X JORNADA DEL PROGRAMA DE VACUNACIONES DE LA REGIÓN DE MURCIA

Vacunas frente al VRS en el adulto: el futuro próximo

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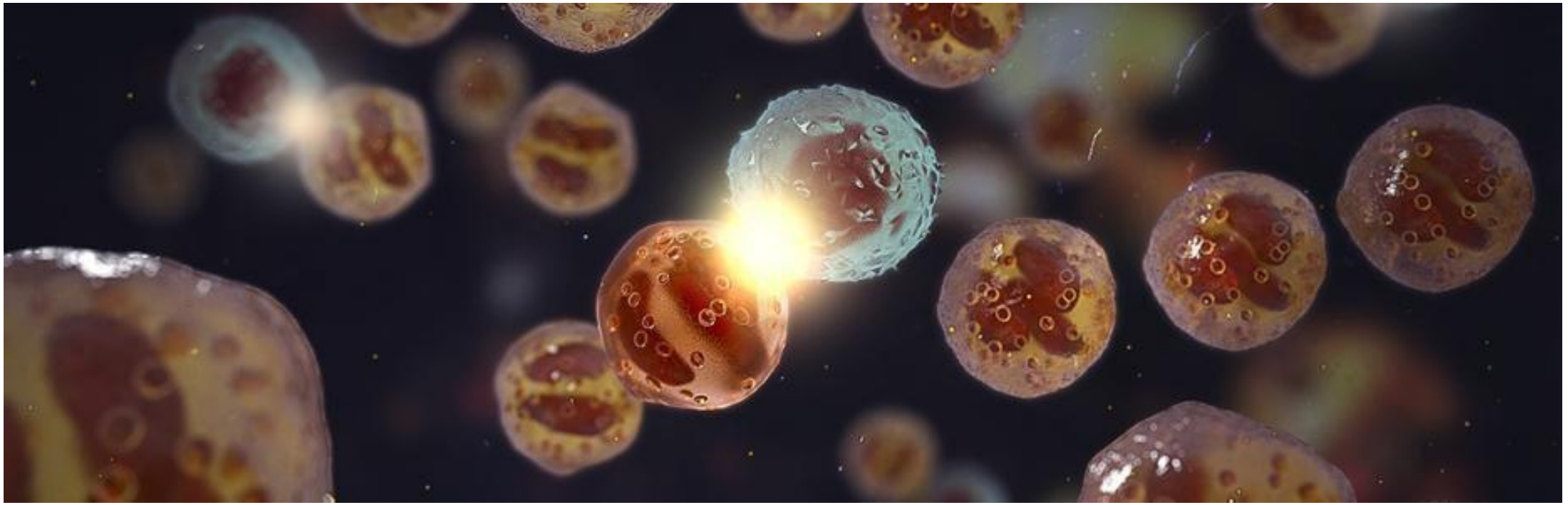
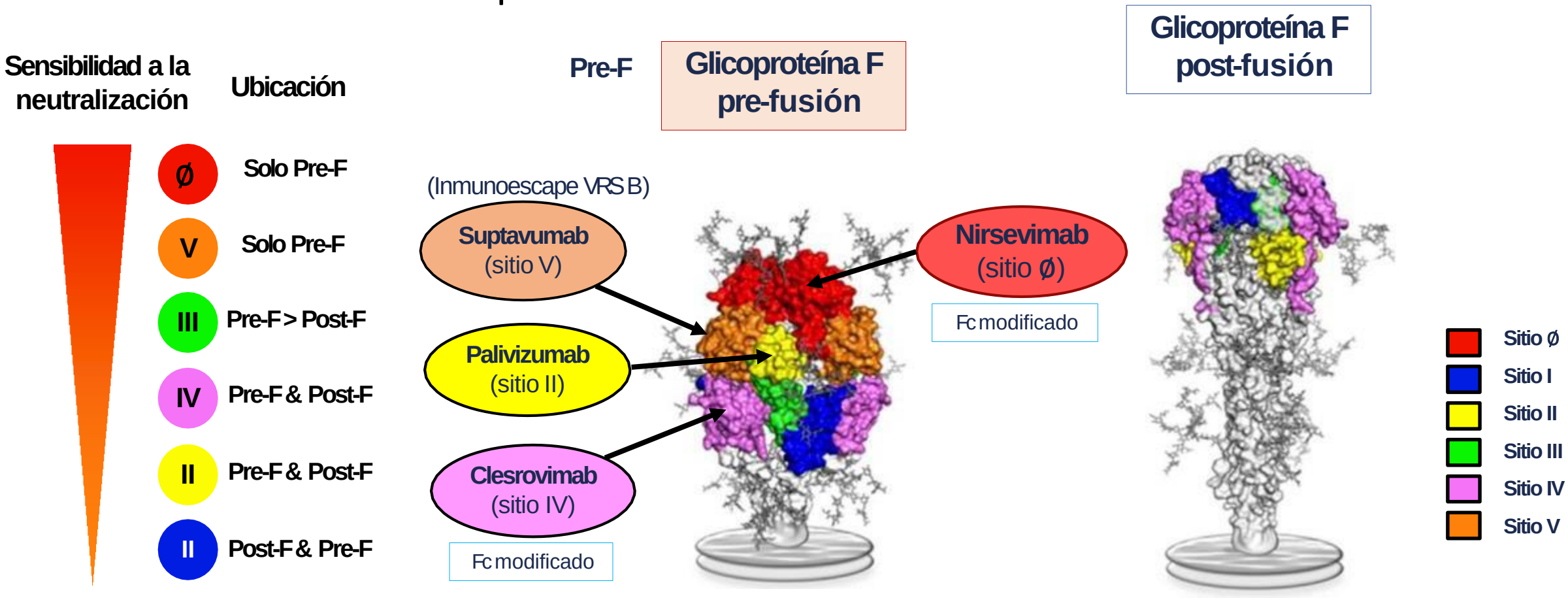


Declaración de conflicto de interés:

He recibido durante los últimos años ayudas de viajes y/o honorarios por conferencias y/o el patrocinio de proyectos y/o consultorías
de SANOFI, MSD, GSK, SEQIRUS, MODERNA, HIPRA, JANSSEN, AZ y PFIZER

Inmunodominancia y poder neutralizante de sitios antigénicos de la proteína F de VRS



Sitios antigénicos de la glicoproteína F del VRS y Acs monoclonales.

