MISSOURI PQC
Perinatal Quality Collaborative

Updates on RSV Immunizations for Infants and Pregnant People

Missouri Hospital Association

IN PARTNERSHIP WITH THE MHA MISSOURI HOSPITAL ASSOCIATION

Abrysvo and Nirsevimab for the prevention of severe RSV infection

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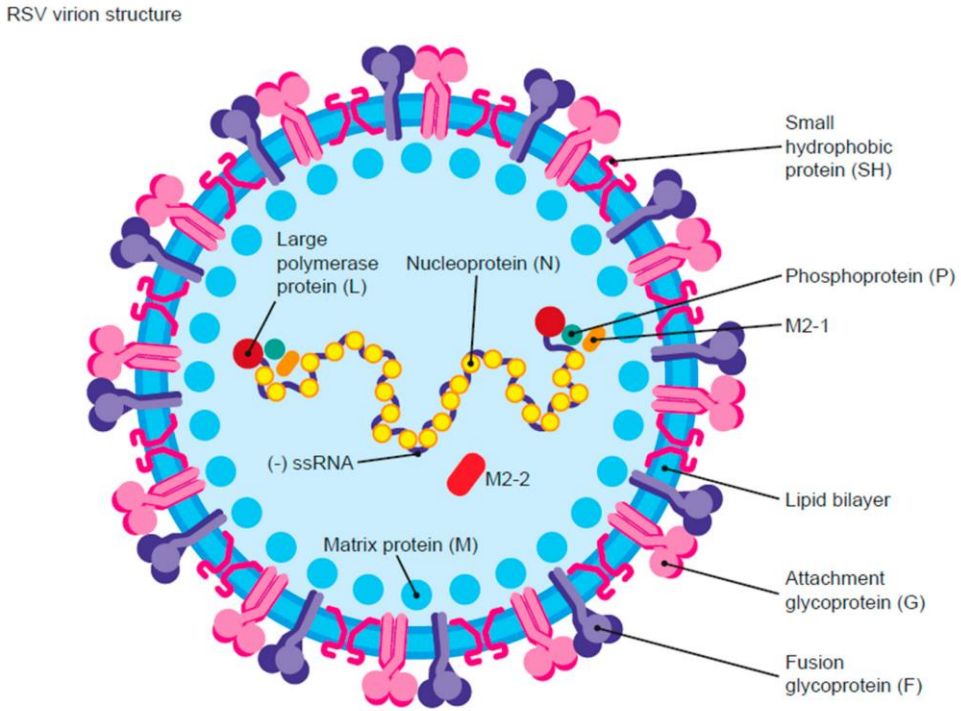
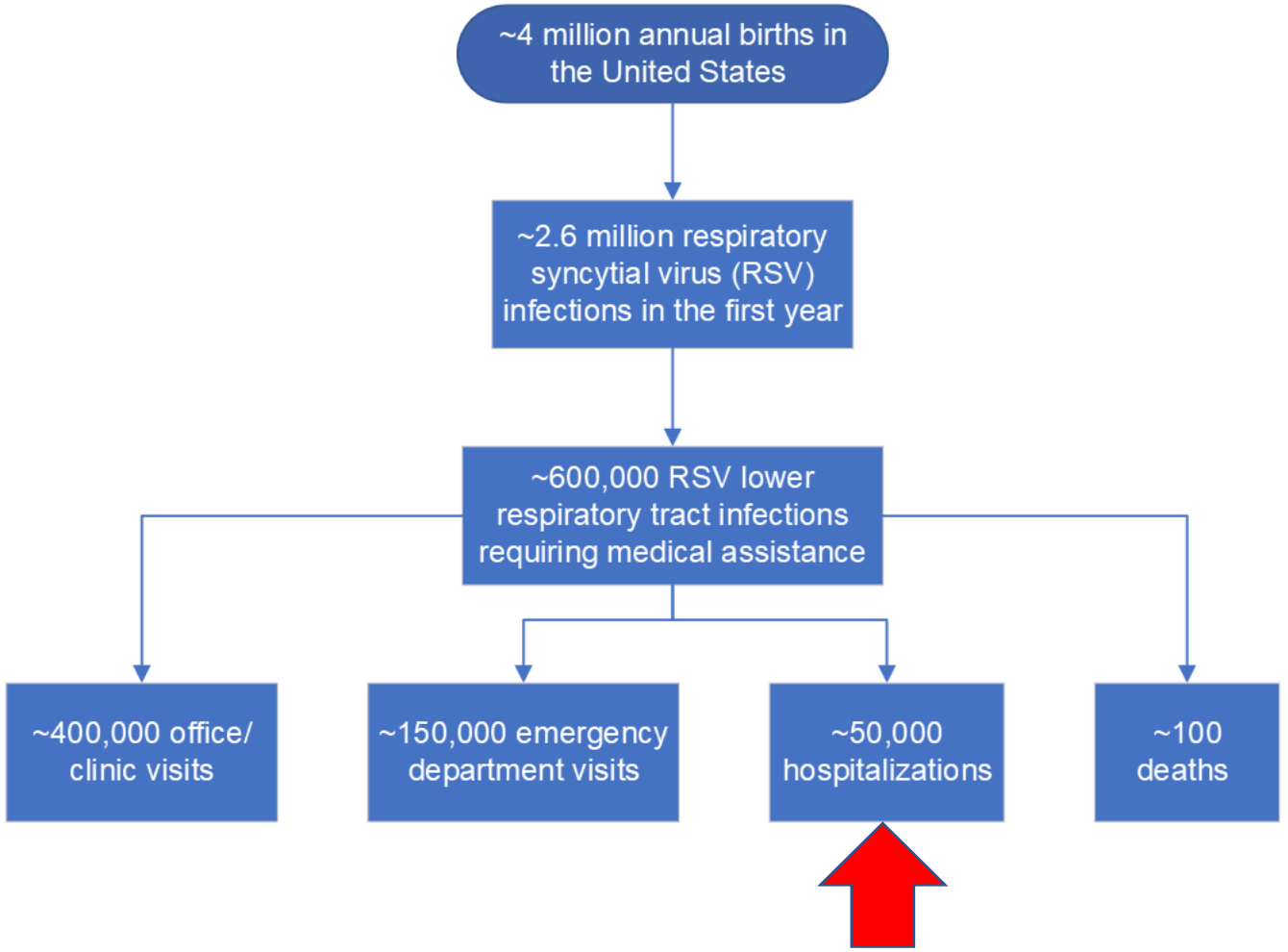




