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RSVPreF3 Vaccine for Respiratory Syncytial Virus (RSV) in Older Adults

March 1, 2023

Vaccines and Related Biological Products Advisory Committee

GSK plc.

Introduction

Bishoy Rizkalla, PhD

Vice President & Global Medical Affairs Lead

Respiratory Vaccines

GSK

Agenda

Introduction	**Bishoy Rizkalla, PhD** Vice President & Global Medical Affairs Lead GSK
Burden of Respiratory Disease in Older Adult Populations	**Ann Falsey, MD** Professor of Medicine University of Rochester, NY
Efficacy & Immunogenicity	**Bishoy Rizkalla, PhD** Vice President & Global Medical Affairs Lead GSK
Safety / Benefit-Risk	**Peggy Webster, MD, MBA** Vice President & Head of Vaccine Safety GSK

About RSV and GSK's RSVPreF3 Older Adult (OA) Candidate Vaccine

RSV Infection represents significant health threat for OAs

Currently no vaccine available

Single dose

High level of protection from broad spectrum of RSV-A and RSV-B associated diseases

Well tolerated with acceptable safety profile

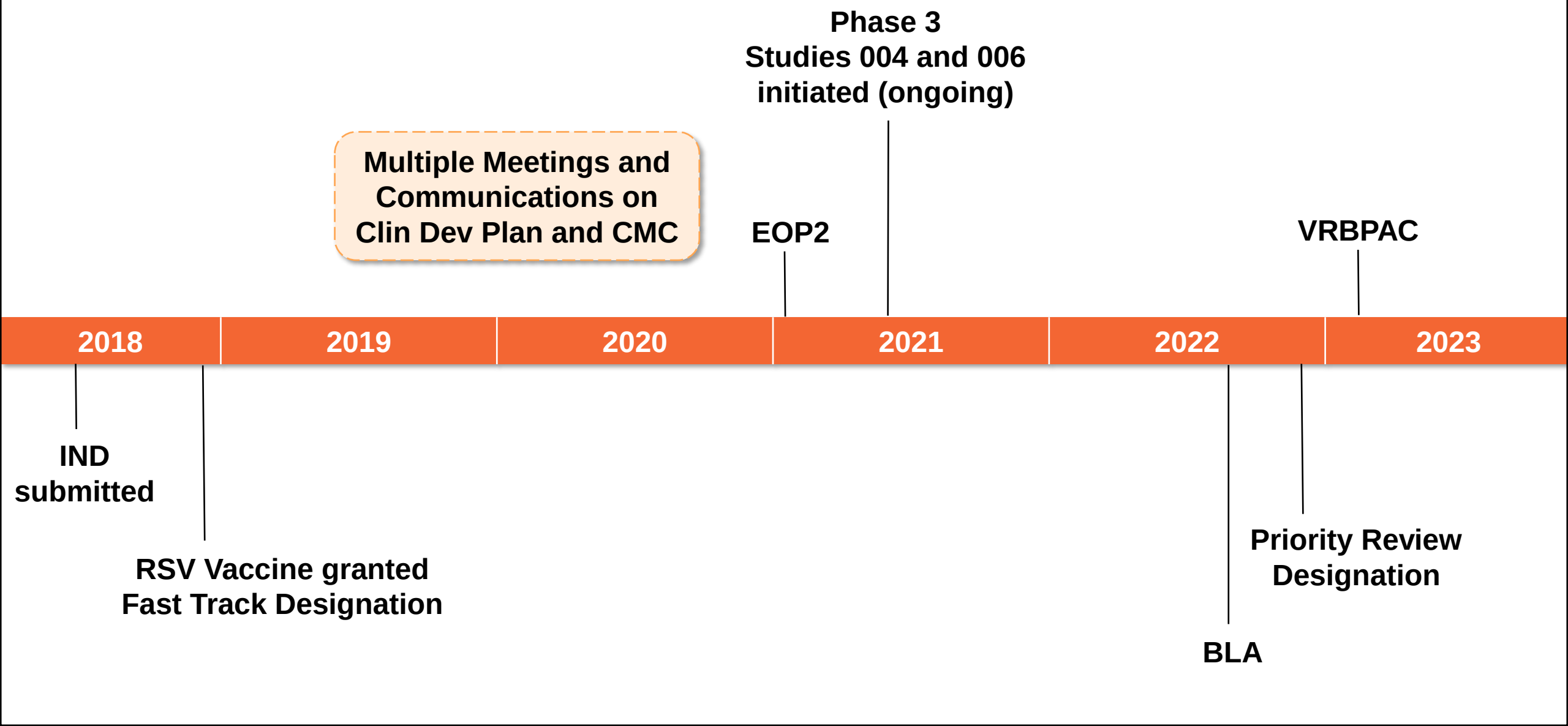
RSV OA Vaccine Proposed Indication, Dosing, and Administration

- Proposed indication
  - Active immunization for the prevention of lower respiratory tract disease (LRTD) caused by RSV-A and RSV-B subtypes in adults ≥ 60 YOA

- Proposed administration and dosage
  - Single IM administration of 120 µg RSVPreF3 adjuvanted with $AS01_E$

YOA: Years of age; IM: intramuscular; RSV: Respiratory syncytial virus; PreF: Prefusion

RSV Vaccine Regulatory Timeline



RSV Vaccine Clinical Program Supporting BLA

Phase 1/2
(Adults 18-40 YOA and older adults 60-80 YOA)

Study 002
Dose and formulation selection

Phase 3
(Older adults ≥ 60 YOA)

Study 006
Pivotal efficacy, immunogenicity, and safety

Study 004
Immunogenicity and safety

Study 007
Co-administration with FLU-QIV

Study 009
Lot-to-lot consistency

Clinical Program Supports Efficacy and Safety of RSV Vaccine

- Efficacy of 82.6% in prevention of RSV LRTD in adults ≥ 60 YOA
- Consistent protection regardless of
  - RSV disease severity
  - Advancing age
  - Comorbidities of interest
  - RSV-A and RSV-B subtypes
- Well tolerated with acceptable safety profile

Burden of Respiratory Disease in Older Adult Populations

Ann Falsey, MD

Professor of Medicine

University of Rochester, NY

Epidemiology of RSV

- RSV is highly contagious human pathogen that causes yearly epidemics during winter season in temperate climates
- RSV has 2 major subtypes, A and B, which may co-circulate
- RSV infection does not confer long-term immunity
  - Reinfection with RSV occurs throughout life and common in all ages[1,2]
  - Adult symptoms range from mild colds to pneumonia and respiratory failure
- Major groups at risk for severe disease
  - Young children
  - Older adults
  - Adults with comorbid conditions

1.Simoes,1999; 2. Krilov, 2011

Infection Rates/100 Persons Per Season

	4 Seasons 1999-2003[1] N = 1849 (375-551)	2 Seasons 2017-2019[2] N = 1040 (513-527)
RSV	**5.5** (3.2 – 7.7)	**5.7** (4.2 – 7.2)
Influenza A	**2.4** (1.1 – 4.3)	**3.0** (2.7 – 3.3)
Influenza B	**1.0** (0 – 2.2)	**2.8** (0 – 5.5)

- Using PCR + serology for diagnosis – 10% asymptomatic
- Conservative estimate of symptomatic infection – 3-4% per year

1. Falsey et al., 2005; 2. Korsten et al., 2021

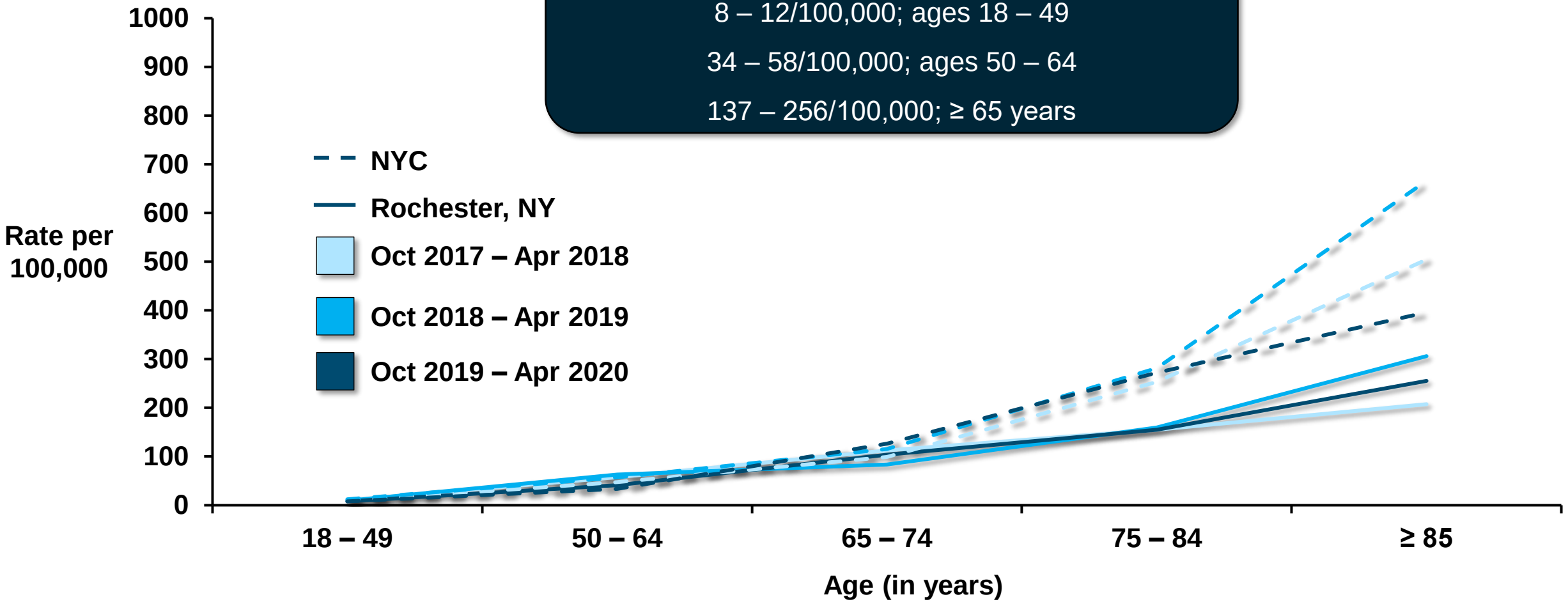
Adult RSV Hospitalization Rates in Upstate and NYC

Age-group specific incidence ranged from

8 – 12/100,000; ages 18 – 49

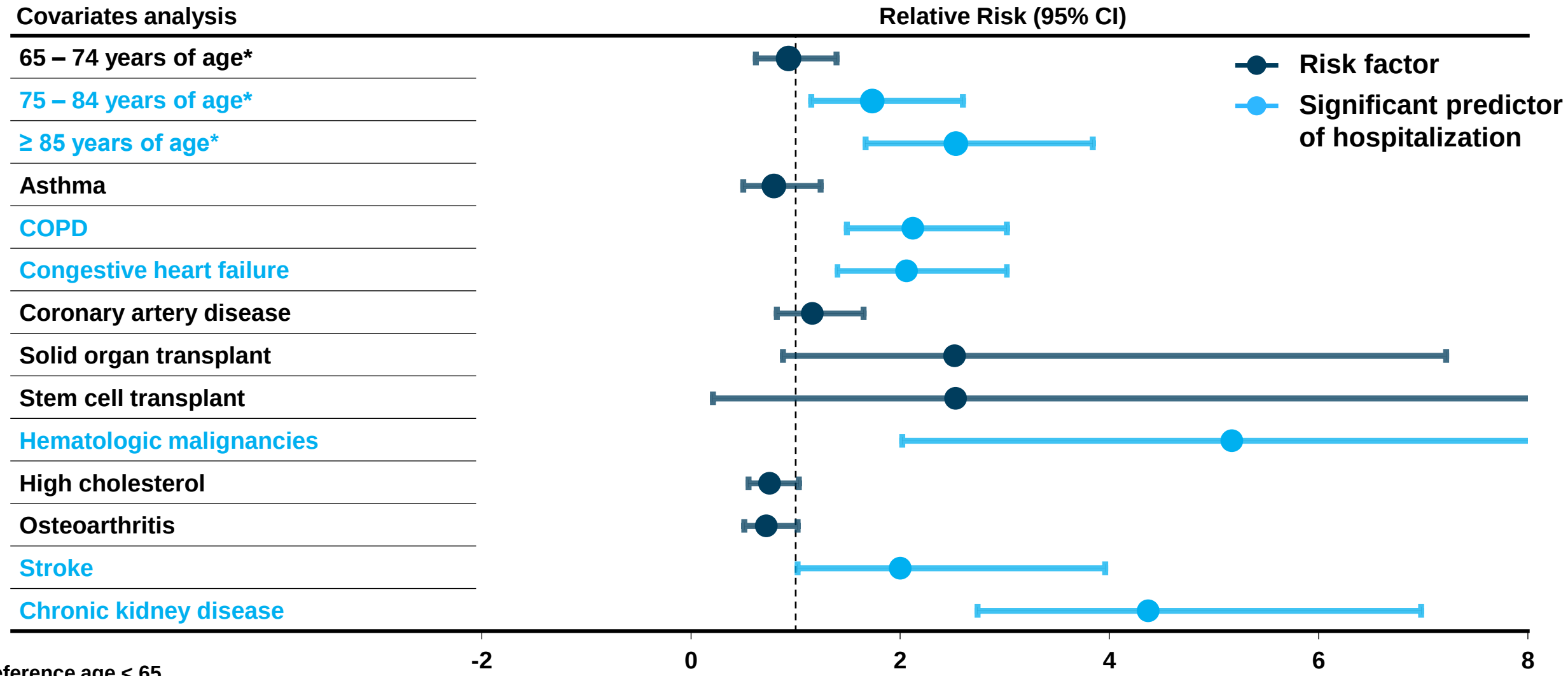
34 – 58/100,000; ages 50 – 64

137 – 256/100,000; ≥ 65 years



Adapted from Branche AR et al., 2022

Age and Comorbidities Increase Risk of Hospitalization Among Older Adults Who Develop RSV



