GSK's RSVPreF3 OA Vaccine (AREXVY)

AREXVY was approved by FDA on May 3, 2023, and is indicated for the prevention of LRTD caused by RSV in adults 60 and older, as a single dose.

ACIP June 21, 2023

Leonard Friedland, MD

Vice President, Scientific Affairs and Public Health

GSK

Presentation Overview

Efficacy and safety results over 2 full RSV seasons from pivotal Phase 3 Study

- 1 dose of AREXVY provides durable efficacy against RSV-associated LRTD over 2 full RSV seasons, including against severe RSV disease, in adults with underlying comorbidities, and across advancing ages
- 2nd dose 12 months after 1st dose does not appear to confer additional efficacy in overall population

Immunogenicity and safety results from 2 co-administration trials with influenza vaccines (adjuvanted, high dose)

- AREXVY can be administered with all types of commonly used influenza vaccines

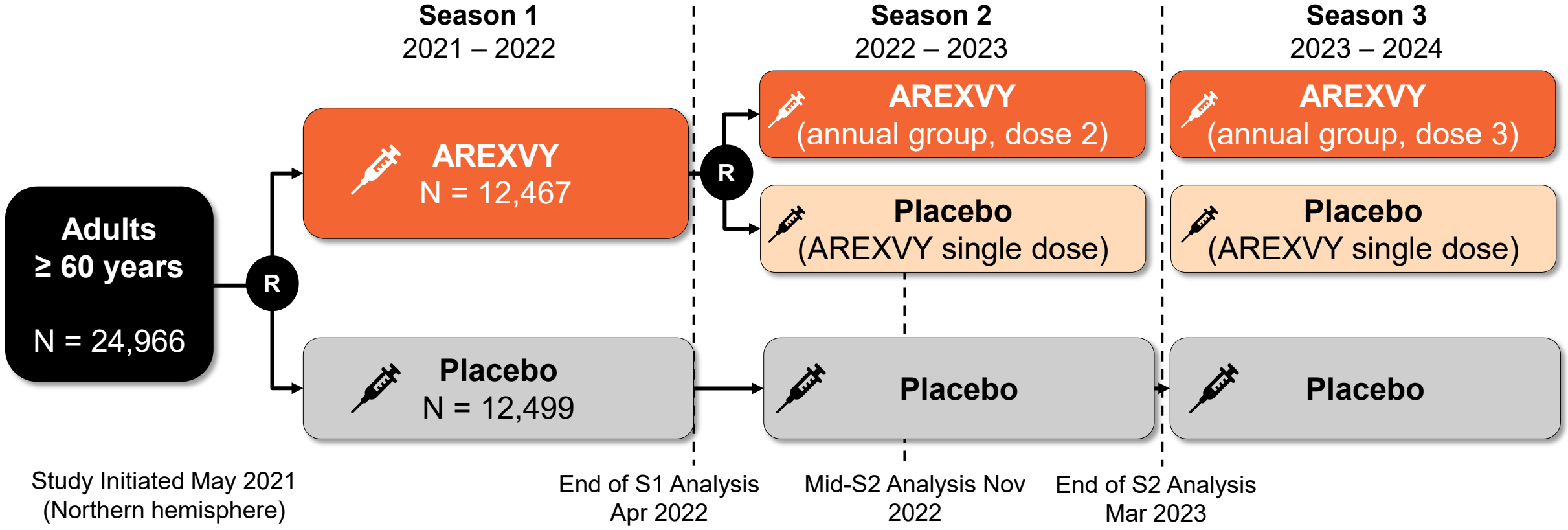
LRTD: lower respiratory tract disease

Pivotal Efficacy and Safety Study (AReSVi-006): Results Through 2 Full RSV Seasons

Phase 3, randomized, placebo-controlled, multi-country study to demonstrate efficacy and safety of single and annual revaccination doses in adults 60 years and older

Ongoing AReSVi-006 Phase 3 Trial Design

Randomized, placebo-controlled, observer-blind, multi-country efficacy study



Confirmatory secondary endpoint: Evaluate efficacy of AREXVY in prevention of RSV*-LRTD† in adults ≥ 60 YOA over 2 seasons, following a single dose of AREXVY and following annual revaccination dose

- All RSV-LRTD cases adjudicated by independent external adjudication committee
- Success criterion: lower limit of 2-sided 97.5% CI for vaccine efficacy > 20%

***RT-PCR confirmed; †LRTD defined as ≥ 2 lower respiratory symptoms/signs for ≥ 24 hours including ≥1 lower respiratory sign OR ≥ 3 lower respiratory symptoms for ≥ 24 hours; RT-PCR: reverse transcriptase polymerase chain reaction**

AReSVi-006 Case Definitions

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
- O2 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
- O2 supplement

