Meeting of the Advisory Committee on Immunization Practices (ACIP)

Centers for Disease Control and Prevention

October 24, 2024

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Medical Director

GSK

AREXVY Indications

AREXVY is indicated for active immunization for prevention of lower respiratory tract disease (LRTD) caused by RSV in

- Individuals **≥ 60 YOA**
- Individuals **50-59 YOA** at increased risk for LRTD caused by RSV

- ~ 9 million AREXVY doses administered in US to date

YOA, years of age

FDA, 2024. AREXVY Prescribing Information (PI); https://www.fda.gov/media/167805/download (URL accessed Aug 2024)

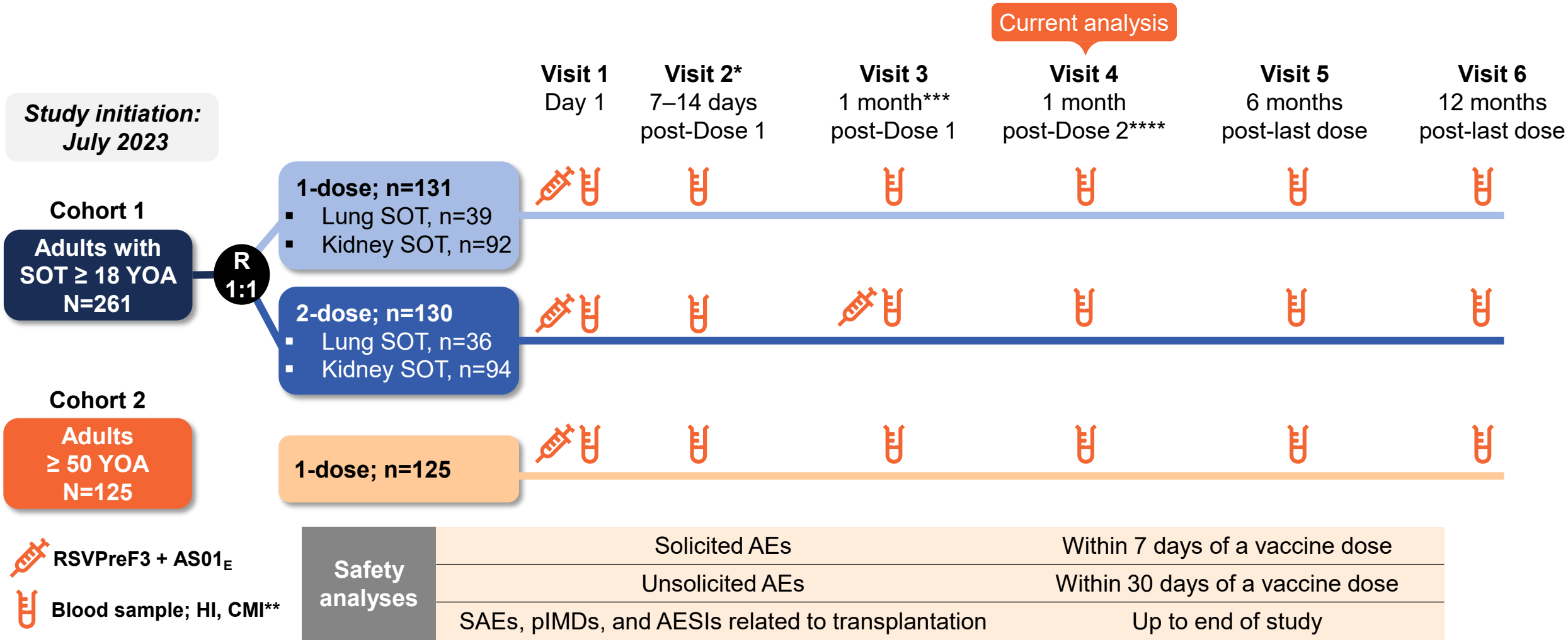
RSV-OA=ADJ-023: Immune response and safety among adult lung and kidney transplant recipients ≥ 18 years of age Preliminary results

A Phase 2b, randomized, controlled, open-label study to evaluate the immune response and safety of the RSVPreF3 + $AS01_E$ vaccine in adults (≥18 years of age) when administered to lung and kidney transplant recipients comparing a 1 versus a 2-dose schedule and compared to adults (≥50 years of age) receiving 1 dose

NCT 05921903

RSV-OA=ADJ-023: Phase 2b Study Design

Descriptive immunogenicity and safety study in lung and kidney transplant recipients ≥ 18 YOA versus adults ≥ 50 YOA



Safety analyses		
	Solicited AEs	Within 7 days of a vaccine dose
	Unsolicited AEs	Within 30 days of a vaccine dose
	SAEs, pIMDs, and AESIs related to transplantation	Up to end of study

*Only in subset of study population, ~30% of participants; **Blood sample for CMI analysis collected at each visit only in subset of study population (~30% of participants);
***Allowed interval range: 30-60 days; ****For Adults with SOT 1-dose group and Adults ≥ 50 YOA, Visit 4 refers to 1-month post-Visit 3; AE, adverse event; AESI, adverse event of special interest; CMI, cell-mediated immunity; HI, humoral immunity; pIMD, potential immune-mediated disorder; SAE, serious adverse event; SOT, solid organ transplant; YOA, years of age

Key Inclusion and Exclusion Criteria

Adults with SOT (kidney & lung) ≥ 18 YOA

Inclusion criteria:

- **ABO compatible allogeneic kidney or lung transplant (allograft) > 12 months prior to first study intervention**
- **Receiving maintenance immunosuppressive therapy for prevention of allograft rejection**

Exclusion criteria:

- Allograft rejection in 3 months prior to first dose
- Current diagnosis of malignancy
- Use of anti-CD20 or other B-cell mAb agents for prevention of allograft rejection within 9 months of first dose

Kidney

Inclusion criteria: Stable renal function

Exclusion criteria:

- Previous allograft loss secondary to recurrent primary kidney disease
- Significant proteinuria/albuminuria

Lung

Inclusion criteria: Stable lung function

Exclusion criteria:

- Acute pulmonary infection with 2 weeks of study intervention visit
- Diagnosis of chronic lung allograft dysfunction

Adults ≥ 50 YOA

Inclusion criteria:

- **Medically stable in investigator's opinion**
- **Participants with chronic stable conditions with or without specific treatment (e.g., diabetes mellitus, hypertension, cardiac disease)**

Exclusion criteria:

- Immunosuppressive or immunodeficient conditions
- Unstable chronic illness

ABO, ABO blood group system; CD, cluster of differentiation; mAb, monoclonal antibody; SOT, solid organ transplant; YOA, years of age

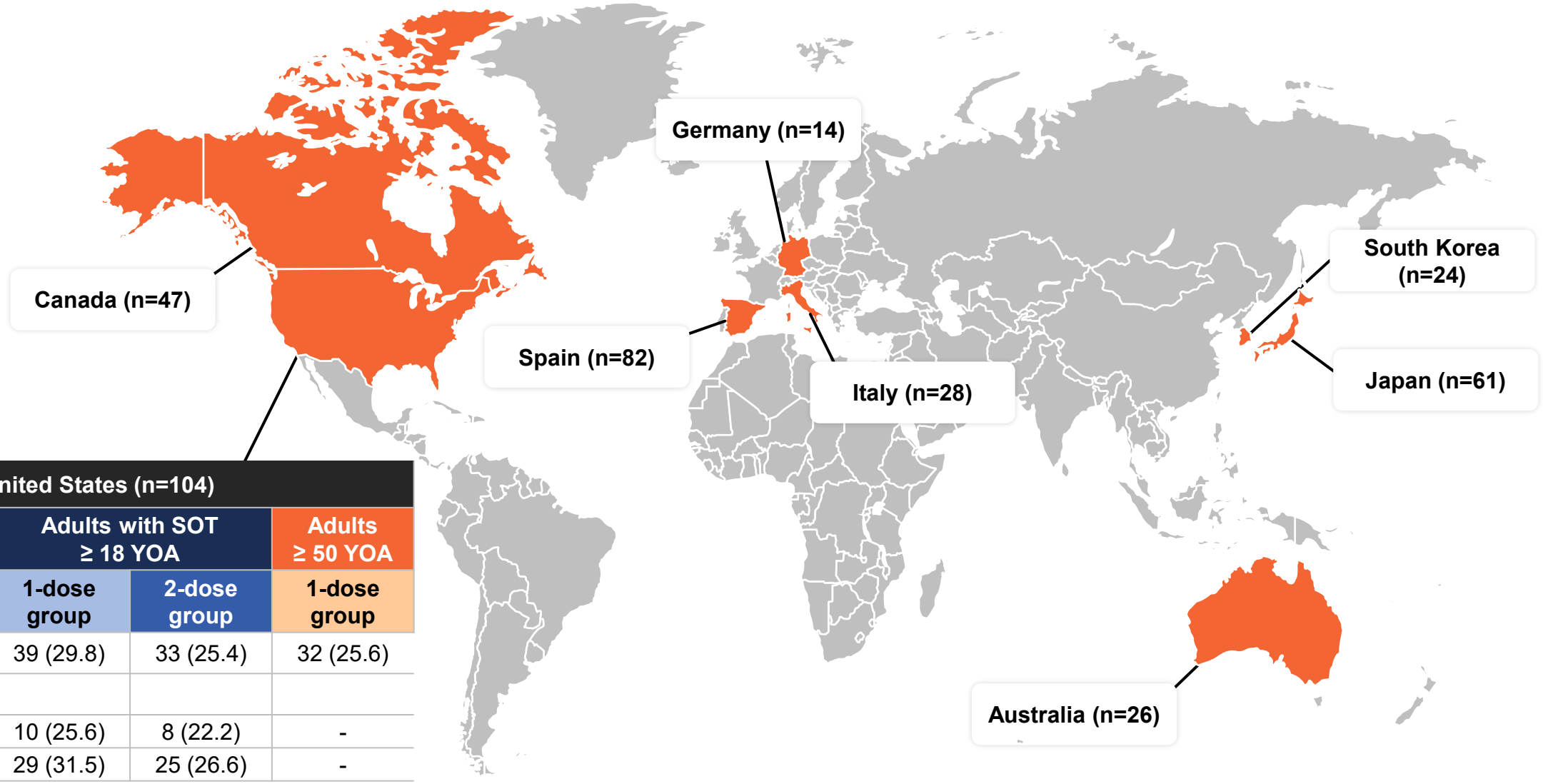
ClinicalTrials.gov. NCT05921803. https://www.clinicaltrials.gov/study/NCT05921903 (accessed September 2024)