*Reference age < 65

Wyffels, 2020

RSV Disease and Medically Attended Illness

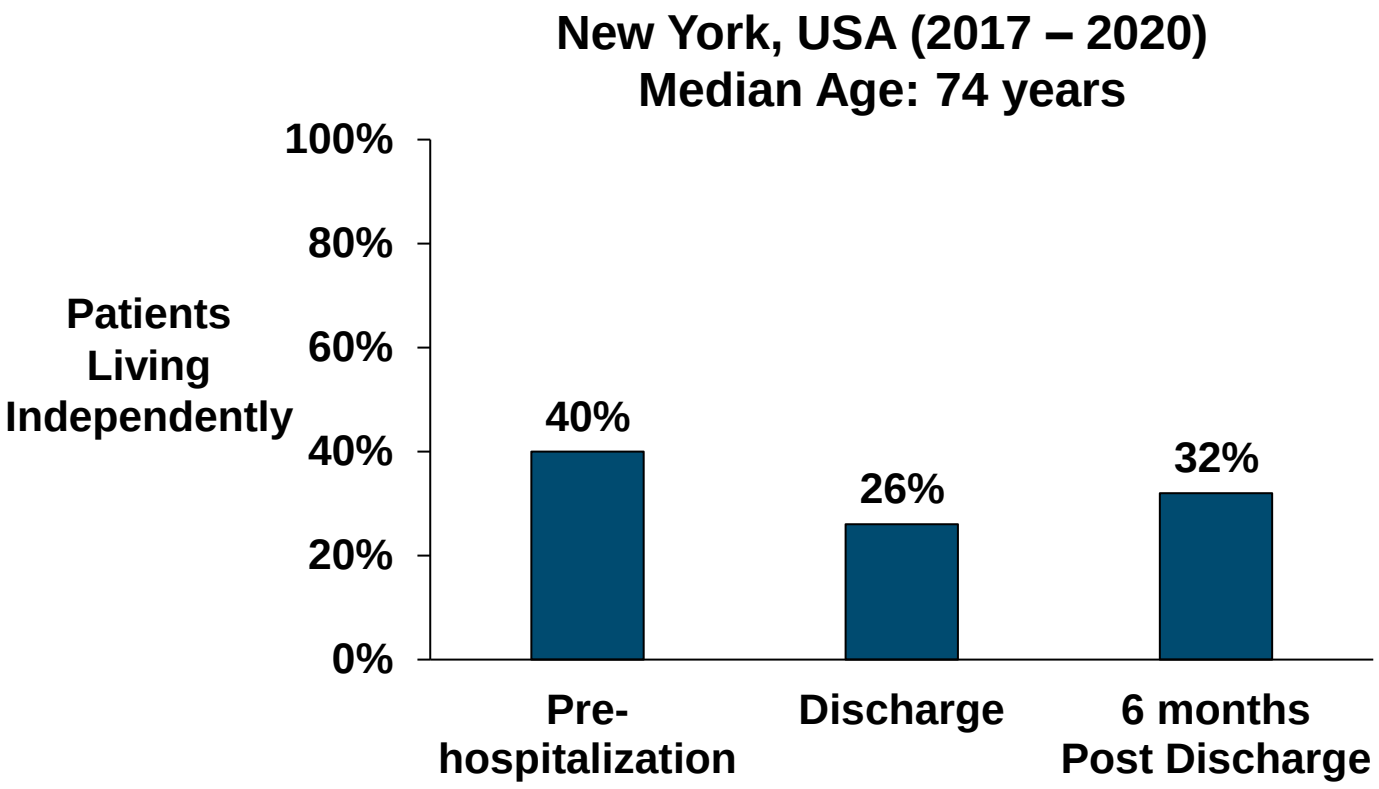
Medically Attended RSV Infection in Community Cohort of Adults ≥ 50 Years Old

	Seasonal Incidence / 1000 (95% CI)
Overall	**15.4** (13.2, 18.0)
Season	
06-07	**11.0** (7.5, 16.1)
07-08	**17.9** (13.2, 24.4)
08-09	**16.6** (12.5, 22.1)
09-10	**15.9** (12.2, 20.8)
Age Group, years	
50-59	**12.4** (9.9, 15.6)
60-69	**14.7** (11.0, 19.6)
> 70	**19.9** (15.3, 25.8)

6% of those with outpatient visits progressed to hospitalization

McClure et al., 2014

Considerable Long-Term Impact of Hospitalizations on Functional Status and Health



14% had loss of independence at discharge after hospitalization following RSV infection[1]

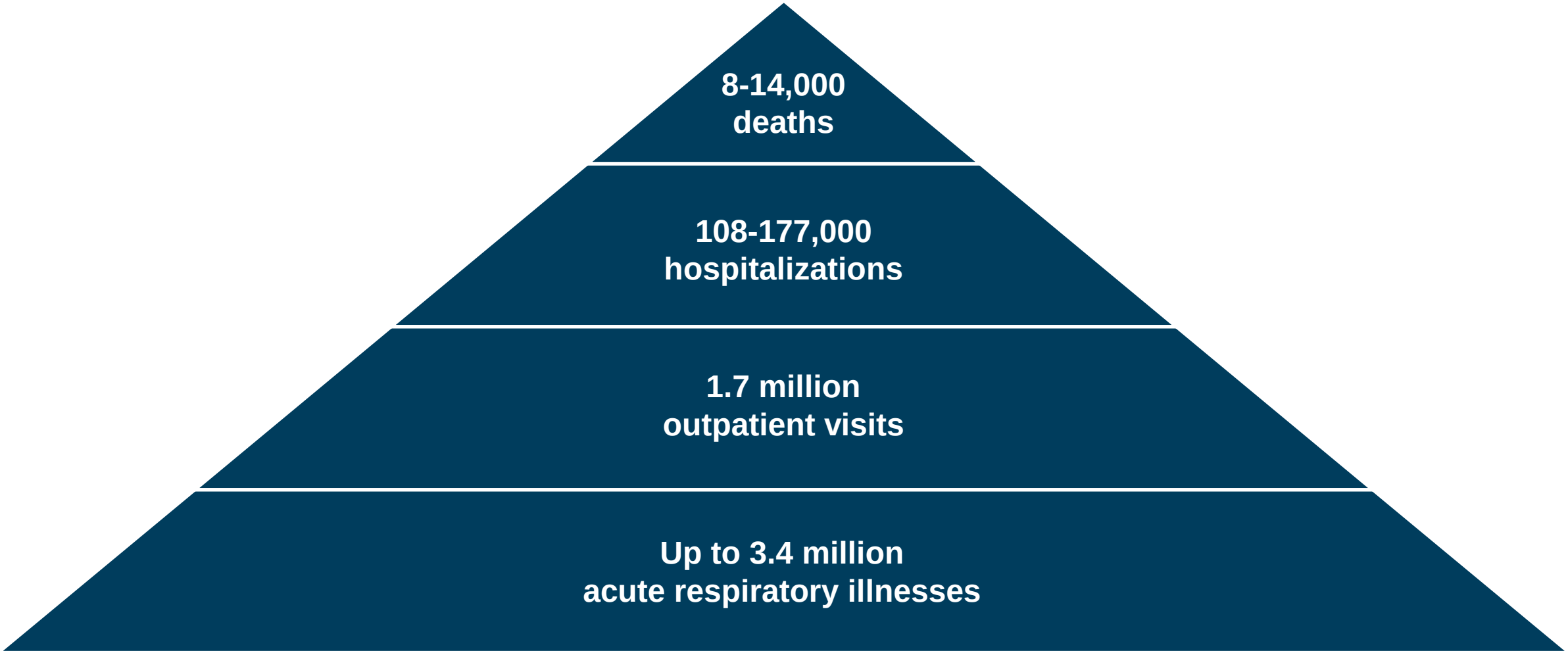
8% reported ongoing loss of independence 6 months after hospitalization following RSV infection[1]

Data accumulating that RSV leads to decompensation of heart failure, arrhythmia, and thromboembolic events similar to influenza[2,3]

Graphs independently created for GSK from original data

1. Branche A et al., 2022; 2. Falsey et al., 2005; 3. Volling, et al., 2014

Annual US Burden of Disease in OAs ≥ 60 Years of Age



1. Falsey, 2005; 2. Korsten, 2021; 3. McClure, 2014; 4. Savic & Penders, 2022; 5. Branche, 2022

Unmet Need Summary

- RSV is frequent cause of respiratory tract disease in adults
- Older age and underlying medical conditions are risks for severe disease
- RSV-positive ARI in OAs associated with significant long-term lower QoL
- Adult RSV results in high burden on healthcare system
- Just beginning to understand the substantial non-respiratory impact of adult RSV with functional loss and cardiovascular complications
- Effective treatment for RSV infections not available
- Prevention with effective vaccine may be highly impactful

Efficacy & Immunogenicity

Bishoy Rizkalla, PhD

Vice President & Global Medical Affairs Lead

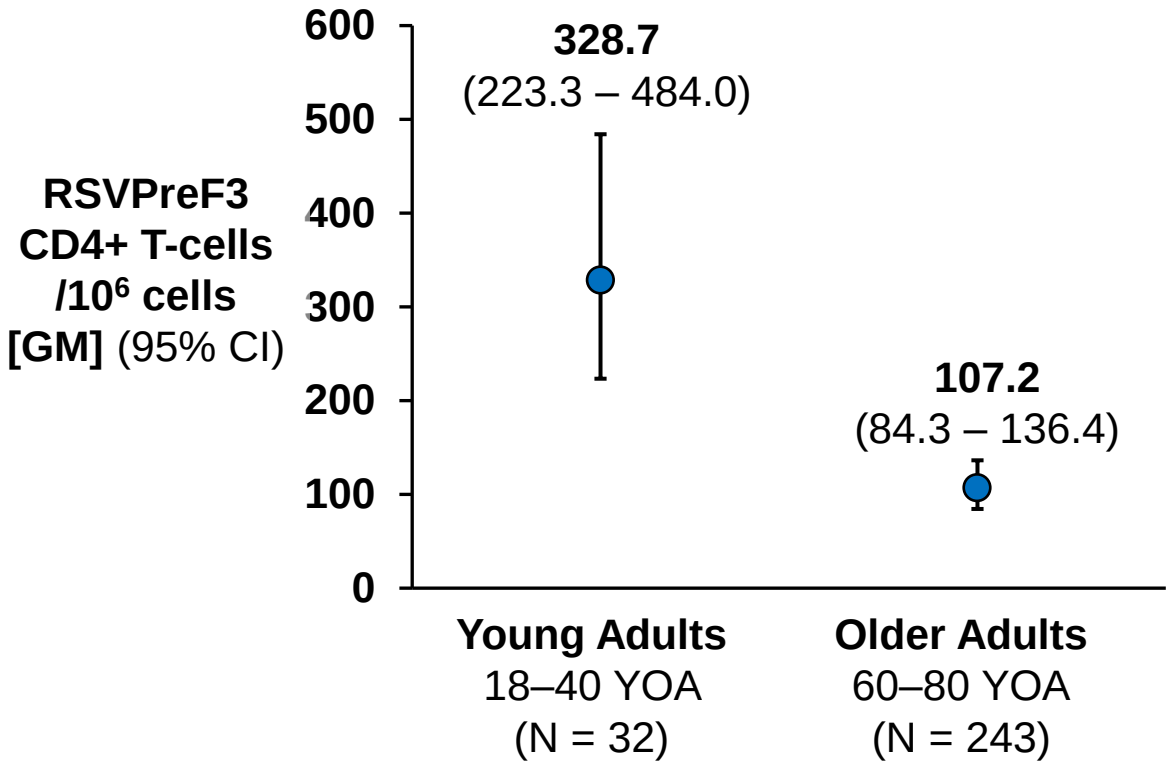
Respiratory Vaccines

GSK

Age-Related Decline in Immunity and Challenges in Protecting OAs Against Severe RSV Disease

- Quality and quantity of immune cells diminishes with older age[1]
- RSV F protein-specific T-cell responses shown deficient in OAs vs younger individuals[2,3]
- Age-related decline in RSV-specific T-cell and NAb responses may be associated with higher risk of RSV disease severity[1,2]

Baseline RSV-Specific Cellular Immune Response[3]

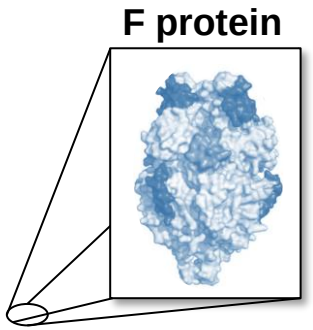


Lower levels in OAs vs young adults

Graph independently created for GSK from original data
CD = cluster of differentiation; GM = geometric mean

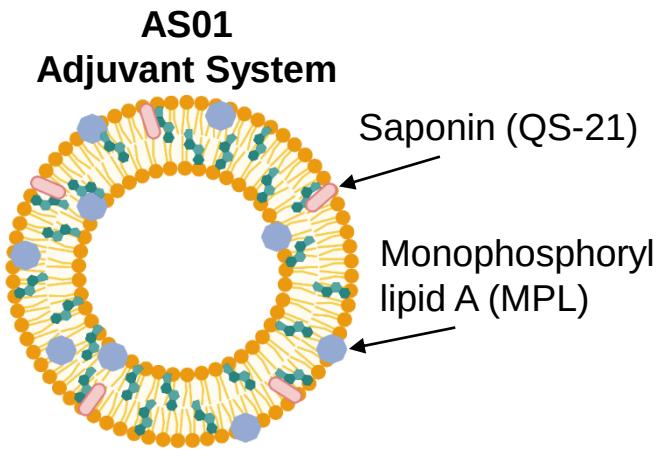
1. Stephens LM and Varga SM, 2021; 2. Cherukuri A et al., 2013; 3. Leroux-Roels I et al., 2022

RSV Vaccine: 120 µg RSVPreF3 + AS01$_E$ Adjuvant Formulation Selected for Phase 3 Development



RSV OA Vaccine

RSV PreF3 Antigen (120µg) + **AS01$_E$ Adjuvant System**



- High serum neutralization titers for RSV-A and RSV-B
- High polyfunctional RSVPreF3 specific CD4+ T-cell responses in OAs approaching levels seen in young adults following vaccination
- Th1 dominant response
- Well tolerated with acceptable safety profile

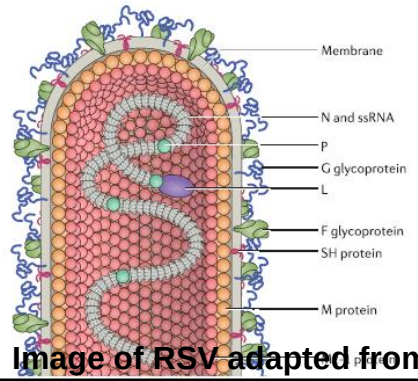


Image of RSV adapted from Battles & McLellan, 2019; image of PreF protein adapted from Joyce et al., 2019; image of AS01 created by GSK using BIORENDER.com

Efficacy & Immunogenicity

RSV Vaccine Clinical Development Program

Phase 1/2
(Adults 18-40 YOA and older adults 60-80 YOA)

Study 002
Dose and formulation selection
Total = 1,067
Exposed = 100

Phase 3
(Older adults ≥ 60 YOA)

Study 006
Pivotal efficacy, immunogenicity, and safety
Total = 25,040
Exposed = 12,467

Study 004
Immunogenicity and safety
Total = 1,660
Exposed = 1,653

Study 007
Co-administration with FLU-QIV
Total = 890
Exposed = 868

Study 009
Lot-to-lot consistency
Total = 758
Exposed = 757

Study 006: Pivotal Efficacy, Immunogenicity and Safety Study

Phase 1/2

(Adults 18-40 YOA and older adults 60-80 YOA)