80% of hospitalizations occur in term infants with no past medical history

https://www.cdc.gov/rsv/research/

Palivizumab in <= 35 weeks GA or BPD (N=1502)

TABLE 2. Summary of Analysis of RSV Hospitalization

	Placebo	Palivizumab	% Reduction (95% CI)	*P* Value
Primary analysis (incidence of RSV hospitalizations)*	53/500 (10.6%)	48/1002 (4.8%)	55% (38, 72)	<.001
Alternative analysis (Kaplan-Meier†)	53/500 (10.6%)	48/1002 (4.8%)	55% (38, 72)	<.001
Sensitivity analyses				
Dropout before 150 days and no endpoint‡	53/500 (10.6%)	49/1002 (4.9%)	55% (38, 72)	<.001
Respiratory hospitalization but no RSV test done§	56/500 (11.2%)	54/1002 (5.4%)	52% (35, 69)	<.001
Primary inclusion populations				
Premature (no BPD)	19/234 (8.1%)	9/506 (1.8%)	78% (66, 90)	<.001
BPD	34/266 (12.8%)	39/496 (7.9%)	39% (20, 58)	.038

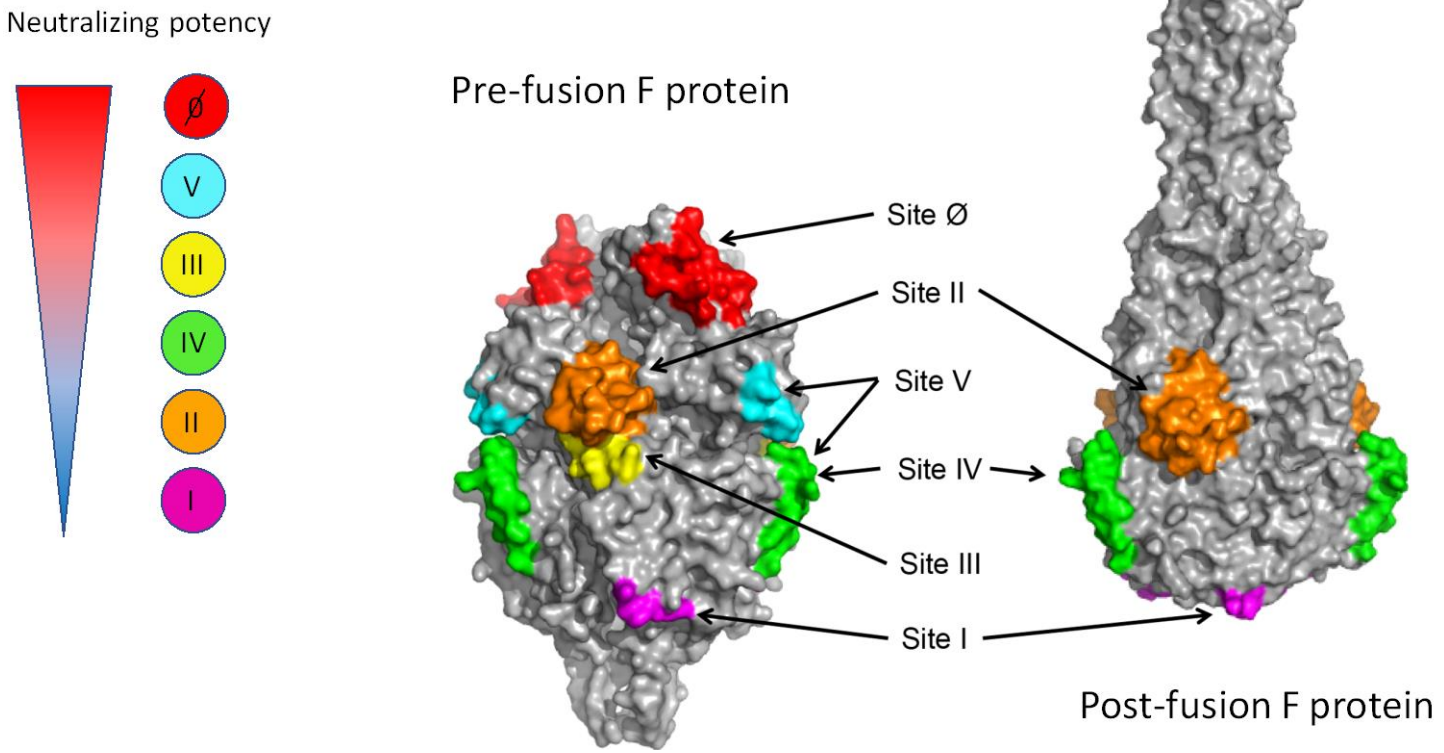
- Fewer days of hospitalization (-0.33 days, p<0.001)
- Fewer ICU admissions (3% vs. 1.3%, p = 0.026)