Severe LRTD*

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

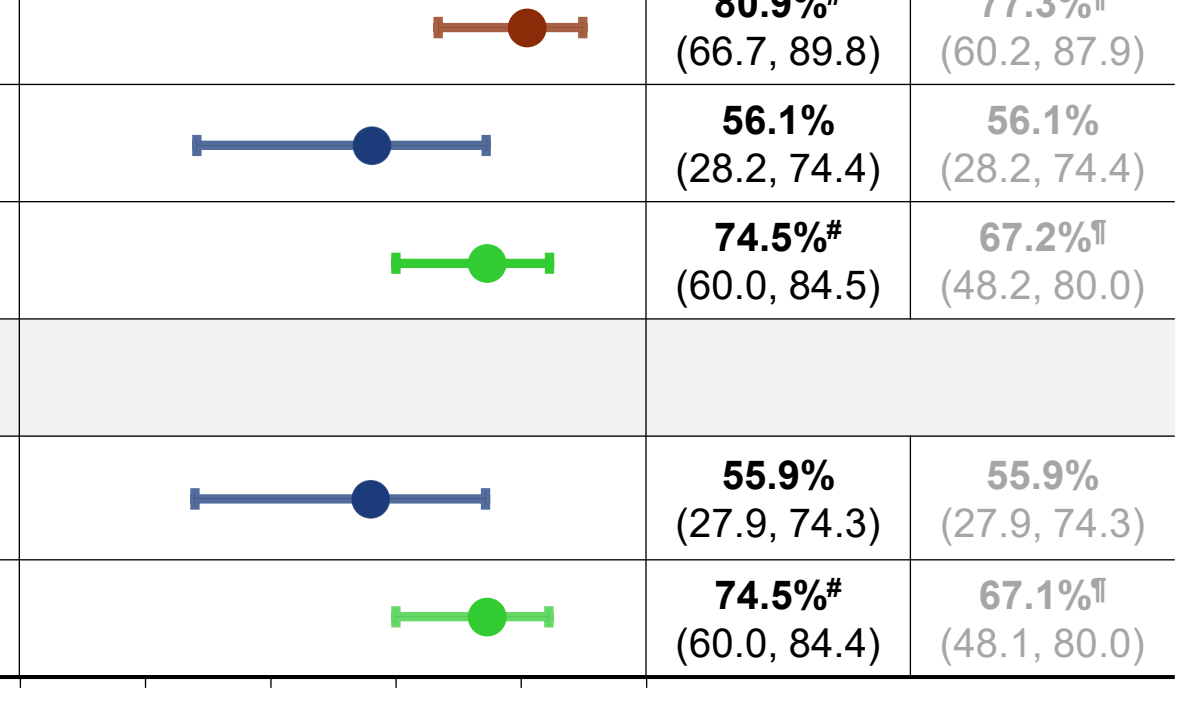
Lower respiratory signs

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

*USPI case definitions

AREXVY Produces Durable Vaccine Efficacy Against RSV-LRTD Over 2 Full Seasons

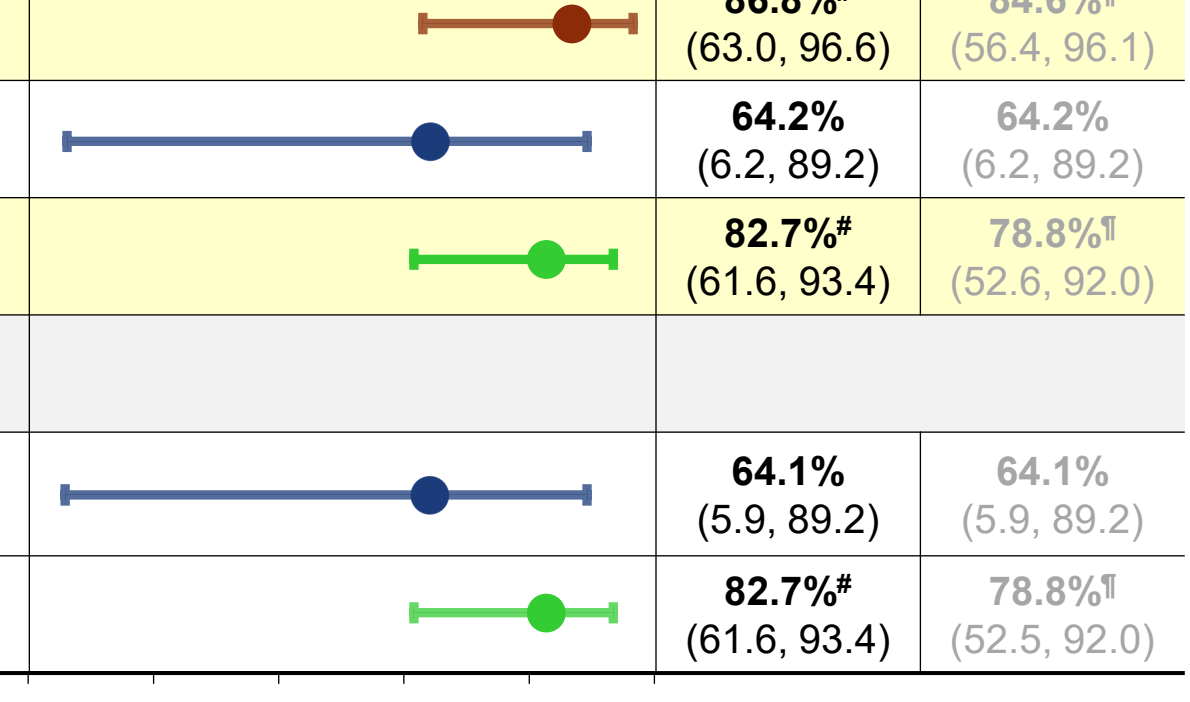
	Median Follow-Up (months)	AREXVY	Placebo	VE (95% CI)	VE (95% CI)
		Number of events			
Single Dose				*W/o season as covariate#*	*W/ season as covariate¶*
Season 1* VE 1	**6.7**	**7** / 12,466	**40** / 12,494	**82.6%** (57.9, 94.1)	**82.6%** (57.9, 94.1)
Mid Season 2 Post dose 1	**14**	**15** / 12,469	**85** / 12,498	**80.9%#** (66.7, 89.8)	**77.3%¶** (60.2, 87.9)
Season 2 Only Post dose 2	**6.4**	**20** / 4,991	**91** / 10,031	**56.1%** (28.2, 74.4)	**56.1%** (28.2, 74.4)
Season 1 + 2**	**18**	**30** / 12,469	**139** / 12,498	**74.5%#** (60.0, 84.5)	**67.2%¶** (48.2, 80.0)
Annual (2 doses, ~12 months apart)					
Season 2 Only Post dose 2	**6.4**	**20** / 4,966	**91** / 10,031	**55.9%** (27.9, 74.3)	**55.9%** (27.9, 74.3)
Seasons 1 + 2**	**18**	**30** / 12,469	**139** / 12,498	**74.5%#** (60.0, 84.4)	**67.1%¶** (48.1, 80.0)



Modified exposed set
***96.95% CI for VE 1; **97.5% CI for Season 1 + 2**

AREXVY Produces Durable Vaccine Efficacy Against RSV-Severe LRTD Over 2 Full Seasons

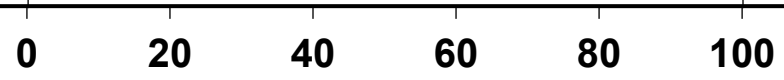
	Median Follow-Up (months)	AREXVY Number of events	Placebo Number of events	VE (95% CI) *W/o season as covariate#*	VE (95% CI) *W/ season as covariate¶*
Single Dose					
Season 1* VE 1	**6.7**	**1** / 12,466	**17** / 12,494	**94.1%** (62.4, 99.9)	**94.1%** (62.4, 99.9)
Mid Season 2 Post dose 1	**14**	**4** / 12,469	**33** / 12,498	**86.8%#** (63.0, 96.6)	**84.6%¶** (56.4, 96.1)
Season 2 Only Post dose 2	**6.4**	**5** / 4,991	**28** / 10,031	**64.2%** (6.2, 89.2)	**64.2%** (6.2, 89.2)
Season 1 + 2**	**18**	**7** / 12,469	**48** / 12,498	**82.7%#** (61.6, 93.4)	**78.8%¶** (52.6, 92.0)
Annual (2 doses, ~12 months apart)					
Season 2 Only Post dose 2	**6.4**	**5** / 4,966	**28** / 10,031	**64.1%** (5.9, 89.2)	**64.1%** (5.9, 89.2)
Seasons 1 + 2**	**18**	**7** /12,469	**48** / 12,498	**82.7%#** (61.6, 93.4)	**78.8%¶** (52.5, 92.0)



Modified exposed set
***96.95% CI for VE 1; **97.5% CI for Season 1 + 2**

AREXVY Produces Durable Vaccine Efficacy Against RSV-LRTD in Vulnerable Populations Over 2 Full Seasons

	AREXVY	Placebo	VE (95% CI)	VE (95% CI)
	Number of events			
Season 1* (Median follow-up = 6.7 months)				
≥ 1 pre-existing comorbidity of interest	**1** / 4,973	**18** / 4,861	**94.6%** (65.9, 99.9)	**94.6%** (65.9, 99.9)
Pre-frail	**1** / 4,792	**14** / 4,778	**92.9%** (53.4, 99.8)	**92.9%** (53.4, 99.8)
Single dose over 2 seasons† (Median follow-up = 18 months)			*W/o season as covariate#*	*W/ season as covariate¶*
≥ 1 pre-existing comorbidity of interest	**16** / 4,983	**72** / 4,919	**74.5%#** (55.7, 86.1)	**66.7%¶** (41.8, 82.0)
Pre-frail	**1** / 4,792	**14** / 4,778	**80.0%#** (57.3, 91.8)	**73.3%¶** (42.4, 89.2)



