AREXVY (Adjuvanted RSVPreF3) 2-Year Update

ACIP June 26, 2024

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GSK

AREXVY Indications

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

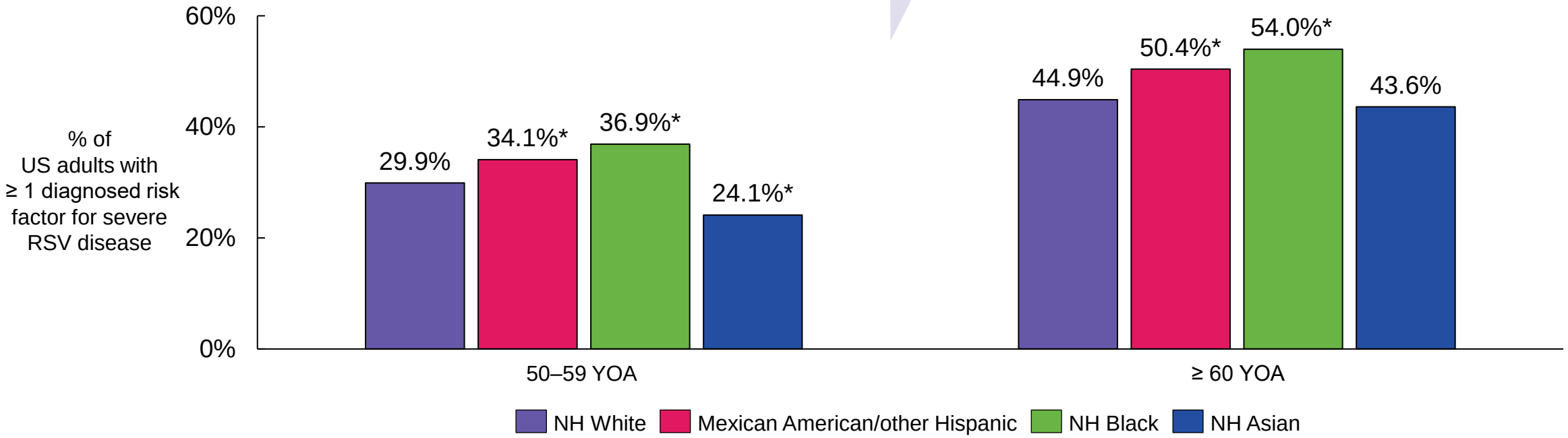
- Individuals **≥ 60 YOA**
- Individuals **50-59 YOA** at increased risk for LRTD caused by RSV

YOA: years of age

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

Risk Factors for Severe RSV Disease Are Highly Prevalent Among Adults ≥ 50 Years with Disparities Observed by Race and Ethnicity

- **31.4%** of adults **50–59 YOA** and **46.9%** of adults **≥ 60 YOA** are **diagnosed with ≥ 1 risk factor for severe RSV disease**[a]
- **Mexican American/other Hispanic and NH Black adults** have **significantly higher** prevalence of **≥ 1 diagnosed risk factor** in each of these age groups (vs. NH White adults)[b]