El diseño basado en la estructura funcional de la glicoproteína F permitió obtener una pre-F estable e inmunógena que induce Acs protectores.

Mejias A, et al. Ann Allergy Asthma Immunol. 2020;125:36–46. Graham BS. NEJM 388;7 2023 https://www.nejm.org/doi/10.1056/NEJMp2216358

Kanekiyo et al JID 2019:219 (Suppl 1) https://doi.org/10.1093/infdis/jiy745

Carga clínica del VRS en adultos mayores de la comunidad o de residencias

Tasa de ataque en residencias 30 % más que en la comunidad.

Comunidad

Edad media 65,1 (+/- 8,8)
91 % alguna comorbilidad crónica.

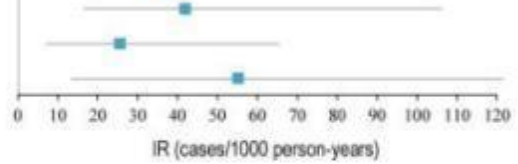
8,4%
Fragilidad

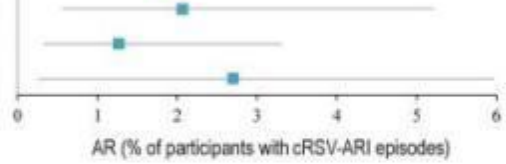
x 3,6

x 1,3

A

CD cohort	N	n	Person-years	IR	95% CI LL	95% CI UL	AR	95% CI LL	95% CI UL
Overall	1251	23	617.37	37.25	22.62	61.35	1.84	1.00	3.08
By RSV type									
RSV-A	1251	18	618.73	29.09	17.44	48.52	1.44	0.77	2.44
RSV-B	1251	5	621.68	8.04	2.30	28.13	0.40	0.06	1.37
By age group*									
50-59	382	8	189.37	42.25	18.24	83.24	2.09	0.91	4.09
60-64	238	4	116.01	34.48	11.58	102.68	1.68	0.33	4.94
65-69	242	5	119.33	41.90	16.53	106.21	2.07	0.56	5.22
70-79	315	4	156.45	25.57	6.97	65.46	1.27	0.33	3.31
≥80	74	2	36.22	55.22	13.43	227.09	2.70	0.26	10.13





Residencia

Edad media 82,7 (+/- 8,5)
99,2 % alguna comorbilidad crónica.

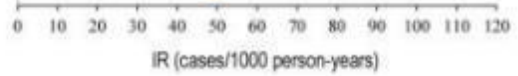
63,1%
Fragilidad

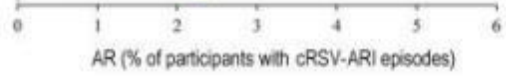
x 1,5

x 2,2

B

LTCF cohort	N	n	Person-years	IR	95% CI LL	95% CI UL	AR	95% CI LL	95% CI UL
Overall	664	15	313.47	47.85	22.58	101.41	2.26	0.88	4.69
By RSV type									
RSV-A	664	9	315.31	28.54	11.01	73.96	1.36	0.38	3.39
RSV-B	664	6	315.64	19.01	5.08	71.18	0.90	0.12	3.11
By age group*									
65-69	59	3	27.37	109.60	24.08	498.77	5.09	0.44	19.05
70-79	172	2	82.25	24.32	2.94	87.84	1.16	0.14	4.14
≥80	433	10	203.84	49.06	21.40	112.44	2.31	0.80	5.14





Narejos S, et al. Respiratory Syncytial Virus Disease Burden in Community-Dwelling and Long-Term Care Facility Older Adults in Europe and the United States: A Prospective Study. Open Forum Infectious Diseases. 2023;10(4):ofad111. doi: 10.1093/ofid/ofad111. eCollection 2023 Apr

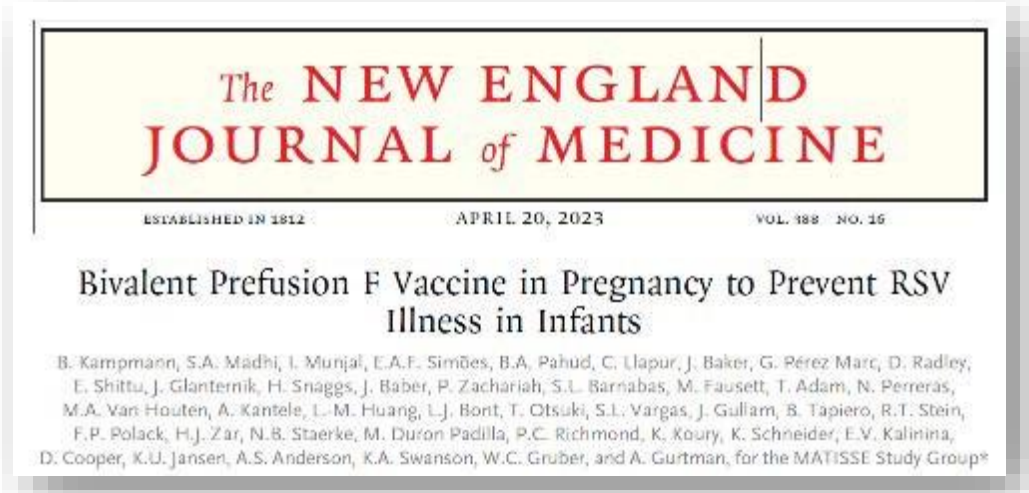
Vacuna frente a VRS bivalente para adultos y embarazadas


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults

E.E. Walsh, G. Pérez Marc, A.M. Zareba, A.R. Falsey, Q. Jiang, M. Patton, F.P. Polack, C. Llapur, P.A. Doreski, K. Ilangovan, M. Rämet, Y. Fukushima, N. Hussen, L.J. Bont, J. Cardona, E. DeHaan, G. Castillo Villa, M. Ingilizova, D. Eiras, T. Mikati, R.N. Shah, K. Schneider, D. Cooper, K. Koury, M.-M. Lino, A.S. Anderson, K.U. Jansen, K.A. Swanson, A. Gurtman, W.C. Gruber, and B. Schmoele-Thoma, for the RENOIR Clinical Trial Group*