Study 002
Dose and formulation selection
Total = 1,067
Exposed = 100

Phase 3

(Older adults ≥ 60 YOA)

Study 006
Pivotal efficacy, immunogenicity, and safety
Total = 25,040
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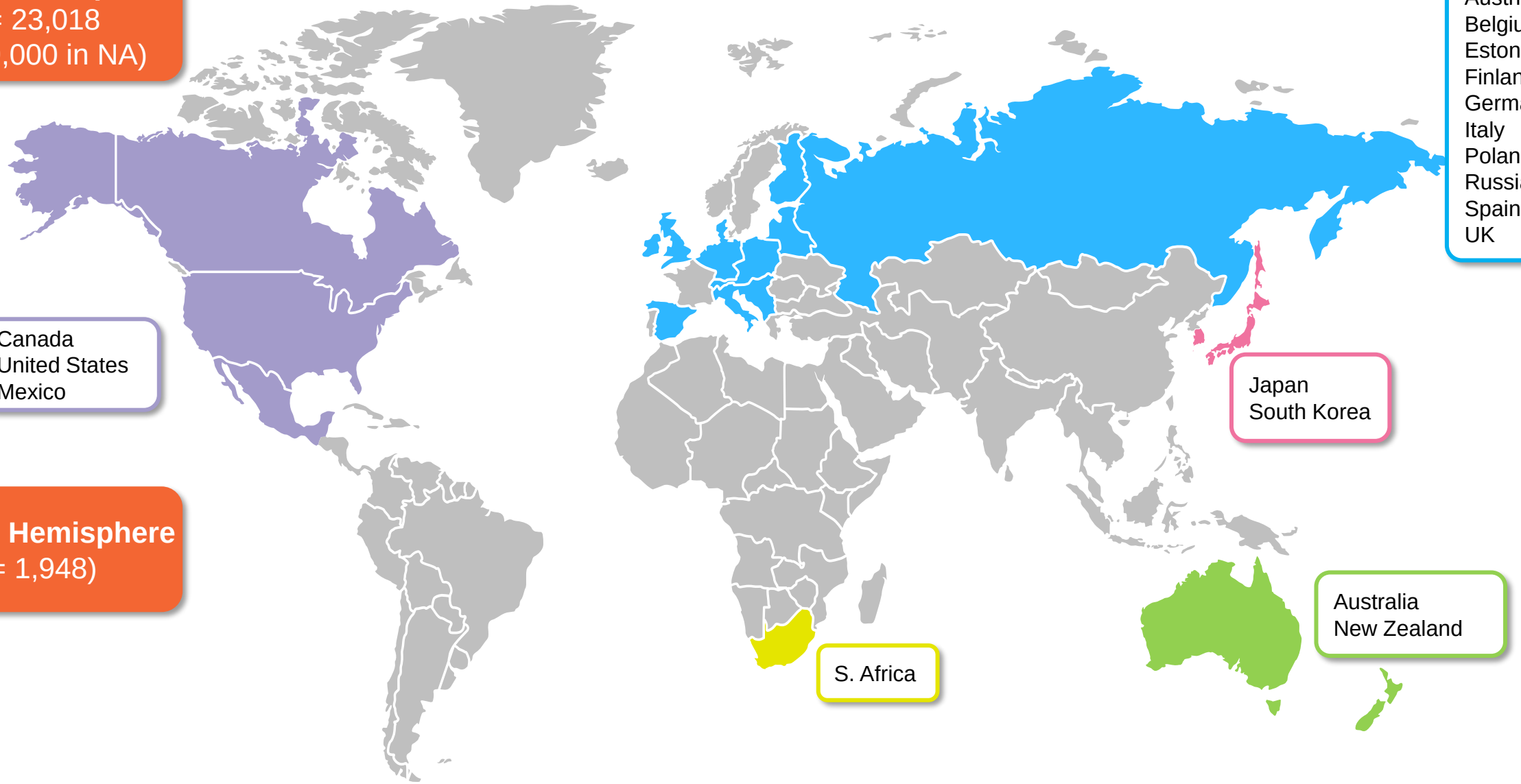
Study 007
Co-administration with FLU-QIV
Total = 890
Exposed = 868

Study 009
Lot-to-lot consistency
Total = 758
Exposed = 757

Study 006: ~ 25,000 Participants Randomized in 17 Countries

Northern Hemisphere
(N = 23,018
incl. ~ 9,000 in NA)



Canada
United States
Mexico

Austria
Belgium
Estonia
Finland
Germany
Italy
Poland
Russia
Spain
UK

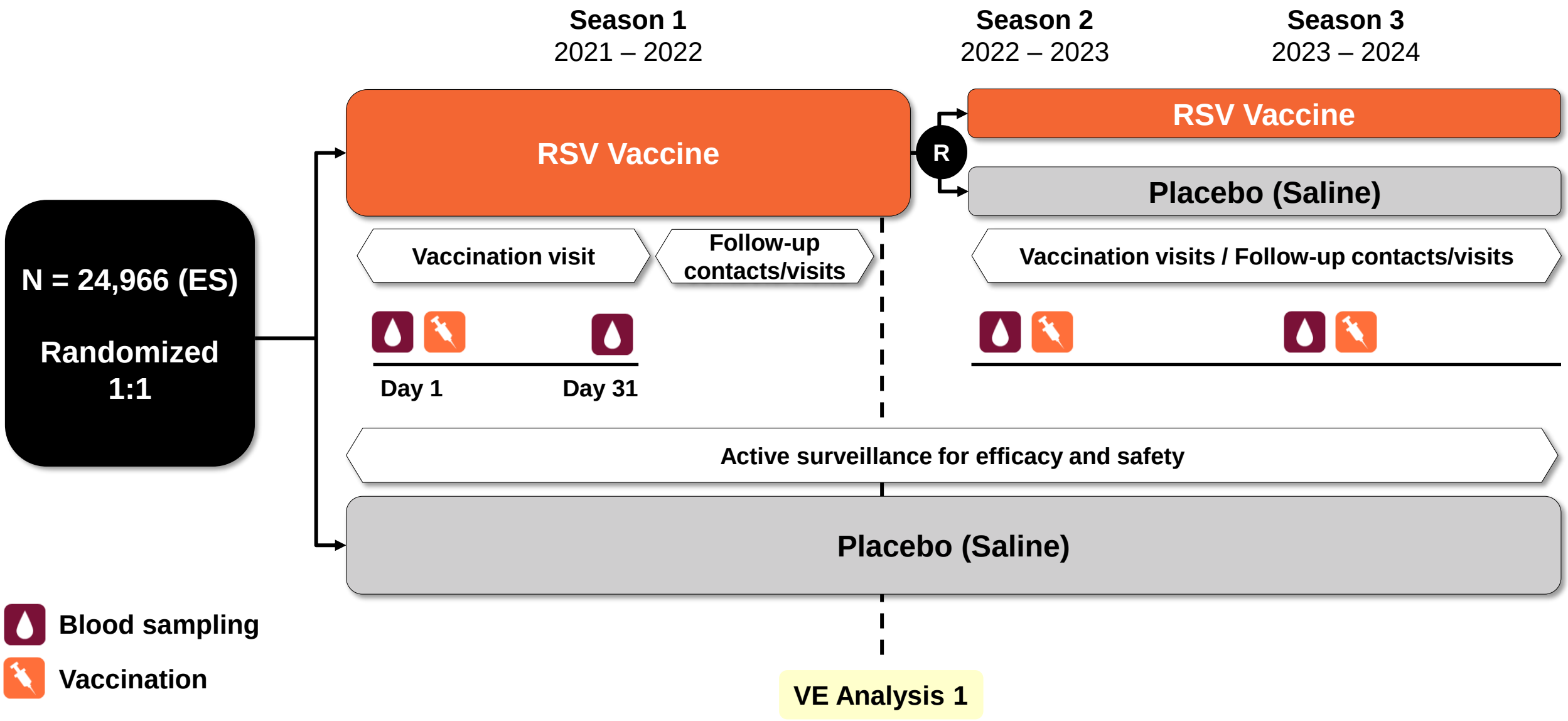
Japan
South Korea

Southern Hemisphere
(N = 1,948)

S. Africa

Australia
New Zealand

Study 006: Study Design



ES = Exposed Set; Reactogenicity and humoral immunity assessed in subset of participants; R = randomized

Study 006: Primary and Secondary Objectives

Primary Objective

Demonstrate efficacy of RSV vaccine in preventing RT-PCR-confirmed RSV LRTD in adults ≥ 60 YOA during first season

Main Secondary Objectives

- **Efficacy against RT-PCR-confirmed RSV LRTD by:**
  - RSV subtype (RSV-A and RSV-B)
  - Age category
  - Baseline comorbidities of interest and frailty status
- **Efficacy against RT-PCR-confirmed severe RSV LRTD**
- **Efficacy against RT-PCR-confirmed RSV ARI**
- **Impact of RSV vaccine on Patient-Reported Outcomes**
- **Immunogenicity/reactogenicity and safety**

All RSV-LRTD cases and severity of LRTD adjudicated by independent external adjudication committee (EAC)

Study 006: Case Definitions

ARI

≥ 2 respiratory symptoms or signs
OR
≥ 1 respiratory and 1 systemic symptom or sign

Systemic symptoms or signs

- Fever/feverishness
- Fatigue
- Body aches
- Headache
- Decreased appetite

Respiratory symptoms or signs

Upper respiratory symptoms or signs

- Nasal congestion
- Sore throat

Lower respiratory symptoms

- Sputum
- Cough
- Dyspnea

Lower respiratory signs

- Wheezing
- Crackles/rhonchi
- Tachypnea
- Hypoxemia
- O2 supplement

LRTD

≥ 2 lower respiratory symptoms or signs (≥ 1 sign)
OR
≥ 3 lower respiratory symptoms

Lower respiratory symptoms

- Sputum
- Cough
- Dyspnea

Lower respiratory signs

- Wheezing
- Crackles/rhonchi
- Tachypnea
- Hypoxemia
- O2 supplement

Severe LRTD

Definition 1: ≥ 2 lower respiratory **signs** or assessed 'severe' by PI
OR
Definition 2: Need of additional supportive therapy*

Lower respiratory signs

- Wheezing
- Crackles/rhonchi
- Tachypnea
- Hypoxemia
- O2 supplement

***O2 supplementation, positive airway pressure therapy or other types of mechanical ventilation**

Study 006: Efficacy and Immunogenicity Analyses Sets

Exposed Set (ES)

All participants who received study intervention

N = 24,966

Modified Exposed Set (mES)

Primary population for efficacy analyses

All participants who did not report RSV-confirmed ARI before Day 15 post vaccination

N = 24,960

Per-Protocol Set for Immunogenicity (PPSi)

All participants with post-vaccination immunogenicity data and did not have protocol deviations leading to elimination

N = 1,702

Study 006: Demographic Characteristics Balanced Between Groups (ES)

Characteristic	RSV Vaccine (N = 12,467)	Placebo (N = 12,499)	United States (ES) (N = 6,949)
Mean age, years	**69.5**	**69.6**	**Proportion of Exposed Set = 28%**
Age category			
60–69	6963 **(56%)**	6980 **(56%)**	4290 **(62%)**
70–79	4487 **(36%)**	4491 **(36%)**	2275 **(33%)**
≥ 80	1017 **(8%)**	1028 **(8%)**	384 **(6%)**
Female	6488 **(52%)**	6427 **(51%)**	3562 **(51%)**
Race			
White	9887 **(79%)**	9932 **(80%)**	5728 **(82%)**
Black or African American	1064 **(9%)**	1101 **(9%)**	1025 **(15%)**
Asian	953 **(8%)**	956 **(8%)**	74 **(1%)**
Other*	563 **(5%)**	510 **(4%)**	65 **(1%)**

***Includes Native American, Alaska Native, Native Hawaiian, and other Pacific Islanders**

Baseline Characteristics Balanced Between Study Groups (ES)

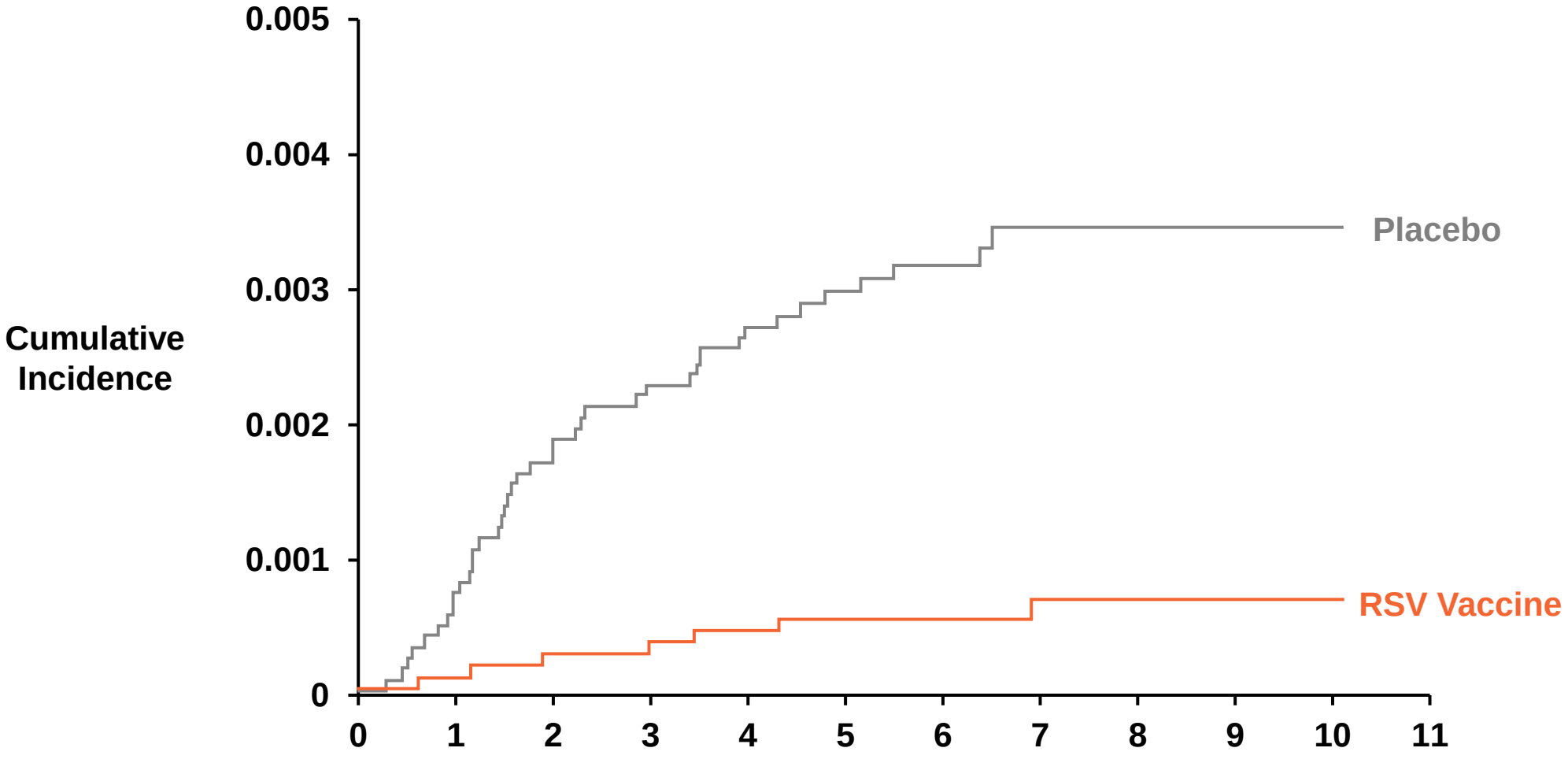
Characteristic	RSV Vaccine (N = 12,467)	Placebo (N = 12,499)	United States (ES) (N = 6,949)
Frailty status			
Frail	2%	1%	2%
Pre-frail	38%	38%	42%
Fit	60%	60%	56%
Pre-existing comorbidities			
≥ 1 Pre-existing comorbidity	96%	95%	98%
≥ 1 Pre-existing comorbidity of interest	40%	39%	40%
≥ 1 Cardiorespiratory condition	20%	19%	20%
≥ 1 Endocrinometabolic condition	26%	26%	26%