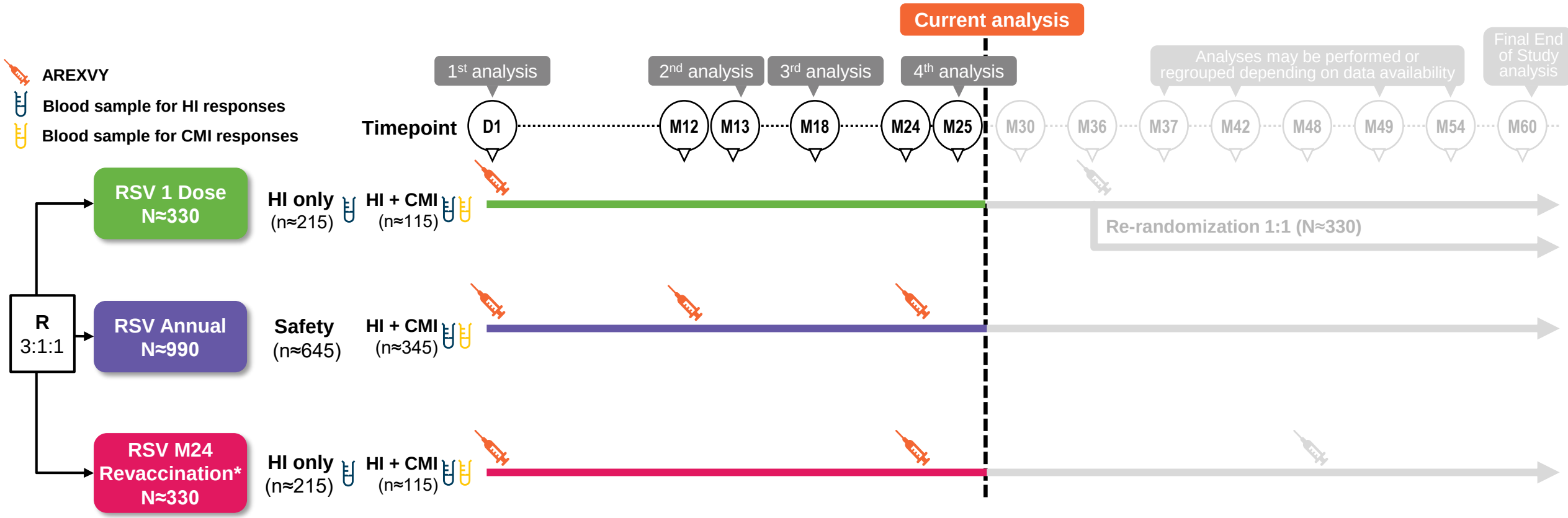
Horn et al. NFID ACVR, May 8-10, 2024

[a]Self-reported diagnosis of the following conditions: CHF, CHD, stroke, angina pectoris, MI, COPD (COPD, emphysema, or current chronic bronchitis), asthma (current), diabetes, liver disease (current), renal disease. [b]Other race/multi-racial results not presented.
*Statistically significant based on two-sided P < 0.05. P-values were calculated based on pairwise chi-square analysis on 2x2 tables using non-Hispanic White adults as the reference group.
Notes: Retrospective, cross-sectional analysis of pooled NHANES data spanning the period 2011-March 2020.Weighting to the United States population conducted in accordance with NHANES published guidelines: https://wwwn.cdc.gov/nchs/nhanes/tutorials/weighting.aspx. CHD, coronary heart disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; NH, Non-Hispanic; NHANES, National Health and Nutrition Examination Survey; YOA, years of age.

AReSVi-004: Immunogenicity, Safety, Reactogenicity and Persistence of Single Dose of AREXVY Vaccine and Different Revaccination Schedules in Adults ≥ 60 YOA

Randomized, open-label, multi-country study (NCT04732871)

AReSVi-004 Phase 3 Study Design[1-3]