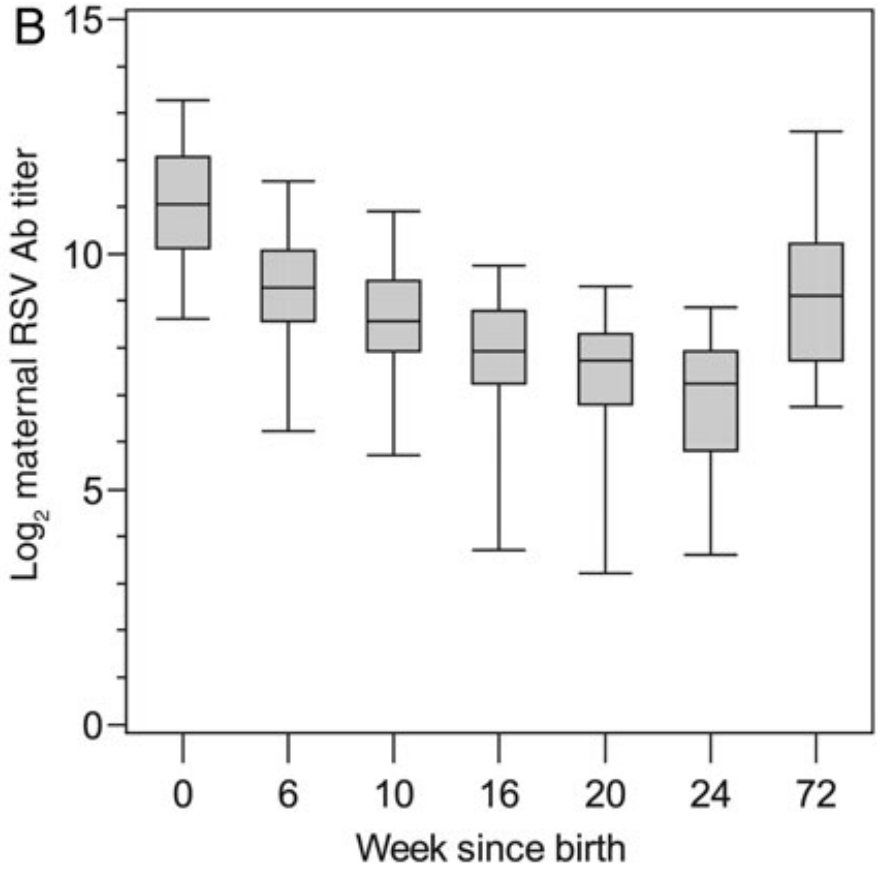
- NNT to prevent one hospitalization = 17

$3,400 per vial;
$20,000 per course

Impact-RSV Study Group. Pediatrics 1998; 102: 531-7.

Abrysvo (FDA approved 8/21/2023)





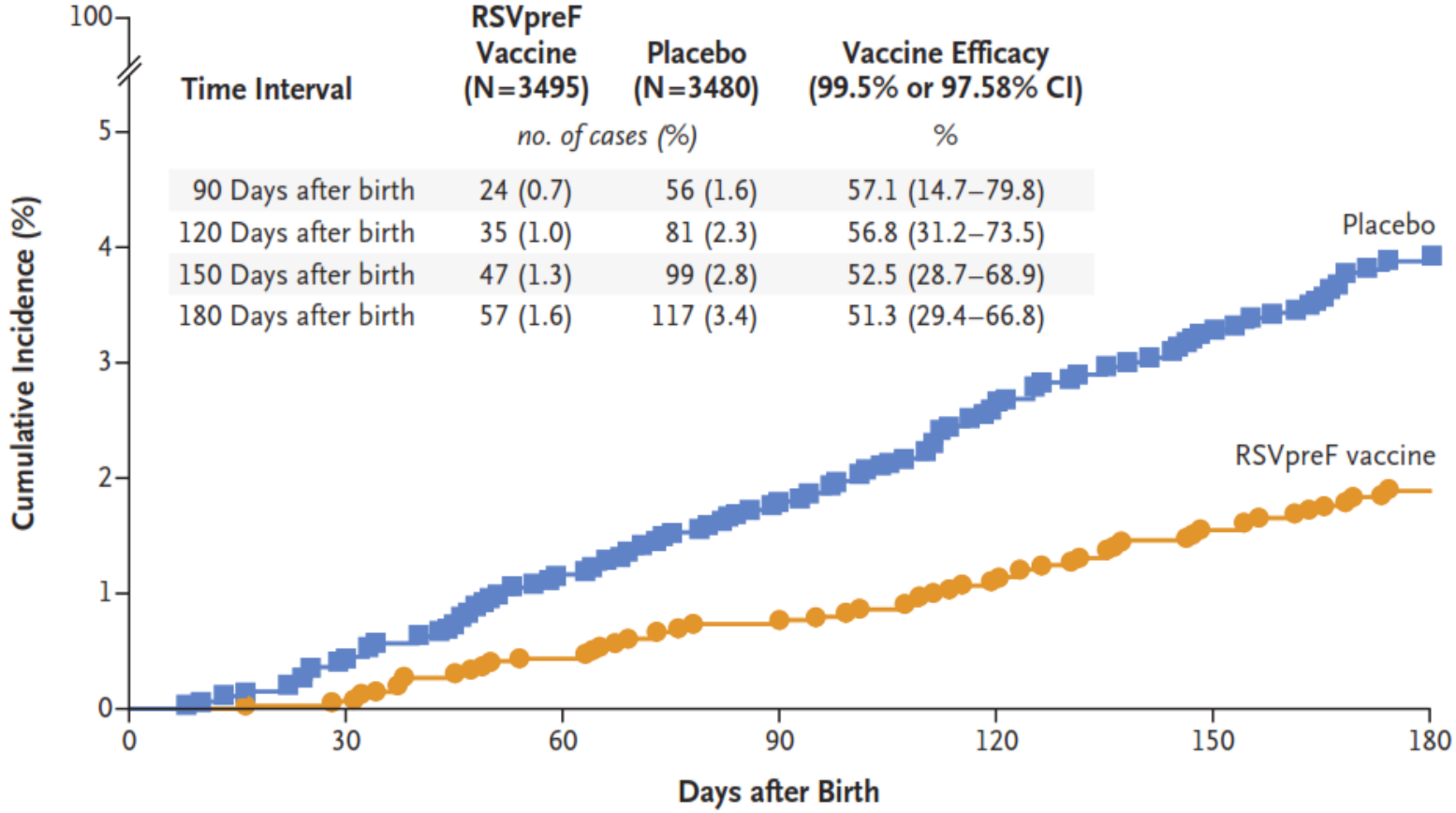
Bivalent vaccine to target RSV A and RSV B subtypes.