Demographic Characteristics Generally Balanced Between Groups (Exposed Set)

Characteristic	Adults with SOT ≥ 18 YOA		Adults ≥ 50 YOA	Total (N=386)
	1-dose group (N=131)	2-dose group (N=130)	1-dose group (N=125)	
Age (years) at vaccination, mean (SD)	61.9 (9.3)	61.4 (8.4)	63.8 (8.2)	62.4 (8.7)
Age category, n (%)				
18–49 YOA	9 (6.9)	8 (6.2)	0 (0.0)	17 (4.4)
50–59 YOA	37 (28.2)	41 (31.5)	44 (35.2)	122 (31.6)
≥ 60 YOA	85 (64.9)	81 (62.3)	81 (64.8)	247 (64.0)
Sex, n (%)				
Female	54 (41.2)	50 (38.5)	66 (52.8)	170 (44.0)
Ethnicity, n (%)				
Hispanic or Latino	12 (9.2)	5 (3.8)	22 (17.6)	39 (10.1)
Race, n (%)				
American Indian or Alaska Native	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.3)
Asian	26 (19.8)	33 (25.4)	10 (8.0)	69 (17.9)
Black or African American	11 (8.4)	8 (6.2)	4 (3.2)	23 (6.0)
White	89 (67.9)	79 (60.8)	95 (76.0)	263 (68.1)
Not reported or unknown	4 (3.1)	9 (6.9)	15 (12.0)	28 (7.3)
Multiple	1 (0.8)	0 (0.0)	1 (0.8)	2 (0.5)
SOT type, n (%)				
Lung transplant	39 (29.8)	36 (27.7)	-	-
Kidney transplant	92 (70.2)	94 (72.3)	-	-
Interval between last transplantation and Visit 1 (months), median (min, max)	67 (12, 386)	60 (14, 450)	-	-

Adults with SOT 1-dose group: adults with kidney and lung transplant ≥18 YOA receiving 1 dose of RSVPreF3 + $AS01_E$ at Visit 1 (Day 1); Adults with SOT 2-dose group: adults with kidney and lung transplant ≥18 YOA receiving 2 doses of RSVPreF3 + $AS01_E$ at Visit 1 (Day 1) and Visit 3 (30–60 days post-Dose 1); Adults ≥50 YOA group: adults ≥50 YOA receiving 1 dose of RSVPreF3 + $AS01_E$ at Visit 1 (Day 1); SD, standard deviation; SOT, solid organ transplant; YOA, years of age

Worldwide Study Including 8 Countries



United States (n=104)			
	Adults with SOT ≥ 18 YOA		Adults ≥ 50 YOA
	1-dose group	2-dose group	1-dose group
n (%)	39 (29.8)	33 (25.4)	32 (25.6)
SOT type, n (%)			
Lung	10 (25.6)	8 (22.2)	-
Kidney	29 (31.5)	25 (26.6)	-

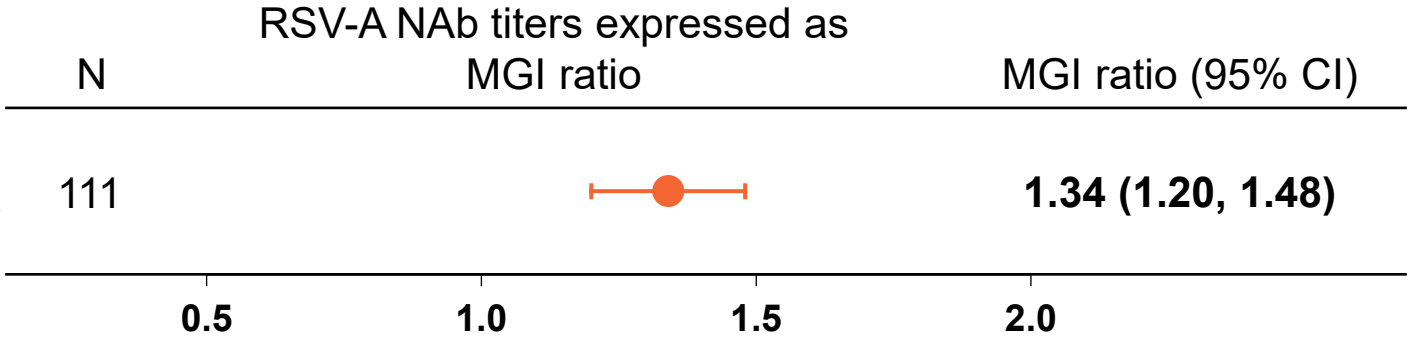
Immunogenicity

Preliminary results

Co-primary Endpoints: RSV-A and RSV-B NAbs Higher at 1 Month Post-Dose 2 vs Post-Dose 1 in Adults with SOT ≥ 18 YOA Receiving 2 Doses of RSVPreF3 + $AS01_E$*

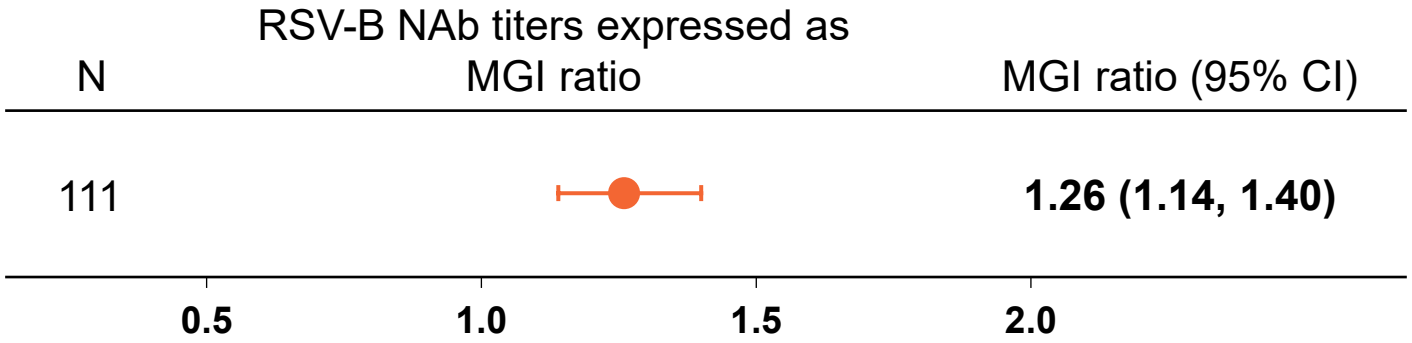
RSV-A

$$\text{MGI} = \frac{\text{1 month post−Dose 2 (Visit 4)}}{\text{1 month post−Dose 1 (Visit 3)}}$$



RSV-B

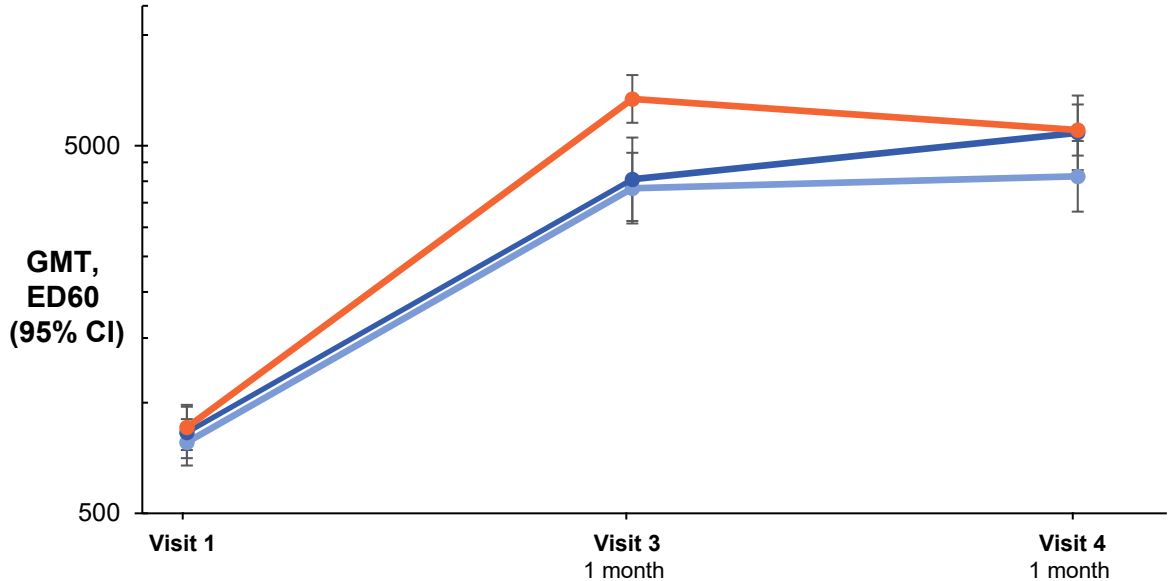
$$\text{MGI} = \frac{\text{1 month post−Dose 2 (Visit 4)}}{\text{1 month post−Dose 1 (Visit 3)}}$$



*Adults with SOT ≥ 18 YOA receiving 2 doses of RSVPreF3 + $AS01_E$ at Visit 1 (Day 1) and Visit 3 (30–60 days post-Dose 1)
CI, confidence interval; MGI, mean geometric increase; NAb, neutralizing antibody; SOT, solid organ transplant; YOA, years of age