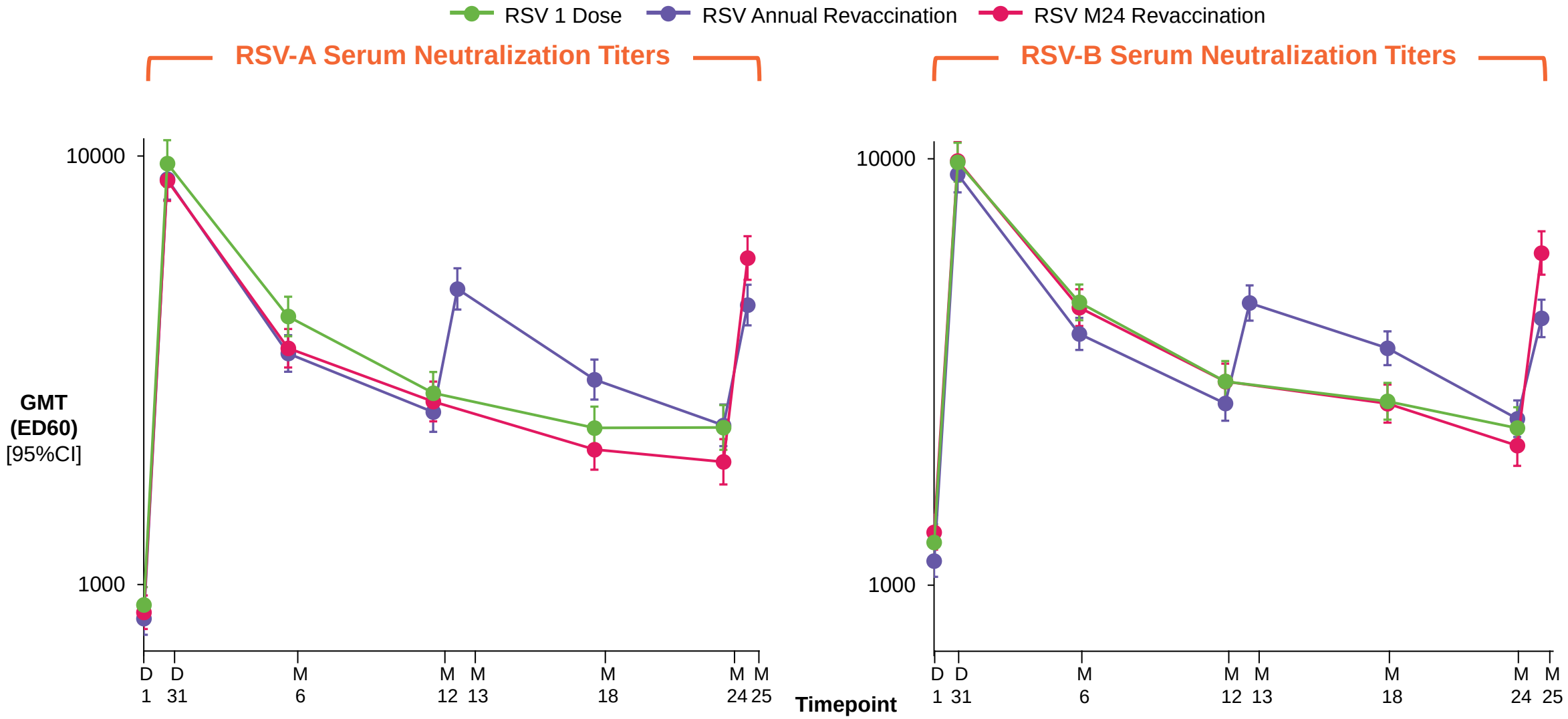
All participants followed for safety

Primary objective: To evaluate humoral immune response following 1-dose primary schedule up to 12 months post-dose 1**

Key secondary objectives: To evaluate humoral and CMI*** responses following 1-dose primary schedule and re-vaccination doses, up to study end (M60); safety and reactogenicity also assessed

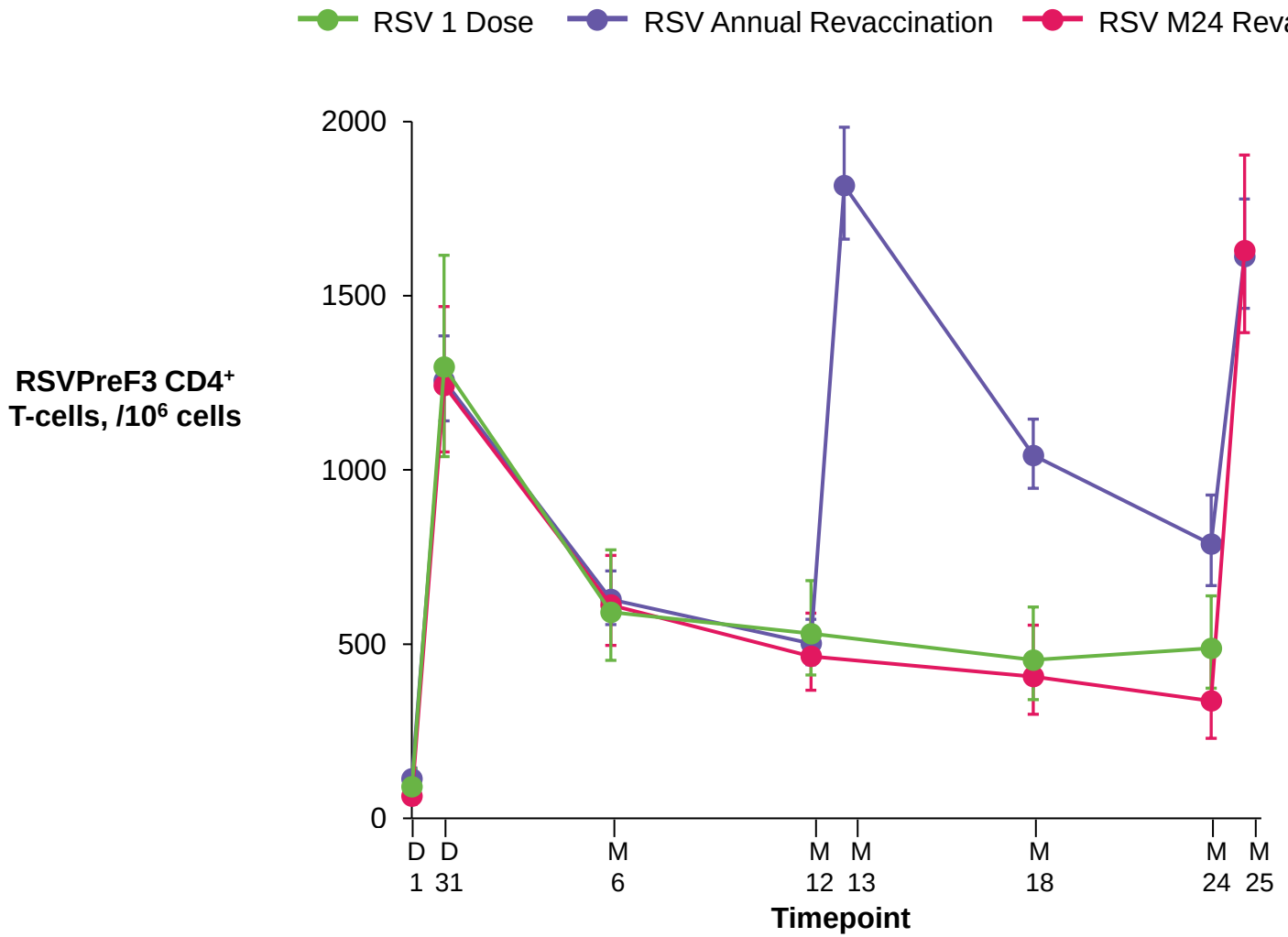
***RSV M24 revaccination: Participants receiving first dose (Dose 1) of AREXVY at Day 1 followed by revaccination dose at 24 months post Dose 1; **Primary endpoints: NAb (neutralizing antibody) geometric mean titers (RSV-A and RSV-B) at Day 1 (pre-vaccination), D31, M6, and M12 post-dose 1; ***CMI response in terms of frequency of RSVPreF3-specific CD4+ and/or CD8+ T-cells expressing > 2 activation markers; CMI, cell-mediated immunity; HI, humoral immunity; 1. Schwarz TF et al. 2023; 2. ClinicalTrials.gov. NCT04732871; 3. GSK, 2024 https://www.gsk-studyregister.com/en/trial-details/?id=212496 (All URLs accessed June 2024)**