Study 006: Primary Objective Met
High Efficacy Against RSV-Confirmed LRTD (mES)

RSV Vaccine (N = 12,466)		**Placebo** (N = 12,494)		
n	Incidence Rate (/1000 PY)	n	Incidence Rate (/1000 PY)	**VE** (96.95% CI)
7	1.0	**40**	5.8	**82.6%** (58, 94)

Lower limit of 96.95% CI pre-defined threshold for licensure > 20%

Study 006: Cumulative Incidence Curves for RSV-Confirmed LRTD (mES)



Number at Risk

RSV Vaccine	12466	12392	12286	11892	11655	11046	8320	5495	2727	571	2	0
Placebo	12494	12403	12290	11887	11640	11022	8291	5464	2709	559	2	0

Study 006: Consistent Efficacy Against RSV Disease (mES)

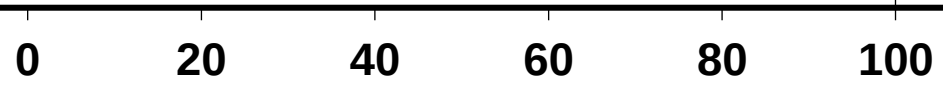
	RSV Vaccine (N = 12,466)	Placebo (N = 12,494)	Vaccine Efficacy (CI*)
	Number of events		
RSV-confirmed ARI	**27**	**95**	**71.7%** (56.2, 82.3)
RSV-confirmed LRTD	**7**	**40**	**82.6%** (57.9, 94.1)
RSV-confirmed severe LRTD[1]	**1**	**17**	**94.1%** (62.4, 99.9)

***95% CI for RSV-ARI and RSV-confirmed severe LRTD; 96.95% CI for RSV-confirmed LRTD**

1. RSV-confirmed severe LRTD definition 1

Study 006: Consistent Efficacy Against RSV-Confirmed LRTD by Age Stratum (mES)

	RSV Vaccine (N = 12,466)	Placebo (N = 12,494)	Vaccine Efficacy (CI*)
	Number of events/participants		
≥ 60	**7 / 12,466**	**40 / 12,494**	**82.6%** (57.9, 94.1)
60 – 69	**4 / 6,963**	**21 / 6,979**	**81.0%** (43.6, 95.3)
70 – 79	**1 / 4,487**	**16 / 4,487**	**93.8%** (60.2, 99.9)



≥ 80 YOA

- Events: RSV Vaccine = 2 / 1,016, Placebo = 3 / 1,028
- *Due to too few cases observed in adults ≥ 80 years of age, cannot conclude VE*

***96.95% CI for ≥ 60 YOA, 95% CI for age subgroups**

Study 006: Consistent Efficacy Against RSV-Confirmed LRTD for Each RSV Subtype (mES)

	RSV Vaccine (N = 12,466)	Placebo (N = 12,494)	Vaccine Efficacy (CI*)
	Number of events		
RSV-confirmed LRTD	**7**	**40****	**82.6%** (57.9, 94.1)
RSV-A	**2**	**13**	**84.6%** (32.1, 98.3)
RSV-B	**5**	**26**	**80.9%** (49.4, 94.3)

*96.95% CI for RSV-confirmed LRTD, 95% CI for RSV-confirmed LRTD by RSV subtype
**1 case confirmed by local test without confirmation of subtype

Study 006: High Efficacy Against RSV-Confirmed LRTD in Vulnerable Populations (mES)

	RSV Vaccine (N = 12,466)	Placebo (N = 12,494)	Vaccine Efficacy (95% CI)
	Number of events		
≥ 1 Pre-existing comorbidity of interest	**1**	**18**	**94.6%** (65.9, 99.9)
≥ 1 cardiorespiratory condition	**1**	**12**	**92.1%** (46.7, 99.8)
≥ 1 endocrine metabolic	**0**	**13**	**100%** (74.0, 100)
Pre-frail	**1**	**14**	**92.9%** (53.4, 99.8)

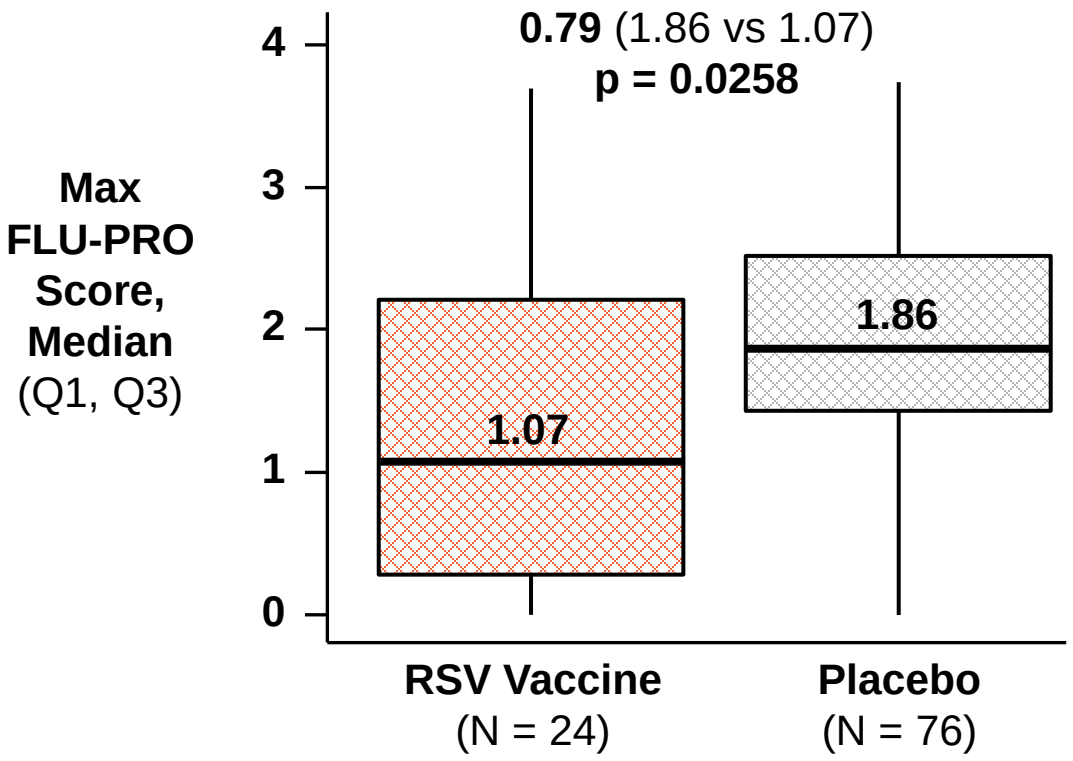
Frail

- Events: RSV Vaccine = 1/ 189, Placebo = 1/ 177
- *Due to too few cases observed in frail participants, cannot conclude VE*

Study 006: FLU-PRO Maximum Chest/Respiratory Score*

Participants in RSVPreF3 group with breakthrough cases had less severe chest / respiratory symptoms vs participants in placebo group

FLU-PRO Chest/Respiratory Score During First 7 Days of RSV Confirmed ARI Episode



- Difference between groups > 3x higher than Minimal Clinically Significant Change = 0.26[1**]
- Results represent overall reduction = 42% (0.79/1.86) in severity of cough, trouble breathing, chest tightness symptoms vs placebo

***82% of participants completed at least 1 FLU-PRO questionnaire during first 7 days of RSV ARI episode; ** AReSVi-006: Improvement in symptom's severity, change of one point in PGI-S score associated with -0.26 mean change in both FLU-PRO total and chest score; 1. Yu J et al.,2019**

Study 006 and 004: Immunogenicity Studies

Phase 1/2

(Adults 18-40 YOA and older adults 60-80 YOA)

Study 002
Dose and formulation selection
Total = 1,067
Exposed = 100

Phase 3

(Older adults ≥ 60 YOA)

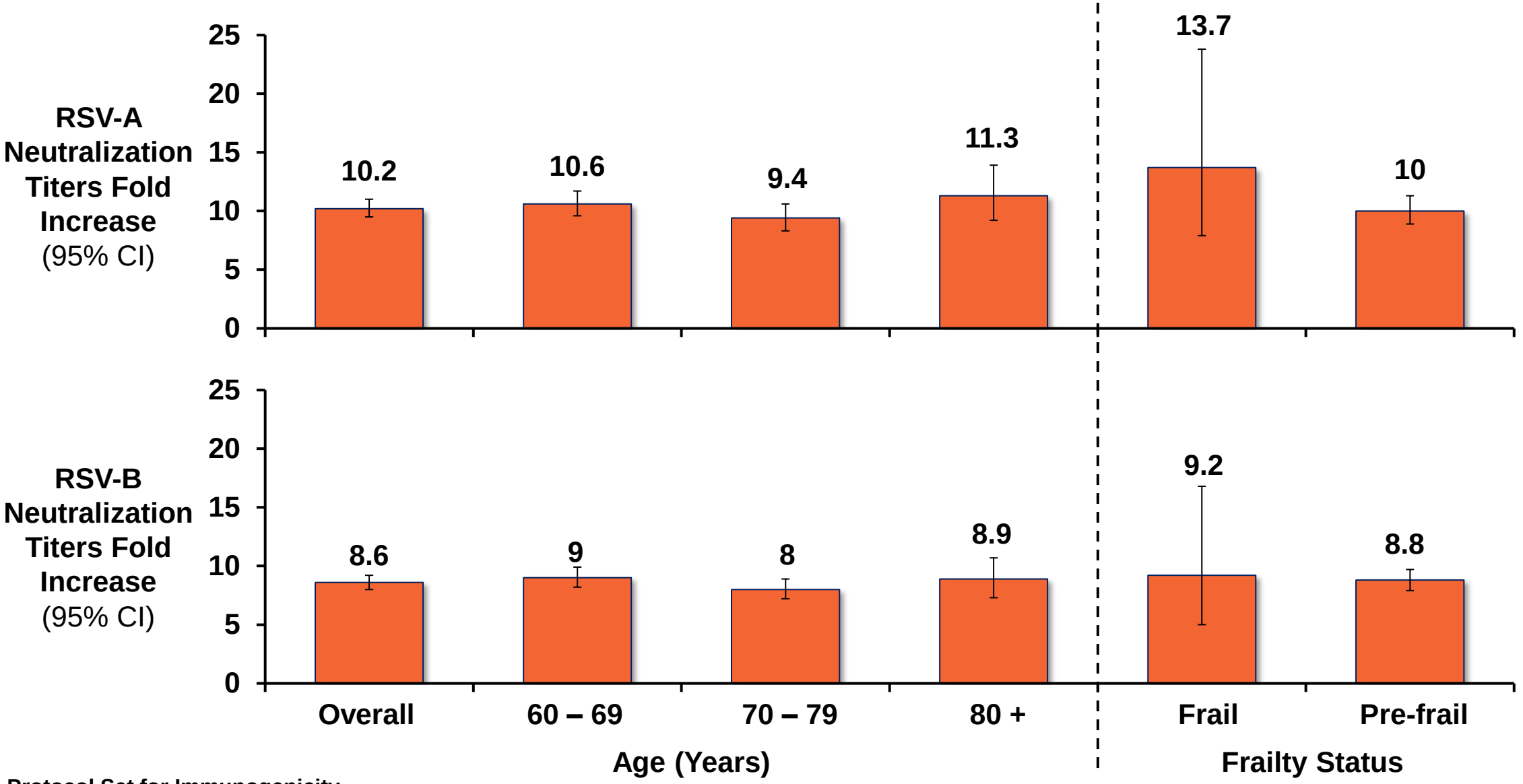
Study 006
Pivotal efficacy, immunogenicity, and safety
Total = 25,040
Exposed = 12,467

Study 004
Immunogenicity and safety
Total = 1,660
Exposed = 1,653

Study 007
Co-administration with FLU-QIV
Total = 890
Exposed = 868

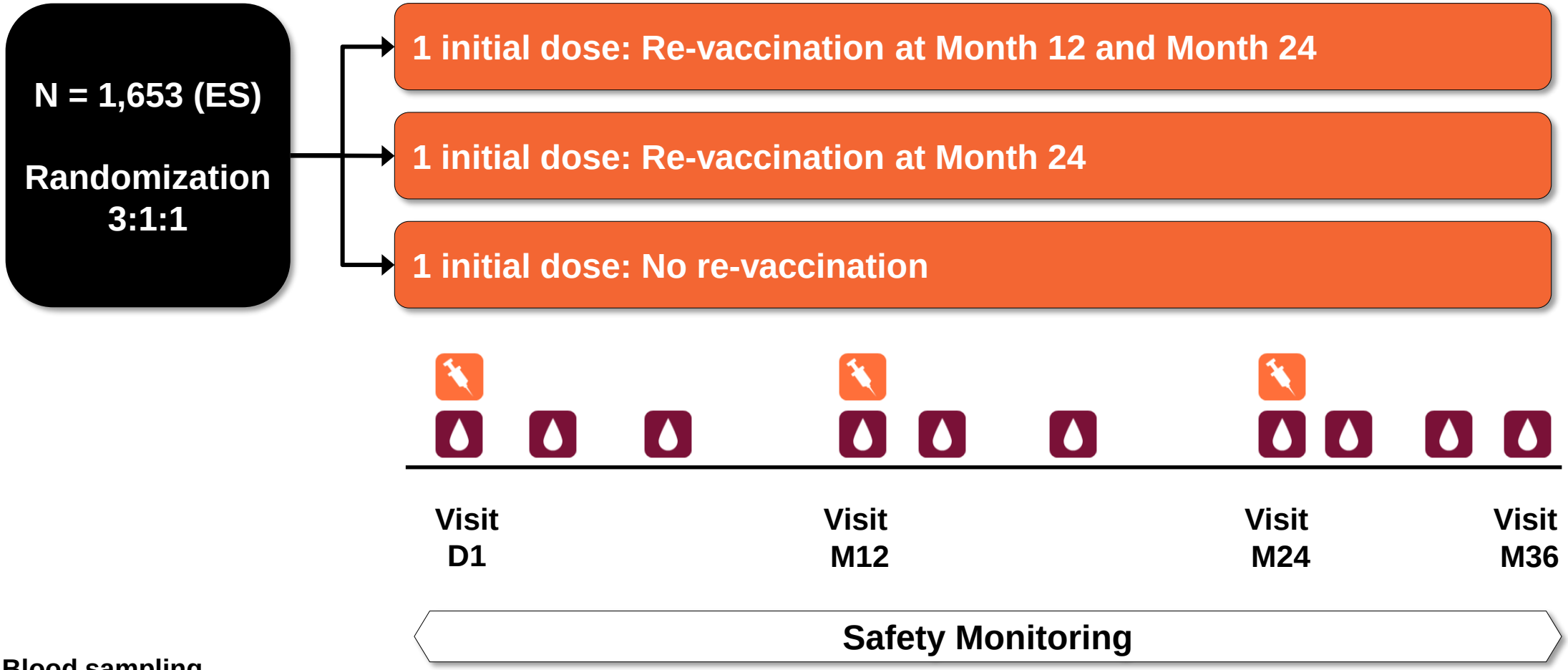
Study 009
Lot-to-lot consistency
Total = 758
Exposed = 757