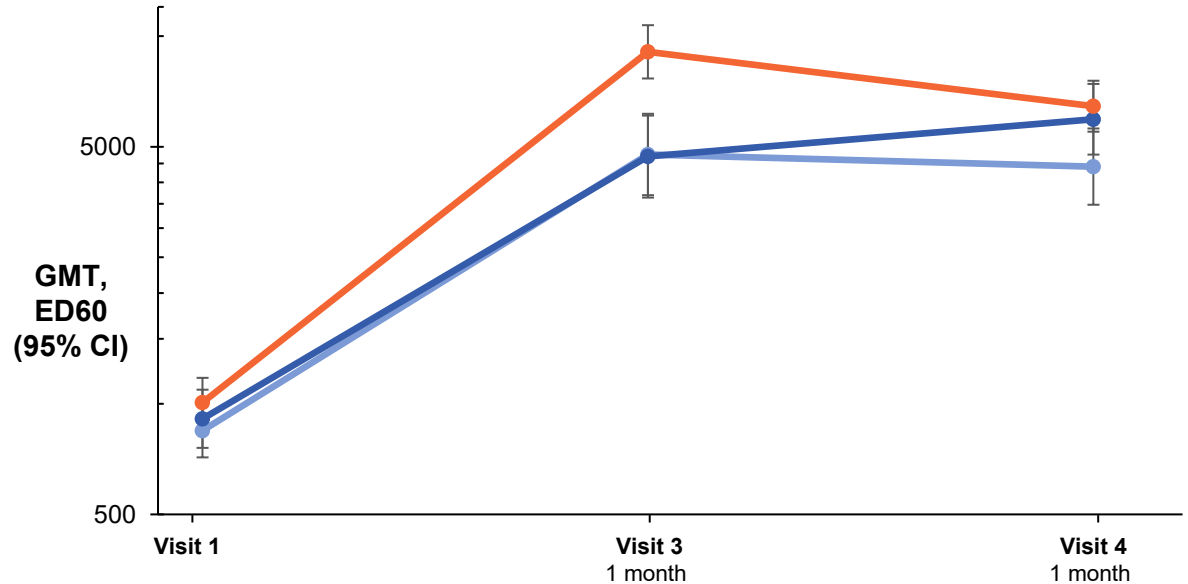
RSVPreF3 + AS01$_E$ Elicits Robust Humoral Immune Responses in Kidney and Lung Transplant Recipients

RSV-A NAbs*



n	Visit 1	Visit 3 1 month post-Dose 1	Visit 4 1 month post-Dose 2**
SOT 1-dose	114	114	114
SOT 2-dose	110	110	110
≥ 50 YOA	105	105	105

RSV-B NAbs*



n	Visit 1	Visit 3 1 month post-Dose 1	Visit 4 1 month post-Dose 2**
SOT 1-dose	114	114	114
SOT 2-dose	110	110	110
≥ 50 YOA	105	105	105

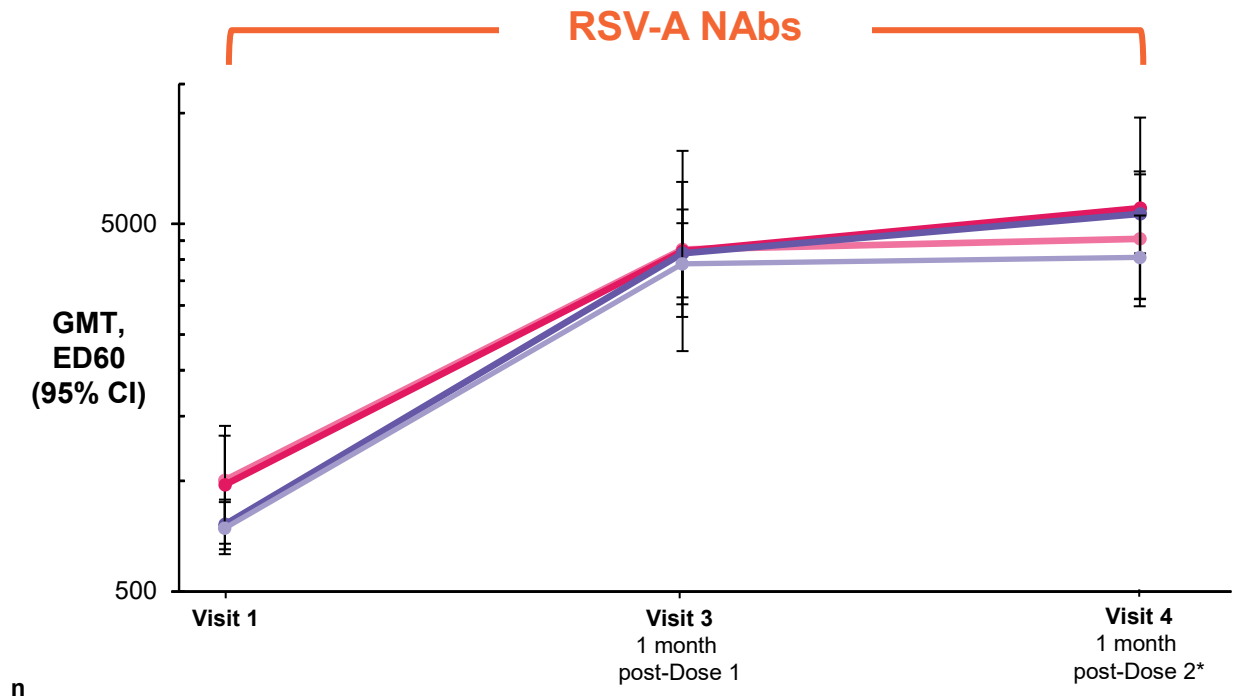
Adults with SOT ≥ 18 YOA 1-dose

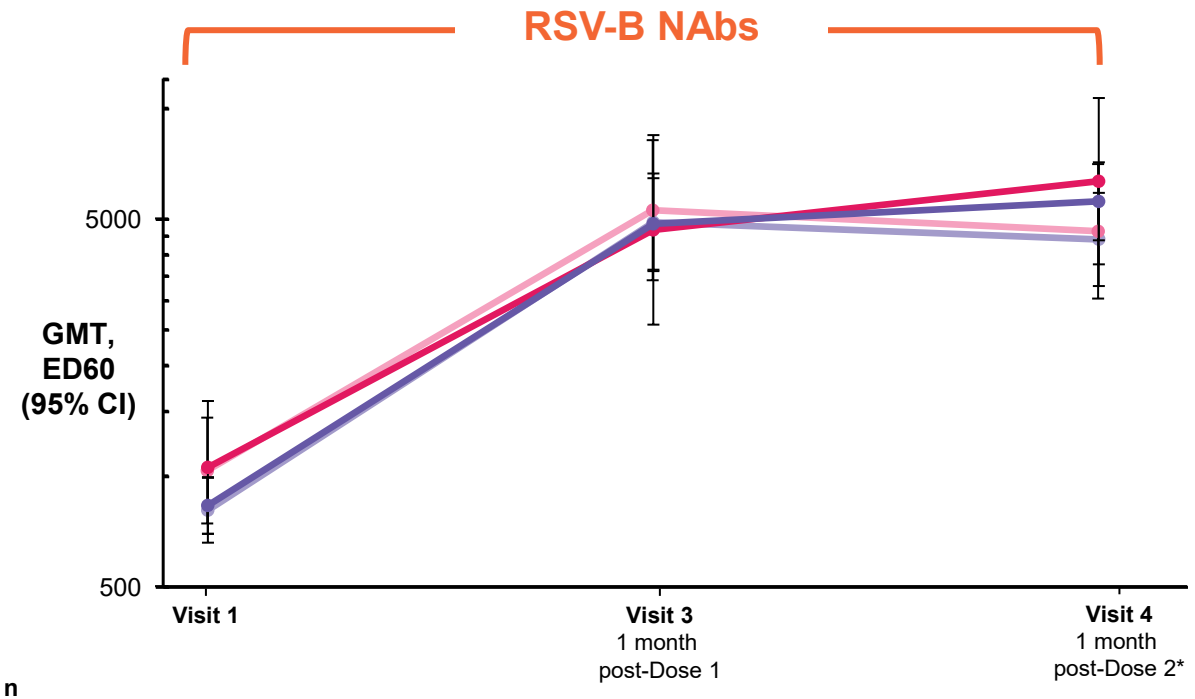
Adults with SOT ≥ 18 YOA 2-dose

Adults ≥ 50 YOA

***In participants with results available at all timepoints; **For Adults with SOT 1-dose group and Adults ≥50 YOA, Visit 4 refers to 1 month post-Visit 3**
Adults with SOT 1-dose group: adults with kidney and lung transplant ≥18 YOA receiving 1 dose of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1); Adults with SOT 2-dose group: adults with kidney and lung transplant ≥18 YOA receiving 2 doses of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1) and Visit 3 (30–60 days post-Dose 1); Adults ≥50 YOA group: adults ≥50 YOA receiving 1 dose of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1); CI, confidence interval; ED60, estimated dilution 60; GMT, geometric mean titer; NAb, neutralizing antibody; SOT, solid organ transplant; YOA, years of age

RSVPreF3 + AS01$_E$ Induced Similar RSV-A and RSV-B Neutralizing Antibody Responses in Kidney and Lung Transplant Recipients





n			
Kidney 1 dose	89	88	83
Kidney 2 dose	90	84	81
Lung 1 dose	34	35	33
Lung 2 dose	33	30	30

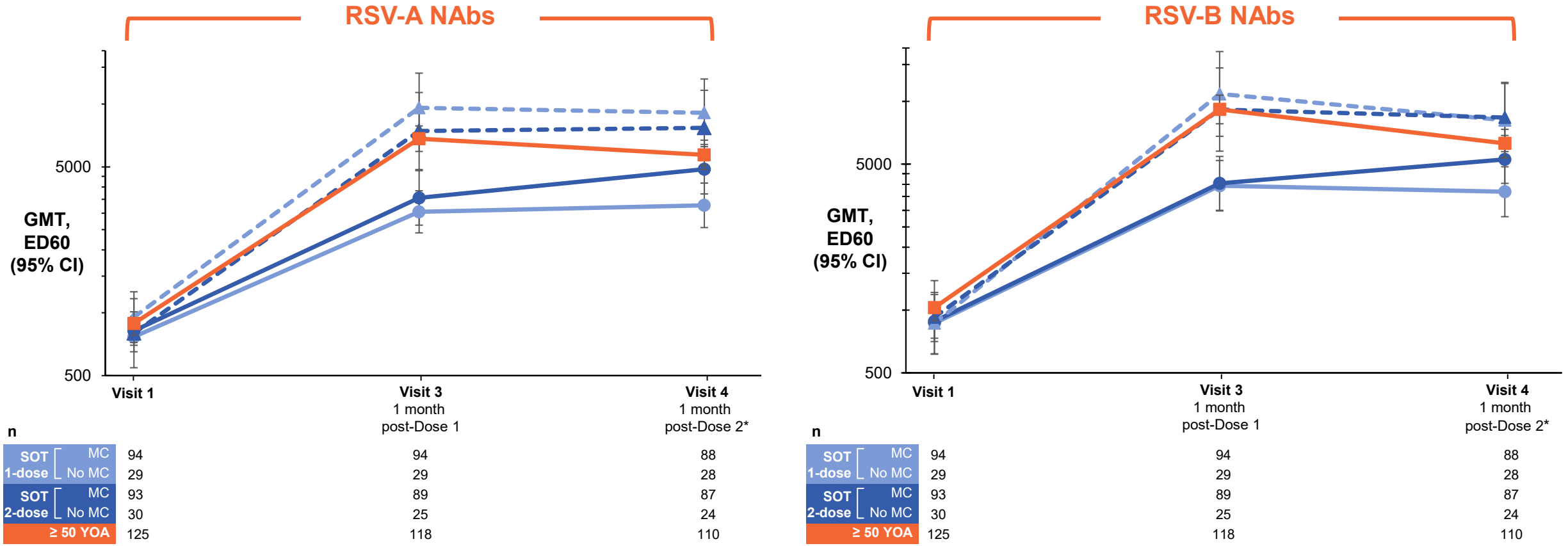
n			
Kidney 1 dose	89	88	83
Kidney 2 dose	90	84	81
Lung 1 dose	34	35	33
Lung 2 dose	33	30	30

