GSK's RSVPreF3 + AS01$_E$ Vaccine (AREXVY)

AREXVY approved by FDA for the prevention of LRTD caused by RSV in adults ≥ 60 years, as a single dose.

ACIP recommends that persons aged ≥ 60 years may receive a single dose of RSV vaccine, using shared clinical decision-making.

ACIP October 25, 2023

Susan Gerber, MD

Medical Director

GSK

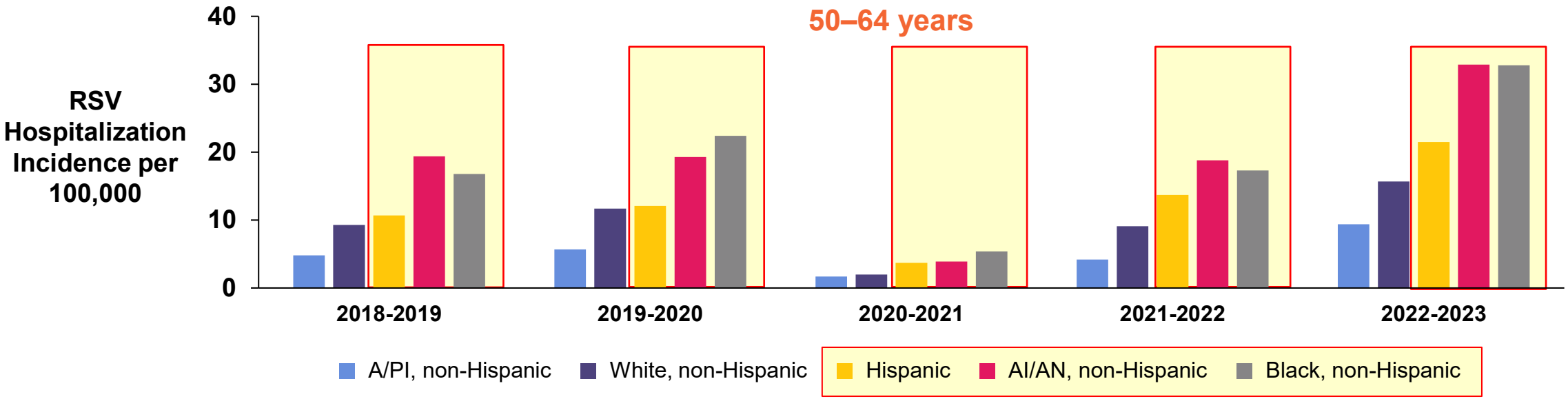
Substantial RSV Disease Burden and Unmet Medical Need in US Adults Aged 50–59 Years

1. RSV-associated hospitalizations and medically-attended RSV illnesses are substantial among 50-59 YOA
2. Published incidence rates likely substantially underestimate RSV burden due to lack of awareness, standardized testing, and underdetection within surveillance studies
3. Comorbidities associated with severe RSV disease are prevalent among adults 50–59 YOA
4. Observed disparities by race and ethnicity are particularly pronounced with respect to hospitalization rates among middle aged adults 50–64 YOA

YOA, years of age

Disparities by Race and Ethnicity in RSV Hospitalization Rates Particularly Pronounced in Adults 50–64 Years

Unadjusted RSV-related hospitalization incidence per 100,000 by race / ethnicity and season from RSV-NET data[1]



Among adults aged **50–64 YOA**, **unadjusted RSV-related hospitalization rates** (vs White, non-Hispanic) during 2018–2023 were:

- **Hispanic:** **1.0-1.9 times higher**
- **AI/AN, non-Hispanic:** **1.6-2.1 times higher**
- **Black, non-Hispanic:** **1.8-2.7 times higher**

Graphs independently created for GSK from original data; A/PI, Asian and Pacific Islander, AI/AN, America Indian or Alaska Native;

1. CDC, https://www.cdc.gov/rsv/research/rsv-net/dashboard.html. (accessed October 2023)

Immune Response and Safety Among Adults 50–59 Years of Age (RSV-OA=ADJ-018): Day 31 Analysis

Phase 3, observer-blind, randomized, placebo-controlled study to evaluate non-inferiority of the immune response and safety of RSVPreF3 + $AS01_E$ vaccine in adults 50–59 years of age, including adults at increased risk of RSV lower respiratory tract disease, compared with adults 60 years of age and older

Primary Objective

Primary objective: To demonstrate the non-inferiority of the humoral immune response in participants 50–59 YOA with and without comorbidities well-documented to be related to RSV-associated severe disease compared with older adults (≥ 60 YOA) after RSVPreF3 + $AS01_E$ vaccine administration

ClinicalTrials.gov. NCT05590403. https://www.clinicaltrials.gov/study/NCT05590403; (accessed September 2023)
1. RSV OA=ADJ-018 study protocol

Primary Endpoints

Primary objective: To demonstrate the non-inferiority of the humoral immune response in participants 50–59 YOA with and without comorbidities well-documented to be related to RSV-associated severe disease compared with older adults (≥ 60 YOA) after RSVPreF3 + $AS01_E$ vaccine administration

Study populations:

50–59 YOA with comorbidities associated with RSV-LRTD vs **≥ 60 YOA**

50–59 YOA without comorbidities associated with RSV-LRTD vs **≥ 60 YOA**

Primary Endpoints

- RSV-A neutralization titers at 1 month after RSVPreF3 + $AS01_E$ administration
- RSV-B neutralization titers at 1 month after RSVPreF3 + $AS01_E$ administration