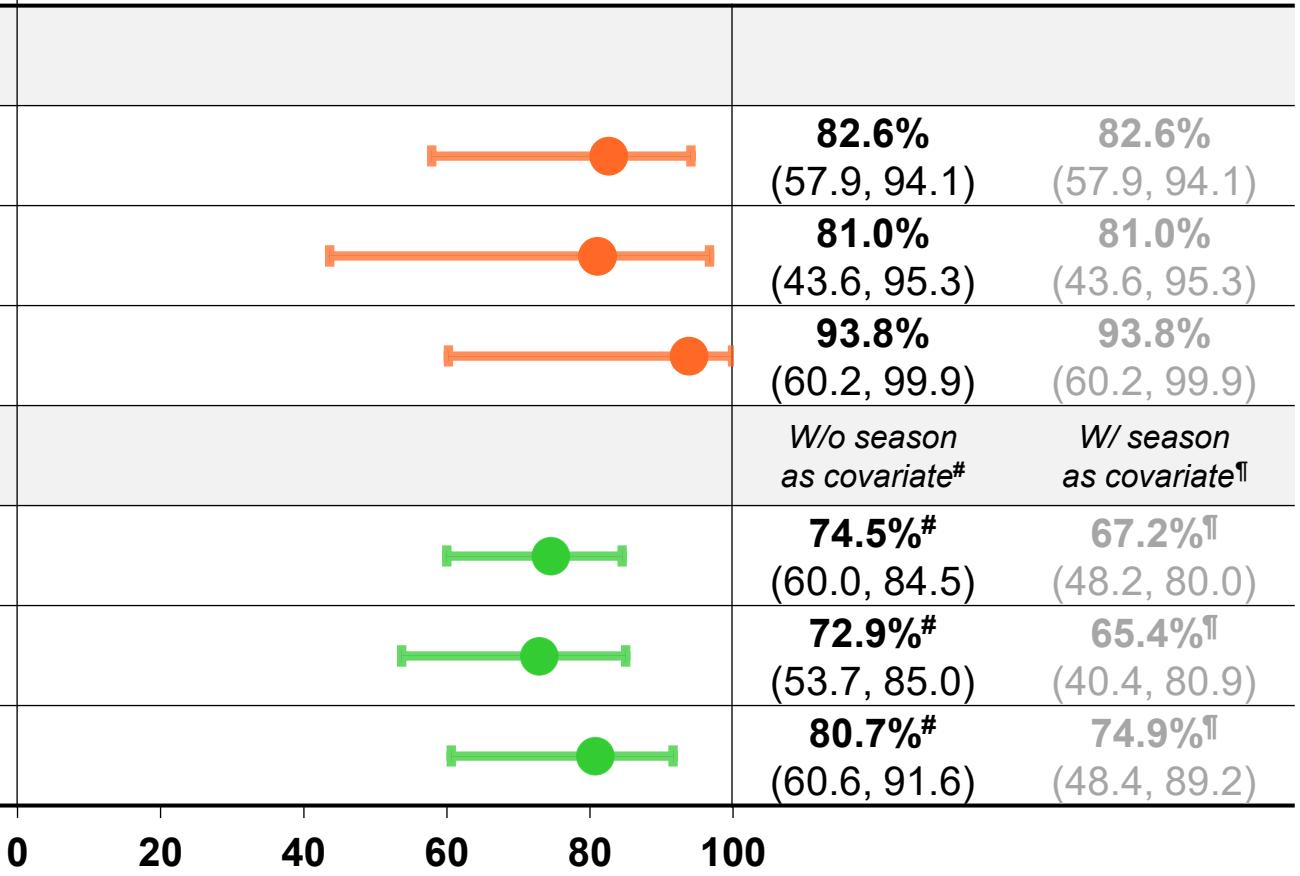
Vaccine efficacy in frail participants cannot be concluded due to low number of cases accrued

Comorbidities of interest include chronic obstructive pulmonary disease, asthma, any chronic respiratory or pulmonary disease, and chronic heart failure (cardiorespiratory condition) and diabetes mellitus type 1 or type 2 and advanced liver or renal disease (endocrine or metabolic condition

***April 2022 analysis; †From 15 days post Dose 1 up to end of Season 2 in Northern Hemisphere**

AREXVY Produces Durable Vaccine Efficacy Against RSV LRTD Across Advancing Ages Over 2 Full Seasons

	AREXVY	Placebo	VE (95% CI)	VE (95% CI)
	Number of events			
Season 1* (Median follow-up = 6.7 months)				
≥ 60 YOA* **	**7** / 12,466	**40** / 12,494	**82.6%** (57.9, 94.1)	82.6% (57.9, 94.1)
60 – 69 YOA	**4** / 6,963	**21** / 6,979	**81.0%** (43.6, 95.3)	81.0% (43.6, 95.3)
70 – 79 YOA	**1** / 4,487	**16** / 4,487	**93.8%** (60.2, 99.9)	93.8% (60.2, 99.9)
Single dose over 2 seasons† (Median follow-up = 18 months)			*W/o season as covariate#*	*W/ season as covariate¶*
≥ 60 YOA** **	**30** / 12,469	**139** / 12,498	**74.5%#** (60.0, 84.5)	67.2%¶ (48.2, 80.0)
60 – 69 YOA	**17** / 6,963	**74** / 6,981	**72.9%#** (53.7, 85.0)	65.4%¶ (40.4, 80.9)
70 – 79 YOA	**9** / 4,489	**55** / 4,489	**80.7%#** (60.6, 91.6)	74.9%¶ (48.4, 89.2)

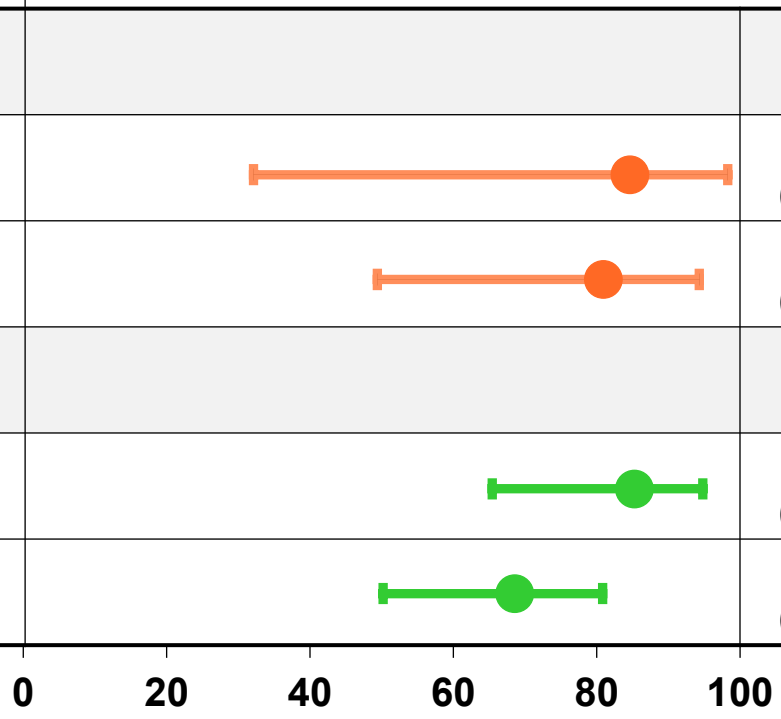


Vaccine efficacy in adults ≥ 80 years of age cannot be concluded due to low number of cases accrued

***April 2022 analysis; ***96.95% CI; ****97.5% CI; YOA: years of age;**
†From 15 days post Dose 1 up to end of Season 2 in Northern Hemisphere

AREXVY Produces Durable Vaccine Efficacy Against RSV-A LRTD and RSV-B LRTD Over 2 Full Seasons