Study 006: Robust Immune Response for RSV Subtypes Across All Age Groups and Frailty Status (Day 31)



Per-Protocol Set for Immunogenicity

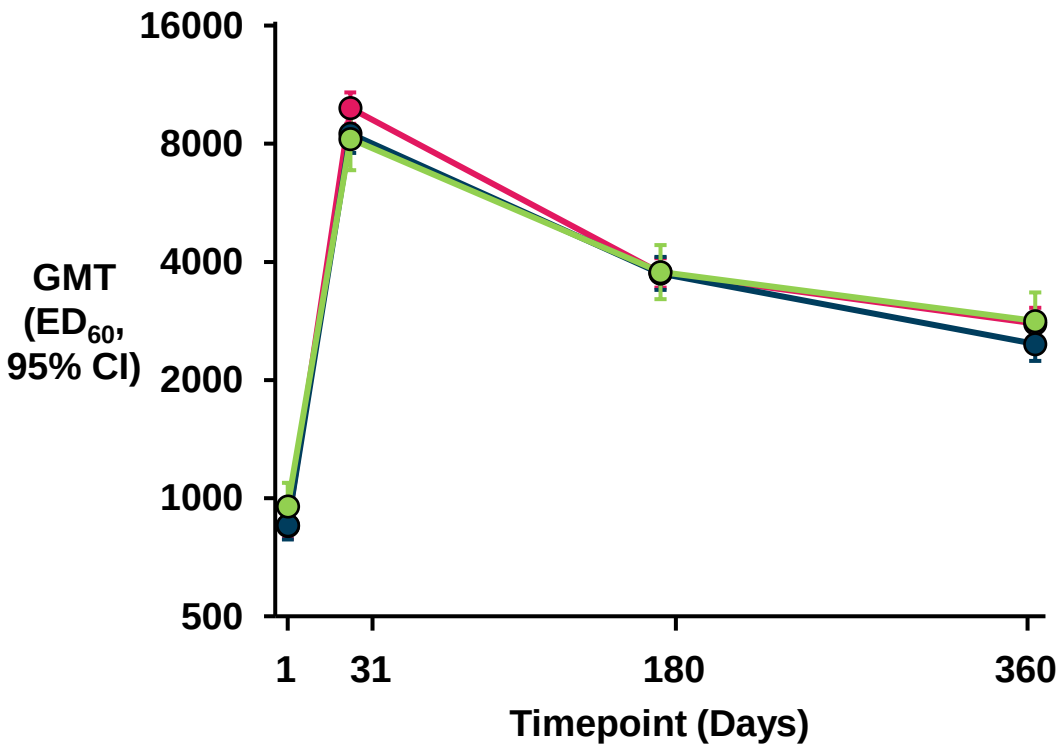
Study 004: Study Design



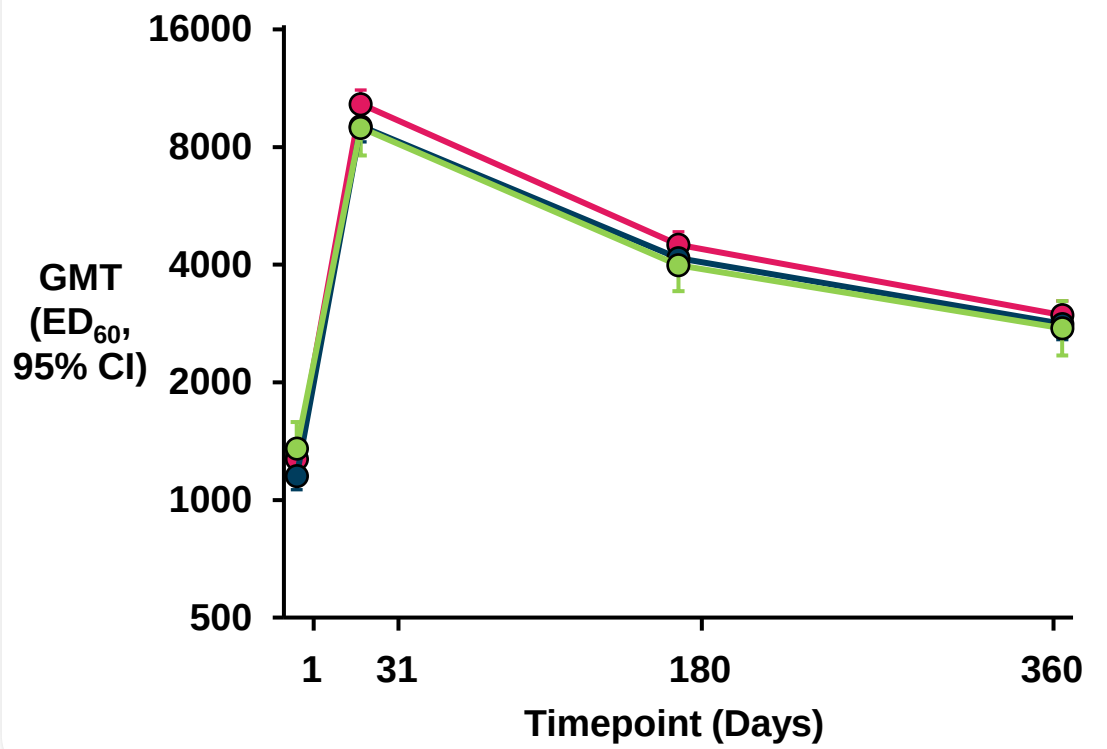
Immunogenicity assessed in subset of participants

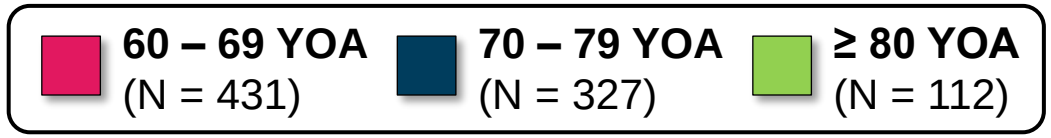
Study 004: Durable RSV-A and RSV-B Serum Neutralization Titers Across All Age Groups 12 Months Post Vaccination

RSV-A Serum Neutralization Titers



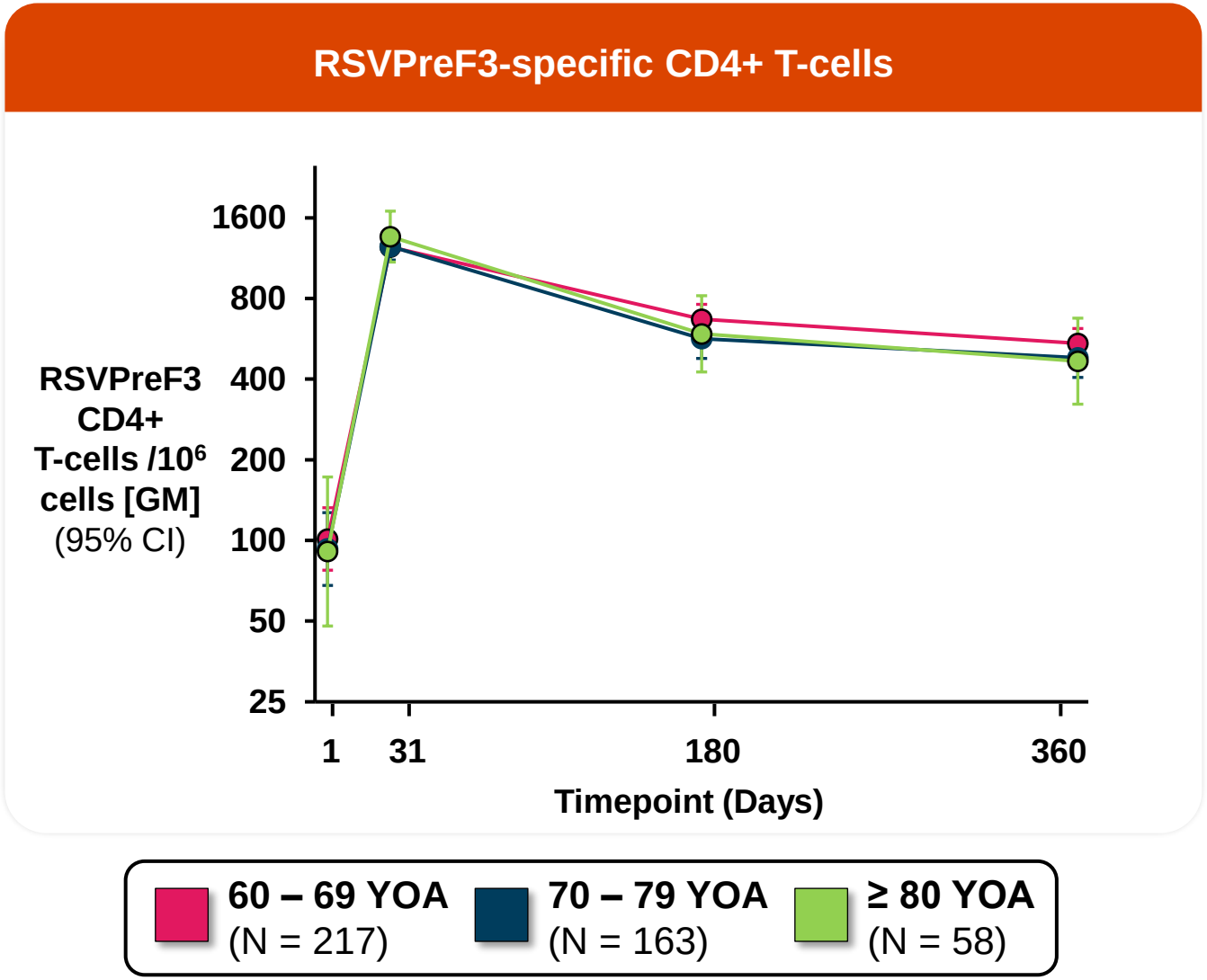
RSV-B Serum Neutralization Titers





Per-Protocol Set for Humoral Response

Study 004: Durable CD4+ T-Cell Responses Across All Age Groups 12 Months Post Vaccination



Per-Protocol Set for Humoral Response

***CD4+ T-cells expressing ≥ 2 activation markers including ≥ 1 cytokine among CD40L, 4-1BB, IL-2, TNF-α, IFN-γ, IL-13, IL-17 (events/10^6 cells; by intracellular staining)**

Study 007: Co-Administration of RSV Vaccine with Licensed Influenza Vaccine

Phase 1/2

(Adults 18-40 YOA and older adults 60-80 YOA)

Study 002
Dose and formulation selection
Total = 1,067
Exposed = 100

Phase 3

(Older adults ≥ 60 YOA)

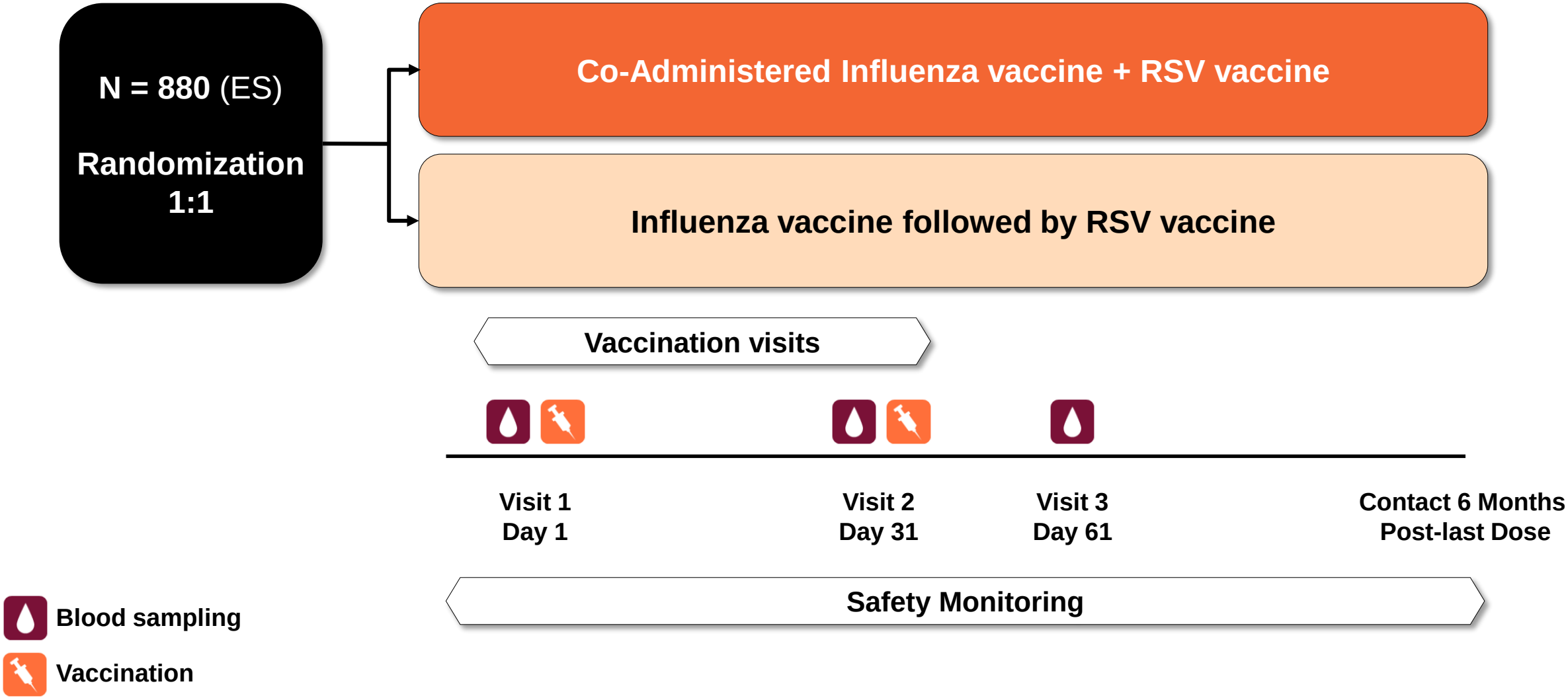
Study 006
Pivotal efficacy, immunogenicity, and safety
Total = 25,040
Exposed = 12,467