Success criteria[1]: Upper limit of 2-sided 95% CI for GMT ratio is ≤ 1.5 and SRR difference is ≤10%

CI, confidence interval; SRR: SeroResponse Rate (% of participants with ≥4-fold increase from pre-vaccination serum antibody titers); GMT, geometric mean titer;ClinicalTrials.gov. NCT05590403. https://www.clinicaltrials.gov/study/NCT05590403; (accessed September 2023) 1. RSV OA=ADJ-018 study protocol

Immunogenicity Endpoints

Primary objective: To demonstrate the non-inferiority of the humoral immune response in participants 50–59 YOA with and without comorbidities well-documented to be related to RSV-associated severe disease compared with older adults (≥ 60 YOA) after RSVPreF3 + $AS01_E$ vaccine administration

Study populations:

50–59 YOA with comorbidities associated with RSV-LRTD vs **≥ 60 YOA**

50–59 YOA without comorbidities associated with RSV-LRTD vs **≥ 60 YOA**

Primary Endpoints

- RSV-A neutralization titers at 1 month after RSVPreF3 + $AS01_E$ administration
- RSV-B neutralization titers at 1 month after RSVPreF3 + $AS01_E$ administration

Success criteria[1]: Upper limit of 2-sided 95% CI for GMT ratio is ≤ 1.5 and SRR difference is ≤10%

Immunogenicity Endpoints

- RSV-A / RSV-B GMT pre vaccination and at 1, 6, and 12 months after vaccination
  - Tertiary endpoint: analysis by baseline comorbidities
- Frequency of RSVPreF3 + $AS01_E$ specific CD4+ T cells expressing at least 2 activation markers at pre-vaccination and at 1, 6, and 12 months after vaccination

ClinicalTrials.gov. NCT05590403. https://www.clinicaltrials.gov/study/NCT05590403; (accessed September 2023)
1. RSV OA=ADJ-018 study protocol

Safety Endpoints

Primary objective: To demonstrate the non-inferiority of the humoral immune response in participants 50–59 YOA with and without comorbidities well-documented to be related to RSV-associated severe disease compared with older adults (≥ 60 YOA) after RSVPreF3 + $AS01_E$ vaccine administration

Study populations:

50–59 YOA with comorbidities associated with RSV-LRTD vs **≥ 60 YOA**

50–59 YOA without comorbidities associated with RSV-LRTD vs **≥ 60 YOA**

Primary Endpoints

- RSV-A neutralization titers at 1 month after RSVPreF3 + $AS01_E$ administration
- RSV-B neutralization titers at 1 month after RSVPreF3 + $AS01_E$ administration

Success criteria[1]: Upper limit of 2-sided 95% CI for GMT ratio is ≤ 1.5 and SRR difference is ≤10%

Immunogenicity Endpoints

- RSV-A / RSV-B GMT pre vaccination and at 1, 6, and 12 months after vaccination
  - Tertiary endpoint: analysis by baseline comorbidities
- Frequency of RSVPreF3 + $AS01_E$ specific CD4+ T cells expressing at least 2 activation markers at pre-vaccination and at 1, 6, and 12 months after vaccination

Safety Endpoints

- Solicited administration site / systemic event with onset within 4 days
- Unsolicited AEs within 30 days
- SAEs and pIMDs up to Month 6
- Related SAEs, fatal SAEs and related pIMDs up to study end (Month 12)

AE, adverse events; SAE; serious adverse events; pIMD, potential immune mediated disease

ClinicalTrials.gov. NCT05590403. https://www.clinicaltrials.gov/study/NCT05590403; (accessed September 2023)

1. RSV OA=ADJ-018 study protocol

Study Design

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

Inclusion Criteria[1]