Higher RSV-A and RSV-B Neutralizing Antibody Titers Observed After 24 Month Vaccination Interval



RSV Annual revaccination (N=250-341): Participants receiving first dose (Dose 1) of AREXVY at Day 1, followed by revaccination dose at 12 months post Dose 1 and at 24 months post Dose 1;
RSV M24 revaccination (N= 223-319): Participants receiving first dose (Dose 1) of AREXVY at Day 1 followed by revaccination dose at 24 months post Dose 1;
RSV 1 dose (N=281-318): Participants receiving single dose (Dose 1) of AREXVY at Day 1; ED60: estimated dilution 60; GMT: geometric mean titer

CD4+ T-Cell Responses Increased 1-Month Post Each Vaccination Dose

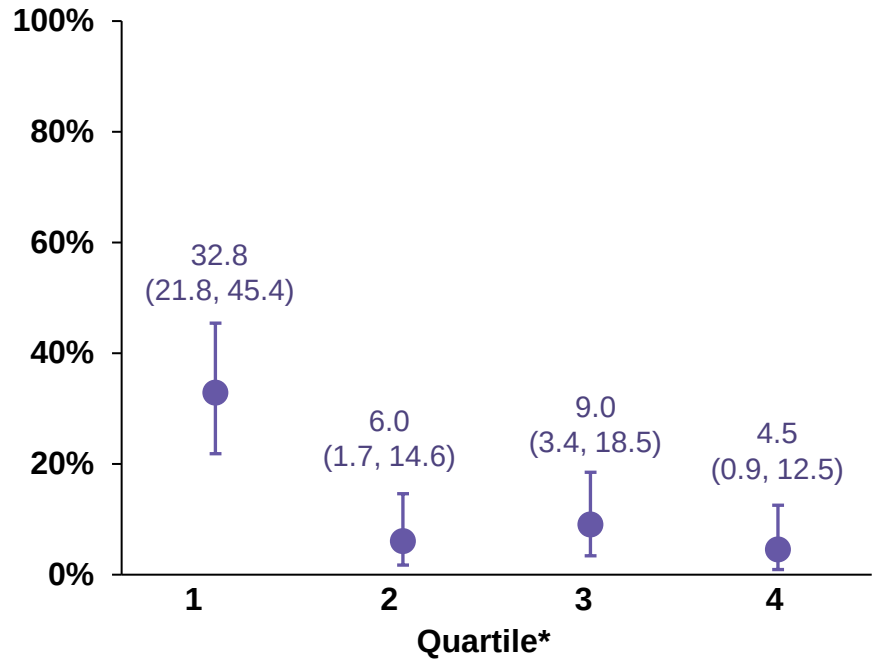


RSV Annual revaccination (N=216-286): Participants receiving first dose (Dose 1) of AREXVY at Day 1, followed by revaccination dose at 12 months post Dose 1 and at 24 months post Dose 1; RSV M24 revaccination (N=68-94): Participants receiving first dose (Dose 1) of AREXVY at Day 1 followed by revaccination dose at 24 months post Dose 1; RSV 1 dose (N=83-95): Participants receiving single dose (Dose 1) of AREXVY at Day 1; 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)