Chu et al. J Infect Dis 2014; 210: 1582-9.

Abrysvo decreases clinic and ED visits

B **Medically Attended RSV-Associated Lower Respiratory Tract Illness**

Time Interval	RSVpreF Vaccine (N=3495)	Placebo (N=3480)	Vaccine Efficacy (99.5% or 97.58% CI)
	no. of cases (%)		%
90 Days after birth	24 (0.7)	56 (1.6)	57.1 (14.7–79.8)
120 Days after birth	35 (1.0)	81 (2.3)	56.8 (31.2–73.5)
150 Days after birth	47 (1.3)	99 (2.8)	52.5 (28.7–68.9)
180 Days after birth	57 (1.6)	117 (3.4)	51.3 (29.4–66.8)



No. at Risk							
Placebo	3480	3288	2964	2879	2804	2738	2700
RSVpreF vaccine	3495	3348	3035	2968	2898	2845	2792

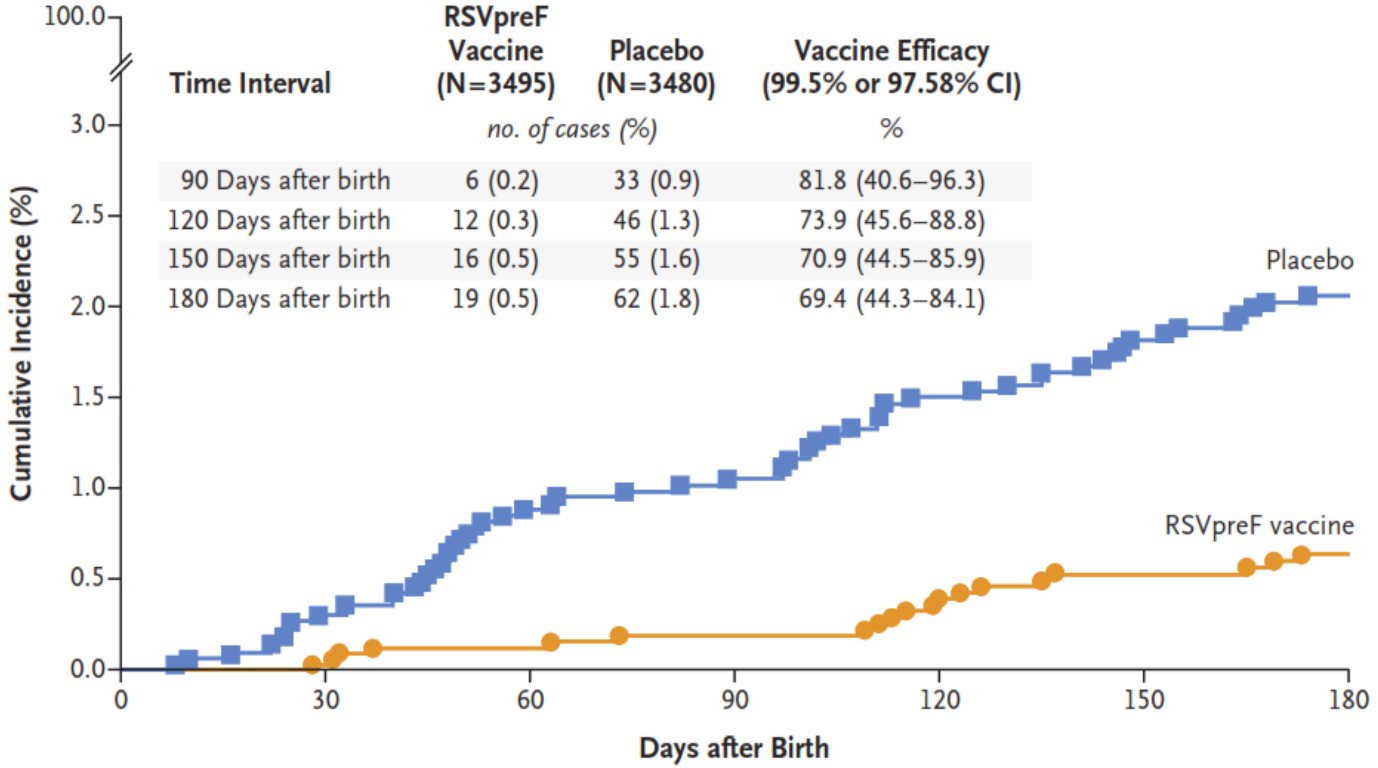
- Number needed to treat = 56

Kampmann et al. N Engl J Med 2023; 388: 1451-64.

Abrysvo reduces the risk of severe disease*

A Medically Attended Severe RSV-Associated Lower Respiratory Tract Illness

Time Interval	RSVpreF Vaccine (N=3495)	Placebo (N=3480)	Vaccine Efficacy (99.5% or 97.58% CI)
	no. of cases (%)		%
90 Days after birth	6 (0.2)	33 (0.9)	81.8 (40.6–96.3)
120 Days after birth	12 (0.3)	46 (1.3)	73.9 (45.6–88.8)
150 Days after birth	16 (0.5)	55 (1.6)	70.9 (44.5–85.9)
180 Days after birth	19 (0.5)	62 (1.8)	69.4 (44.3–84.1)



No. at Risk							
Placebo	3480	3292	2973	2899	2833	2776	2749
RSVpreF vaccine	3495	3349	3042	2981	2916	2867	2820

- Number needed to treat = 77

*Severe defined as tachypnea, hypoxia, requiring respiratory support, ICU admission, or unconscious

Kampmann et al. N Engl J Med 2023; 388: 1451-64.