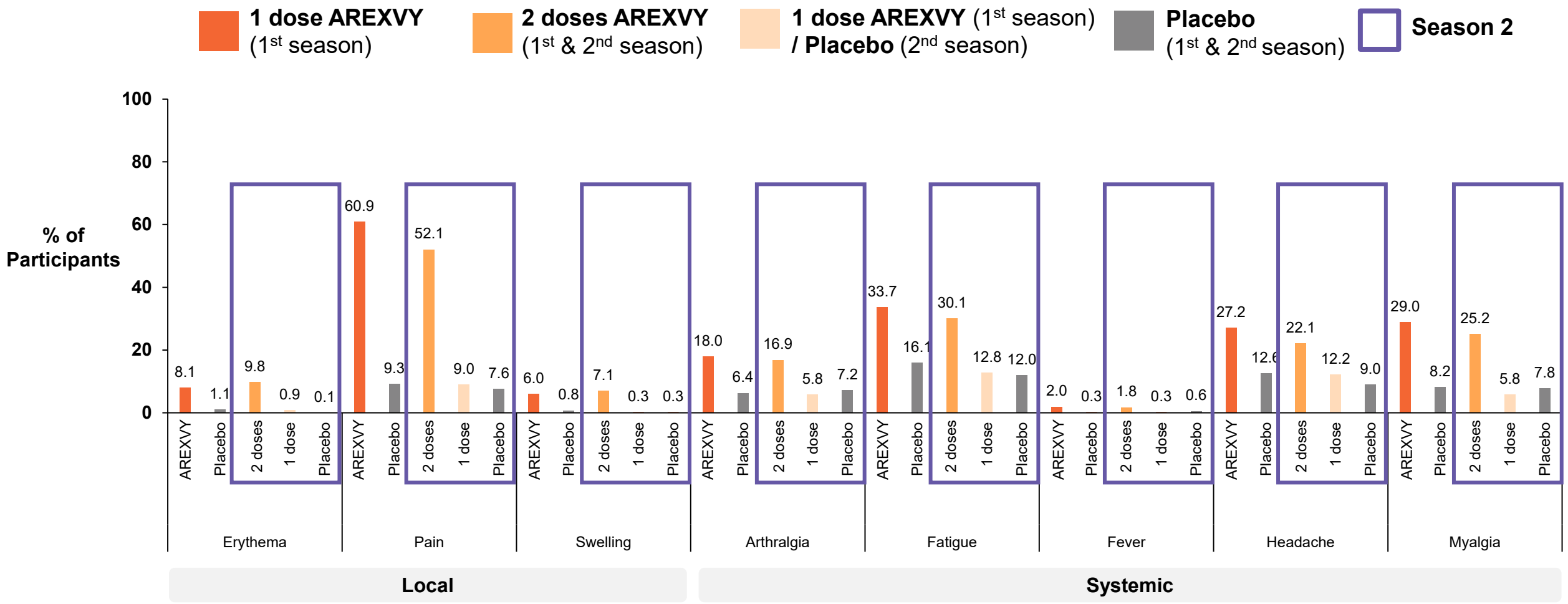
	AREXVY	Placebo	VE (95% CI)	VE (95% CI)
	Number of events			
Season 1* (Median follow-up = 6.7 months)				
RSV-A	**2** / 12,466	**13** / 12,494	**84.6%** (32.1, 98.3)	**84.6%** (32.1, 98.3)
RSV-B	**5** / 12,466	**26** / 12,494	**80.9%** (49.4, 94.3)	**80.9%** (49.4, 94.3)
Single dose over 2 seasons† (Median follow-up = 18 months)			*W/o season as covariate#*	*W/ season as covariate¶*
RSV-A	**6** / 12,469	**48** / 12,498	**85.2%#** (65.4, 94.8)	**80.5%¶** (54.0, 93.2)
RSV-B	**24** / 12,469	**90** / 12,498	**68.5%#** (50.2, 80.8)	**59.7%¶** (35.8, 75.5)



*April 2022 analysis; †From 15 days post Dose 1 up to end of Season 2 in Northern Hemisphere

Reactogenicity Profile of 2nd Dose in Line with 1st Dose

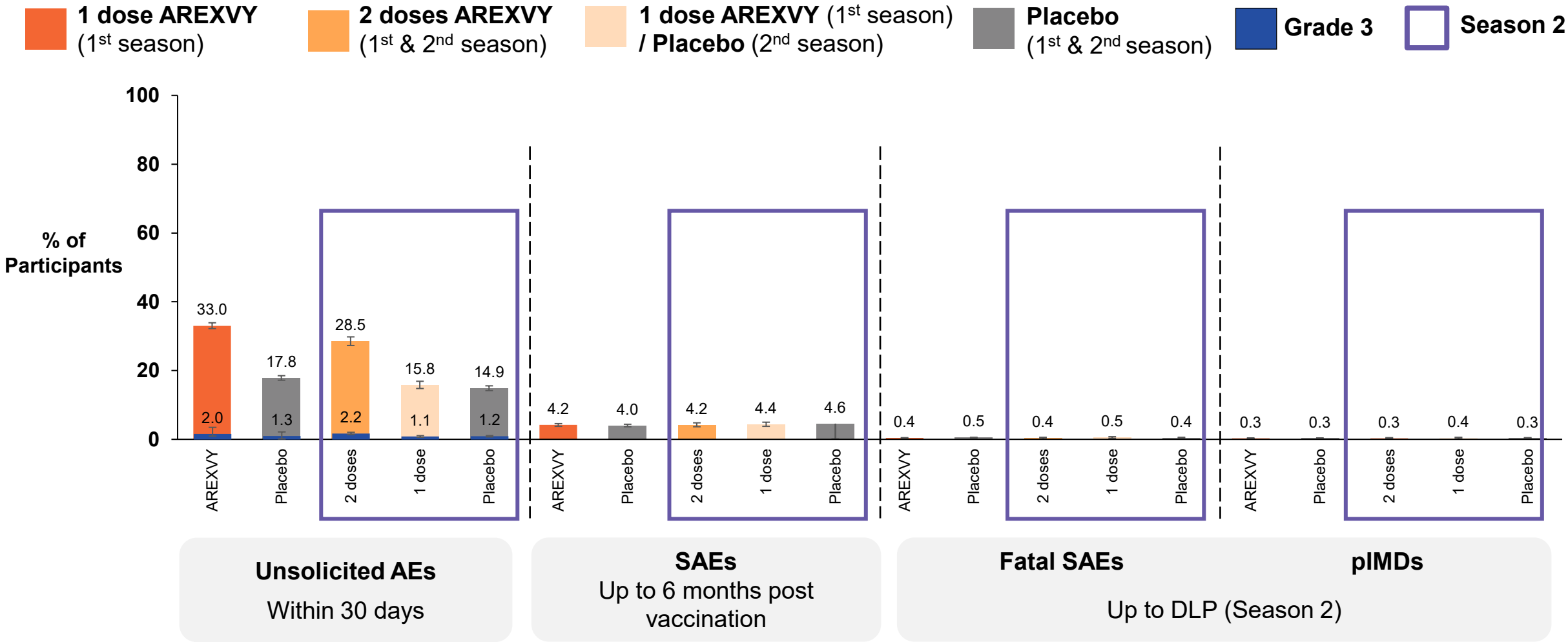
Solicited AEs Reported Within 4 Days of Vaccination (Solicited Safety Set)



AREXVY Season 1 n=879; Placebo Season 1 n=878; 2 doses Season 2 n=326 (received AREXVY in Season 1 and Season 2);
1 dose Season 2 n=345 (received AREXVY in Season 1 and Placebo in Season 2);
Placebo Season 2 n=666 (received Placebo in Season 1 and Season 2)