Cohort 1a:
Adults with comorbidities associated with RSV-LRTD

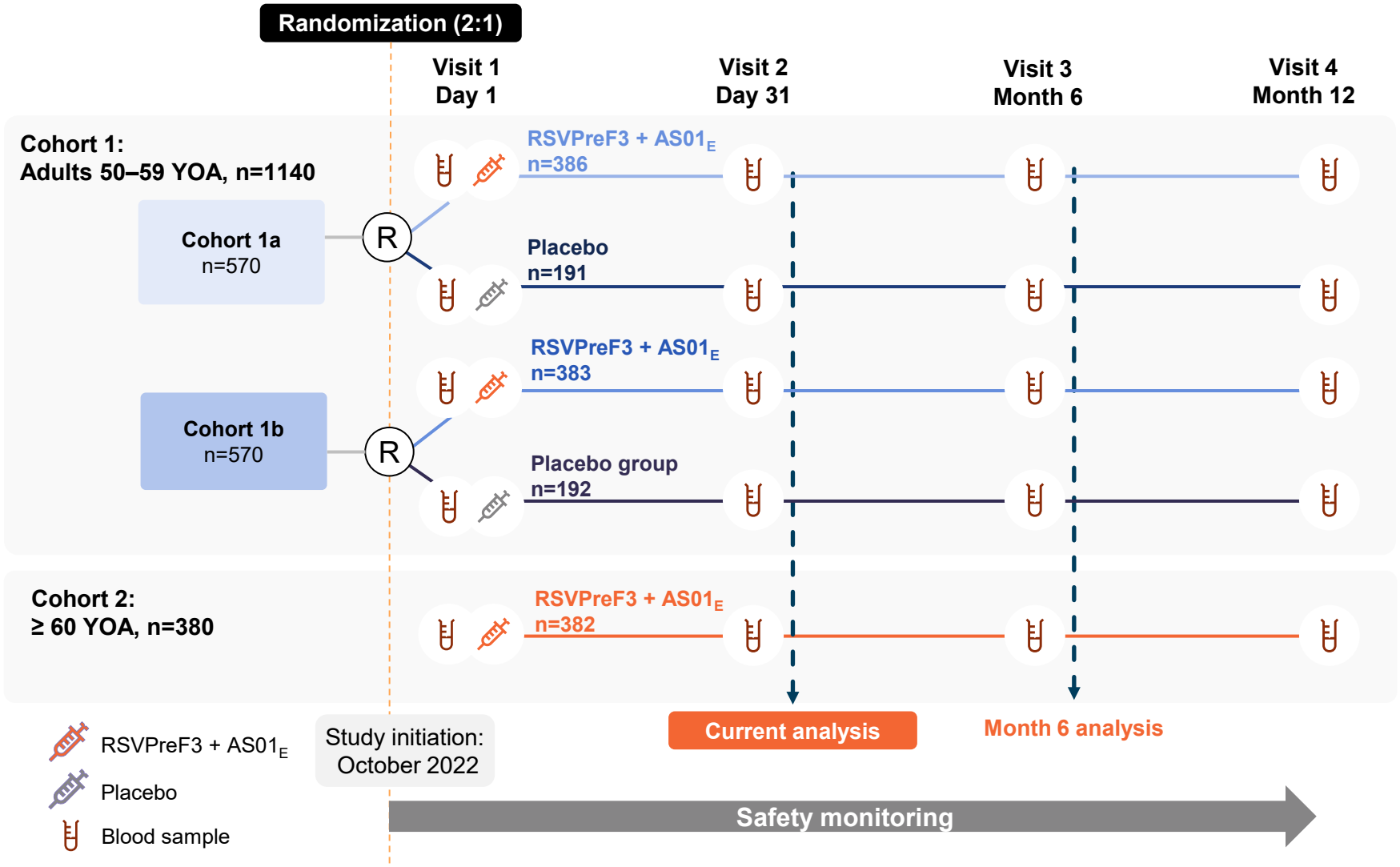
- Participants with ≥ 1 of following medical conditions:
  - Chronic pulmonary disease resulting in activity restricting symptoms or use of long-term medication
  - Chronic cardiovascular disease
  - Diabetes mellitus types 1 and 2
  - Chronic kidney disease
  - Chronic liver disease

Cohort 1b:
Adults w/o comorbidities associated with RSV-LRTD

- Participants with chronic stable medical conditions with or without specific treatment, such as hypertension, hypercholesterolemia, or hypothyroidism, and not at increased risk for RSV-LRTD

Cohort 2: ≥ 60 YOA cohort

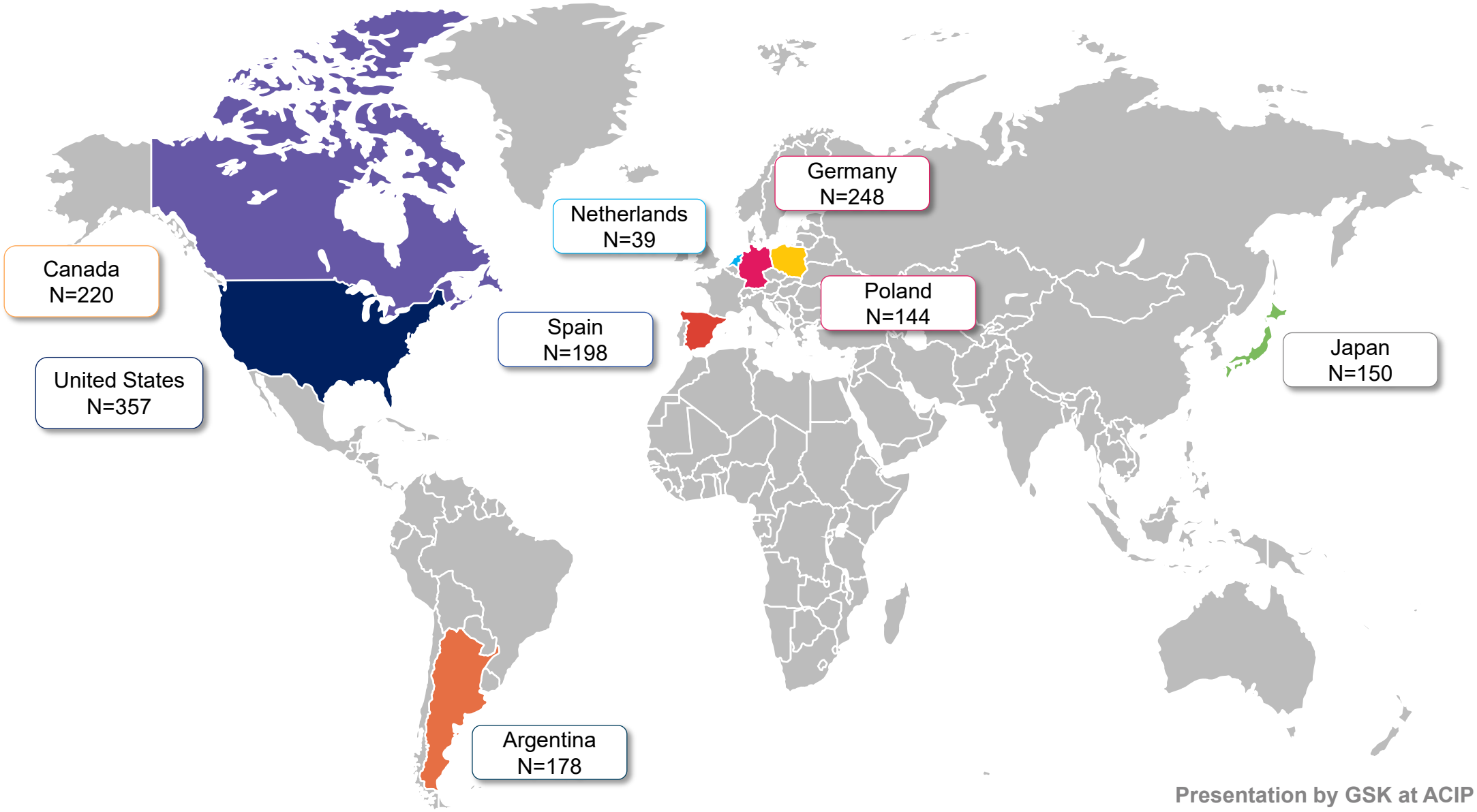
- Participants with chronic stable medical conditions