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 20, 2023 VOL. 388 NO. 16

Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants

B. Kampmann, S.A. Madhi, I. Munjal, E.A.F. Simões, B.A. Pahud, C. Llapur, J. Baker, G. Pérez Marc, D. Radley, E. Shittu, J. Glanternik, H. Snaggs, J. Baber, P. Zachariah, S.L. Barnabas, M. Fausett, T. Adam, N. Perreras, M.A. Van Houten, A. Kantele, L.-M. Huang, L.J. Bont, T. Otsuki, S.L. Vargas, J. Guliam, B. Tapiero, R.T. Stein, F.P. Polack, H.J. Zar, N.B. Staerke, M. Duron Padilla, P.C. Richmond, K. Koury, K. Schneider, E.V. Kalinina, D. Cooper, K.U. Jansen, A.S. Anderson, K.A. Swanson, W.C. Gruber, and A. Gurtman, for the MATISSE Study Group*

1ª temporada

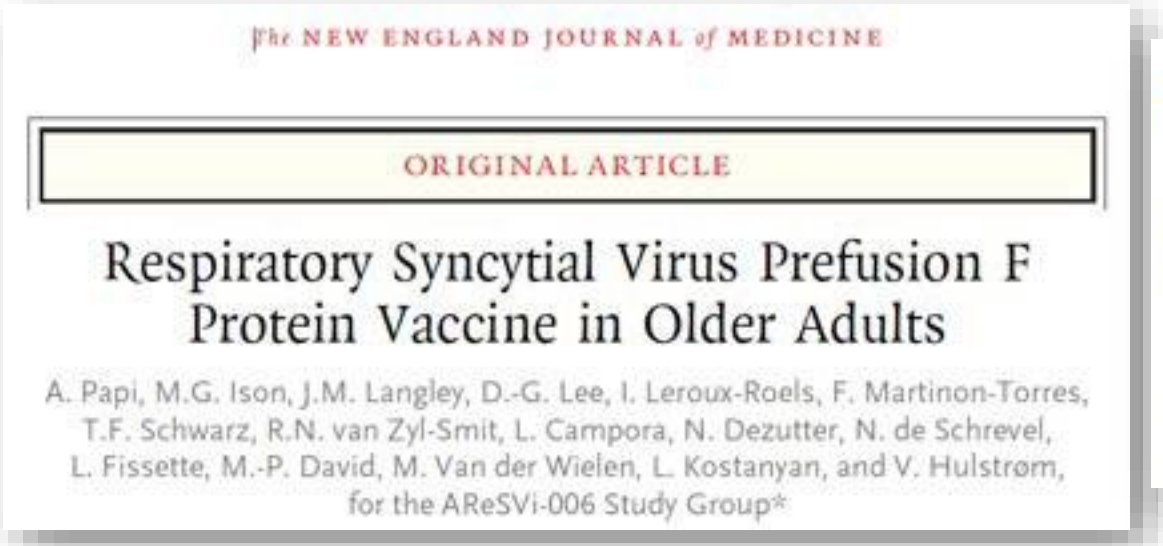
Eficacia 66,7 % (IC 96,6 % de 28,8 a 85,8) frente a enfermedad del tracto respiratorio inferior asociada al VRS **con ≥2 síntomas**.
Eficacia 85,7 % (IC 96,6 % de 32,0 a 98,7) frente a enfermedad del tracto respiratorio inferior asociada al VRS **con ≥3 síntomas**.
Eficacia 62,1 % (IC 95 % de 37,1 a 77,9) frente a **IRA por VRS.**

2ª temporada

Eficacia 78,6 % frente a enfermedad del tracto respiratorio inferior asociada al VRS **con ≥3 síntomas** y 48,9 % **con ≥2 síntomas**.

Walsh EE et al NEJM 2023 DOI: 10.1056/NEJMoa2213836 Kampmann B et al. N Engl J Med 2023;388:1451-64. DOI: 10.1056/NEJMoa2216480. Walsh EE et al. 8th Resvinet Conference, Feb 2024, pág:100

Primera vacuna adyuvada frente a VRS autorizada para adultos

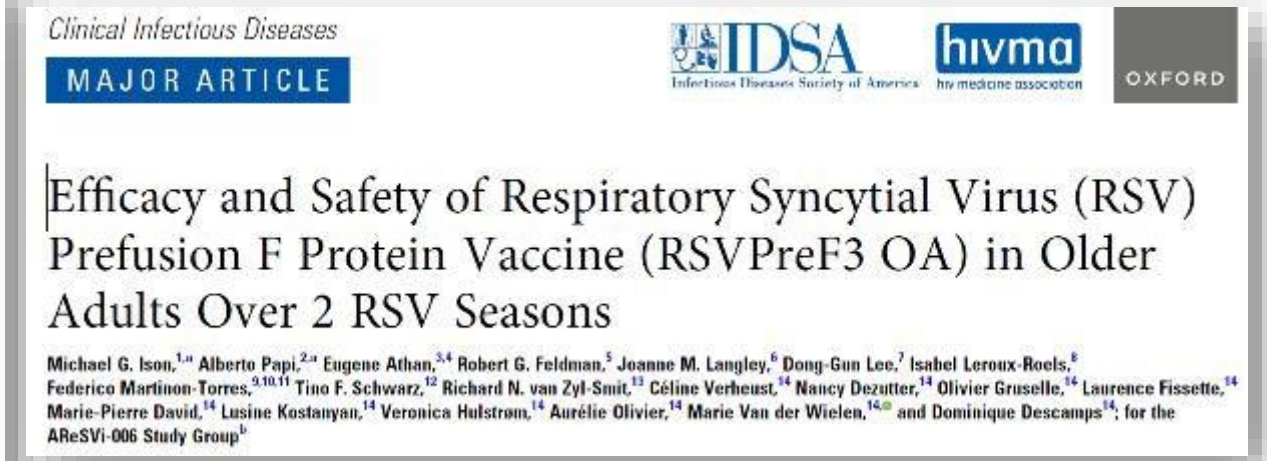


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults

A. Papi, M.G. Ison, J.M. Langley, D.-G. Lee, I. Leroux-Roels, F. Martinon-Torres, T.F. Schwarz, R.N. van Zyl-Smit, L. Campora, N. Dezutter, N. de Schrevel, L. Fissette, M.-P. David, M. Van der Wielen, L. Kostanyan, and V. Hulstrøm, for the AReSVi-006 Study Group*



Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

Efficacy and Safety of Respiratory Syncytial Virus (RSV) Prefusion F Protein Vaccine (RSVPreF3 OA) in Older Adults Over 2 RSV Seasons

Michael G. Ison,[1,a] Alberto Papi,[2,a] Eugene Athan,[3,4] Robert G. Feldman,[5] Joanne M. Langley,[6] Dong-Gun Lee,[7] Isabel Leroux-Roels,[8] Federico Martinon-Torres,[9,10,11] Tino F. Schwarz,[12] Richard N. van Zyl-Smit,[13] Céline Verheust,[14] Nancy Dezutter,[14] Olivier Gruselle,[14] Laurence Fissette,[14] Marie-Pierre David,[14] Lusine Kostanyan,[14] Veronica Hulstrøm,[14] Aurélie Olivier,[14] Marie Van der Wielen,[14,@] and Dominique Descamps[14]; for the AReSVi-006 Study Group[b]

Eficacia del 94,1 % (IC95 %, 62,4 a 99,9) frente a **enfermedad grave de vías respiratorias inferiores VRS** (sobre la base de los signos clínicos o por el investigador).

Eficacia del 71,7 % (IC95 %, 56,2 a 82,3) **frente a IRA relacionada con VRS.**

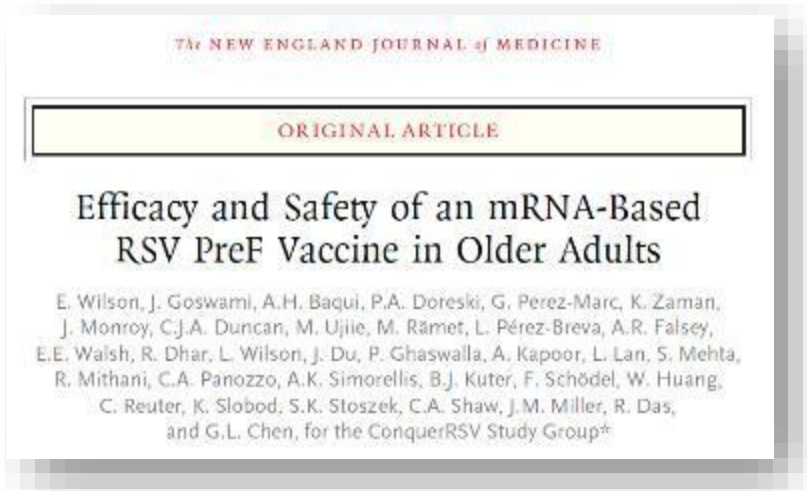
La eficacia fue similar frente a los subtipos A y B del VRS:

1. Para enfermedad del tracto respiratorio inferior relacionada con el VRS: 84,6 % para VRS-A y 80,9 % para VRS-B.
2. Para IRA relacionada con el VRS: 71,9 % para VRS-A y 70,6 %, para VRS-B.

Papi A et al. N Engl JMed 2023;388:595-608 DOI: 10.1056/NEJMoa2209604

Ison MG et al. Efficacy and safety of respiratory syncytial virus prefusion F protein vaccine (RSVPreF3 OA) in older adults over 2 RSV seasons, Clinical Infectious Diseases, 2024. doi: 10.1093/cid/ciae010

Vacunas VRS en desarrollo (RNAm-1345)



La eficacia fue del 68,4 % (IC 95 %, 50,9-79,7) frente a enfermedad respiratoria aguda asociada a VRS.

Table 2. Vaccine Efficacy against RSV-Associated Lower Respiratory Tract Disease with at Least Two or at Least Three Signs or Symptoms (Per-Protocol Efficacy Population).*

End Point	mRNA-1345		Placebo		Vaccine Efficacy (CI)†
	no. of participants	*no. of events*	*no. of participants*	*no. of events*	%
RSV-associated lower respiratory tract disease with ≥2 signs or symptoms‡					
Overall	17,572	9	17,516	55	83.7 (66.0 to 92.2)
RSV subtype					
RSV A	17,572	3	17,516	36	91.7 (73.0 to 97.4)
RSV B	17,572	6	17,516	19	68.5 (21.1 to 87.4)
Age group					
60–69 yr	11,168	8	11,118	33	76.0 (48.0 to 88.9)
70–79 yr	5,440	1	5,416	22	95.4 (65.9 to 99.4)
≥80 yr	964	0	982	0	NE (NE to NE)
RSV-associated lower respiratory tract disease with ≥3 signs or symptoms§					
Overall	17,572	3	17,516	17	82.4 (34.8 to 95.3)
RSV subtype					
RSV A	17,572	1	17,516	10	90.0 (22.0 to 98.7)
RSV B	17,572	2	17,516	7	71.5 (−37.0 to 94.1)
Age group					
60–69 yr	11,168	3	11,118	11	72.9 (2.8 to 92.4)
70–79 yr	5,440	0	5,416	6	100 (NE to 100)
≥80 yr	964	0	982	0	NE (NE to NE)

Wilson E et al. N Engl J Med 2023;389:2233-44 DOI: 10.1056/NEJMoa2307079

Vacuna Recombinante de Subunidades Proteicas Bivalente PreF frente al Virus Respiratorio Sincitial (VRS) de Pfizer (Abrysvo®)

Vacuna Bivalente RSVpreF no adyuvada

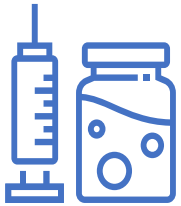
Dos indicaciones:

Protección pasiva frente a la enfermedad del tracto respiratorio inferior causada por el virus respiratorio sincitial (VRS) en los lactantes desde el nacimiento hasta los 6 meses de edad tras la inmunización materna durante el embarazo.