Kidney transplant — 1 dose, 2 dose

Lung transplant — 1 dose, 2 dose

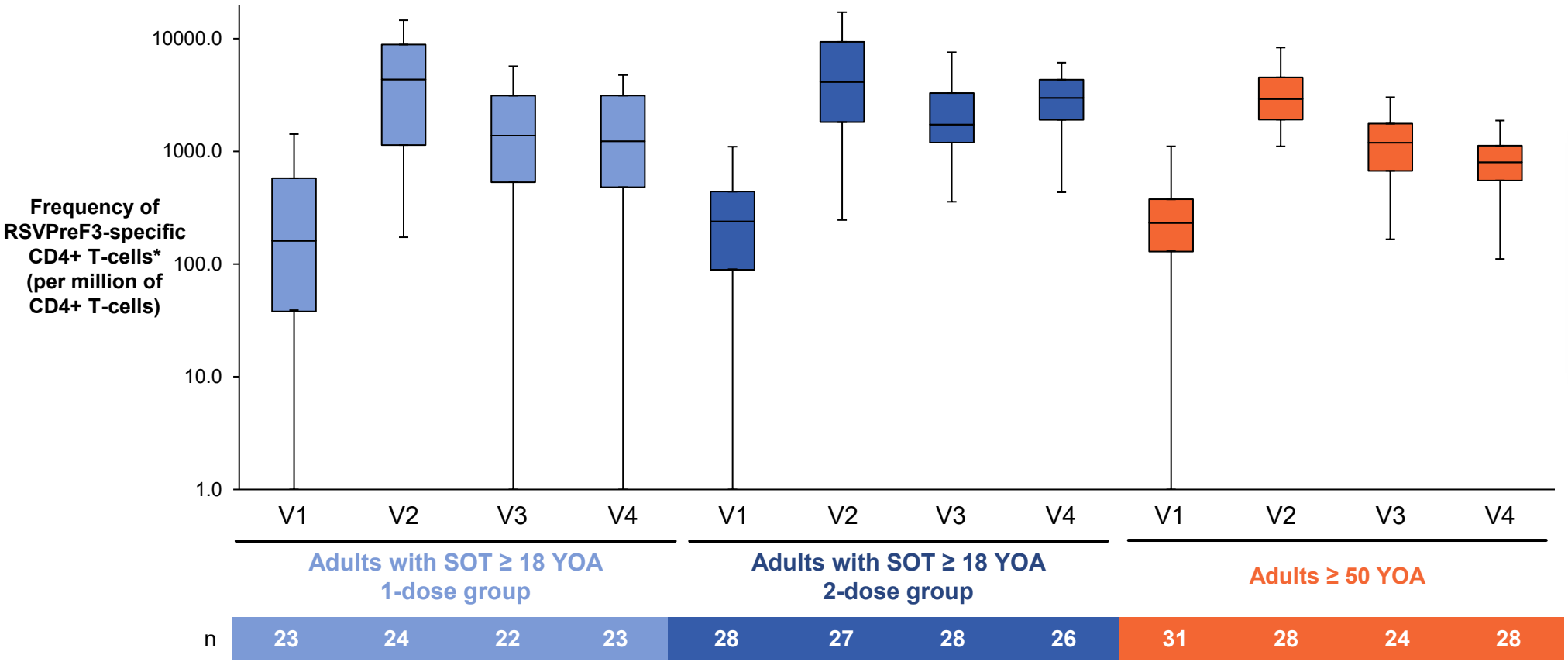
*For Adults with SOT 1-dose group, Visit 4 refers to 1 month post-Visit 3; Adults with SOT 1-dose group: adults with kidney and lung transplant ≥18 YOA receiving 1 dose of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1); Adults with SOT 2-dose group: adults with kidney and lung transplant ≥18 YOA receiving 2 doses of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1) and Visit 3 (30–60 days post-Dose 1);CI, confidence interval; ED60, estimated dilution 60; GMT, geometric mean titer; SOT, solid organ transplant; YOA, years of age

Differences in RSV-A and RSV-B Neutralizing Antibody Responses Induced by RSVPreF3 + AS01$_E$ by Presence or Absence of Mycophenolate

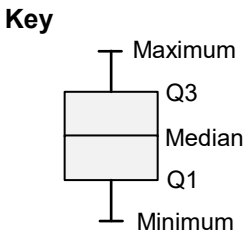


*For Adults with SOT 1-dose group and Adults ≥50 YOA, Visit 4 refers to 1 month post-Visit 3; Adults with SOT 1-dose group: adults with kidney and lung transplant ≥18 YOA receiving 1 dose of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1); Adults with SOT 2-dose group: adults with kidney and lung transplant ≥18 YOA receiving 2 doses of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1) and Visit 3 (30–60 days post-Dose 1); CI, confidence interval; ED60, estimated dilution 60; GMT, geometric mean titer; MC, mycophenolate; SOT, solid organ transplant; YOA, years of age

RSVPreF3 + AS01$_E$ Induces Robust CD4+ T-cell Responses in Kidney and Lung Transplant Recipients



Increased CD4+ T-cell responses were consistent across immunocompromised groups (1-dose, 2-dose) and adults ≥ 50 YOA



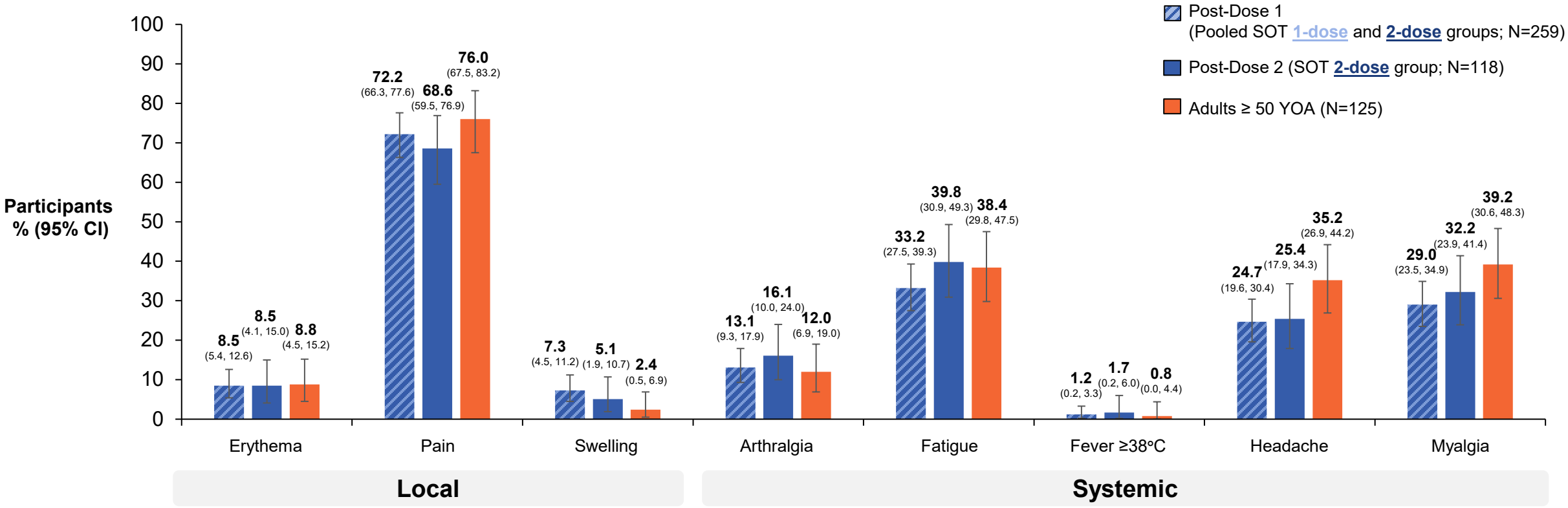
*Expressing ≥ 2 activation markers including ≥1 cytokine among CD40L, 4-1BB, IL-2, TNF-α, IFN-γ, IL-13, and IL-17

Adults with SOT 1-dose group: adults with kidney and lung transplant ≥ 18 YOA receiving 1 dose of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1); adults with SOT 2-dose group: adults with kidney and lung transplant ≥ 18 YOA receiving 2 doses of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1) and Visit 3 (30–60 days post-Dose 1); Adults ≥50 YOA group: adults ≥ 50 YOA receiving 1 dose of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1); CD, cluster of differentiation; IFN, Interferon; IL, interleukin; SOT, solid organ transplant; TNF, tumor necrosis factor; V, Visit; YOA, years of age