Abrysvo safety

- Mild injection site pain (36% vs. 9%), mild redness (5% vs. 0%), swelling (6% vs. 0%), and mild muscle pain (18% vs. 10%) are relatively common

- Preterm birth – smoke or fire?
  - No different in 3,682 patient international phase 3 RCT (5.7% vs. 4.7%)
  - Numerically different in phase 2 trial (6/114 versus 3/116)
  - Arexvy pregnancy trial halted early (N=5,328; 6.8% vs. 5%)
    - Driven by differences in South Africa

Kampmann et al. N Engl J Med 2023; 388: 1451-64.

ACIP recommendations (9/22/2023)

- Administer between 32 and 36 weeks gestation to all pregnant women from September through January (may adjust based on local seasonality)

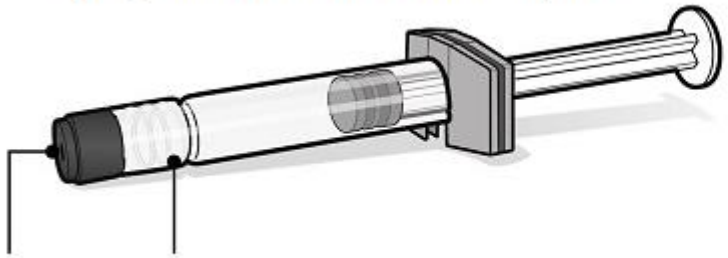
Fleming-Dutra et al. MMWR 2023; 72: 1115-1122.

Package insert specifics

- Follow preparation instructions in kit

Vial of Lyophilized Antigen Component

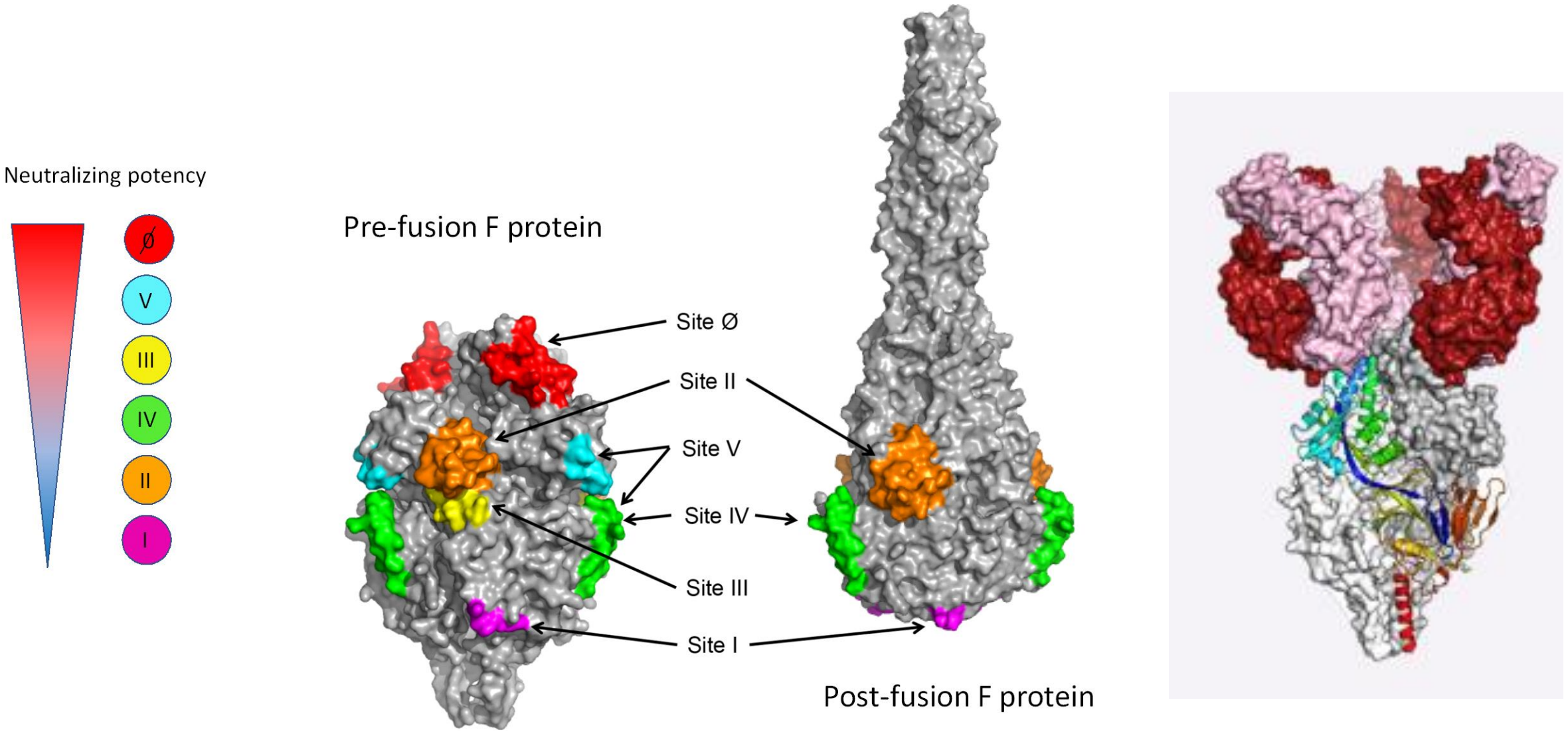
Syringe of Sterile Water Diluent Component



Vial Adapter

- Use within 4 hours of reconstitution
- Flat dose for all – 120 mcg = 0.5 mL
- Preservative free
  - Polysorbate 80 (0.08 mg per 0.5 mL) as an emulsifier
    - 72 mg/kg/day associated with toxicity in preterm neonates
    - Conservative threshold for exposure proposed as 1.4 mg/day in neonates