Inmunización activa de personas de 60 años de edad y mayores para la prevención de la enfermedad del tracto respiratorio inferior causada por el VRS

COMPOSICION

- 120 µg sin adyuvante
- La dosis contiene 60 µg de cada antígeno proteico de prefusión, en una inyección de 0,5 ml



PRESENTACION

- Vial monodosis
- Jeringa precargada
- Adaptador de vial
- Packs de 1 y 10

ALMACENAMIENTO

- Refrigeración entre 2°C y 8°C

Abrysvo, INN-respiratory syncytial virus vaccine (bivalent, recombinant) (europa.eu)

RSVpreF Adult Clinical Development Program

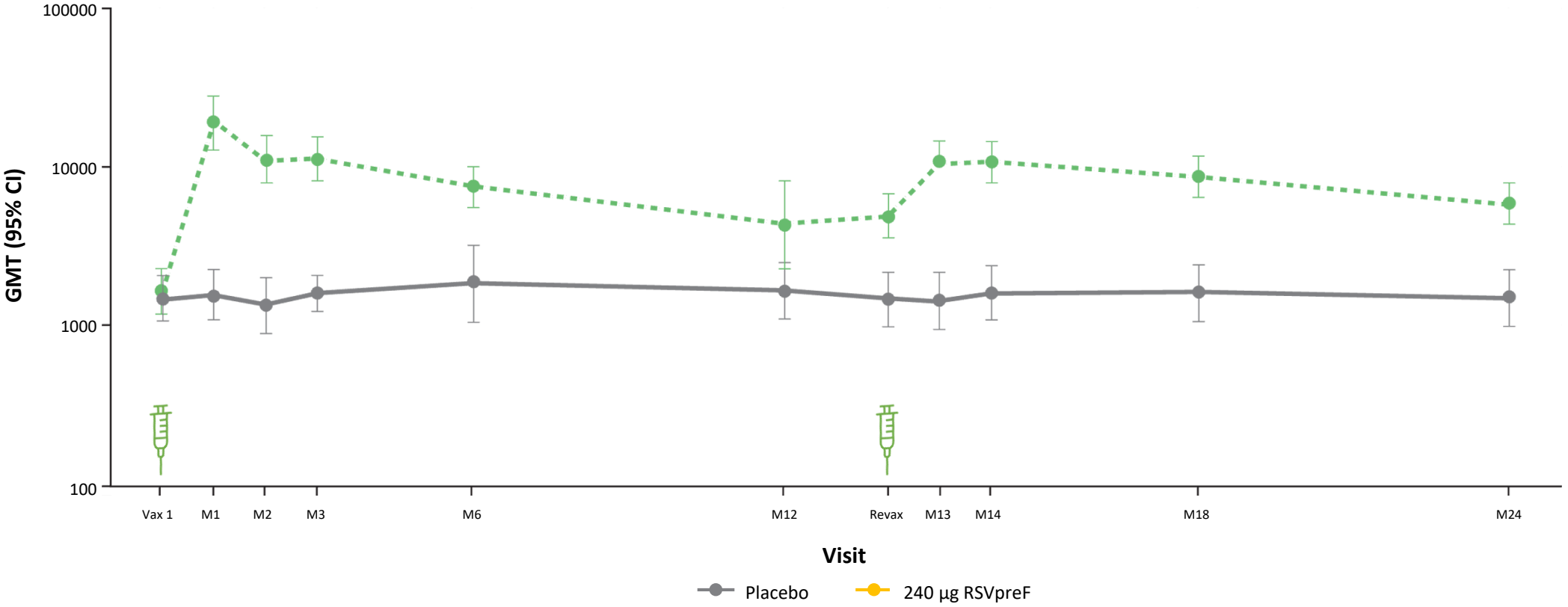
Study	Status	Brief Description	Age Group
C3671001[1] Phase 1/2	Completed	First-in-Human Dose Ranging; +/- $Al(OH)_3$; +/- Influenza Vaccine; Revaccination	18–85 years
C3671002[2] Phase 1/2	Completed	CpG/$Al(OH)_3$ Adjuvant Safety and Immunogenicity	65–85 years
WI257521[3] Phase 2a	Completed	Human Challenge Study	18–50 years
C3671014[4] Phase 3	Completed	Lot Consistency Study	18–49 years
C3671006[5] Phase 3	Completed	Concomitant Influenza Vaccine Study	≥ 65 years
C3671013[6] Phase 3	Ongoing	Pivotal Efficacy	≥ 60 years
C5481001[7] Phase 2	Completed	Combined COVID-19 and RSV Vaccine Study +/- Concomitant Influenza Vaccine	≥ 65 years
C3671023[8] Phase 3	Completed	High-Risk or Immunocompromised Adults	18-60 (high risk) ≥18 (IC)

1. A Study to Describe the Safety and Immunogenicity of a RSV Vaccine in Healthy Adults. NCT03529773; 2. A Study to Evaluate the Safety and Immunogenicity of an Adjuvanted RSV Vaccine in Healthy Older Adults. NCT03572062; 3. Schmoele-Thoma B et al. Vaccine Efficacy in Adults in a Respiratory Syncytial Virus Challenge Study. N Engl J Med 2022; 386:2377-89. 4. Clinical Lot Consistency for RSVpreF in a Population of Healthy Adults 18 to ≤ 49 Years of Age. NCT05096208; 5. Safety and Immunogenicity of RSVpreF Coadministered with SIIV in Adults ≥ 65 Years of Age. NCT05301322; 6. Study to Evaluate the Efficacy, Immunogenicity, and Safety of RSVpreF in Adults (RENOIR). NCT05035212. 7. A Study to Learn About Two or More Vaccines That Are Put Together as One Shot Against Infectious Lung Illnesses, Including COVID-19 and Respiratory Syncytial Virus (RSV); NCT05886777. 8. A Study to Assess the Safety, Tolerability, and Immunogenicity of RSVpreF in Adults at High Risk of Severe RSV Disease (MONET); NCT05842967.`

Revaccination at 1 year yields minimal impact on the sustained immunogenicity achieved with dose 1

Kinetics plot of RSV A neutralizing GMTs

Expanded cohort for revaccination evaluable RSV immunogenicity population study C3671001 (individuals aged 65–85 years)



GMT, geometric mean titer; RSV, respiratory syncytial virus

Gurtman A. VRBPAC Meeting 2022, October 19-23, 2022; Washington, DC [Accessed April 11, 2023]

The RSV Vaccine Efficacy Study iN Older Adults Immunized Against RSV Disease

Renoir

240 Study Sites in 7 Countries

- Argentina
- Canada
- Finland
- Japan
- Netherlands
- South Africa
- U.S.

