled clinical trial for the Pfizer (non-adjuvanted) RSV prefusion F-protein vaccine in adults 60+ years of age
- Report safety and vaccine efficacy (VE) for 1<sup>st</sup> RSV season; following for multiple seasons (N=34,284 participants)
- VE at preventing RSV-related:
  - Lower respiratory tract illness with 2+ signs/symptoms: 67% (11 vs. 33 cases)
  - Lower respiratory tract illness with 3+ signs/symptoms: 86% (2 vs. 14 cases)
  - Acute respiratory illness: 62% (22 vs. 58 cases)



#### Local and Systemic Side Effects





#### **ACIP** Recommendations

 Adults aged 60+ years of age may receive a single dose of an RSV vaccine using shared clinical decision-making taking into account the patient's risk for severe RSV disease

#### Chronic underlying medical conditions associated with increased risk

- Lung disease (such as chronic obstructive pulmonary disease and asthma)
- Cardiovascular diseases (such as congestive heart failure and coronary artery disease)
- Moderate or severe immune compromise\*
- Diabetes mellitus
- Neurologic or neuromuscular conditions
- Kidney disorders
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- Other underlying conditions that a health care provider determines might increase the risk for severe respiratory disease

#### Other factors associated with increased risk

- Frailty<sup>†</sup>
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## **Q&A** and Discussion



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