Study 004
Immunogenicity and safety
Total = 1,660
Exposed = 1,653

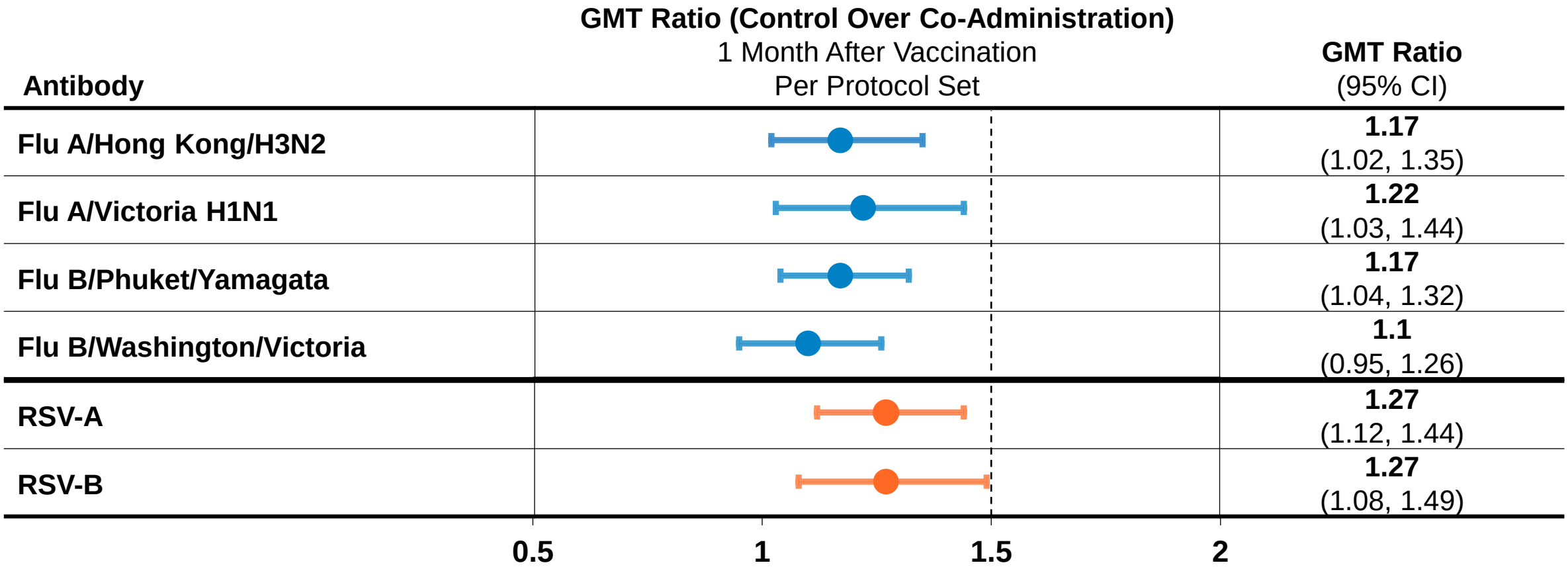
Study 007
Co-administration with FLU-QIV
Total = 890
Exposed = 868

Study 009
Lot-to-lot consistency
Total = 758
Exposed = 757

Study 007: Study Design



Study 007: Co-Administration of RSV Vaccine and Licensed Flu-QIV Met Non-Inferiority Criterion



Success Criteria: Upper limit ≤ 1.5 of 2-sided 95% CI for Group GMT Ratio (RSV-A Neutralizing antibody titers and HI antibody titers in Control Group divided by Co-Ad Group) for RSV vaccine and for each of FLU vaccine strains

HI = haemagglutinin
Flu response evaluated using HI and RSV response evaluated using NAb (ED 60)

Efficacy and Immunogenicity Summary

- 82.6% VE in preventing RSV-confirmed LRTD in adults ≥ 60 YOA
- Protection sustained across full spectrum of symptomatic RSV disease
- Consistent VE against RSV-A and RSV-B and across age groups
- High VE in those at risk of developing severe RSV disease
  - 94.6% pre-existing co-morbidities
  - 92.9% pre-frail

- Robust humoral RSV-A and RSV-B and cell-mediated immune responses
- Immune responses comparable across age groups and shown to persist for ≥ 12 months after vaccination
- RSV vaccine can be co-administered with seasonal influenza vaccine

Safety

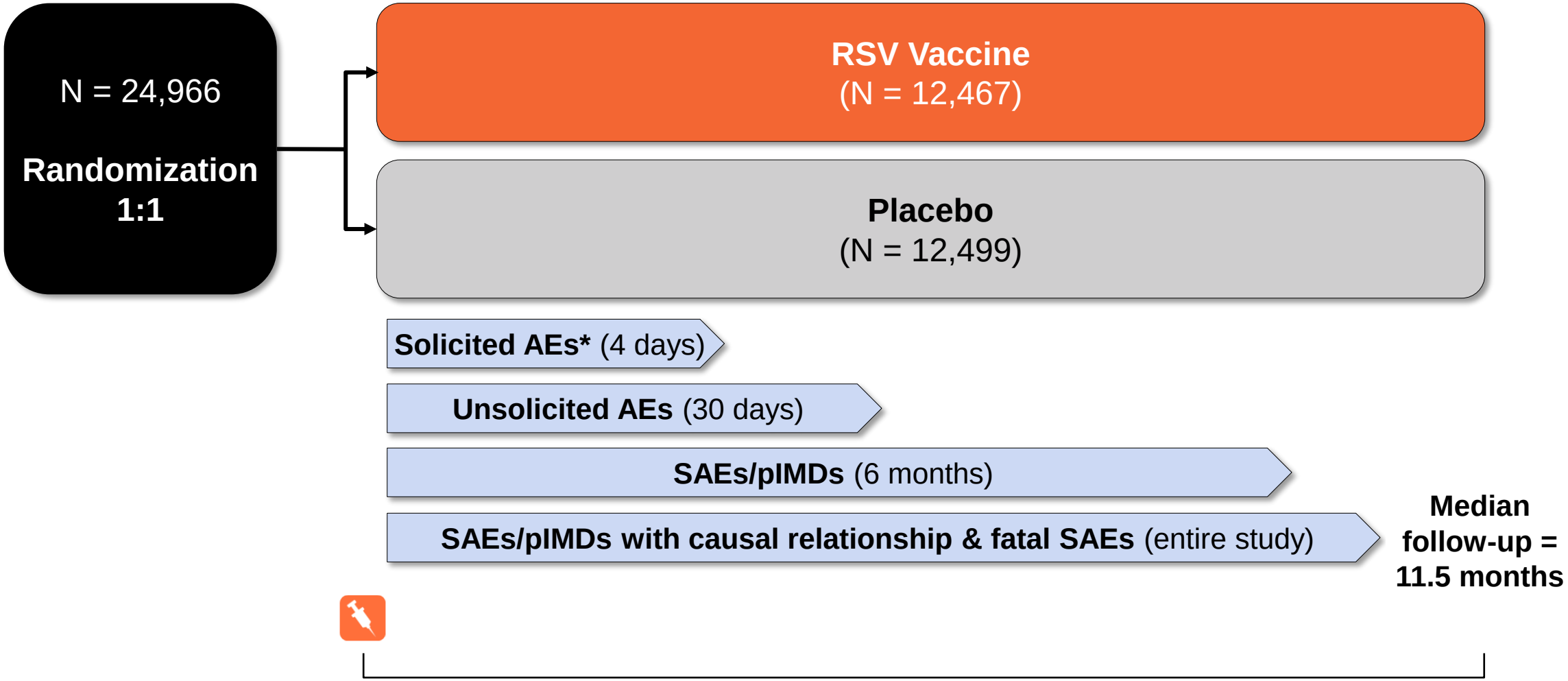
Peggy Webster, MD, MBA

Vice President & Head of Vaccine Safety
GSK

Safety Database Includes > 15,800 Participants

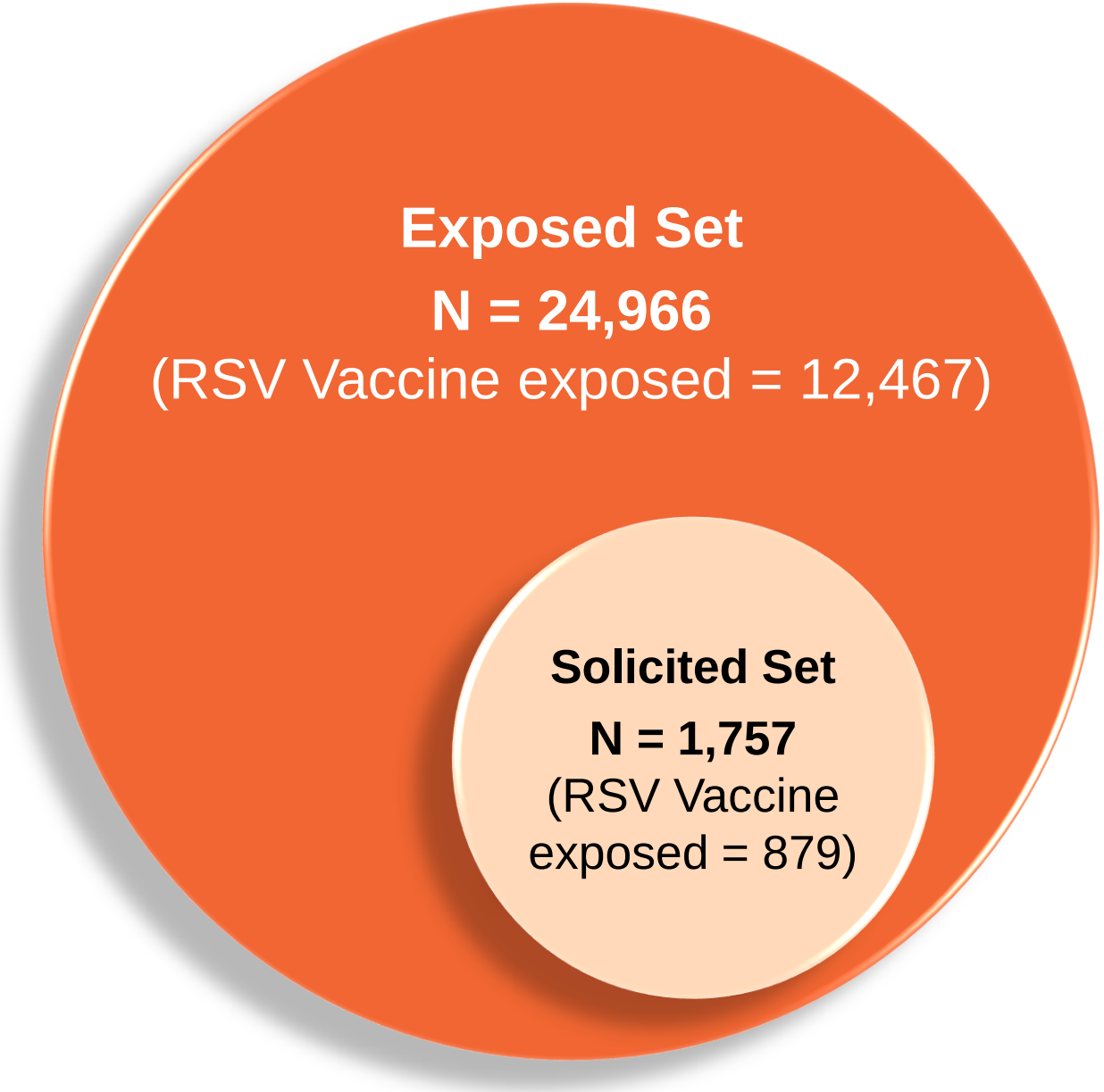
	RSV Vaccine Participants Exposed Set
Phase 1/2 (60 – 80 years)	
Study 002	**100**
Phase 3 (≥ 60 years)	
Study 006	**12,467**
Study 004	**1,653**
Study 007	**868**
Study 009	**757**
Phase 1/2 and Phase 3	**15,845**

Study 006: Safety Follow-Up

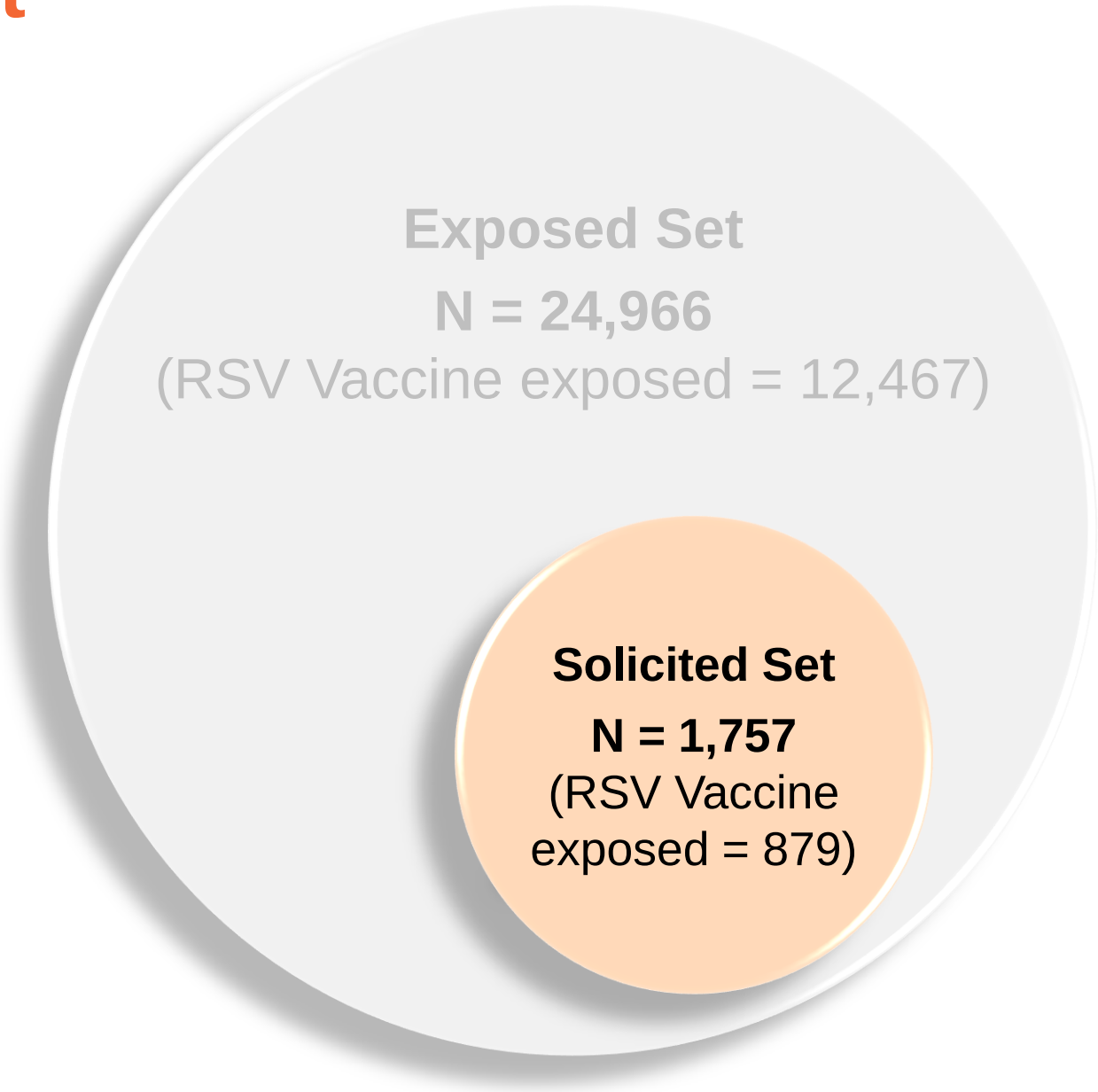


*Solicited Safety Set: reactogenicity events recorded in subset of participants; pIMDs = potential immune-mediated diseases