Safety Profile of 2nd Dose in Line with 1st Dose

Unsolicited AEs, SAEs, fatal SAEs, and pIMDs



AREXVY Season 1 n=12,467; Placebo Season 1 n=12,499; 2 doses Season 2 n=4,966 (received AREXVY in Season 1 and Season 2); 1 dose Season 2 n=4,991 (received AREXVY in Season 1 and Placebo in Season 2); Placebo Season 2 n=10,033 (received Placebo in Season 1 and Season 2)

DLP: data lock point; pIMD: potential immune-mediated disease

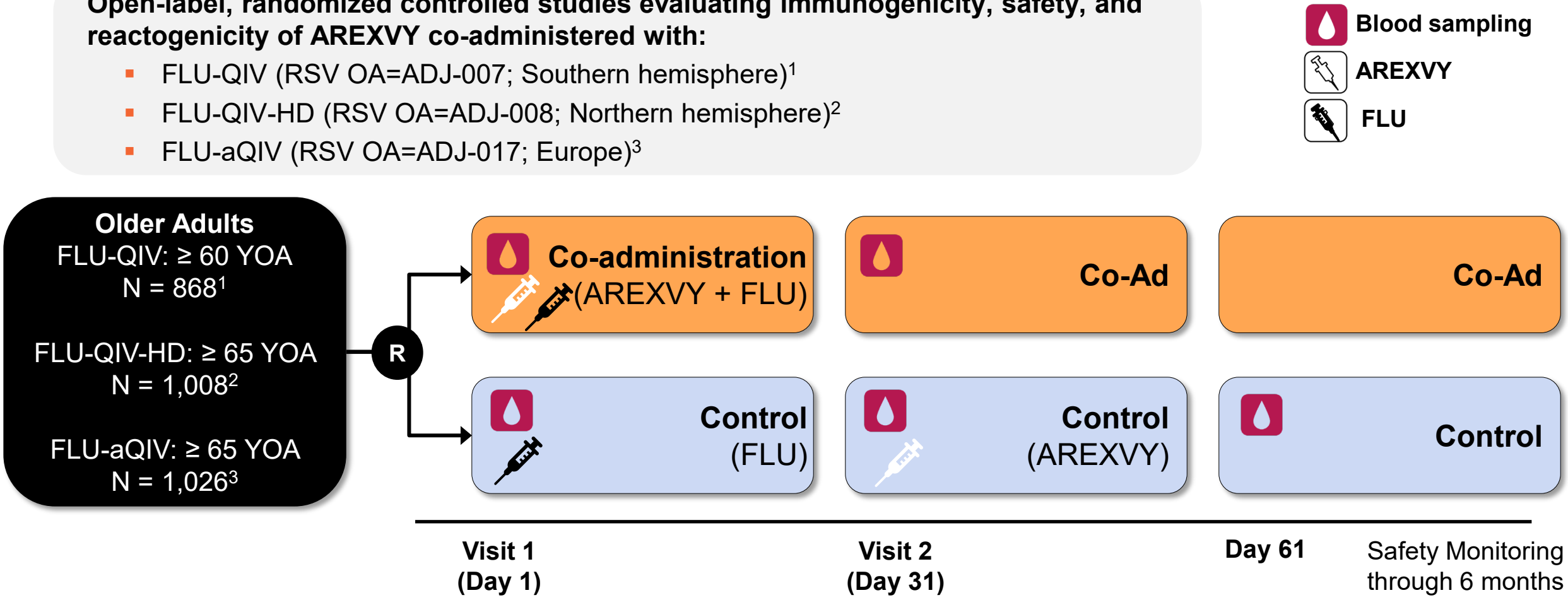
Influenza Vaccine Co-administration Studies: Immunogenicity and Safety

Open-label, randomized, controlled, multi-country studies to evaluate immune response, safety, and reactogenicity of AREXVY when co-administered with influenza vaccines in adults aged 60 years and above (RSV OA=ADJ-007) or 65 years and above (RSV OA=ADJ-008 and RSV OA=ADJ-017)

Phase 3 Influenza Vaccine Co-Administration Studies: Designs[1–3]

Open-label, randomized controlled studies evaluating immunogenicity, safety, and reactogenicity of AREXVY co-administered with:

- FLU-QIV (RSV OA=ADJ-007; Southern hemisphere)[1]
- FLU-QIV-HD (RSV OA=ADJ-008; Northern hemisphere)[2]
- FLU-aQIV (RSV OA=ADJ-017; Europe)[3]



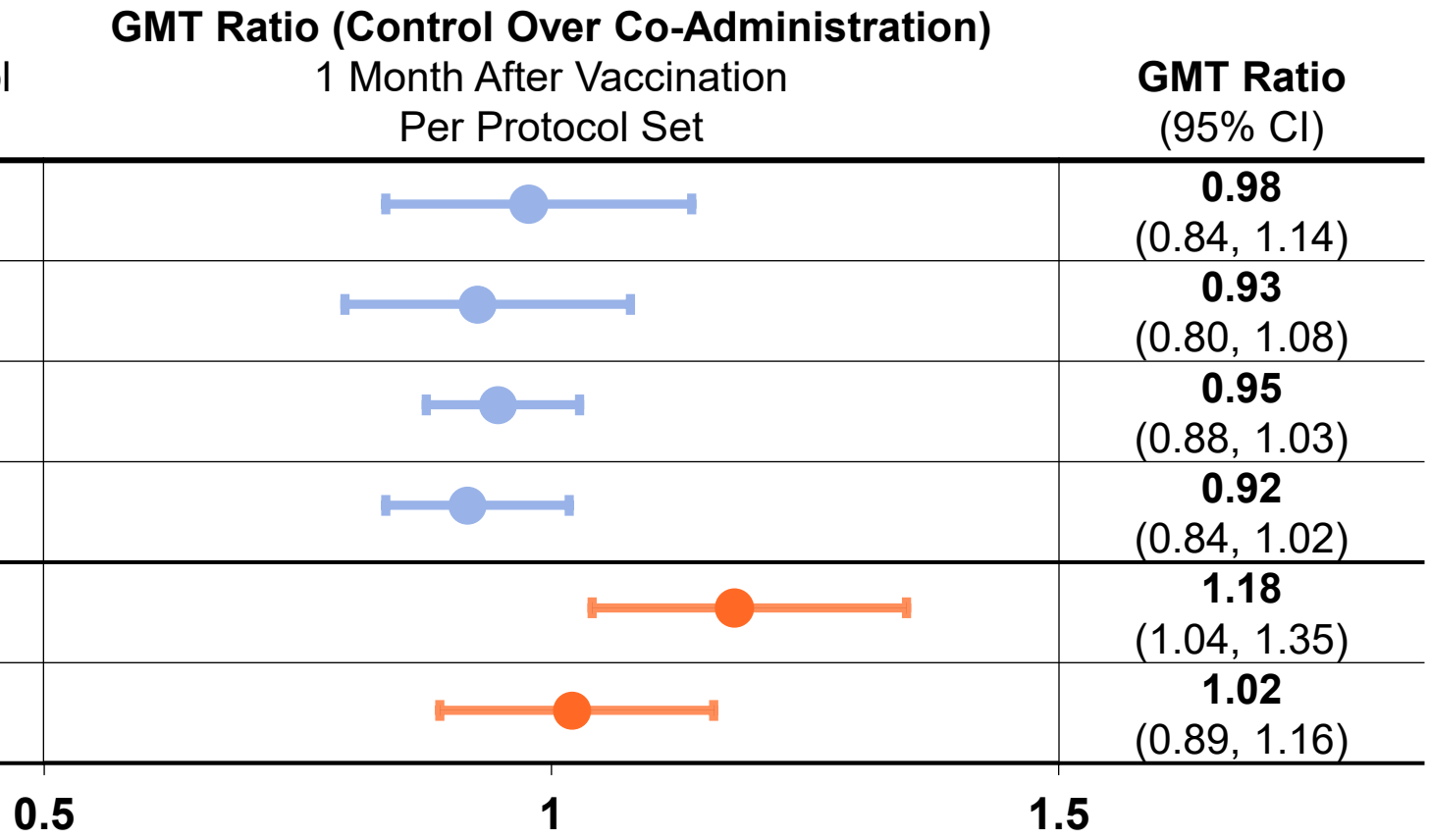
Co-Ad group: Participants receiving single dose of RSVPreF3 OA investigational vaccine and single dose of FLU vaccine at Visit 1. Control group: Participants receiving a single dose of FLU vaccine at Visit 1 (Day 1), followed by a single dose of the RSVPreF3 OA investigational vaccine at Visit 2. FLU-aQIV: adjuvanted quadrivalent influenza vaccine; FLU-QIV: quadrivalent influenza vaccine; FLU-QIV-HD: quadrivalent influenza vaccine-high dose.