YOA, years of age; LRTD, lower respiratory tract disease; w/o, without; ClinicalTrials.gov. NCT05590403. https://www.clinicaltrials.gov/study/NCT05590403; (accessed September 2023) 1. RSV OA=ADJ-018 study protocol

8 Countries with Enrolled Participants

N=1,534 (Exposed Set)



Demographic Characteristics Well-Balanced

Exposed Set

Characteristic	50 – 59 YOA Cohort 1a: Adults with comorbidities associated with RSV-LRTD		50 – 59 YOA Cohort 1b: Adults without comorbidities associated with RSV-LRTD		≥ 60 YOA	Total
	RSVPreF3 + AS01$_E$ (N=386)	Placebo (N=191)	RSVPreF3 + AS01$_E$ (N=383)	Placebo (N=192)	RSVPreF3 + AS01$_E$ (N=382)	(N=1534)
Mean age, years (SD)	55.3 (2.8)	55.6 (2.8)	54.8 (2.8)	54.7 (2.8)	69.5 (6.9)	58.6 (7.5)
Age category, n (%)						
50–59 YOA	386 (100)	191 (100)	383 (100)	192 (100)	0	1152 (75.1)
60–69 YOA	0	0	0	0	203 (53.1)	203 (13.2)
70–79 YOA	0	0	0	0	130 (34.0)	130 (8.5)
≥ 80 YOA	0	0	0	0	49 (12.8)	49 (3.2)
Female, n (%)	186 (48.2)	85 (44.5)	221 (57.7)	119 (62.0)	188 (49.2)	799 (52.1)
Body Mass Index (BMI) kg/m^2, mean (SD)	30.9 (6.8)	31.3 (7.3)	28.4 (5.9)	28.4 (6.7)	28.1 (6.0)	29.3 (6.6)
Race, n (%)						
American Indian or Alaska Native	4 (1.0)	3 (1.6)	1 (0.3)	0 (0)	1 (0.3)	9 (0.6)
Asian	42 (10.9)	23 (12.0)	41 (10.7)	22 (11.5)	44 (11.5)	172 (11.2)
Black or African American	15 (3.9)	3 (1.6)	14 (3.7)	8 (4.2)	11 (2.9)	51 (3.3)
Native Hawaiian or Other Pacific Islander	0 (0)	2 (1.0)	0 (0)	0 (0)	1 (0.3)	3 (0.2)
White	324 (83.9)	158 (82.7)	320 (83.6)	158 (82.3)	324 (84.8)	1284 (83.7)
Multiple	1 (0.3)	1 (0.5)	4 (1.0)	3 (1.6)	0 (0)	9 (0.6)
Unknown	0 (0)	1 (0.5)	3 (0.8)	1 (0.5)	1 (0.3)	6 (0.4)
Ethnicity, n (%)						
Hispanic or Latino	63 (16.3)	35 (18.3)	48 (12.5)	23 (12.0)	50 (13.1)	219 (14.3)
Unknown	0 (0)	0 (0)	0 (0)	1 (0.5)	1 (0.3)	2 (0.1)

SD, standard deviation; *Participants with underlying medical conditions such as chronic pulmonary and cardiovascular diseases, diabetes mellitus types 1 and 2, and chronic liver and renal diseases

Clinical Characteristics Well-Balanced

Exposed Set

Characteristic	50 – 59 YOA Cohort 1a: Adults with comorbidities associated with RSV-LRTD		50 – 59 YOA Cohort 1b: Adults without comorbidities associated with RSV-LRTD		≥ 60 YOA	Total
	RSVPreF3 + AS01$_E$ (N=386)	Placebo (N=191)	RSVPreF3 + AS01$_E$ (N=383)	Placebo (N=192)	RSVPreF3 + AS01$_E$ (N=382)	(N=1534)
Comorbidity of interest, n (%)						
1 pre-existing comorbidity of interest	269 (69.7)	140 (73.3)	0 (0)	0 (0)	93 (24.3)	502 (32.7)
≥ 2 pre-existing comorbidities of interest	117 (30.3)	51 (26.7)	0 (0)	0 (0)	51 (13.4)	219 (14.3)
Chronic pulmonary disease	147 (38.1)	77 (40.3)	0 (0)	0 (0)	58 (15.2)	282 (18.4)
Chronic cardiovascular disease	124 (32.1)	58 (30.4)	0 (0)	0 (0)	56 (14.7)	238 (15.5)
Diabetes mellitus	188 (48.7)	91 (47.6)	0 (0)	0 (0)	68 (17.8)	347 (22.6)
Chronic liver or renal disease	56 (14.5)	23 (21.0)	0 (0)	0 (0)	18 (4.7)	97 (6.3)
Smoking status for tobacco, n (%)						
Current smoker	83 (21.5)	49 (25.7)	66 (17.2)	36 (18.8)	45 (11.8)	279 (18.2)
Former smoker	133 (34.5)	50 (26.2)	99 (25.8)	37 (19.3)	133 (34.8)	452 (29.5)
Never smoker	170 (44.0)	92 (48.2)	217 (56.7)	119 (62.0)	204 (53.4)	802 (52.3)
Unknown	0 (0)	0 (0)	1 (0.3)	0 (0)	0 (0)	1 (0.1)