Lower Prevaccination RSV-A NAb Titers Associated with Higher Seroresponse Rates (≥ 4-Fold Increase) Following Revaccination

RSV Annual Revaccination

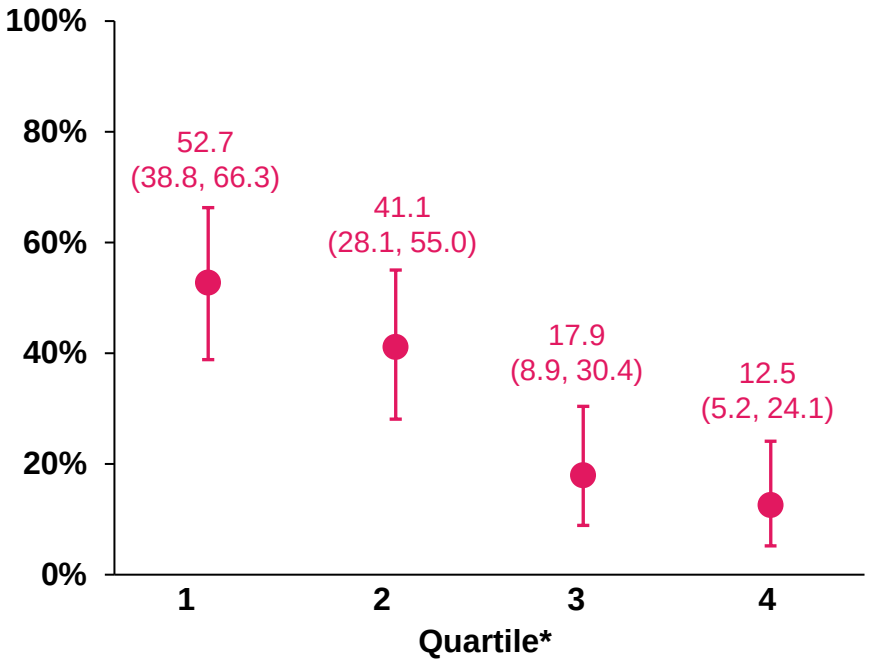
Participants with ≥ 4-fold increase in RSV-A NAb titers at M13 vs M12 [95% CI]



n/N	22 / 67	4 / 67	6 / 67	3 / 67
NAb baseline GMT (ED60)	193 – <1,304	1,304 – <2,381	2,381 – <4,078	4,078 – 123,535

RSV M24 Revaccination

Participants with ≥ 4-fold increase in RSV-A NAb titers at M25 vs M24 [95% CI]

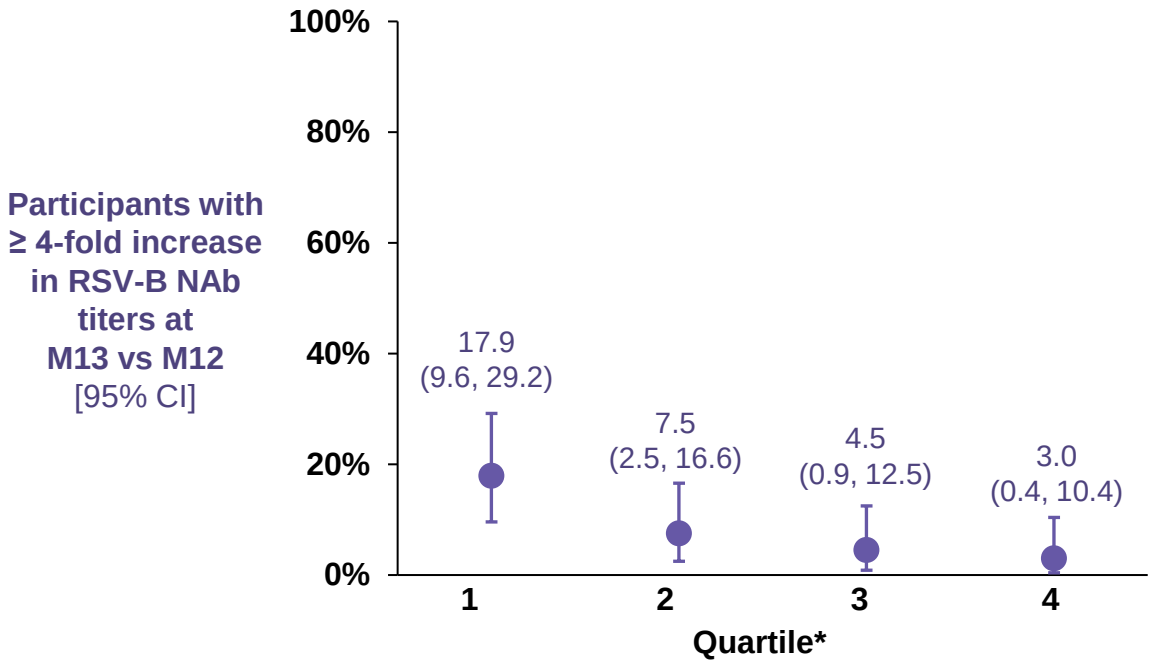


29 / 55	23 / 56	10 / 56	7 / 56
283 – <1,000	1,000 – <1,849	1,849 – <3,736	3,736 – 38,840