1. ClinicalTrials.gov, 2022. NCT04841577. https://clinicaltrials.gov/ct2/show/NCT04841577; 2. ClinicalTrials.gov, 2023. NCT05559476. https://clinicaltrials.gov/ct2/show/NCT05559476; 3. ClinicalTrials.gov, 2023. NCT05568797. https://clinicaltrials.gov/ct2/show/NCT05568797. Accessed May 2023

Co-Administration of AREXVY and Licensed FLU-QIV-HD

GMT Ratio (Control Over Co-Administration)
1 Month After Vaccination
Per Protocol Set

Antibody	Co-Ad N	Control N	GMT Ratio (95% CI)
Flu A/Darwin H3N2	458	441	**0.98** (0.84, 1.14)
Flu A/Victoria H1N1	452	435	**0.93** (0.80, 1.08)
Flu B/Austria/Victoria	458	441	**0.95** (0.88, 1.03)
Flu B/Phuket/Yamagata	456	441	**0.92** (0.84, 1.02)
RSV-A*	459	358	**1.18** (1.04, 1.35)
RSV-B	459	357	**1.02** (0.89, 1.16)



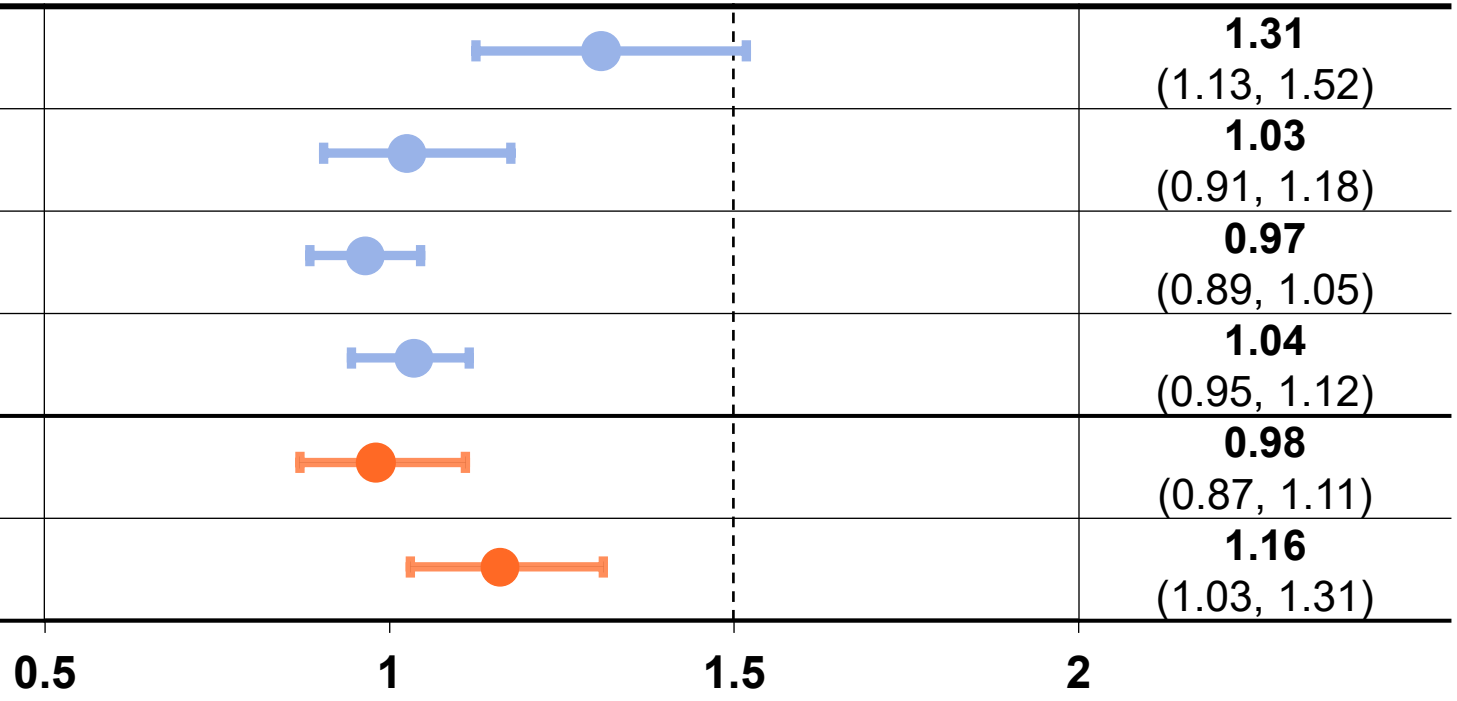
Success Criteria: Upper limit ≤ 1.5 of 2-sided 95% CI for Group GMT Ratio (Control Group divided by Co-Ad Group) for RSV vaccine and for each of FLU vaccine strains

***RSV-A preliminary, final results pending**
Flu response evaluated using HI and RSV response evaluated using NAb (ED 60); HI: Hemagglutination

Co-Administration of AREXVY and Licensed Flu-Adjuvanted QIV

GMT Ratio (Control Over Co-Administration)
1 Month After Vaccination
Per Protocol Set