Comorbidities: Overall, most common comorbidity of interest was diabetes mellitus and least common was chronic liver or renal disease

***Participants with underlying medical conditions such as chronic pulmonary and cardiovascular diseases, diabetes mellitus types 1 and 2, and chronic liver and renal diseases**

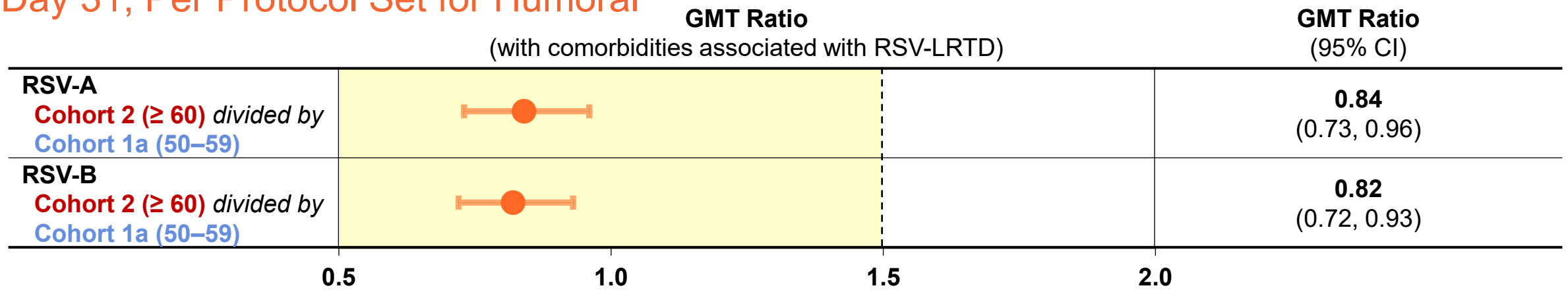
Immunogenicity

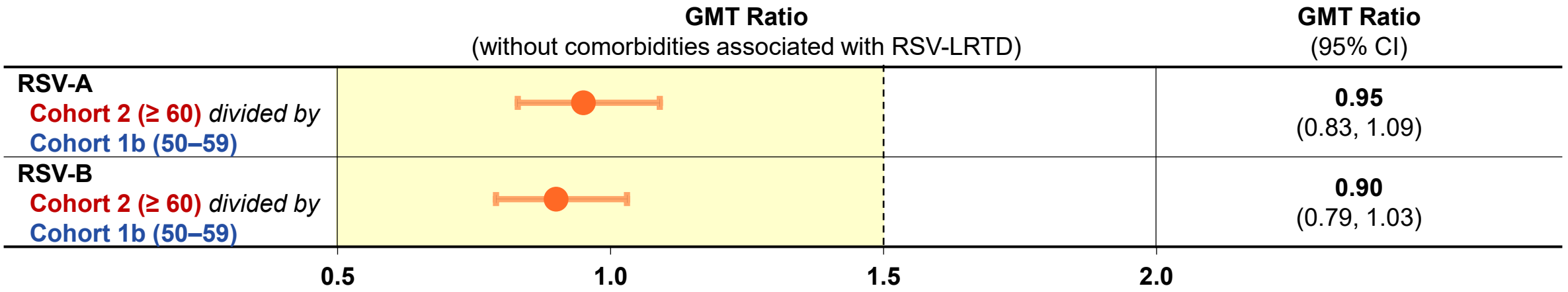
RSV-OA=ADJ-018: Day 31 Analysis (Preliminary)

Data Lock Point: July 26, 2023

Co-Primary Endpoint Met: Humoral Response to RSV Vaccine Demonstrated Non-Inferiority in Adults 50–59 YOA vs Adults ≥ 60 YOA