Enrollment

38,863 participants
Adults **≥60 years**

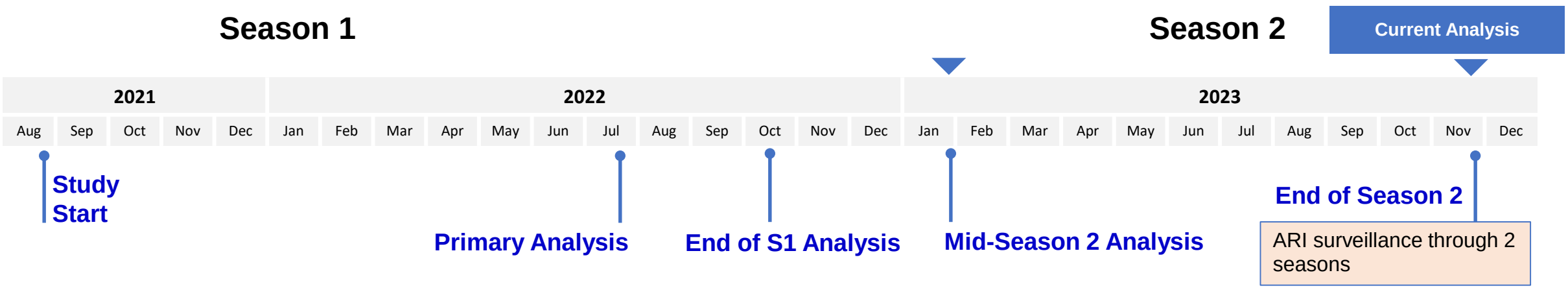
Randomized 1:1 to receive RSVpreF 120 µg or placebo

Stratified by age group
- 60–69, 70-79 & ≥80 years

Key Inclusion/Exclusion Criteria

Healthy or with stable chronic conditions

Immunocompromised persons with serious chronic disorders (e.g., metastatic cancer, end stage renal disease)



11. Gurtman A. RSVpreF older adults clinical development updates. Presentation at ACIP, June 21, 2023. https://www.cdc.gov/vaccines/acip/meetings/slides-2023-06-21-23.html, 3; 2. Walsh EE et al. N Engl J Med 2023;388:1465-1477; 3. Munjal I. A bivalent RSVpreF vaccine to protect against infant illness through immunization of pregnant individuals and older adults via direct immunization. Presentation at World Vaccine Congress, April 1-4, 2024

Phase 3 Study Objectives

Safety	• Describe the safety profile of RSVpreF
	  • Local reactions and systemic events within 7 days post-vaccination
	  • AEs through 1-month post-vaccination
	  • SAEs and NDCMCs throughout study

Primary Efficacy	• Prevention of RSV-LRTD in the 1st RSV season
	  • VE of 1st episode RSV-LRTD involving ≥ 2 signs/symptoms in 1st RSV season
	  • VE of 1st episode RSV-LRTD involving ≥ 3 signs/symptoms in 1st RSV season

Key Secondary Efficacy	• Prevention of RSV-LRTD (VE Endpoints) measured through second season

AE, adverse event; ARI, acute respiratory illness; LRTD, lower respiratory tract disease; NDCMC, newly diagnosed chronic medical condition; RSV, respiratory syncytial virus; SAE, serious adverse event; VE, vaccine efficacy

Walsh EE, et al. *N Engl J Med* 2023;388:1465-77.

Key Study Definitions[1,2]

Weekly active surveillance for ARI symptoms
Symptoms trigger nasal swab and possibly a visit

Acute respiratory illness (ARI) **≥1** of these symptoms (**new or worsened from baseline**), lasting >1 day	**Nasal discharge**	**Nasal congestion**	**Sore throat**	**Cough**	**Sputum production**	**Wheezing**	**Shortness of breath**	
Lower respiratory tract illness (LRTI) **ARI with ≥2 or ≥3 lower respiratory tract** signs or symptoms (new or worsened)				**Cough**	**Sputum production**	**Wheezing**	**Shortness of breath**	**Tachypnea**
Severe LRTI **LRTI criteria plus at least 1 of the following**	**Hospitalization** due to LRTI			New / increased **oxygen supplementation**			New / increased **mechanical ventilation** (including CPAP)	

Positive validated RT-PCR
in central laboratory

RSV-ARI	RSV-LRTI	Severe RSV-LRTI

CPAP, continuous positive airway pressure; RT-PCR, real-time polymerase chain reaction

1. Gurtman A. Safety and efficacy of bivalent RSV prefusion F vaccine in adults ≥60 years of age. Presentation at ACIP, October 22, 2022; 2. Walsh EE et al. N Engl J Med 2023;388:1465-1477

Demographic Characteristics and Prior Conditions

	RSVpreF (N=18,574); n (%)	Placebo (N=18,288); n (%)
Sex		
Male	9460 (50.9)	9183 (50.2)
Race[1]		
White	14844 (79.9)	14625 (80.0)
Black or African American	2193 (11.8)	2161 (11.8)
Asian	1354 (7.3)	1334 (7.3)
Ethnicity		
Hispanic/Latino	7722 (41.6)	7475 (40.9)
Age at Vaccination		
60–69 Years	11619 (62.6)	11470 (62.7)
70–79 Years	5928 (31.9)	5822 (31.8)
≥80 Years	1026 (5.5)	996 (5.4)

	RSVpreF (N=18,574); n (%)	Placebo (N=18,288); n (%)
Any Prespecified Significant Condition	9709 (52.3)	9562 (52.3)
Heart Disease	2494 (13.4)	2462 (13.5)
Lung Disease	2180 (11.7)	2262 (12.4)
With ≥1 Chronic Cardiopulmonary Condition	2917 (15.7)	2954 (16.2)
Asthma	1671 (9.0)	1639 (9.0)
Chronic Obstructive Pulmonary Disease (COPD)	1172 (6.3)	1242 (6.8)
Congestive Heart Failure (CHF)	368 (2.0)	364 (2.0)
Diabetes	3500 (18.8)	3500 (19.1)
Liver Disease	391 (2.1)	394 (2.2)
Renal Disease	578 (3.1)	522 (2.9)
Current Tobacco Use	2885 (15.5)	2737 (15.0)

Safety Population
1. Race was recorded as unknown in 0.2% in each group; race was not reported in 0.3% of each group.
2. One participant enrolled at age <60 years; because this participant received vaccine, the participant is included in the safety reporting.