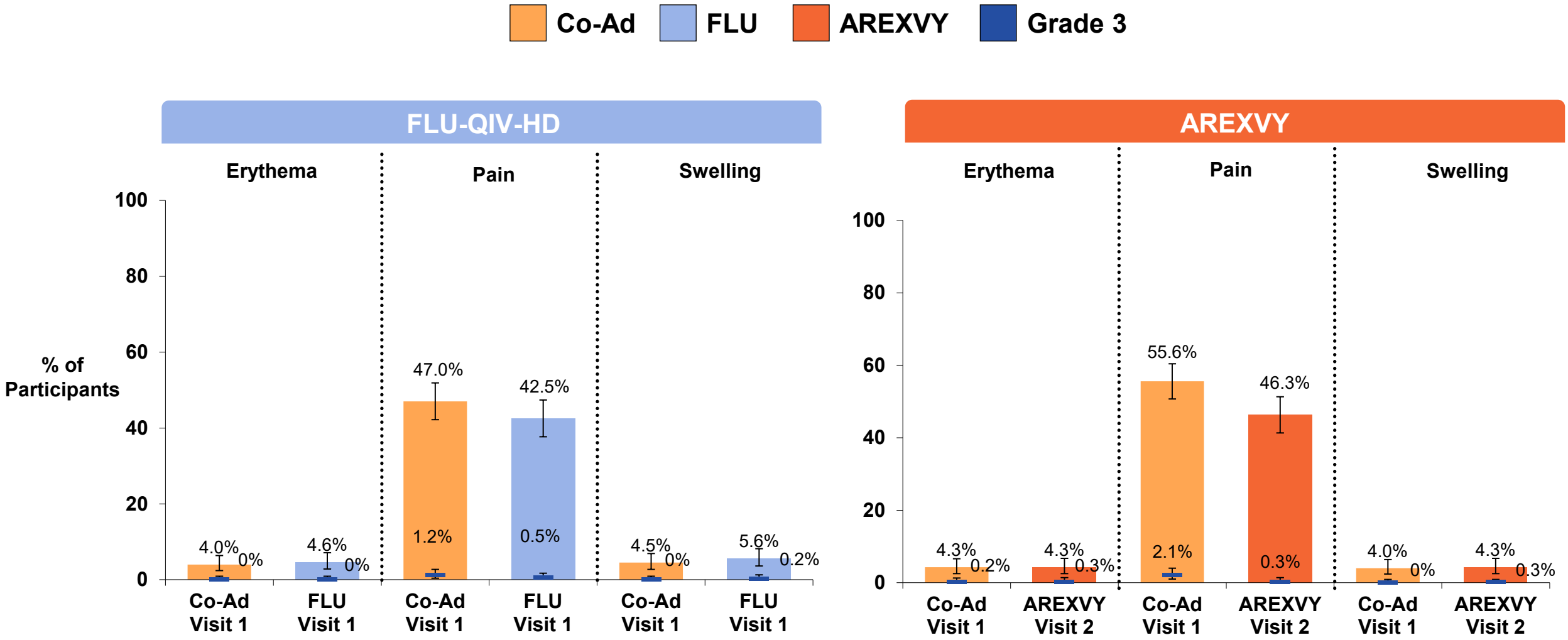
Antibody	Co-Ad N	Control N	GMT Ratio (95% CI)
Flu A/Darwin H3N2*	433	402	**1.31** (1.13, 1.52)
Flu A/Victoria H1N1	424	398	**1.03** (0.91, 1.18)
Flu B/Austria/Victoria	433	402	**0.97** (0.89, 1.05)
Flu B/Phuket/Yamagata	432	402	**1.04** (0.95, 1.12)
RSV-A**	475	377	**0.98** (0.87, 1.11)
RSV-B	473	377	**1.16** (1.03, 1.31)



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

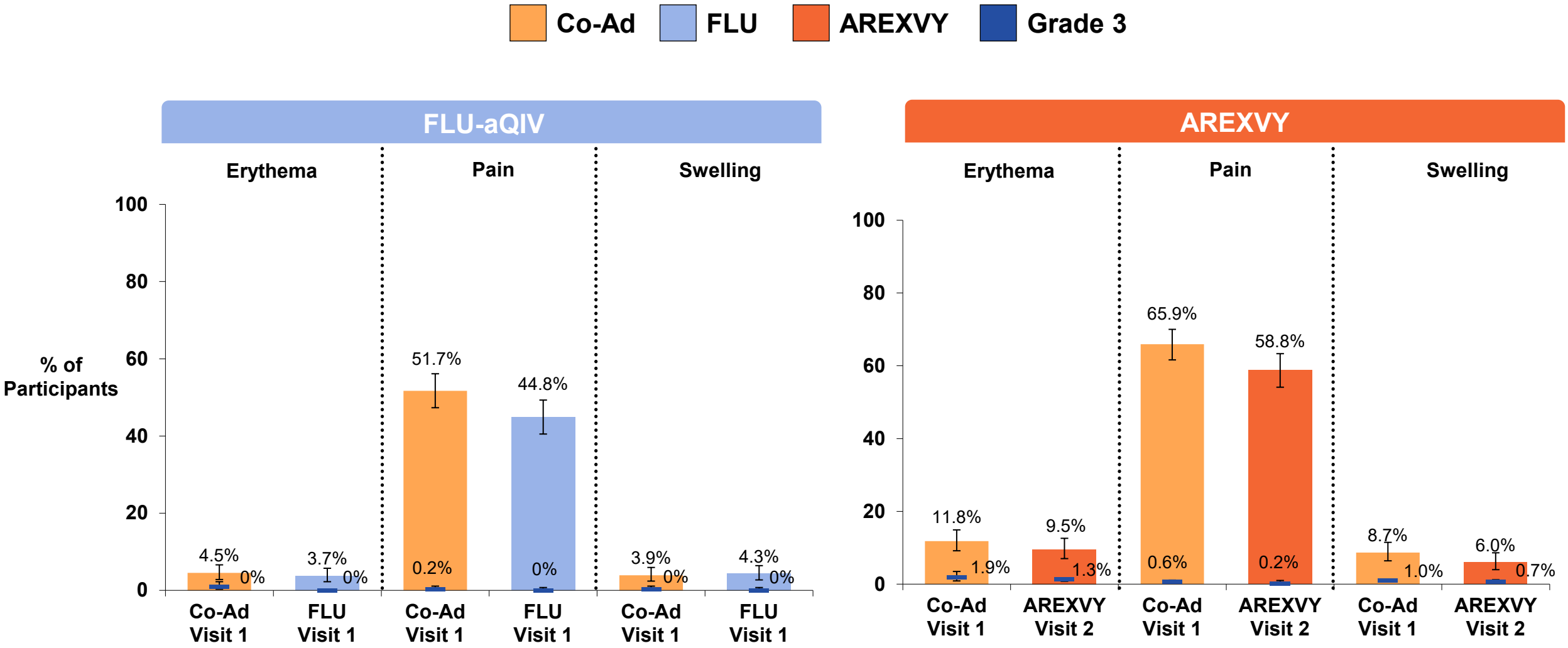
***Lower HI titers observed than expected, investigation ongoing; **RSV-A preliminary, final results pending**
Flu response evaluated using HI and RSV response evaluated using NAb (ED 60); HI: Hemagglutination