***Participants were grouped into quartiles depending on their baseline NAb titers: 1 = baseline NAb min–<1; 2 = baseline NAb 1–<2 (median); 3 = baseline NAb 2 (median)–<3; 4 = baseline NAb 3–4. Participants in the quartile 1 had the lowest pre-revaccination NAb and those in the quartile 4 had the highest; ED60, serum dilution inducing 60% inhibition in plaque-forming units; GMT, geometric mean titer; NAb, neutralizing antibody; RSV Annual revaccination: Participants receiving the first dose (Dose 1) of Arexvy at Day 1, followed by a revaccination dose at 12 months post Dose 1 and at 24 months post Dose 1; RSV M24 revaccination: Participants receiving the first dose (Dose 1) of Arexvy at Day 1 followed by a revaccination dose at 24 months post Dose 1.**

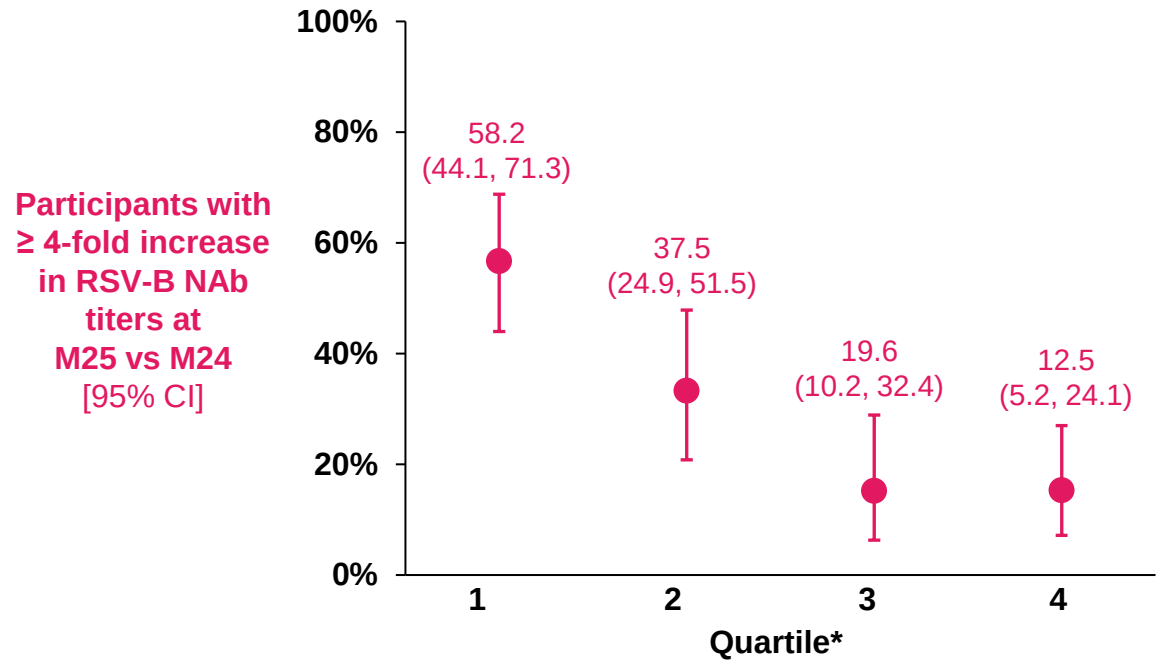
Lower Prevaccination RSV-B NAb Titers Associated with Higher Seroresponse Rates (≥ 4-Fold Increase) Following Revaccination

RSV Annual Revaccination



n/N	12 / 67	5 / 67	3 / 67	2 / 67
NAb baseline GMT (ED60)	351 – <1,607	1,607 – <2,453	2,453 – <4,133	4,133 – 36,391