Safety Evaluation Continued Through the End of Season 2

From vaccination through end of season 2

	RSVpreF (N=18,574)		Placebo (N=18,288)	
	n (%)	95% CI	n (%)	95% CI
NDCMC	1267 (6.8)	6.5, 7.2	1208 (6.6)	6.2, 7.0
SAE	1149 (6.2)	5.8, 6.5	1107 (6.1)	5.7, 6.4
Related SAE	3 (<0.1)	0.0, 0.1	0	0.0, 0.0
AE leading to withdrawal	20 (0.1)	0.1, 0.2	17 (<0.1)	0.1, 0.1
AE leading to death	160 (0.9)	0.7, 1.0	157 (0.9)	0.7, 1.0

Neurological AEs through end of Season 2 (n=9)

RSVPreF	Investigator causality	Days since vaccination
Chronic inflammatory demyelinating polyneuropathy	Related	8
Miller Fisher syndrome	Related	9
Guillain-Barré syndrome	Not related	92
Guillain-Barré syndrome	Not related	250
Peripheral sensory neuropathy	Not related	312

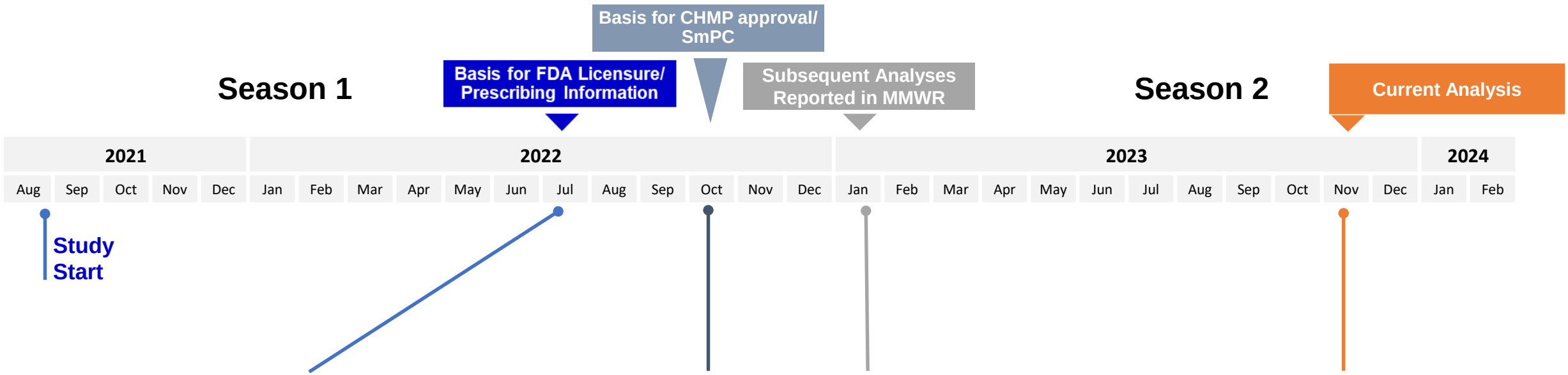
Placebo	Investigator causality	Days since vaccination
Polyneuropathy	Not related	241
Axonal neuropathy	Not related	289
Peripheral sensorimotor neuropathy	Not related	341
Guillain-Barré syndrome	Not related	324

AE, adverse event; CI, confidence interval; NDCMC, newly diagnosed chronic medical condition; preF, prefusion F; RSV, respiratory syncytial virus; SAE, serious adverse event

1. Munjal I. A bivalent RSVpreF vaccine to protect against infant illness through immunization of pregnant individuals and older adults via direct immunization. Presentation at World Vaccine Congress, April 1-4, 2024

RSVpreF Vaccine Efficacy: Timeline

Renoir



Primary Analysis

Vaccine Efficacy against RSV-LRTD with at least **3** signs or symptoms

85.7% (32–98.7)[1]

Vaccine Efficacy against RSV-LRTD with at least **2** signs or symptoms

66.7% (28.8–85.8)[1]

Season 1 Analysis

Vaccine Efficacy against RSV-LRTD with at least **3** signs or symptoms

88.9% (53.6–98.7)[2]

Vaccine Efficacy against RSV-LRTD with at least **2** signs or symptoms

65.1% (35.9-82)[2]

Mid-Season 2 Analysis

Vaccine Efficacy against RSV-LRTD with at least **3** signs or symptoms

78.6% (23.2–96.1)[3]

Vaccine Efficacy against RSV-LRTD with at least **2** signs or symptoms

48.9% (13.7-70.5)

Season 2 Analysis

Vaccine Efficacy against RSV-LRTD with at least **3** signs or symptoms

77.8% (51.4–91.1)[4]

Vaccine Efficacy against RSV-LRTD with at least **2** signs or symptoms

55.7% (34.7–70.4)[4]

1. Pfizer Inc. ABRYSVO USPI, labeling.pfizer.com/ShowLabeling.aspx?id=19589 (accessed 6/26/23). 2. ABRYSVO SmPC https://www.ema.europa.eu/en/medicines/human/EPAR/abrysvo#product-info (accessed 6/10/2024).

3. Walsh EE, et al. *N Engl J Med* 2023;388:1465-77. 4. Melgar M et al. *MMWR Weekly* / July 21, 2023 / 72(29);793–801. Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023 | MMWR (cdc.gov). 45 Pfizer, Inc. Pfizer Announces Positive Top-Line Data for Full Season Two Efficacy of ABRYSVO® for RSV in Older Adults. Press release. February 29, 2024. Accessed February 29, 2024. https://www.pfizer.com/news/press-release/press-release-detail/pfizer-announces-positive-top-line-data-full-season-two

Efficacy of One Dose-Pfizer RSV Vaccine in Adults ≥ 60 Years

Renoir

Efficacy Evaluation Period	Vaccine Efficacy	
	RSV-associated LRTD ≥3 signs/symptoms	RSV-associated LRTD ≥2 signs/symptoms
Season 1*	**88.9** (53.6–98.7)	**65.1** (35.9-82.0)
Season 2**	**77.8** (51.4–91.1)	**55.7** (34.7-70.4)

Cumulative Efficacy RSV-LRTD ≥3 signs/symptoms over 2 Seasons: 81.5% (63.3–91.6)

Efficacy across both seasons after **16.4 months** of disease surveillance

Pfizer, Inc. Pfizer Announces Positive Top-Line Data for Full Season Two Efficacy of ABRYSVO® for RSV in Older Adults. Press release. February 29, 2024. Accessed February 29, 2024. https://www.pfizer.com/news/press-release/press-release-detail/pfizer-announces-positive-top-line-data-full-season-two

*One complete RSV Season for both Hemispheres (Aug 2021-Oct 2022).