Day 31, Per Protocol Set for Humoral



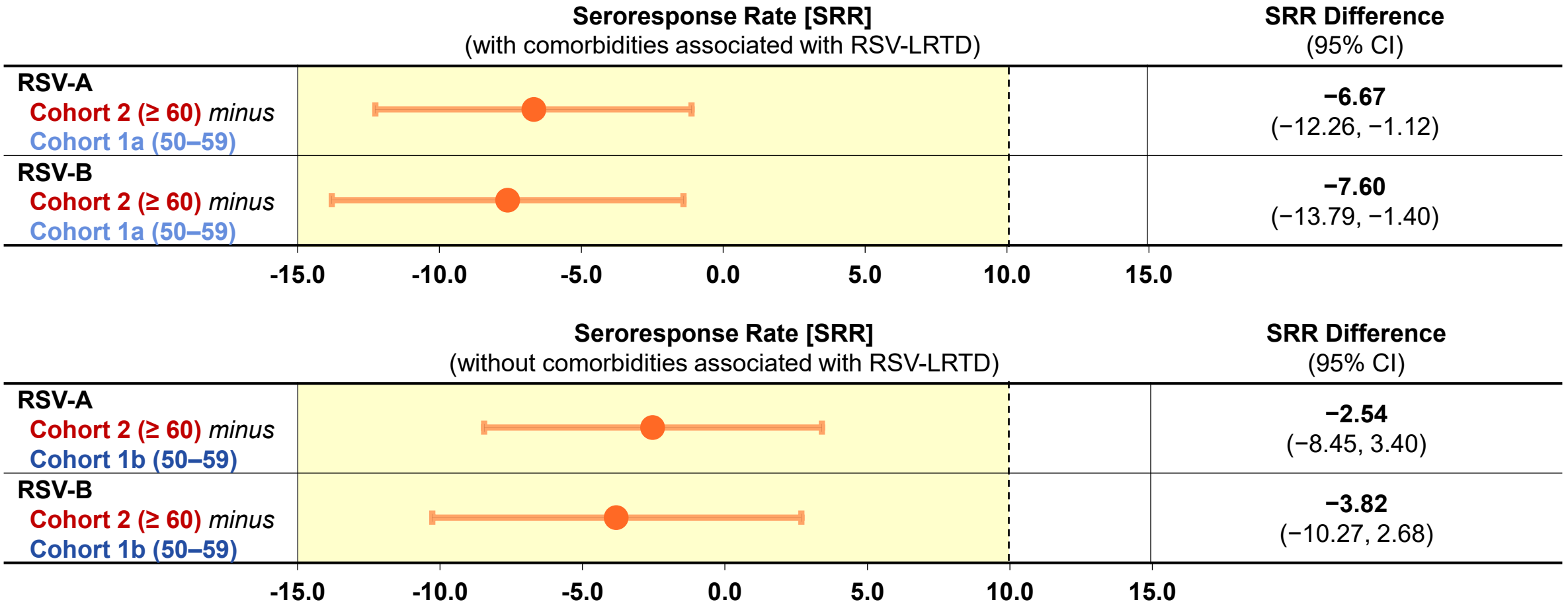


Success Criteria: Upper limit of 2-sided CI for GMT ratio is ≤1.5

Cohort 1a: Adults 50-59 with comorbidities associated with RSV-LRTD ; Cohort 1b: Adults 50-59 without comorbidities associated with RSV-LRTD; Cohort 2: Adults ≥ 60 YOA
GMT, geometric mean titer; CI, confidence interval; LRTD, lower respiratory tract disease; Preliminary data; RSV response evaluated using NAb (ED60);
ED60, serum estimated dilution inducing 60% inhibition in plaque-forming units; Nab, neutralizing antibody

Co-Primary Endpoint Met: SRRs for RSV-A and RSV-B NAbs Demonstrated Non-Inferiority in Adults 50–59 YOA vs Adults ≥ 60 YOA