Study 006: RSV Vaccine Safety Evaluated in 2 Groups



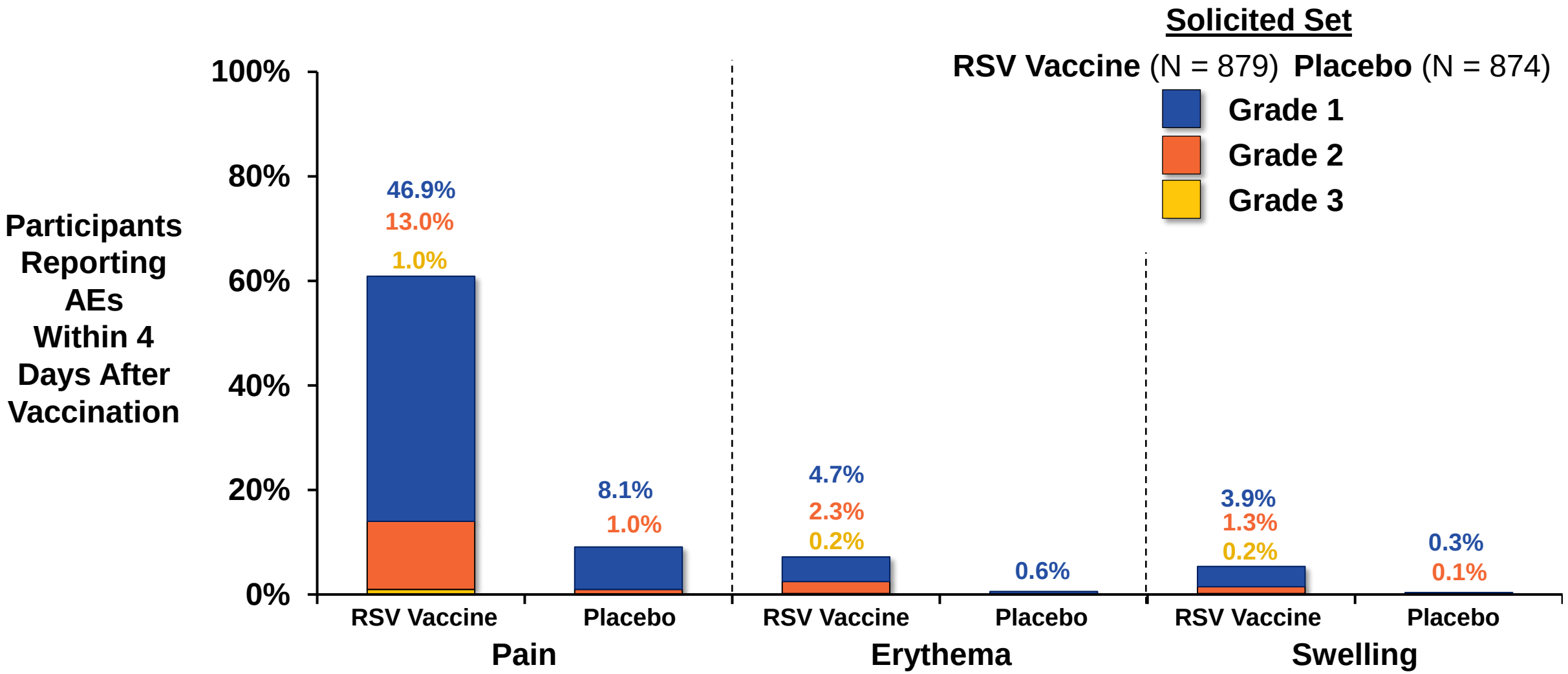
Reactogenicity Profile Primarily Derived from Solicited Set



Study 006: Summary of Adverse Events in Solicited Set

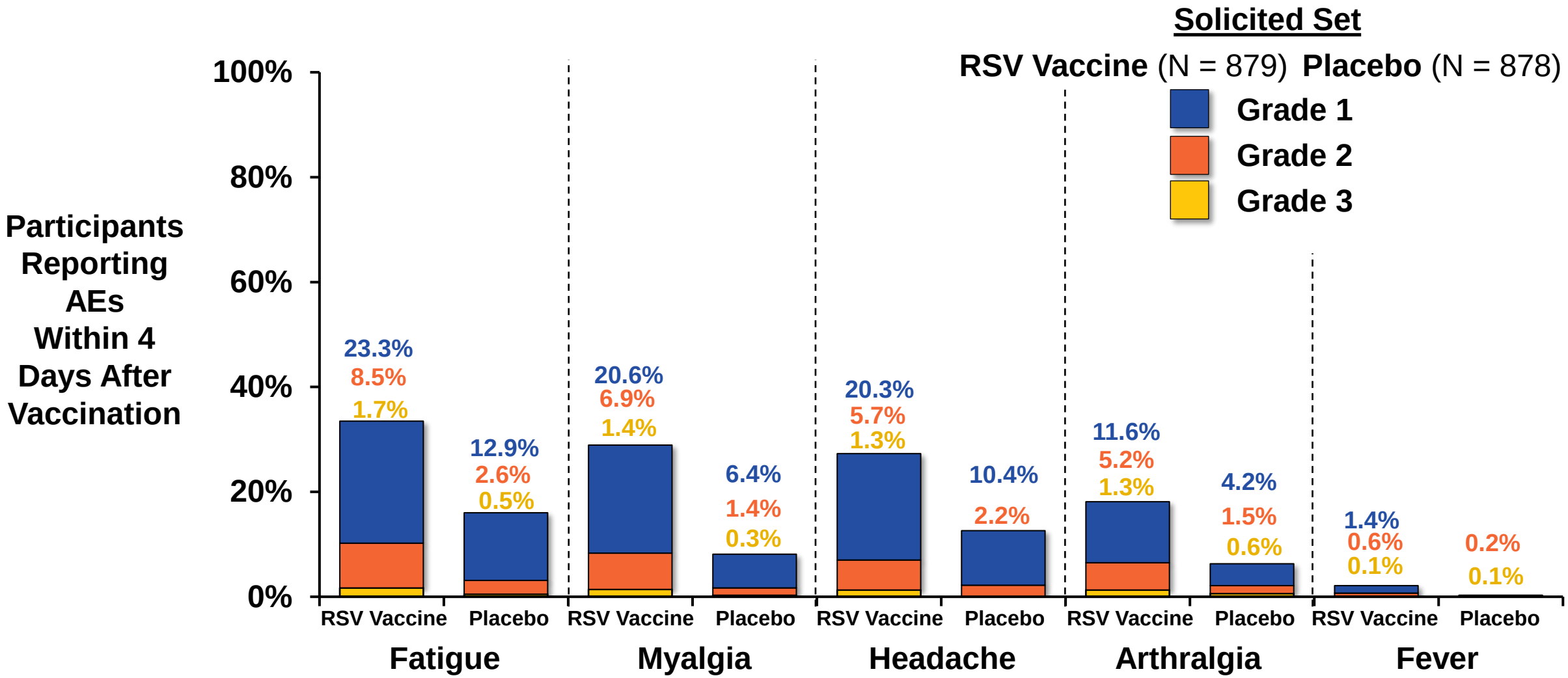
	RSV Vaccine N = 879	Placebo N = 878
Any solicited AE (within 4 days)	**72%**	**28%**
Administration site AEs	**62%**	**10%**
Systemic AEs	**49%**	**23%**
Grade 3 AEs	**4%**	**0.9%**

Study 006: Solicited Administration Site Events Mostly Mild to Moderate and Resolved Quickly



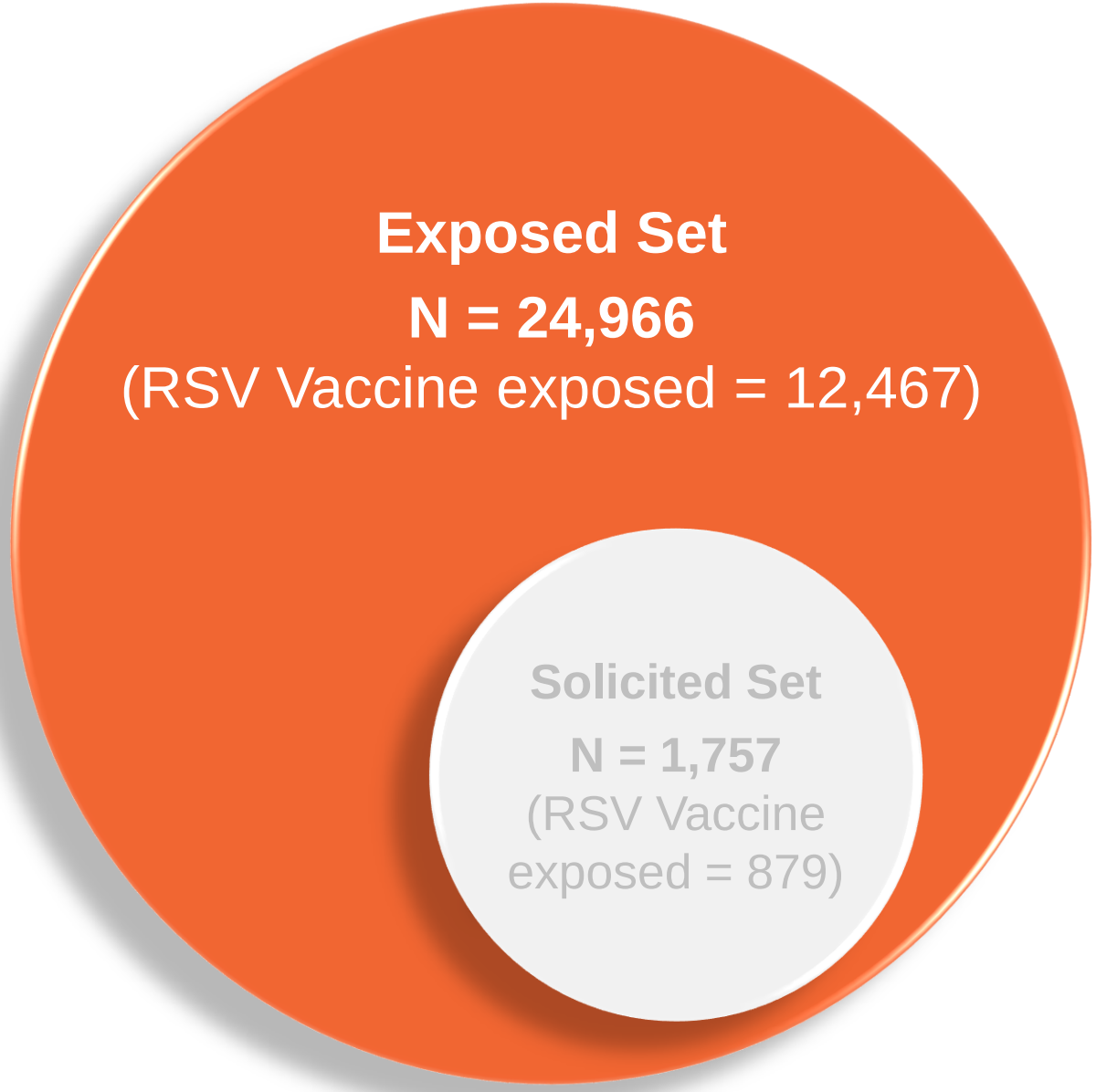
Data Lock Point April 30, 2022; Median duration for RSV Vaccine = 2 days and Placebo = 1-4 days

Study 006: Solicited Systemic Events Mostly Mild to Moderate and Resolved Quickly



Data Lock Point April 30, 2022; Median duration for RSV Vaccine = 1-2 days and Placebo = 1-2 days

Study 006: Unsolicited Events from Exposed Set



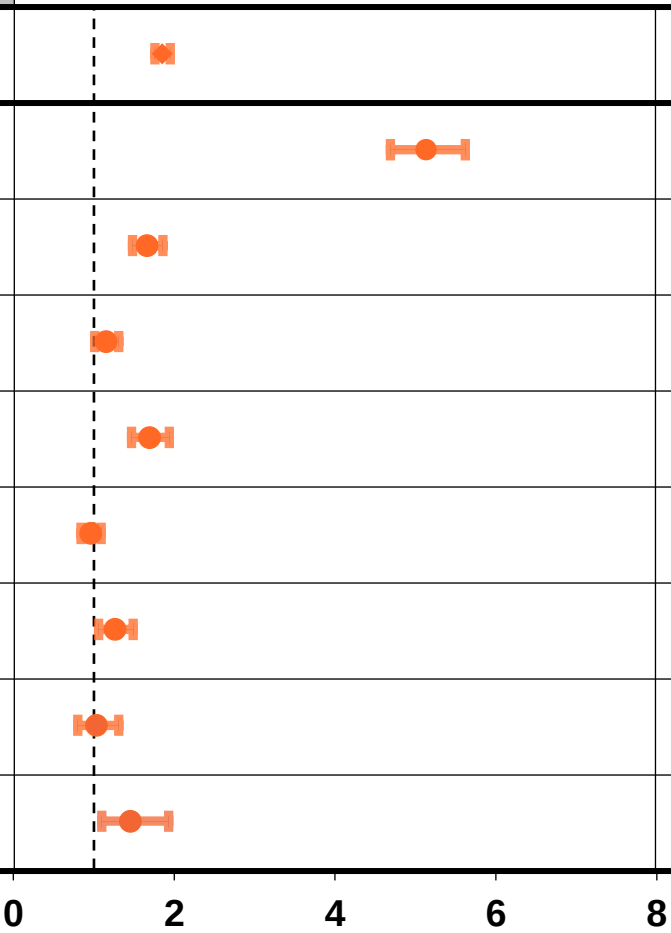
Study 006: Summary of Unsolicited Adverse Events