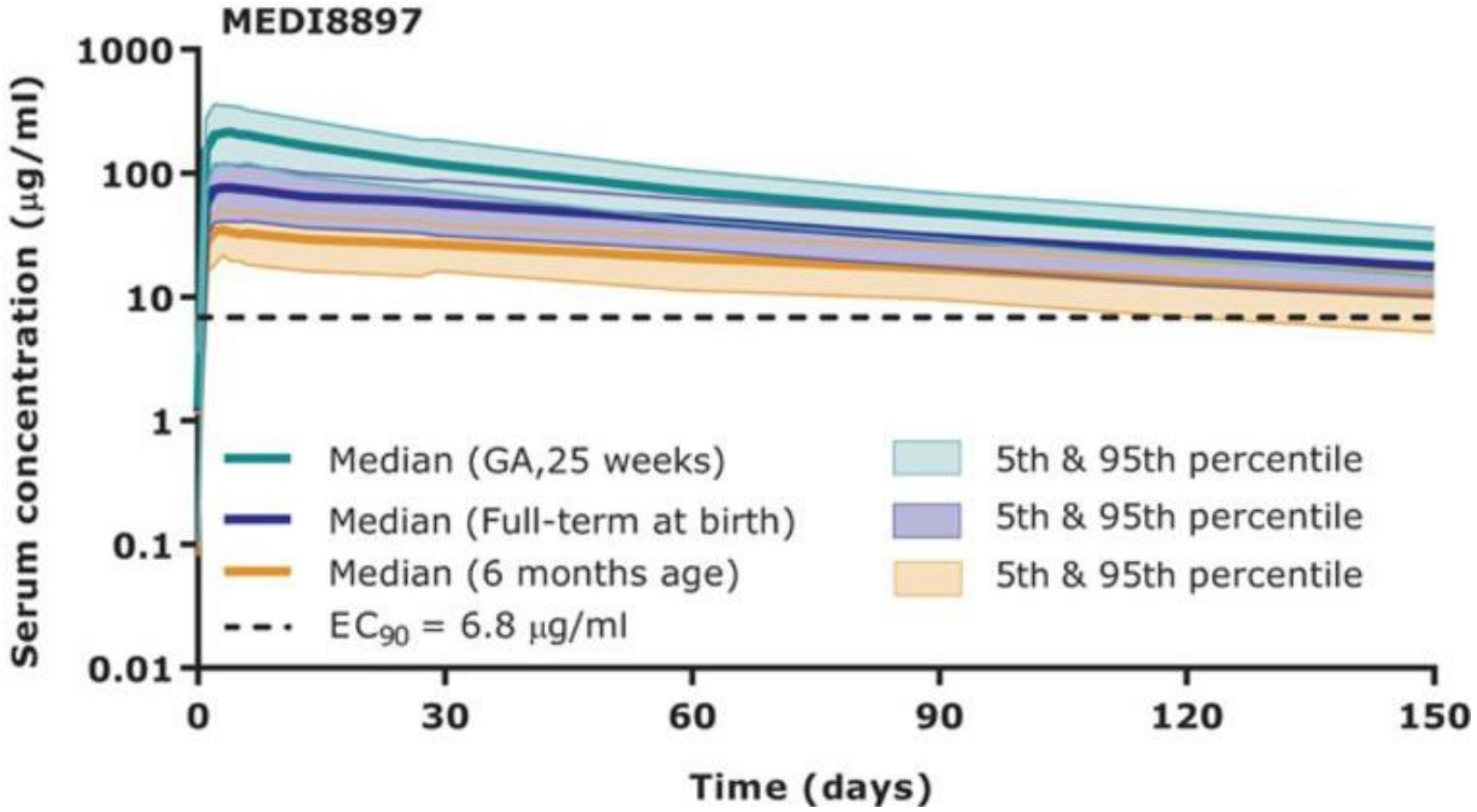
Nirsevimab (FDA approved 7/17/2023)



Zhu et al. Sci Transl Med 2017; 9: eaaj1928.