Safety

Preliminary results

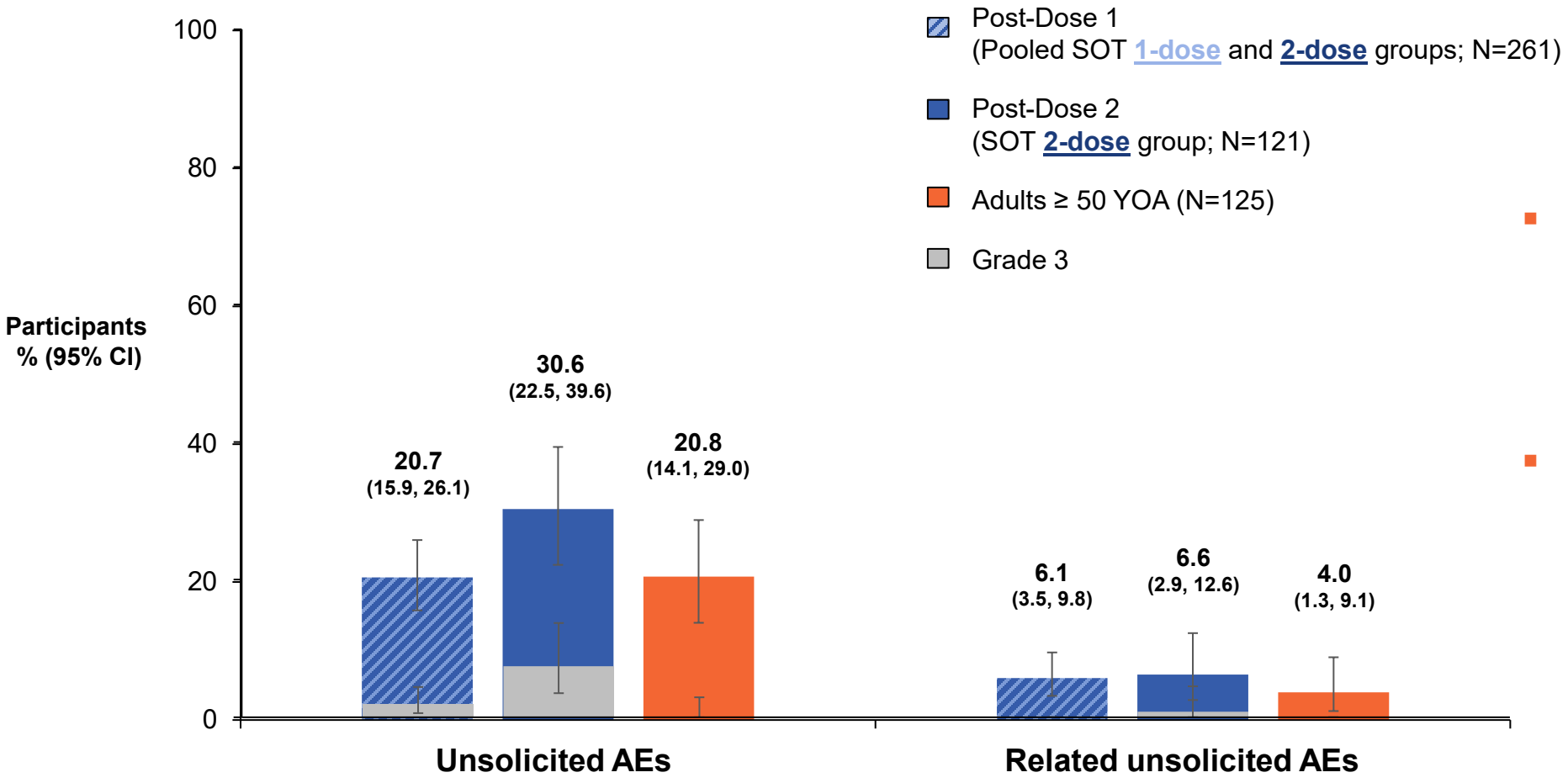
Solicited AEs Broadly Similar Between SOT Groups and ≥ 50 YOA Group (Within 7 Days Post-Vaccination)



Incidence of solicited Grade 3 AEs were low across groups (≤ 3% for any AE in any group)

Grade 3 AEs were defined as administration-site erythema or swelling with a diameter >100 mm, fever with a temperature >39.0°C/102.2°F, and administration-site pain, headache, fatigue, myalgia, and arthralgia that prevented normal activity. Adults with SOT 1-dose group: adults with kidney and lung transplant ≥18 YOA receiving 1 dose of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1); Adults with SOT 2-dose group: adults with kidney and lung transplant ≥18 YOA receiving 2 doses of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1) and Visit 3 (30–60 days post-Dose 1); Adults ≥50 YOA group: adults ≥50 YOA receiving 1 dose of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1); AE, adverse event; CI, confidence interval; SOT, solid organ transplant; YOA, years of age

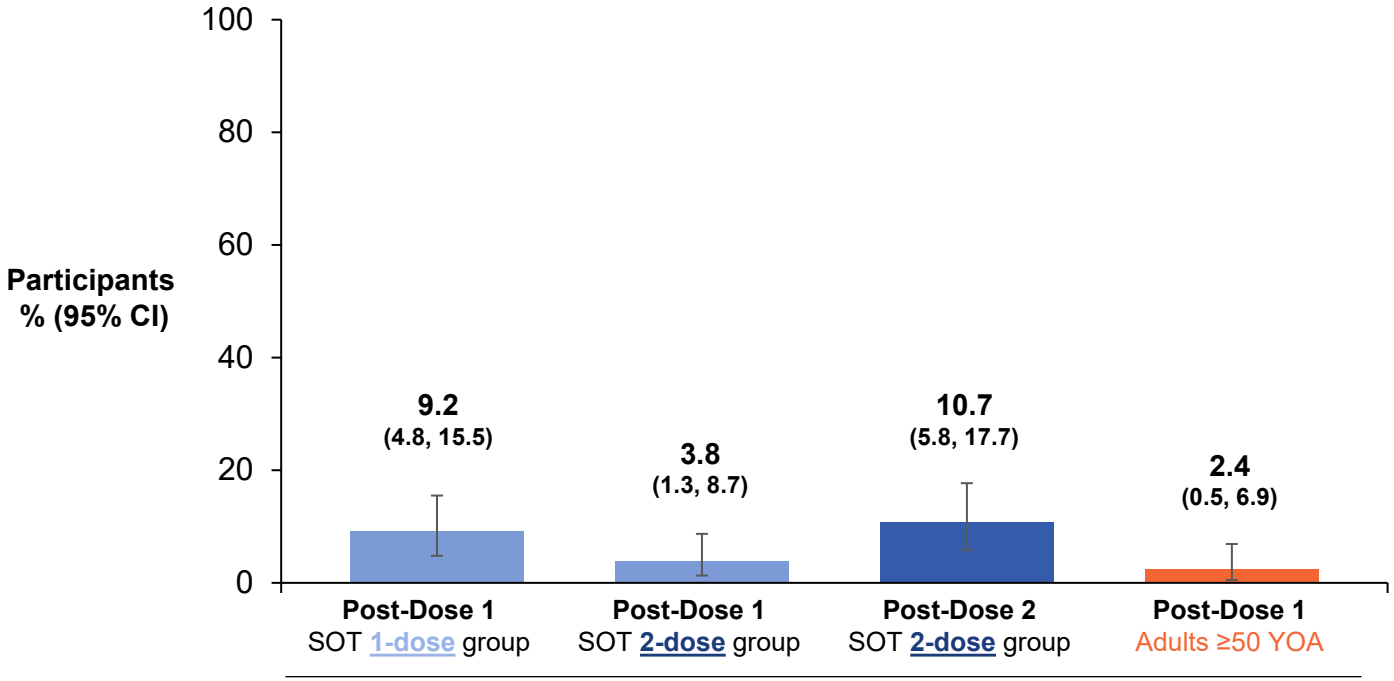
Related Unsolicited AEs Similar Between Groups (Within 30 Days Post-Vaccination)



- Most events in SOT groups reflect background morbidity (e.g. range of infections, gastrointestinal and general AEs)
- No pattern or clustering of events types to suggest a safety concern

Adults with SOT 1-dose group: adults with kidney and lung transplant ≥18 YOA receiving 1 dose of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1); Adults with SOT 2-dose group: adults with kidney and lung transplant ≥18 YOA receiving 2 doses of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1) and Visit 3 (30–60 days post-Dose 1); Adults ≥50 YOA group: adults ≥50 YOA receiving 1 dose of RSVPreF3 + AS01$_E$ at Visit 1 (Day 1); AE, adverse event; CI, confidence interval; SOT, solid organ transplant; YOA, years of age

SAEs Similar Between Dose 1 and Dose 2 SOT Groups (Up to Safety Data Lock Point)



	Post-Dose 1 SOT 1-dose group	Post-Dose 1 SOT 2-dose group	Post-Dose 2 SOT 2-dose group	Post-Dose 1 Adults ≥50 YOA
N	131	130	121	125
Median follow-up	170 days	30-60 days	136 days	171 days

- No specific pattern or clustering of SAEs
- No cases of GBS or atrial fibrillation

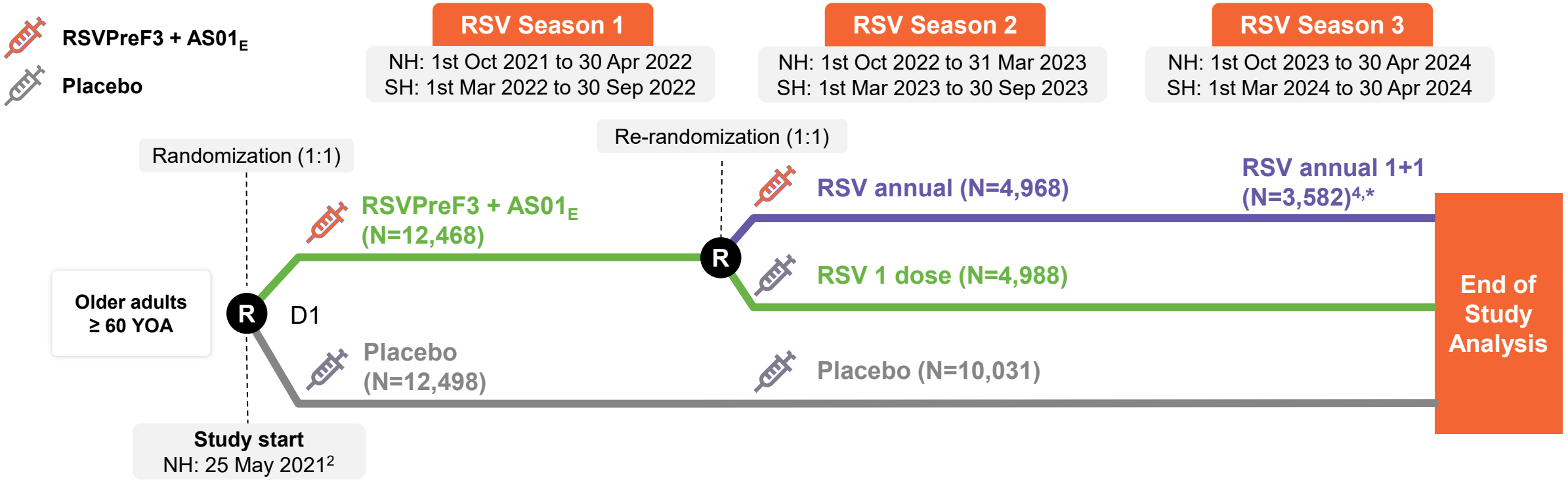
Adults with SOT 1-dose group: adults with kidney and lung transplant ≥18 YOA receiving 1 dose of RSVPreF3 + $AS01_E$ at Visit 1 (Day 1); Adults with SOT 2-dose group: adults with kidney and lung transplant ≥ 18 YOA receiving 2 doses of RSVPreF3 + $AS01_E$ at Visit 1 (Day 1) and Visit 3 (30–60 days post-Dose 1); Adults ≥50 YOA group: adults ≥50 YOA receiving 1 dose of RSVPreF3 + $AS01_E$ at Visit 1 (Day 1); CI, confidence interval; GBS, Guillain-Barré syndrome; pIMD, potential immune-mediated disease; SAE, serious adverse event; SOT, solid organ transplant; YOA, years of age