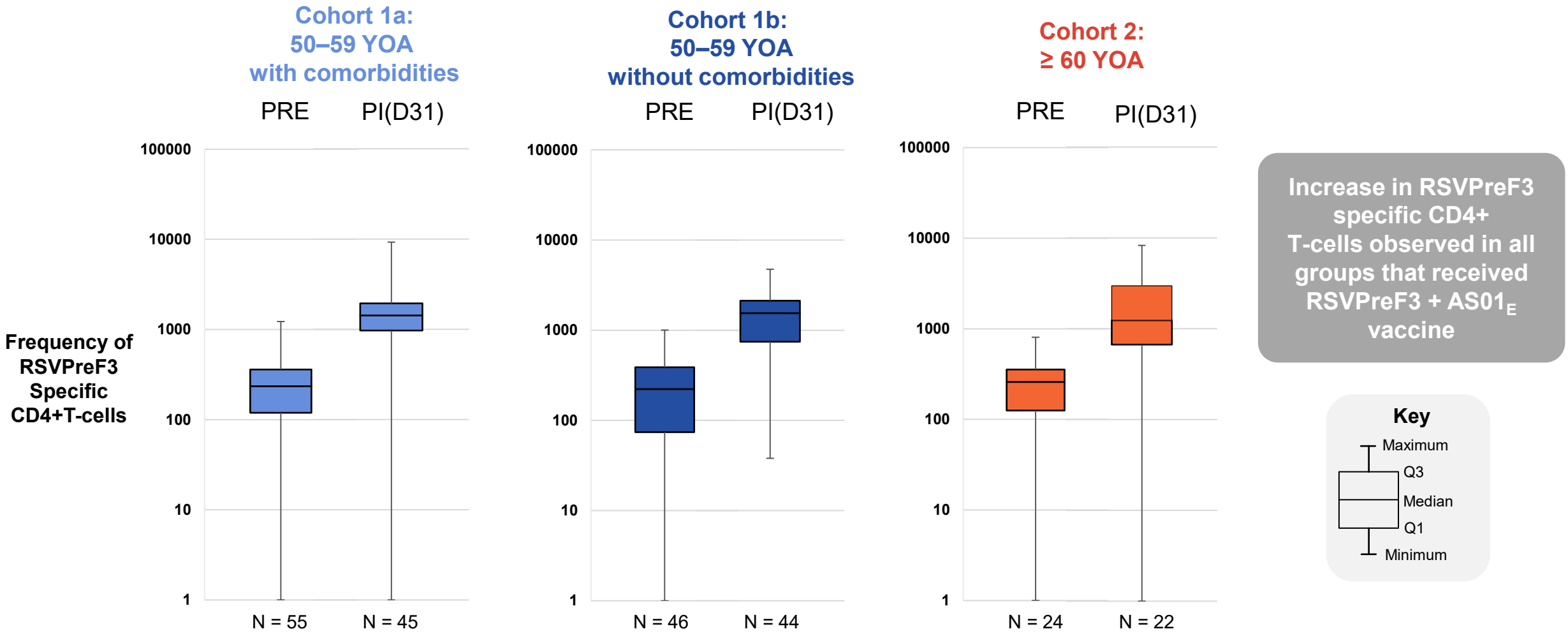
Day 31, Per Protocol Set for Humoral



Success Criteria: Upper limit of 2-sided CI for SRR difference is <10%

Cohort 1a: Adults 50-59 with comorbidities associated with RSV-LRTD ; Cohort 1b: Adults 50-59 without comorbidities associated with RSV-LRTD; Cohort 2: Adults ≥ 60 YOA; Preliminary data; RSV response evaluated using NAb (ED60); SRR, Seroresponse rate defined as % of participants with ≥ 4-fold increase of post-vaccination titers vs pre-vaccination titers (post-vacc titers/pre-vacc titers ≥ 4)

Frequency of RSVPreF3 Specific CD4+ T-Cell Response Consistent for 50–59 YOA Compared with ≥ 60 YOA



Q1 and Q3 are 25th and 75th percentiles. PRE, Pre-vaccination; PI(D31), 1 month post RSV vaccination; Q, quartile; Frequency of RSVPreF3 specific CD4+T-cells expressing ≥ 2 markers including ≥ 1 cytokine (CD40L, 4-1BB, TNF-α, IFN-γ, IL-13, and IL-17 (per million of CD4+T-cells by intracellular cytokine staining) - per protocol set for cell mediated immune response

Safety

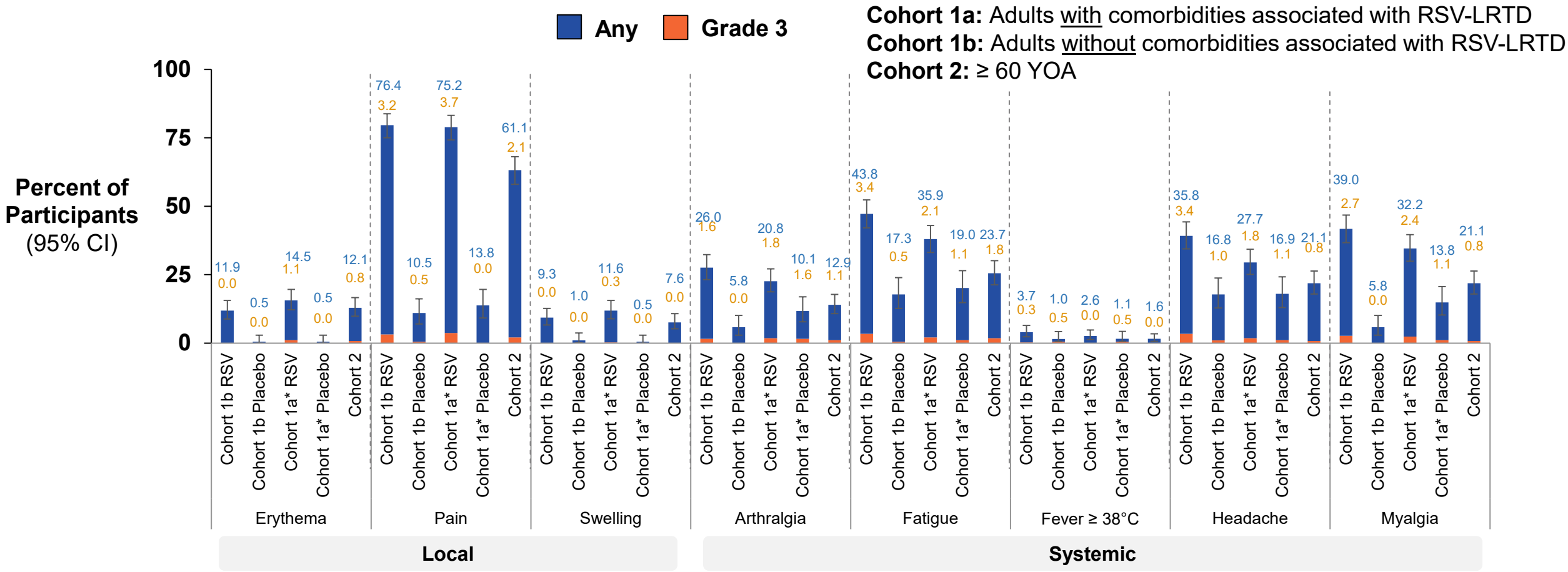
RSV-OA=ADJ-018: 6 Month Analysis

Safety Lock Point: July 21, 2023

Solicited Local and Systemic Adverse Events (AE)

Low reporting (< 5%) of Grade 3 events across groups;
Most common local AE: pain and systemic AEs: fatigue, headache, myalgia