RSV M24 Revaccination

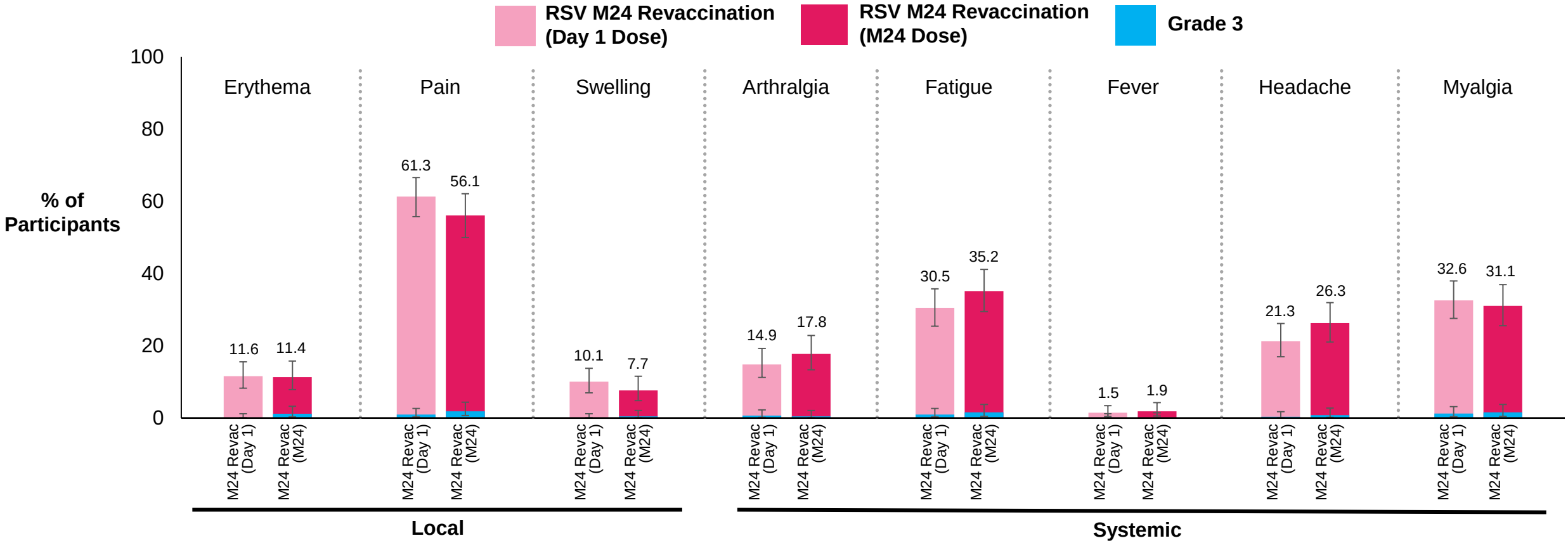


32 / 55	21 / 56	11 / 56	7 / 56
271 – <1,190	1,190 – <2,122	2,122 – <3,845	3,845 – 26,385

***Participants were grouped into quartiles depending on their baseline NAb titers: 1 = baseline NAb min–<1; 2 = baseline NAb 1–<2 (median); 3 = baseline NAb 2 (median)–<3; 4 = baseline NAb 3–4. Participants in the quartile 1 had the lowest pre-revaccination NAb and those in the quartile 4 had the highest; ED60, serum dilution inducing 60% inhibition in plaque-forming units; GMT, geometric mean titer; NAb, neutralizing antibody; RSV Annual revaccination: Participants receiving the first dose (Dose 1) of Arexvy at Day 1, followed by a revaccination dose at 12 months post Dose 1 and at 24 months post Dose 1; RSV M24 revaccination: Participants receiving the first dose (Dose 1) of Arexvy at Day 1 followed by a revaccination dose at 24 months post Dose 1.**

Safety and Reactogenicity Profile in Individuals Revaccinated at Month 24 Similar to First Dose

Solicited AEs reported within 4 days of each vaccine dose (exposed set)



Unsolicited AEs, SAEs, Fatal SAEs and pIMDs of individuals who were revaccinated at Month 24 are also similar to those vaccinated at Day 1

AE, adverse event; M, month; RSV 24M revaccination: Participants receiving the first dose (Day 1 Dose) of RSVPreF3 OA investigational vaccine at Day 1 followed by a revaccination dose at 24 months (M24 Dose) post-Dose 1 (n=270-328). Grade 3: >100 mm for erythema and swelling; significant pain at rest, prevents normal everyday activities for pain; prevents normal activity for headache, fatigue, myalgia, and arthralgia; >39.0°C (102.2°F) for fever.