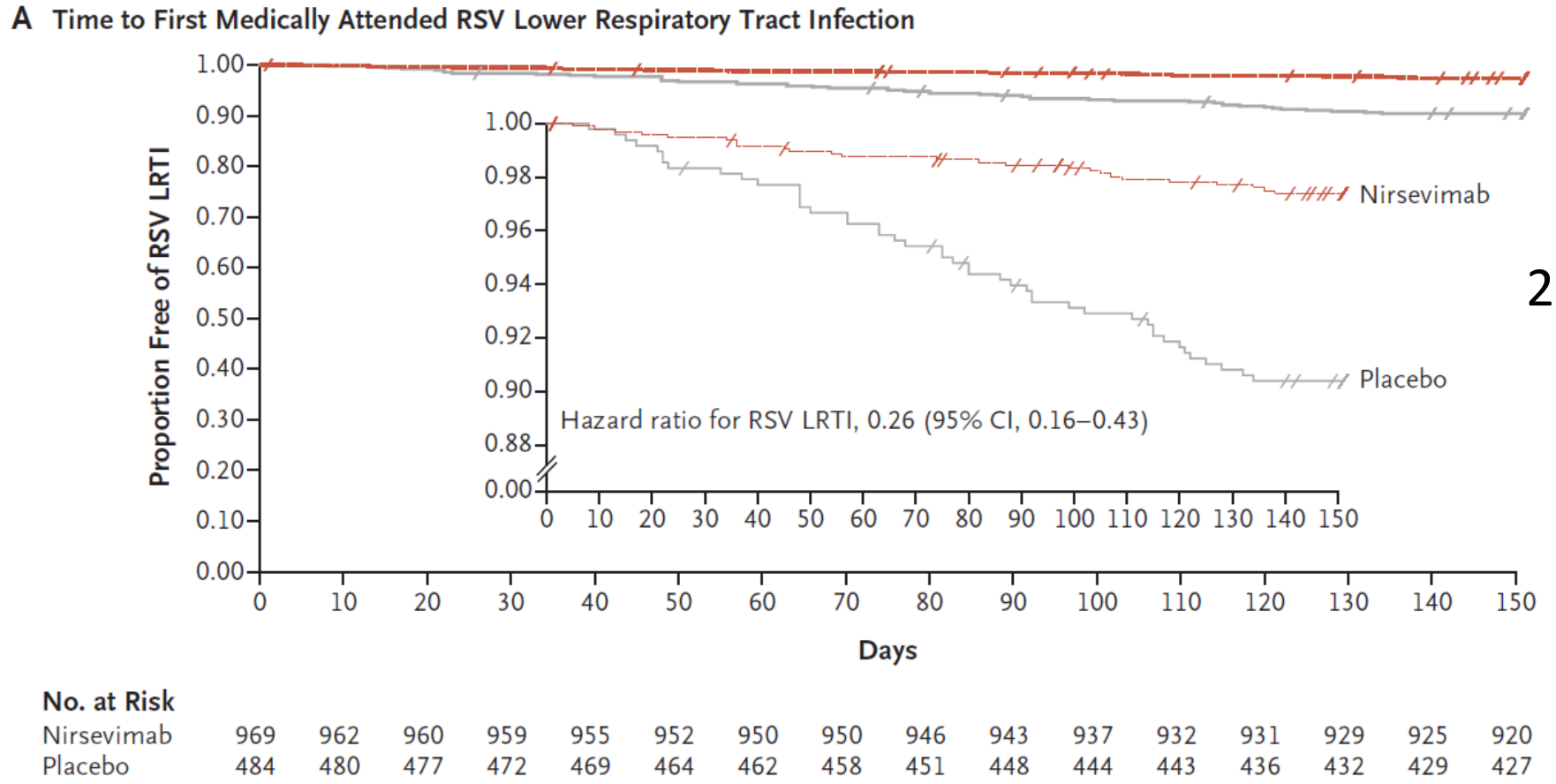
Nirsevimab

- Modified Fc region to extend half-life
  - M252Y/S254T/T256E enhances binding in the acidic environment of the neonatal lysosome, increasing recycling and reducing degradation in the serum



Zhu et al. Sci Transl Med 2017; 9: eaaj1928.

Nirsevimab decreases clinic and ED visits

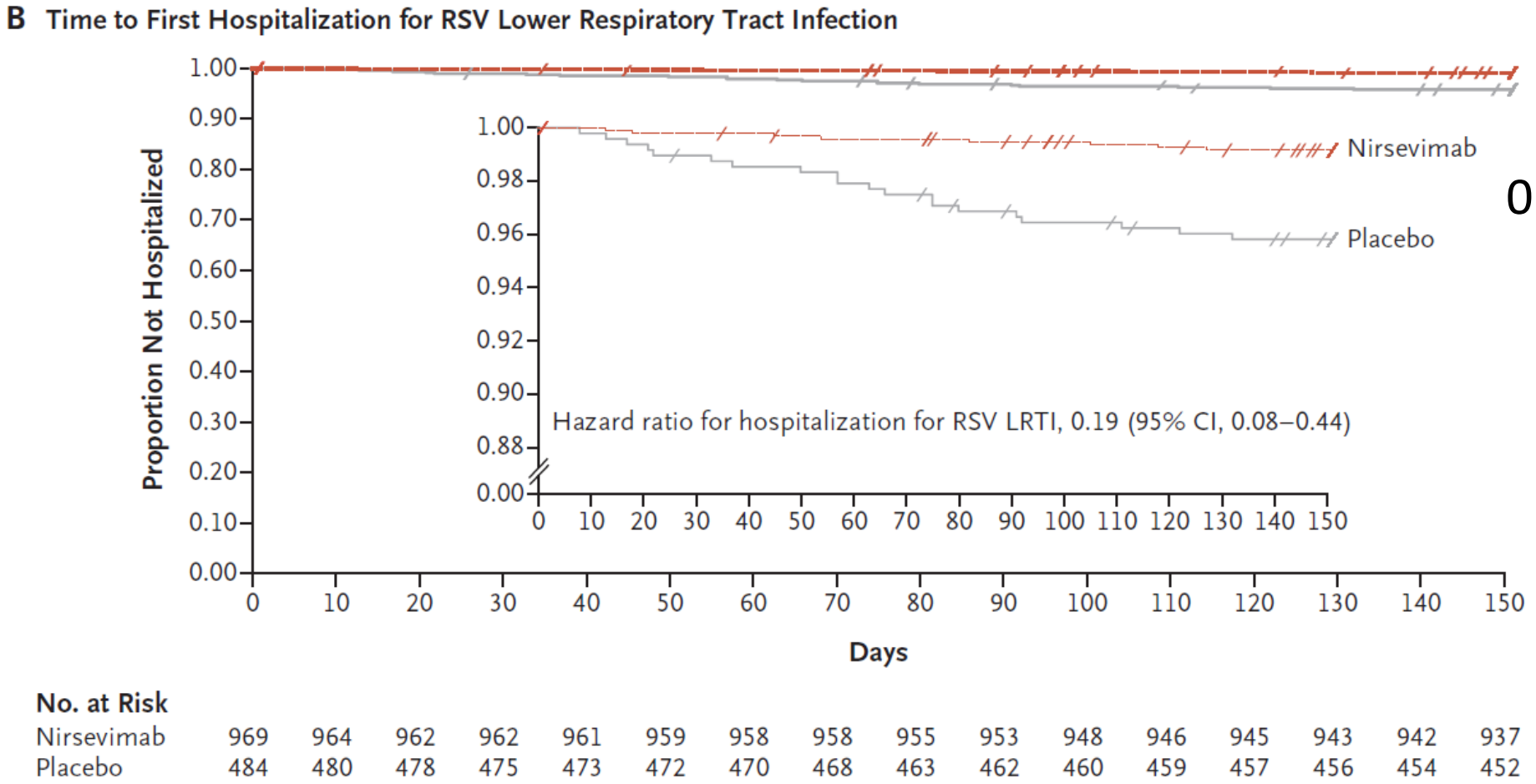


2.6% vs. 9.5%

- NNT to prevent one inpatient or outpatient visit = 14 - 24

Griffin et al. N Engl J Med 2020; 383: 415-25.
Hammitt et al. N Engl J Med 2022; 386: 837-46.
Muller et al. N Engl J Med 2023; 388: 1533-34.