Within 30 days of vaccination	Exposed Set	
	RSV Vaccine N = 12,467	**Placebo** N = 12,499
Any unsolicited AE*	**33%**	**18%**
Any medically attended AE	**6%**	**6%**
Up to 6 months post-vaccination		
Potential immune-mediated diseases (pIMDs)	**0.3%**	**0.3%**
Serious AE (SAE)	**4%**	**4%**
Until Data Lock Point		
Fatal SAE	**0.7%**	**0.8%**

Data Lock Point April 30, 2022 for data within 30 days post-vaccination and September 30, 2022 for SAEs and pIMDs;
***Observed imbalance driven by PTs in SOC General disorders and administration site conditions and Nervous system disorders**

Study 006: Difference in Unsolicited AEs Due to General Disorders and Administration Site Conditions

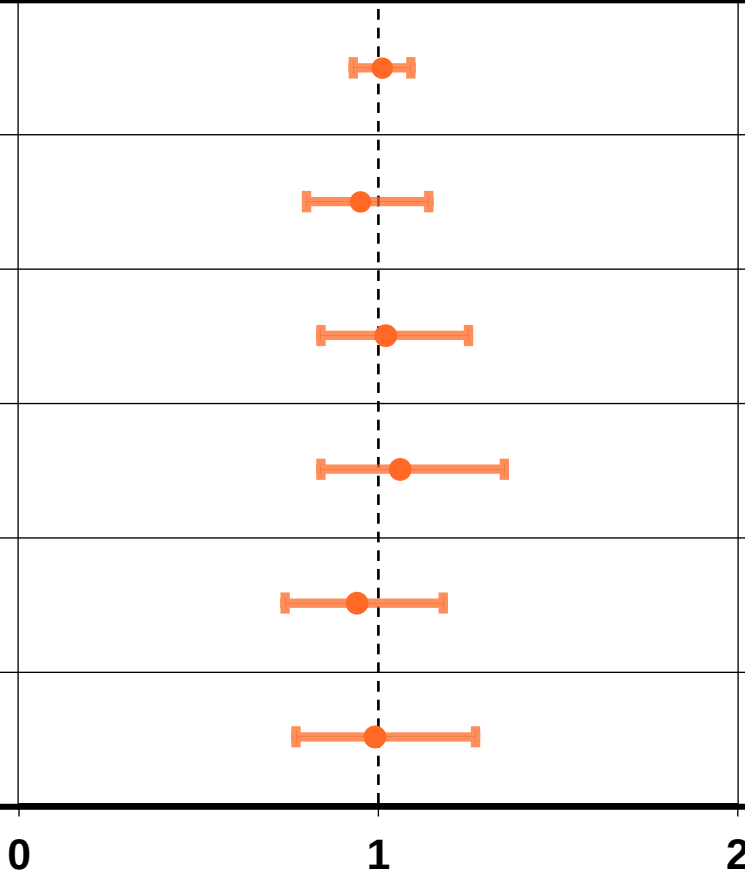
SOC occurring in ≥ 1% in RSV group	Exposed Set: RSV Vaccine N = 12,467	Exposed Set: Placebo N = 12,499	Relative Risk (95% CI)	RR (95% CI)
Any Unsolicited AE (within 30 days)	**33%**	**18%**		**1.85** (1.76, 1.95)
General disorders and admin. site conditions	**24%**	**5%**		**5.13** (4.69, 5.62)
Nervous system disorders	**6%**	**4%**		**1.66** (1.48, 1.86)
Respiratory, thoracic and mediastinal disorders	**4%**	**4%**		**1.15** (1.01, 1.31)
Musculoskeletal and connective tissue disorders	**4%**	**3%**		**1.69** (1.47, 1.94)
Infections and Infestations	**4%**	**4%**		**0.96** (0.84, 1.09)
Gastrointestinal disorders	**3%**	**2%**		**1.26** (1.06, 1.49)
Injury, poisoning and procedural complications	**1%**	**1%**		**1.03** (0.80, 1.31)
Skin and subcutaneous tissue disorders	**1%**	**0.7%**		**1.45** (1.10, 1.93)



Data Lock Point April 30, 2022

Study 006: SAEs Balanced Between Groups

SOC occurring in ≥ 0.5% of participants	Exposed Set: RSV Vaccine N = 12,467	Exposed Set: Placebo N = 12,499	Relative Risk (80% CI)	RR (80% CI)
Any SAE (within 6 months)	**4%**	**4%**		**1.01** (0.93, 1.09)
Infections and infestations	**0.9%**	**0.9%**		**0.95** (0.80, 1.14)
Cardiac disorders	**0.8%**	**0.7%**		**1.02** (0.84, 1.25)
Neoplasms benign, malignant, and unspecified	**0.6%**	**0.5%**		**1.06** (0.84, 1.35)
Nervous system disorders	**0.5%**	**0.5%**		**0.94** (0.74, 1.20)
Injury, poisoning, and procedural complications	**0.5%**	**0.5%**		**0.99** (0.77, 1.27)



Data Lock Point September 30, 2022

Study 006: Incidence of Fatal SAEs Balanced

SOC occurring in ≥ 0.1% of participants	Exposed Set	
	RSV Vaccine N = 12,467	**Placebo** N = 12,499
Any fatal SAE (up to Data Lock Point)	88 **(0.7%)**	95 **(0.8%)**
Cardiac disorders	23 **(0.2%)**	26 **(0.2%)**
Infections and infestations	20 **(0.2%)**	12 **(0.1%)**
General disorders and administration site conditions	14 **(0.1%)**	24 **(0.2%)**
Nervous system disorders	10 **(0.1%)**	11 **(0.1%)**
Respiratory, thoracic, and mediastinal disorders	7 **(0.1%)**	8 **(0.1%)**
Neoplasms benign, malignant, and unspecified (incl. cysts & polyps)	7 **(0.1%)**	6 **(<0.1%)**

Study 007: Safety of RSV Vaccine When Co-Administered with Seasonal Influenza Vaccine

	RSV Vaccine + FLU-QIV N = 442	Control* N = 443
Within 4 days of vaccination		
Any Solicited Administration Site AE	**53.4%**	**39.9%**
Any Solicited Systemic AE	**40.2%**	**34.1%**
Within 30 days of vaccination		
Any Unsolicited AE	**18.8%**	**23.7%**
Any Medically Attended AE	**7.9%**	**11.1%**
During entire study period		
pIMDs	**1.1%**	**0.2%**
SAE	**3.4%**	**4.5%**
Death	**0.9%**	**1.8%**

*Control = FLU-QIV at Day 1 + RSV Vaccine at Day 31

Safety Events of Special Interest

Study 006: Hypersensitivity Reactions Occurring in ≥ 0.1% Participants

Preferred Term	Exposed Set	
	RSV Vaccine N = 12,467	**Placebo** N = 12,499
Rash	31 **(0.2%)**	10 **(0.1%)**
Injection site rash	11 **(0.1%)**	5 **(< 0.1%)**

- SMQs for “hypersensitivity” and “anaphylactic reaction”
  - No case of anaphylaxis related to vaccine

Study 006: Atrial Fibrillation Events Within 30 Days Post-Vaccination

Preferred Term	RSV Vaccine N = 12,467	Placebo N = 12,499
Atrial fibrillation	10 **(0.1%)**	4 **(< 0.1%)**
New onset	4	2
Recurrence	6	2
Outcome		
Recovered	8	3
Not recovered	2	1
Time to Onset, median (min, max)	**18.5** (1 – 30)	**10.5** (1 – 24)

- All participants with new onset have risk factors for development of atrial fibrillation
- IDMC reviewed all events
- Similar incidence in both groups at 6 months post-vaccination (14 RSV Vaccine vs 16 Placebo)

Study 006: Potential Immune-Mediated Diseases (pIMDs) Occurred in < 0.5% of Participants

SOC occurring in ≥ 4 participants	Exposed Set	
	RSV Vaccine N = 12,467	**Placebo** N = 12,499
Any pIMD (within 6 months)	41 **(0.3%)**	34 **(0.3%)**
Metabolism and nutrition disorders	12 **(0.1%)**	11 **(0.1%)**
Musculoskeletal and connective tissue disorders	12 **(0.1%)**	7 **(0.1%)**
Skin and subcutaneous tissue disorders	4 **(< 0.1%)**	4 **(< 0.1%)**
Nervous system disorders	4 **(< 0.1%)**	2 **(< 0.1%)**
Gastrointestinal disorders	4 **(< 0.1%)**	1 **(< 0.1%)**

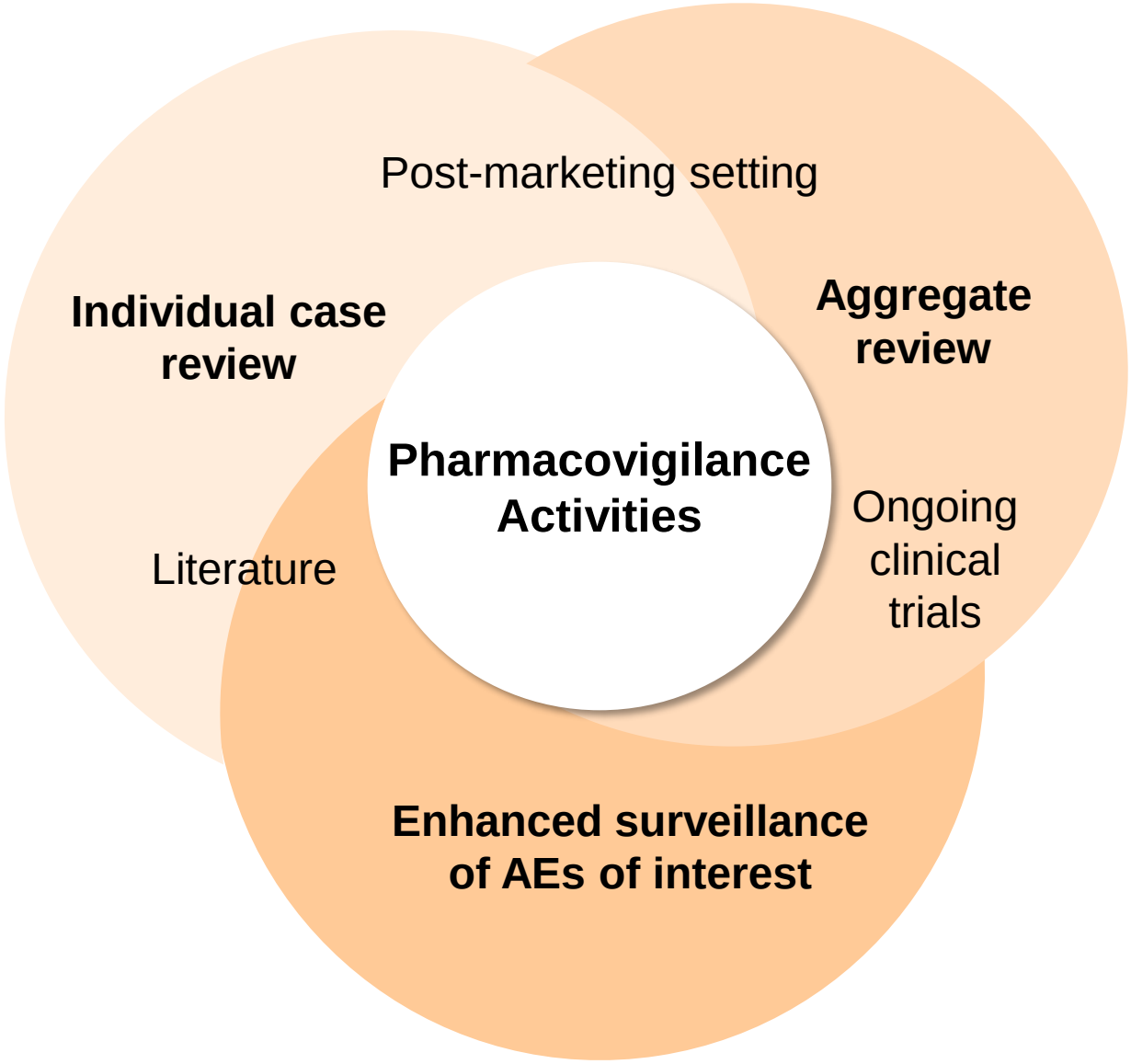
Studies 004 and 007: pIMDs of Medical Interest

Event	Age/ Sex	Country	Time to Onset (Days)	Comment
Guillain Barre Syndrome	78/F	JP	9	Elevated CSF protein, serum GM1-IgG positive; BC Level 3
ADEM	71/M	ZA	7	2 prior strokes with Wallerian demyelination; fatal outcome; BC Level 3
ADEM	71/F	ZA	22	Recovered; no investigations performed; BC Level 3

F = female, M = male, JP = Japan, ZA = South Africa, BC = Brighton Collaboration

Post-Marketing Pharmacovigilance

Proposed Post-Marketing Pharmacovigilance Plan



Enhanced Surveillance: Atrial Fibrillation and pIMDs

- Atrial fibrillation
  - Active surveillance in ongoing and soon-to-start clinical studies

- pIMDs, including GBS and ADEM
  - Continued monitoring and close follow-up in all clinical trials
  - Post-marketing setting
    - Monitoring via Follow-up Questionnaires
    - Custom MedDRA query for pIMD signal detection

Safety Summary

- Exposure in > 15,000 participants in RSV vaccine group
- Clinically acceptable safety profile in adults ≥ 60 YOA
- Well-characterized reactogenicity profile
  - Majority mild to moderate in severity
  - Short duration
- Medically attended AEs, SAEs, pIMDs, and deaths balanced between groups with no clustering of events
- Enhanced pharmacovigilance activities

Benefit / Risk Conclusion

Favorable Benefit / Risk Profile for RSV Candidate Vaccine in OAs

Unmet Need

- OAs at increased risk of morbidity and mortality from RSV infection
- No vaccines or treatments available for vulnerable population

Efficacy

- High and consistent efficacy across spectrum of RSV symptomatic disease regardless of subtype

82.6%	71.7%	94.1%	93.8%	94.6%
RSV-LRTD (≥ 60 YOA)	ARI (≥ 60 YOA)	Severe RSV-LRTD (≥ 60 YOA)	RSV-LRTD (70−79 YOA)	RSV-LRTD (≥ 1 comorbidity of interest)

Safety

- RSV vaccine is well tolerated with acceptable safety profile
- RSV vaccine benefits outweigh risks

RSVPreF3 Vaccine for Respiratory Syncytial Virus (RSV) in Older Adults

March 1, 2023

Vaccines and Related Biological Products Advisory Committee

GSK plc.