AReSVi-004 Summary

1. Revaccination at a 24-month interval provides higher RSV-A and RSV-B neutralizing antibody titers as compared to a 12-month interval
2. The lower the prevaccination RSV-A and RSV-B neutralizing antibody titers observed at 2 years post initial vaccination, the higher the seroresponse rates after revaccination
3. Safety and reactogenicity profiles of second dose comparable with first dose
4. Future results from this trial will help inform optimal revaccination timing

Postmarketing Safety Update

AREXVY: Post-Licensure Safety Surveillance After 1 Year Reflects Acceptable Safety Profile in Clinical Trials

Vaccine Exposure

- **~ 8 million** doses of AREXVY administered in US since launch*

AE

- 1,640 AEs (from US, 1,344 AE reports received) [launch 3 May ’23-2 June ’24]**
- 89% non-serious
- Majority related to labelled reactions

GBS

- Since launch, GSK received **13 reports** of GBS, all from US
- Reports do not exceed expected background incidence[1]
  - 17 cases expected in absence of vaccination

*IQVIA NPA Rapid Weekly TRx, to 13 May 2024
**Based on GSK safety database, spontaneous AE reports not necessarily causally-related to vaccination
1. Sejvar JJ, et al. 2011; AE: adverse event

Overview of Clinical Development Program

AREXVY Clinical Development Program

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-007, RSV OA=ADJ-017, RSV OA=ADJ-008
Safety, reactogenicity, immunogenicity when co-administered with FLU-QIV, FLU-aQIV, FLU-QIV-HD, respectively

AReSVi-006 study
Older adults ≥60 YOA
Pivotal efficacy study

RSV OA=ADJ-019 study
Older adults ≥60 YOA
Safety, reactogenicity, immunogenicity when co-administered with PCV20

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

RSV OA=ADJ-020 study
Older adults ≥50 YOA
Safety, reactogenicity, immunogenicity when co-administered with HZ/su vaccine

RSV OA=ADJ-025 study
Adults 18–49 years of age compared to older adults ≥60 years of age
Safety and immunogenicity

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

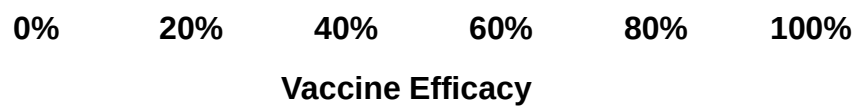
RSV OA=ADJ-013 study
Older adults ≥50 YOA
Safety, reactogenicity, immunogenicity when co-administered with COVID-19 mRNA vaccine

Phase 2b
Phase 3
Completed
Ongoing/ in progress

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; 1MPD1: 1 month post dose 1; PCV20: 20-valent pneumococcal conjugate vaccine; YOA: years of age
All studies ClinicalTrials.gov; All URLs accessed June 2024

Efficacy of a Single Dose of AREXVY over 2 Calendar Years

AREXVY (Single dose)	AREXVY	Placebo	**% VE** (95% CI)	
	Number of events (n/N)		***W/ season covariate***	***W/o season covariate***
RSV-LRTD	**32** / 12,468	**154** / 12,498	**67.7%** (52.3, 78.7)	**73.3%** (60.7, 82.4)
≥ 1 comorbidity of interest*	**17** / 5,000	**79** / 4,942	**67.1%** (43.6, 81.8)	**73.1%** (54.2, 85.1)
≥ 70 years of age	**12** / 5,506	**74** / 5,517	**74.6%** (52.6, 87.5)	**79.1%** (61.3, 89.7)
Pre-frail**	**9** / 4,794	**50** / 4,779	**71.3%** (40.6, 87.7)	**77.0%** (52.7, 90.1)
Severe RSV-LRTD	**9** / 12,468	**54** / 12,498	**74.9%** (48.4, 89.2)	**78.6%** (56.3, 90.7)



Median follow-up: 23.3 months

***Comorbidities of interest: COPD, asthma, any chronic respiratory or pulmonary disease, heart failure (cardiorespiratory condition), diabetes mellitus type 1 or 2, advanced liver or renal disease (endocrine or metabolic condition); **frailty assessed using gait speed test: walking speed < 0.4 m/s or not able to perform test (frail), walking speed 0.4–0.99 m/s (pre-frail), walking speed ≥1 m/s (fit); Due to too few cases observed, cannot conclude VE for frail and ≥ 80 years of age**

Conclusion

- Immunogenicity data supports potential for revaccination with AREXVY
  - Stronger immune responses were observed in those revaccinated after 24-month interval compared to those revaccinated annually
  - Results from ongoing Phase 3 studies will help inform timing of revaccination
- AREXVY provides protection over 2 calendar years
- Acceptable safety profile following administration of ~ 8 million doses
- FDA recently expanded AREXVY's indication to include use in individuals 50–59 YOA at increased risk for RSV-LRTD
  - Will help to close equity gap by broadening access for populations at increased risk for severe disease caused by RSV

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