Nirsevimab decreases hospitalizations



0.8% vs. 4.1%

- NNT to prevent one hospitalization = 33 - 63

Griffin et al. N Engl J Med 2020; 383: 415-25.
Hammitt et al. N Engl J Med 2022; 386: 837-46.
Muller et al. N Engl J Med 2023; 388: 1533-34.

Nirsevimab safety

Table 2 Adverse Reactions Reported at an Incidence Higher Than Placebo in the Safety Population* (Trials 03 and 04)

Adverse Reaction	BEYFORTUS N=2,570 %	Placebo N=1,284 %
Rash† (occurring within 14 days post-dose)	0.9	0.6
Injection site reaction† (occurring within 7 days post-dose)	0.3	0

Number needed to harm = 333

Griffin et al. N Engl J Med 2020; 383: 415-25.
Hammitt et al. N Engl J Med 2022; 386: 837-46.
Muller et al. N Engl J Med 2023; 388: 1533-34.

ACIP recommendation (8/3/2023)

- Born February to September 2023 → give nirsevimab October 1st
- Born October 2023 to March 2024 → give nirsevimab in the first week of life or, if hospitalized after birth, shortly before or promptly after discharge
  - May adjust start time based on local epidemiology

- 2nd season → 8-19 months old with chronic lung disease of prematurity who required medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) any time during the 6-month period before the start of the second RSV season
  - Safe in second season (NEJM 2022; 386: 892-894); waiting on outcome data

- Included in childhood immunization schedule and Vaccines for Children program

Proposed Jones. ACIP Meeting Feb 2023.
Unanimously adopted Jones. ACIP Meeting August 2023.
Jones et al. MMWR 2023; 72: 920-925.

Package insert specifics

- Preservative free
  - Polysorbate 80 (0.1 mg per 0.5 mL) as an emulsifier
    - 72 mg/kg/day associated with toxicity in preterm neonates
    - Conservative threshold for exposure proposed as 1.4 mg/day in neonates

- Flat dosing in commercial sizes (< 5 kg = 50 mg; ≥ 5 kg = 100 mg; second season = 2 x 100 mg)

- Different injection site from vaccines (same leg as HBIG, if required)

Nirsevimab guidance considering Abrysvo

- Give nirsevimab if…
  - No Abrysvo
  - Abrysvo < 14 days prior to birth
  - Maternal immunocompromise or HIV
  - Infant cardiopulmonary bypass
  - Infant significant CHD
  - Infant ICU admission and home oxygen

Fleming-Dutra et al. MMWR 2023; 72: 1115-1122.

Equity

- 39% of Missouri infants miss at least one well-child visit in the first year of life. 12% of Missouri infants have a gap of at least one year in well child visits. 27% of Missouri infants have not received all recommended immunizations by age 2.

- Neonates are 13% less likely to receive immunizations outpatient compared to inpatient
  - NNH = 12

- African American infants 1% less likely to complete hepatitis B series, but 8% less likely to complete childhood immunization series
  - NNH = 20

- African American infants 36% more likely to be hospitalized for RSV

Nation Survey of Children's Health, US DHHS HRSA MCHB
Gomez et al. J Infect Dis 2022; 226: S293-99.
https://stacks.cdc.gov/view/cdc/59414
Rha et al. Pediatrics 2020; 146: e20193611.

Abrysvo logistics

- Cost - $295
  - Contract prices as low as $252
- Inpatient
  - DRG modification?
- Outpatient
  - Covered by VFC and Medicaid; waiting for policy updates from privates
- Requires refrigeration prior to reconstitution
- Required to provide VIS, but not yet updated for pregnancy
  - https://www.cdc.gov/vaccines/hcp/vis/vis-statements/rsv.pdf

Nirsevimab Logistics

- Cost - $495
  - Contract prices as low as $445
- Inpatient
  - VFC enrollment?, DRG modification?
- Outpatient
  - Covered by VFC; covered by UHC, Aetna, Anthem, Tricare.
- Storage – requires refrigeration
- Consent – required in Missouri; IIS now available
  - https://www.cdc.gov/vaccines/vpd/rsv/downloads/Immunization-Information-Statement.pdf

Questions

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Links to additional resources

- Digital and link to print – 2023 Respiratory Virus Infection Vaccine Recommendations for Hospitals and Health Care Providers: https://web.mhanet.com/media-library/2023-rvi-vaccine-recommendations-for-hospitals-and-health-care-providers/
- Digital and link to print – 2023 Respiratory Virus Infection Vaccine Recommendations for the Public: https://web.mhanet.com/media-library/2023-rvi-vaccine-recommendations-for-the-public/
- Other helpful links:
  - CDC Talking to Patients About Vaccine Safety: https://www.cdc.gov/vaccinesafety/hcproviders/talkingtopatients.html
  - CDC Recommendations for RSV Immunizations: https://www.cdc.gov/vaccines/vpd/rsv/index.html

AAP: Nirsevimab Implementation Guide: https://downloads.aap.org/AAP/PDF/Nirsevimab_Implementation_Guide_FINAL.pdf

IIS: https://www.cdc.gov/vaccines/vpd/rsv/immunization-information-statement.html