AReSVi-006 Pivotal Efficacy Study: Preliminary Updates from Season 3

Phase 3, Randomized, Placebo-Controlled, Multi-Country Study to Demonstrate Efficacy & Safety of Single & Annual Revaccination Doses in Adults 60 Years & Older

NCT04886596

AReSVi-006 Phase 3 Trial Design[1-4]



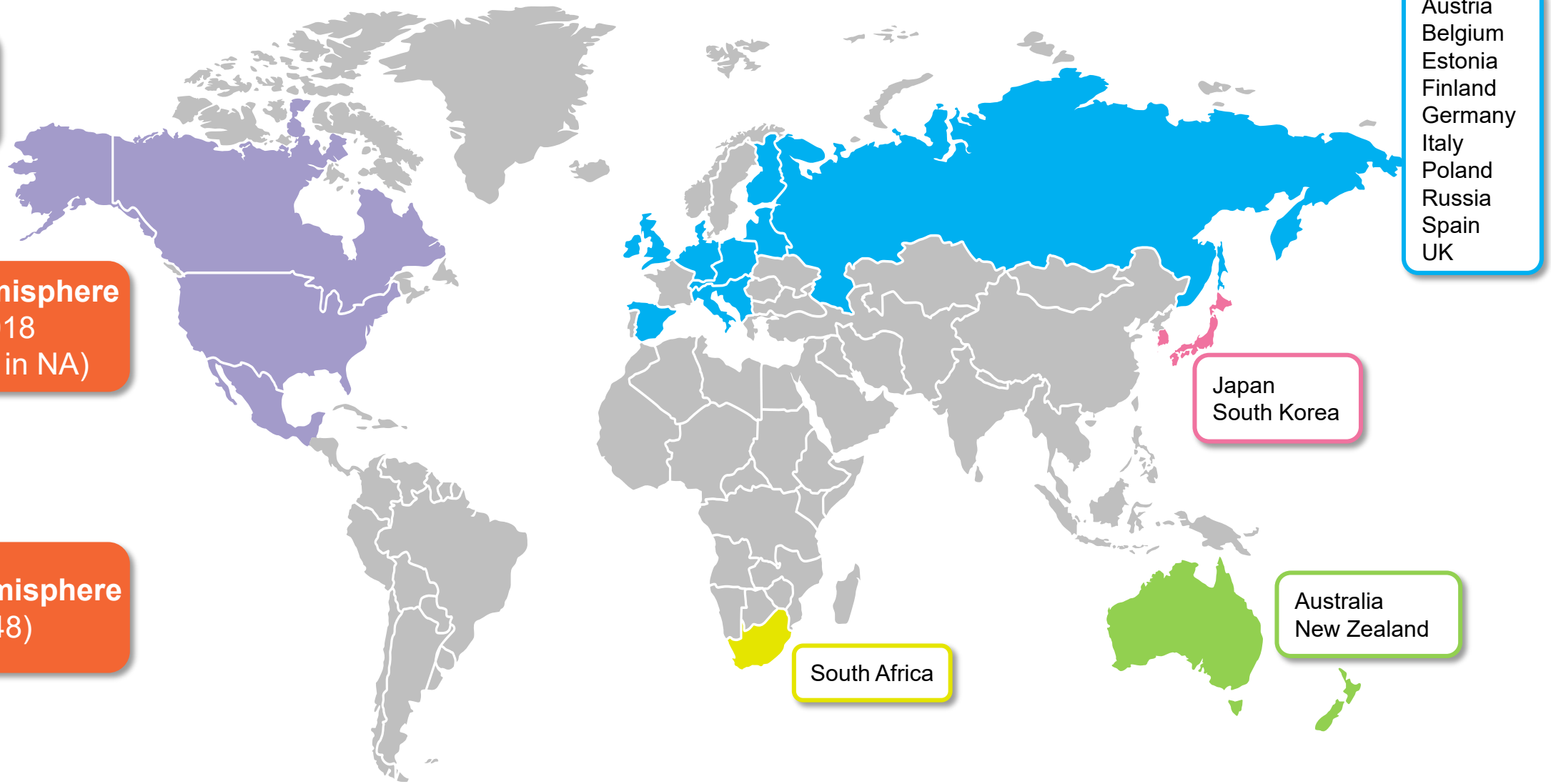
Primary endpoint: To demonstrate efficacy of RSVPreF3 + $AS01_E$ in prevention of RSV LRTD** in adults ≥ 60 YOA during first season[2]

Confirmatory secondary endpoints: To demonstrate efficacy of RSVPreF3 + $AS01_E$ in the prevention of RSV LRTD** in adults ≥ 60 YOA over three seasons, following a single dose and annual revaccination of RSVPreF3 + $AS01_E$, and for each RSV subgroup (A and B) separately[2]

All RSV-LRTD** cases adjudicated by independent external adjudication committee

Figure adapted from Ison MG et al. Clin Infect Dis 2024. under the terms of the CC BY 4.0 Attribution License (https://creativecommons.org/licenses/by/4.0/); *Some participants in NH who came at their Pre-season 3 visit before the approval of protocol amendment 5 received Dose 3; **LRTD defined as ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours. All cases of RSV were RT-PCR confirmed; D, day; LRTD, lower respiratory tract disease; N, number of participants in the modified exposed set (S1), dose 2-modified exposed set (S2), participants in the dose 2-modified exposed set who did not receive dose 3 (RSV annual group);
NH, Northern Hemisphere; RT-PCR, reverse transcription-polymerase chain reaction; S, season; SH, Southern Hemisphere; YOA, years of age;
1. ClinicalTrials.gov, 2024. NCT04886596.; 2. Papi A et al. N Engl J Med 2023;388:595–608; 3. Ison MG et al. Clin Infect Dis 2024;78:1732–1744; 4. Unpublished data

~25,000 Participants Randomized in 17 Countries



RSVPreF3 Vaccine for Respiratory Syncytial Virus (RSV) in Older Adults. Presented at VRBPAC Meeting, March 1, 2023; FDA.gov (URL accessed August 2024);
NA, North America; UK, United Kingdom; VRBPAC, Vaccines and Related Biological Products Advisory Committee

AReSVi-006 Case Definitions[1,2]

Signs and symptoms in addition to ≥ 1 RSV-positive swab detected by qRT-PCR

ARI
≥ 2 respiratory symptoms or signs
OR
≥ 1 respiratory and 1 systemic symptom or sign for at least 24 hours

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
- O_2 supplement

LRTD*
≥ 2 lower respiratory symptoms or signs (≥ 1 sign)
OR
≥ 3 lower respiratory symptoms for at least 24 hours

Lower respiratory symptoms

- Sputum
- Cough
- Dyspnea

Lower respiratory signs

- Wheezing
- Crackles/rhonchi
- Tachypnea
- Hypoxemia
- O_2 supplement

Severe LRTD*
≥ 2 lower respiratory signs
OR
episode preventing normal, everyday activities

Lower respiratory signs

- Wheezing
- Crackles/rhonchi
- Tachypnea
- Hypoxemia
- O_2 supplement

***USPI case definitions; ARI, acute respiratory infection; LRTD, lower respiratory tract disease; qRT-PCR, quantitative reverse transcription-polymerase chain reaction;**

1. GSK's RSVPreF3 OA Vaccine (AREXVY). Presented at ACIP, 21 June 2023 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Adults-Friedland-508.pdf (URL accessed August 2024); 2. Papi A et al. N Engl J Med 2023;388:595–608

Single Dose of RSVPreF3 + AS01$_E$ Demonstrates Clinically Meaningful Vaccine Efficacy Against RSV-LRTD* Over 3 RSV Seasons[1-4]

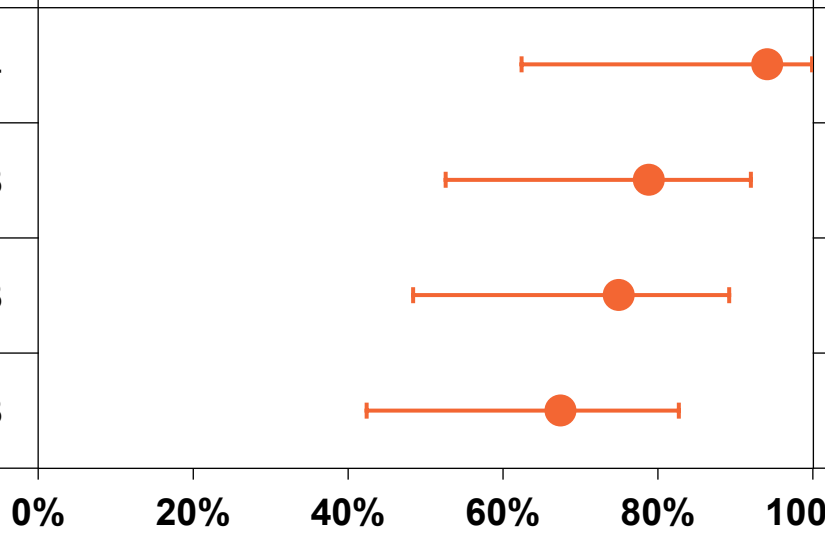
Season (median follow-up time)	RSVPreF3 + AS01$_E$	Placebo	Vaccine Efficacy (CI)*****	% VE (CI)*****	
	Number of events (n/N)			*W/ season covariate*	*W/o season covariate*
Season 1** (end of NH S1; 6.7m)[1]	**7** / 12,466	**40** / 12,494		n/a	**82.6** (57.9, 94.1)
Season 1 + 2*** (end of NH S2; 17.8m)[2]	**30** / 12,469	**139** / 12,498		**67.2** (48.2, 80.0)	**74.5** (60.0, 84.5)
2 calendar years**** (end of SH S2; 23.3m)[3]	**32** / 12,468	**154** / 12,498		**67.7** (52.3, 78.7)	**73.3** (60.7, 82.4)
Season 1–3*** (end of NH S3; 30.6m)[4]	**48** / 12, 468	**215** / 12,498		**62.9** (46.7, 74.8)	**69.1** (55.8, 78.9)

*VE is maintained up to end of Season 3 NH. Confirmatory secondary endpoint is demonstrated with LL >20%; **96.95% CI; ***97.5% CI; ****95% CI; *****VE was estimated using a Poisson model adjusted for age, region, and season ("with season as a covariate") or for age and region ("without season as a covariate"; post-hoc analyses). For Season only VE, season could not be considered a covariate, so data are presented in the "without season as a covariate" column; CI, confidence interval; LRTD, lower respiratory tract disease; m, month; n/a, not applicable; NH, Northern Hemisphere; S, Season; SH, Southern Hemisphere; VE, vaccine efficacy.