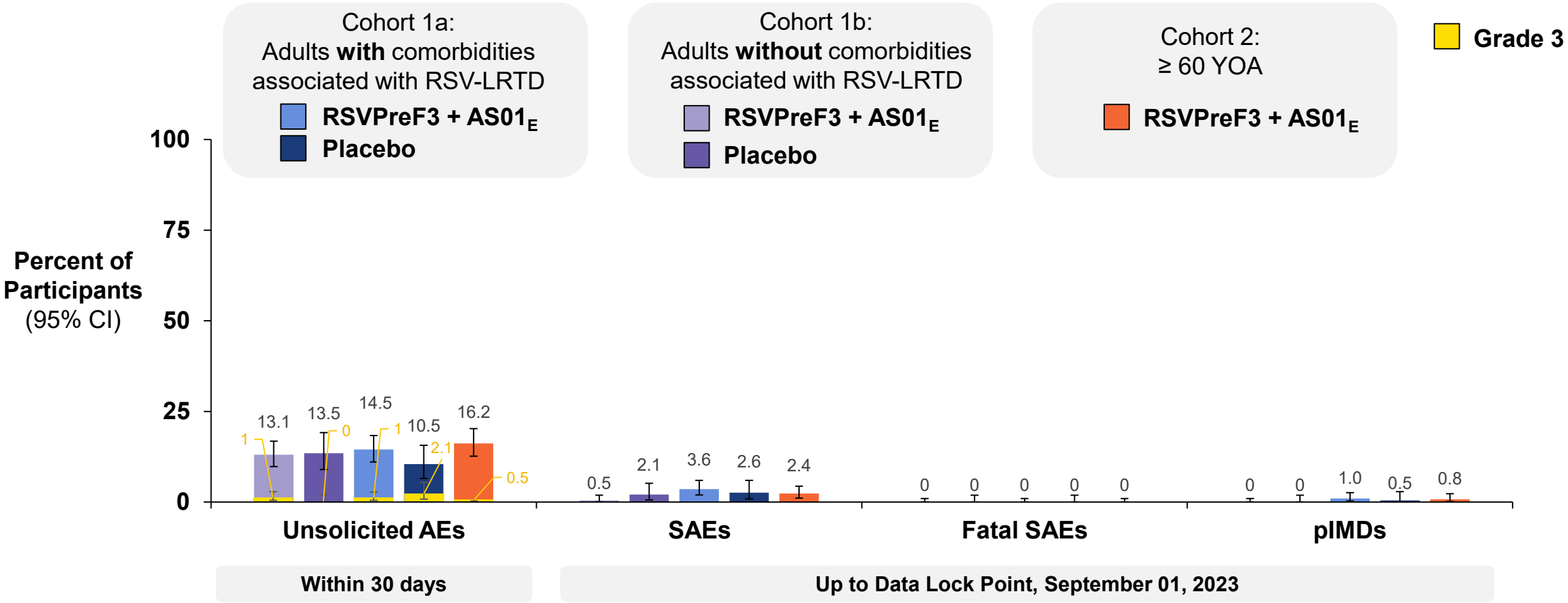
Solicited AEs Reported Within 4 Days of Vaccination (Exposed Set)



Error bars show 95% CIs for total AEs. 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

Unsolicited AEs, SAEs, Fatal SAEs, and pIMDs

Exposed Set



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; SAE; serious adverse events; pIMD, potential immune mediated disease

Summary of RSV-OA=ADJ-018 Results

Summary: Immune Response Among Adults 50–59 YOA

Non-inferiority success criteria met in adults **50–59 YOA with and without comorbidities** associated with RSV-LRTD compared with **adults ≥ 60 YOA**

Vaccine efficacy can be inferred **in adults 50–59 YOA,** including those with **comorbidities associated with RSV-LRTD**

High vaccine efficacy from pivotal Phase 3 in adults ≥ 60 YOA

- RSV-LRTD = 82.6% for season 1
- Severe RSV-LRTD = 94.1% for season 1
- ≥ 1 comorbidity associated with RSV-LRTD = 94.6%
- Durable efficacy across 2 full seasons

Summary: Immune Response and Safety Among Adults 50–59 YOA

Non-inferiority success criteria met in adults **50–59 YOA with and without comorbidities** associated with RSV-LRTD compared with **adults ≥ 60 YOA**

Vaccine efficacy can be inferred **in adults 50–59 YOA,** including those with **comorbidities associated with RSV-LRTD**

Safety profile for 50–59 YOA groups **consistent** with profile observed in adults ≥ 60 YOA

Overall AREXVY Safety Update

Safety Update

Clinical studies

- As of Oct. 16, 2023, no reports of ADEM in GSK database
  - Two unconfirmed reports of ADEM in Co-administration Study (RSV OA=ADJ-007) with AREXVY + FLU-QIV[1]
    - Both diagnoses updated by investigator and no longer reported as ADEM

Post Authorization

- As of Oct. 13, 2023, ≥ 2.1 million doses of AREXVY administered* in US
  - Reported AEs reflect known safety profile**

1. https://clinicaltrials.gov/study/NCT04841577
*IQVIA NPA Rapid Weekly TRx; **Based on GSK safety database lock Oct. 16
ADEM, acute disseminated encephalomyelitis

Overall Summary

1. Severe RSV disease among adults 50–59 YOA with certain comorbidities presents significant unmet medical need

2. RSV-OA=ADJ-018 provides data to address this medical need; showing comparable immunogenicity to those ≥ 60 YOA, inferring vaccine efficacy

3. AREXVY is well tolerated with a favorable safety profile in 50–59 YOA

GSK's RSVPreF3 + AS01$_E$ Vaccine (AREXVY)

AREXVY approved by FDA for the prevention of LRTD caused by RSV in adults ≥ 60 years, as a single dose.

ACIP recommends that persons aged ≥ 60 years may receive a single dose of RSV vaccine, using shared clinical decision-making.

ACIP October 25, 2023

Susan Gerber, MD

Medical Director

GSK