Modified Set: Solicited Local AEs Within 4 Days Post Vaccination



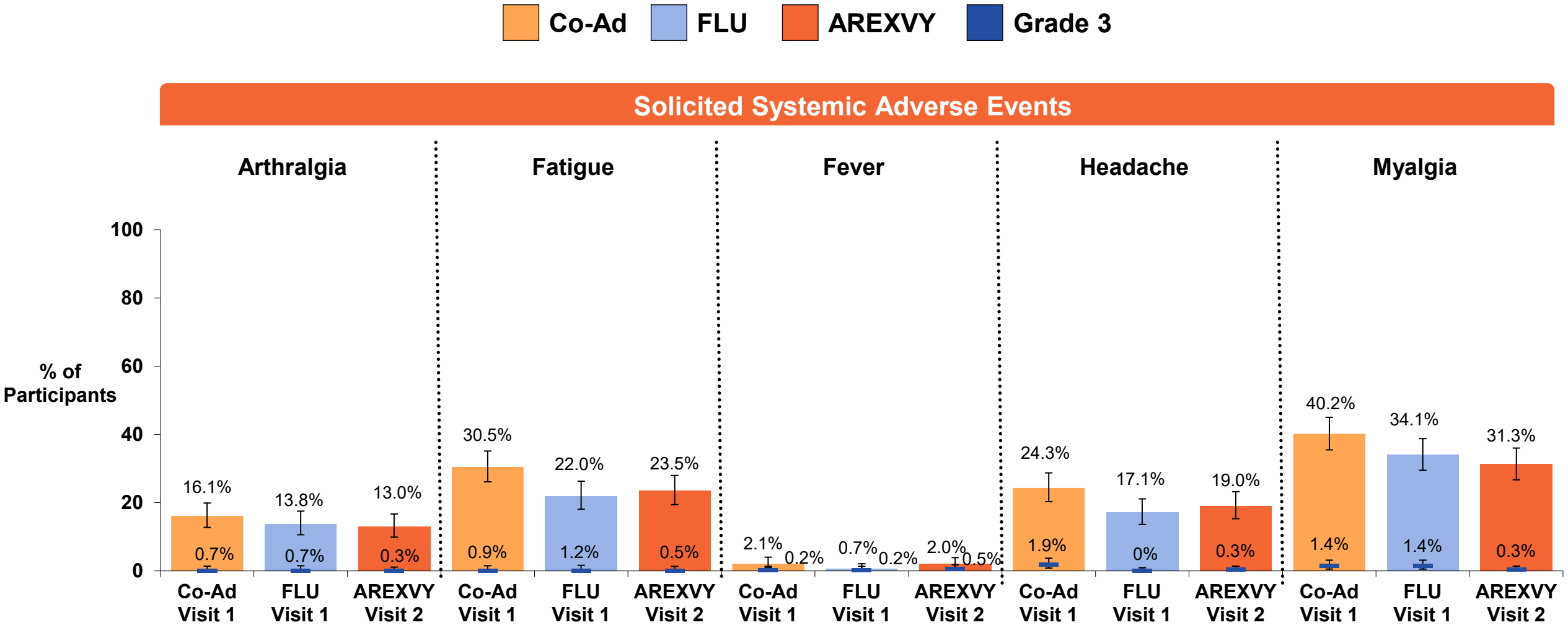
Grade 3: > 100 mm for erythema and swelling; Grade 3 pain: significant pain at rest; prevents normal everyday activities. Fever: temperature ≥ 38.0 C/100.4 F by any route (oral, axillary or tympanic); Grade 3 fever: > 39.0 C/102.2 F.
Grade 3 headache, fatigue, myalgia, arthralgia: preventing normal activity

Exposed Set: Solicited Local AEs Within 7 Days Post Vaccination



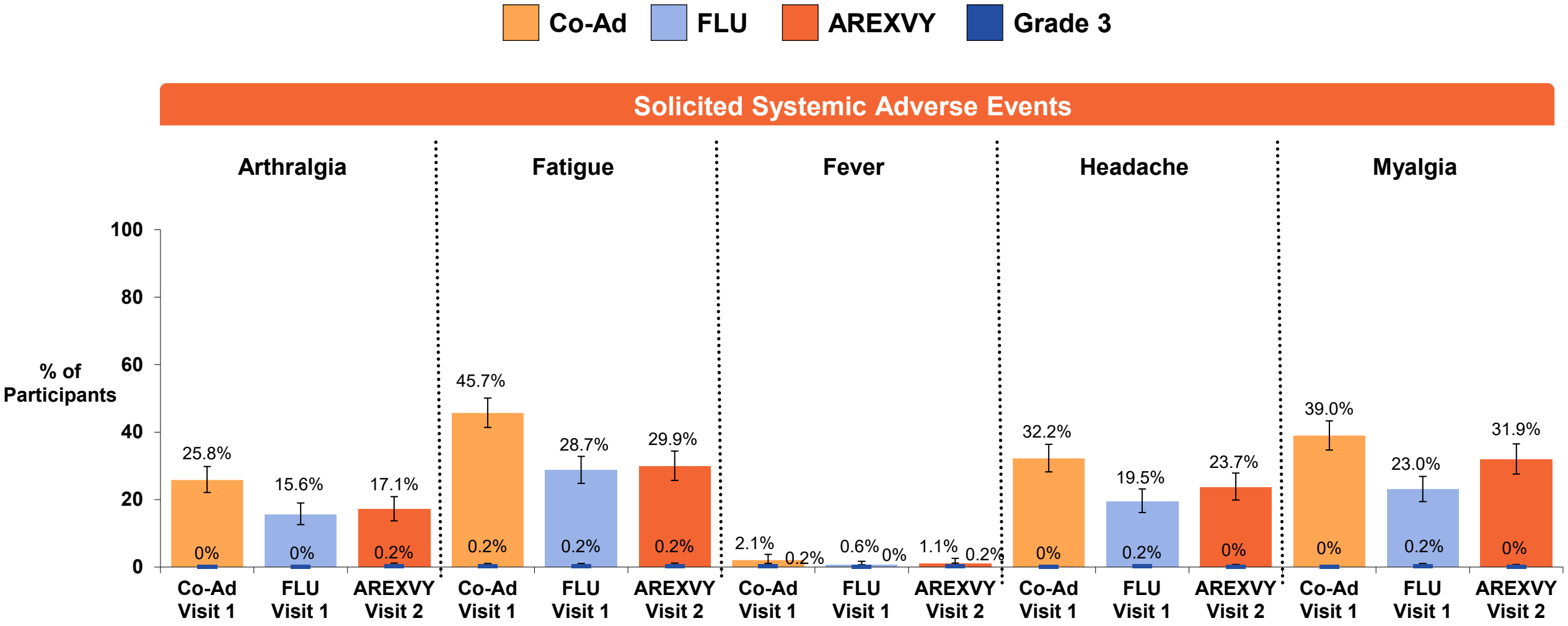
Grade 3: > 100 mm for erythema and swelling; Grade 3 pain: significant pain at rest; prevents normal everyday activities. Fever: temperature ≥ 38.0 C/100.4 F by any route (oral, axillary or tympanic); Grade 3 fever: > 39.0 C/102.2 F.
Grade 3 headache, fatigue, myalgia, arthralgia: preventing normal activity

Modified Set: Solicited Systemic AEs Within 4 Days Post Vaccination



Grade 3: >100 mm for erythema and swelling. Grade 3 pain: significant pain at rest; prevents normal everyday activities.
Fever: temperature ≥ 38.0°C/100.4°F by any route (oral, axillary or tympanic); Grade 3 fever: > 39.0°C/102.2°F.
Grade 3 headache, fatigue, myalgia, arthralgia: preventing normal activity

Exposed Set: Solicited Systemic AEs Within 7 Days Post Vaccination



Grade 3: >100 mm for erythema and swelling. Grade 3 pain: significant pain at rest; prevents normal everyday activities.
Fever: temperature ≥ 38.0°C/100.4°F by any route (oral, axillary or tympanic); Grade 3 fever: > 39.0°C/102.2°F.
Grade 3 headache, fatigue, myalgia, arthralgia: preventing normal activity

Summary of Findings

1 dose of AREXVY provides durable efficacy against RSV-associated LRTD for 2 full RSV seasons, including against severe RSV disease, in adults with underlying comorbidities, and across advancing ages

Revaccination after 12 months does not appear to confer additional efficacy benefit for overall population; future data will inform optimal timing of revaccination

AREXVY can be administered with all types of commonly used influenza vaccines

Reactogenicity and safety profiles of 2nd dose in line with 1st dose; important for future revaccination consideration

Across all studies no new cases of GBS, ADEM, or other neuroinflammatory demyelinating disorders with additional exposure

GSK's RSVPreF3 OA Vaccine (AREXVY)

AREXVY was approved by FDA on May 3, 2023, and is indicated for the prevention of LRTD disease caused by RSV in adults 60 and older, as a single dose.

ACIP June 21, 2023