1. Papi A et al. N Engl J Med 2023;388:595–608; 2. Ison MG et al. Clin Infect Dis 2024;78:1732–1744; 3. Gerber S. AREXVY (Adjuvanted RSVPreF3) 2-Year Update. Presented at ACIP 26 June 2024. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2024-06-26-28/03-RSV-Adult-Gerber-508.pdf (accessed August 2024); 4. Unpublished data

Vaccine Efficacy of Single Dose of RSVPreF3 + AS01$_E$ Against Severe RSV-LRTD Over 3 RSV Seasons[1-4]

Season (median follow-up time)	RSVPreF3 + AS01$_E$	Placebo	% VE (95% CI)*	
	Number of events (n/N)		*W/ season covariate*	*W/o season covariate*
Season 1 (end of NH S1; 6.7m)[1]	**1** / 12,466	**17** / 12,494	n/a	**94.1** (62.4, 99.9)
Season 1 + 2 (end of NH S2; 17.8.m)[2]	**7** / 12,469	**48** / 12,498	**78.8** (52.6, 92.0)	**82.7** (61.6, 93.4)
2 calendar years (end of SH S2; 23.3m)[3]	**9** / 12,468	**54** / 12,498	**74.9** (48.4, 89.2)	**78.6** (56.3, 90.7)
Season 1–3 (end of NH S3; 30.6m)[4]	**15** / 12,468	**75** / 12,498	**67.4** (42.4, 82.7)	**72.3** (51.3, 85.2)



*VE estimated using Poisson model adjusted for age, region, and season ("with season as a covariate") or for age and region ("without season as a covariate"; post hoc analyses). For Season only VE, season could not be considered a covariate, so data are presented in the "without season as a covariate" column; CI, confidence interval; LRTD, lower respiratory tract disease; m, month; n/a, not applicable; NH, Northern Hemisphere; S, Season; SH, Southern Hemisphere; VE, vaccine efficacy; 1. Papi A et al. N Engl J Med 2023; 2. Ison MG et al. Clin Infect Dis 2024; 3. Gerber S. AREXVY (Adjuvanted RSVPreF3) 2-Year Update. Presented at ACIP 26 June 2024. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2024-06-26-28/03-RSV-Adult-Gerber-508.pdf (accessed August 2024); 4. Unpublished data

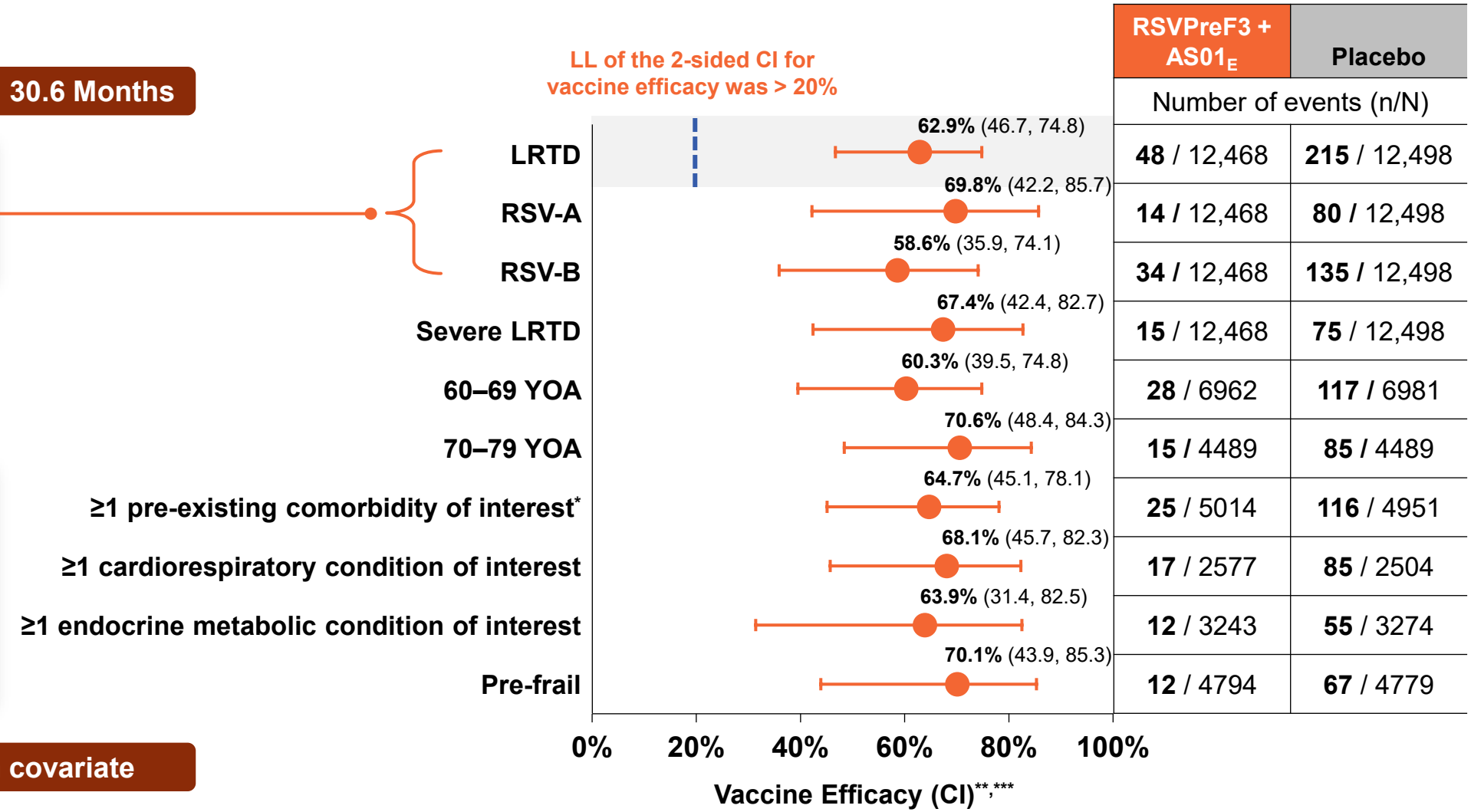
Single Dose of RSVPreF3 + AS01$_E$ Shows Consistent Vaccine Efficacy for Subgroups Over 3 RSV Seasons

Median Follow-up: 30.6 Months

Confirmatory secondary endpoints

VE cannot be reliably estimated for **adults ≥ 80 YOA and frail group** as **too few cases** were observed

VE with season covariate

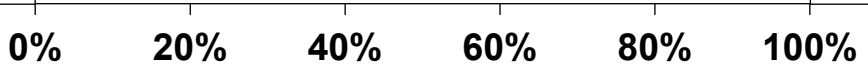


	RSVPreF3 + AS01$_E$	Placebo
	Number of events (n/N)	
LRTD	**48** / 12,468	**215** / 12,498
RSV-A	**14** / 12,468	**80** / 12,498
RSV-B	**34** / 12,468	**135** / 12,498
Severe LRTD	**15** / 12,468	**75** / 12,498
60–69 YOA	**28** / 6962	**117** / 6981
70–79 YOA	**15** / 4489	**85** / 4489
≥1 pre-existing comorbidity of interest*	**25** / 5014	**116** / 4951
≥1 cardiorespiratory condition of interest	**17** / 2577	**85** / 2504
≥1 endocrine metabolic condition of interest	**12** / 3243	**55** / 3274
Pre-frail	**12** / 4794	**67** / 4779

*COPD, asthma, any chronic respiratory/pulmonary disease, diabetes type 1 or type 2, chronic heart failure, advanced liver or renal disease; **97.5% CI for confirmatory secondary endpoint; 95% CI for other endpoints; ***Vaccine efficacy was estimated using a Poisson model adjusted for age, region, and season ("with season as a covariate");
COPD, chronic obstructive pulmonary disease; CI, confidence interval; LL, lower limit; LRTD, lower respiratory tract disease; VE, vaccine efficacy; YOA, years of age. Unpublished data

Vaccine Efficacy of Single Dose of RSVPreF3 + AS01$_E$ Against RSV-LRTD by RSV Season[1-4]

Season (median follow-up time)	RSVPreF3 + AS01$_E$	Placebo	Vaccine Efficacy (CI)*	% VE (CI)*
	Number of events (n/N)			
Season 1 (end of NH S1; 6.7m)[1]	**7** / 12,466	**40** / 12,494		**82.6** (57.9, 94.1)
Season 2 only (end of NH S2; 6.3m)[2]	**20** / 4991	**91** / 10,031		**56.1** (28.2, 74.4)
Season 2 only (end of SH S2; 11.9m)[3]	**22** / 4988	**106** / 10,031		**58.5** (33.9, 75.0)
Season 3 only (end of NH S3; 7m)[4]	**16** / 4988	**61** / 10,031		**48.0** (8.7, 72.0)



*96.95% CI for the primary endpoint (S1 RSV-LRTD, overall); 95% CI for other endpoints; CI, confidence interval; LRTD, lower respiratory tract disease; m, month; n/a, not applicable; NH, Northern Hemisphere; S, Season; SH, Southern Hemisphere; VE, vaccine efficacy

1. Papi A *et al. N Engl J Med* 2023;388:595–608; 2. Ison MG *et al. Clin Infect Dis* 2024;78:1732–1744; 3. GSK. Data on File; 2024N557587_00; 4. Unpublished data

Vaccine Efficacy of Single Dose of RSVPreF3 + AS01$_E$ Against RSV-LRTD in Adults with ≥ 1 Comorbidity of Interest* by RSV Season[1-4]

Season (median follow-up time)	RSVPreF3 + AS01$_E$	Placebo	Vaccine Efficacy (95% CI)	% VE (95% CI)
	Number of events (n/N)			
Season 1 (end of NH S1; 6.7m)[1]	**1** / 4937	**18** / 4861		**94.6** (65.9, 99.9)
Season 2 only (end of NH S2; 6.3m)[2]	**12** / 1981	**48** / 3895		**51.5** (7.4, 76.6)
Season 2 only (end of SH S2; 11.9m)[3]	**13** / 1990	**55** / 3916		**54.2** (15.1, 77.1)
Season 3 only (end of NH S3; 7m)[4]	**8** / 2000	**37** / 3924		**57.8** (8.0, 83.0)

*Conditions of interest included any chronic respiratory/pulmonary disease (including chronic obstructive pulmonary disease and asthma) and chronic heart failure (cardiorespiratory), and diabetes mellitus type 1 or type 2 and advanced liver or renal disease (endocrine or metabolic); CI, confidence interval; COPD, chronic obstructive pulmonary disease; LRTD, lower respiratory tract disease; m, month; NH, Northern Hemisphere; S, Season; SH, Southern Hemisphere; VE, vaccine efficacy; YOA, years of age

1. Papi A *et al. N Engl J Med* 2023;388:595–608; 2. Ison MG *et al. Clin Infect Dis* 2024;78:1732–1744; 3. GSK. Data on File; 2024N557587_00; 4. Unpublished data

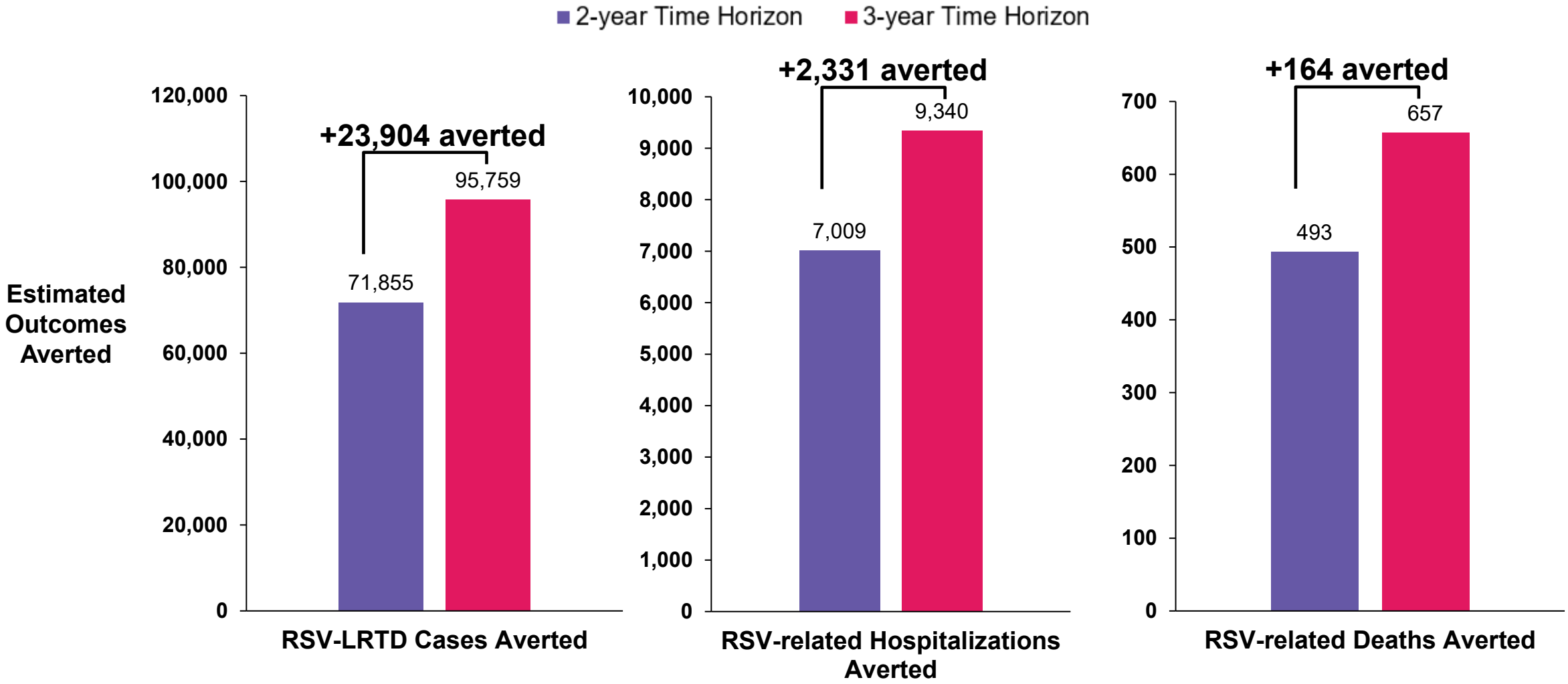
Safety Profile Remains Consistent and Acceptable Over 3 Seasons

- ~ 25,000 participants in pivotal efficacy trial
  - Cumulative follow-up occurred across all groups for median of 31.7 months
  - Safety profile of vaccine in adults ≥ 60 YOA remains acceptable and consistent with label[1]
- Frequency of SAEs/pIMDs remained low and similar across groups
  - No reports of GBS, ADEM

ADEM, acute disseminated encephalomyelitis; GBS, Guillain-Barré syndrome; pIMD, potential immune-mediated disease; SAE, serious adverse event; YOA, years of age; 1. FDA, 2024. AREXVY Prescribing Information (PI); https://www.fda.gov/media/167805/download (URL accessed Aug 2024)

Public Health Benefits with RSVPreF3 + AS01$_E$ Vaccination Over 3 Years

Potential RSV outcomes averted with vaccination vs no vaccination over 3 years based on 30.6-month follow up from Study 006 and over 2 years based on 23.3-month follow-up from Study 006 among US adults aged 50-59 years with COPD



Assuming same vaccination coverage as influenza vaccines from 2022-2023 season (https://www.cdc.gov/flu/fluvaxview/interactive-general-population.htm); Analysis includes 3,299,241 US adults with COPD aged 50-59 years, with 1,652,920 (50.1%) receiving RSVPreF3 + AS01$_E$; Estimated health outcomes over 2 years based on vaccine efficacy estimates using 23.3-month follow-up data from RSV OA=ADJ-006 Phase 3 Trial; Estimated health outcomes over 3 years based on vaccine efficacy estimates using 30.6-month follow-up data from RSV OA=ADJ-006 Phase 3 Trial

Overview of Clinical Development Program

Overview of Clinical Development

RSV OA=ADJ-002 study
Adults 18–40 or 60–80 YOA
First-in-human safety, immunogenicity, formulation, and dosing selection

RSV OA=ADJ-011 study (Extension of Study 002)
Adults ≥ 60 YOA
Persistence and safety and immunogenicity of a re-vaccination dose

RSV OA=ADJ-023 study
Immunocompromised adults ≥ 18 YOA (lung and kidney transplant recipients)
Safety and immunogenicity

AReSVi-006 study
Adults ≥ 60 YOA
Pivotal efficacy study

AReSVi-004 study
Adults ≥ 60 YOA
Safety, reactogenicity, immunogenicity, persistence, and re-vaccination

RSV OA=ADJ-018 study
Adults 50−59 YOA (incl. adults at increased risk of RSV-LRTD) vs ≥ 60 YOA
Safety, reactogenicity, immunogenicity

RSV OA=ADJ-012 study (Extension of Study 006)
Extension & crossover study in adults ≥ 60 YOA
Immunogenicity and safety of different re-vaccination schedules and persistence of single dose

RSV OA=ADJ-025 study
Adults 18–49 YOA at increased risk vs adults ≥ 60 YOA
Immunogenicity and safety

Co-administration
Safety, reactogenicity, and Immunogenicity

RSV OA=ADJ-007 study
Adults ≥ 60 YOA
Co-administration with FLU-QIV

RSV OA=ADJ-017 study
Adults ≥ 65 YOA
Co-administration with FLU-aQIV

RSV OA=ADJ-008 study
Adults ≥ 65 YOA
Co-administration with FLU-QIV-HD

RSV OA=ADJ-020 study
Adults ≥ 50 YOA
Co-administration with HZ/su vaccine

RSV OA=ADJ-019 study
Adults ≥ 60 YOA
Co-administration with PCV20

RSV OA=ADJ-013 study
Adults ≥ 50 YOA
Co-administration with COVID-19 mRNA vaccine

Phase 1/2 | Phase 2b | Phase 3
Completed | Ongoing/in progress/ data not yet public

FLU-aQIV: adjuvanted quadrivalent influenza vaccine; FLU-QIV: quadrivalent influenza vaccine; FLU-QIV-HD: high-dose quadrivalent influenza vaccine; HZ/su: herpes zoster recombinant subunit; M: month; PCV20, 20-valent pneumococcal conjugate vaccine; RSV-LRTD: respiratory syncytial virus lower respiratory tract disease; YOA: years of age
All studies ClinicalTrials.gov; All URLs accessed October 2024

Summary

Conclusions

1. One dose of RSVPreF3 + AS01$_E$ provides robust RSV-A and RSV-B neutralizing antibody responses and high CD4+ T-cell responses; acceptable safety profile in kidney and lung transplant recipients ≥ 18 YOA

2. For solid organ transplant recipients on mycophenolate, a second dose of RSVPreF3 + AS01$_E$ resulted in RSV-A and RSV-B neutralizing antibody responses close to levels observed in adults ≥ 50 YOA at same time point

3. RSVPreF3 + AS01$_E$ provides clinically meaningful efficacy over 3 seasons (median follow up time 30.6 months) in ≥ 60 YOA, with a continued acceptable safety profile

4. Estimated public health benefits of RSVPreF3 + AS01$_E$ are increased given its efficacy over 3 seasons as compared to previous efficacy estimates

5. Ahead of this year's RSV season, it is important to protect vulnerable individuals ≥ 50 YOA who are at high-risk for severe RSV disease

Meeting of the Advisory Committee on Immunization Practices (ACIP)

Centers for Disease Control and Prevention

October 24, 2024

Susan Gerber, MD

Medical Director

GSK