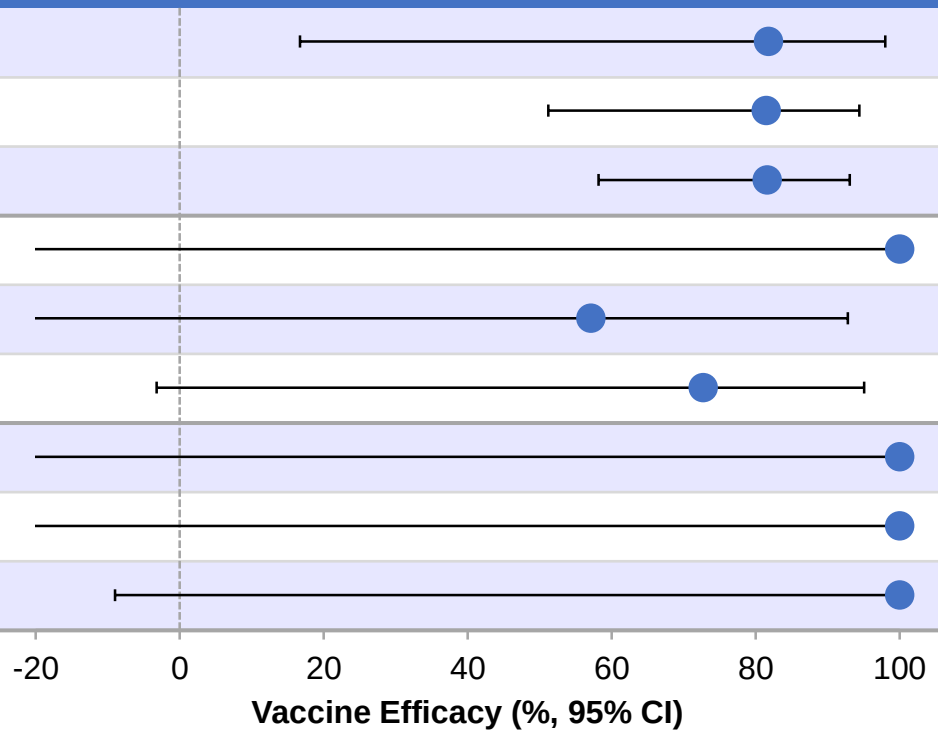
**Second complete RSV Season for both hemispheres (July 2022-Nov 2023).

Abbreviation: LRTD: lower respiratory tract disease

Primary endpoint:
RSV-LRTI with ≥3 symptoms

Consistent Efficacy was Observed Across **Age Groups**

RSV-LRTI with ≥ 3 Symptoms		Number of Events		Vaccine Efficacy (95% CI)
		RSVpreF	Placebo	
60–69 Years	Season 1	2	11	**81.8%** (16.7, 98.0)
	Season 2	5	27	**81.5%** (51.2, 94.4)
	Across 2 Seasons	7	38	**81.6%** (58.2, 93.1)
70–79 Years	Season 1	0	4	**100%** (-51.5, 100)
	Season 2	3	7	**57.1%** (-87.7, 92.8)
	Across 2 Seasons	3	11	**72.7%** (-3.2, 95.1)
≥80 Years	Season 1	0	3	**100%** (-142, 100)
	Season 2	0	2	**100%** (-432.5, 100)
	Across 2 Seasons	0	5	**100%** (-9.1, 100)

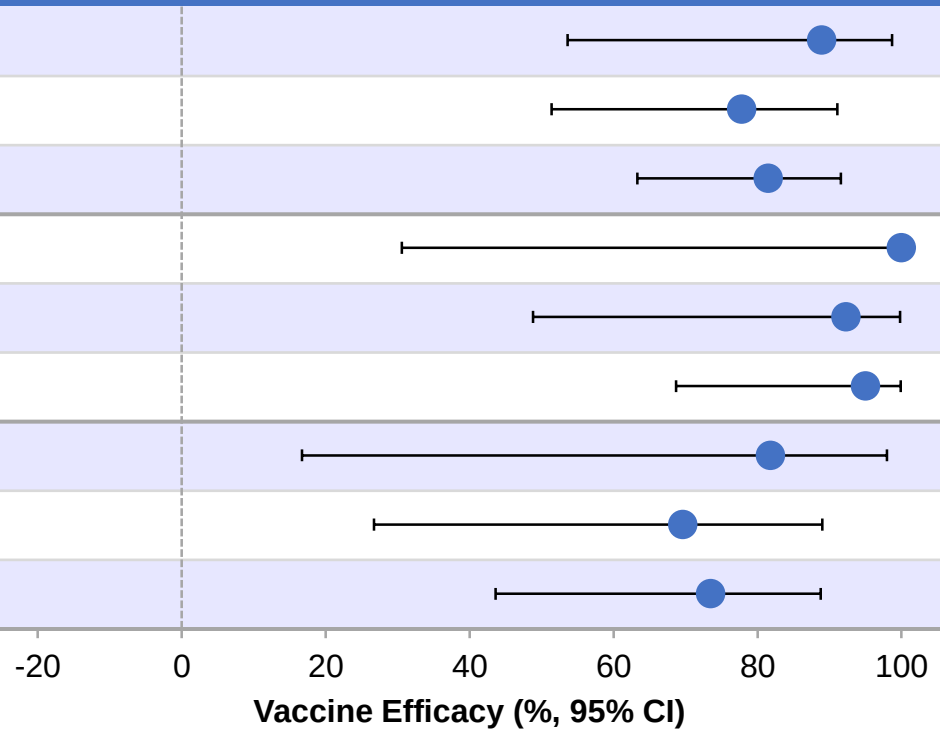


1. Munjal I. A bivalent RSVpreF vaccine to protect against infant illness through immunization of pregnant individuals and older adults via direct immunization. Presentation at World Vaccine Congress, April 1-4, 2024

Primary endpoint:
RSV-LRTI with ≥3 symptoms

Consistent Efficacy was Observed Across Subgroups with **Prespecified High Risk Conditions**

RSV-LRTI with ≥ 3 Symptoms		Number of Events		Vaccine Efficacy (95% CI)
		RSVpreF	Placebo	
Overall	**Season 1**	2	18	**88.9%** (53.6, 98.7)
	Season 2	8	36	**77.8%** (51.4, 91.1)
	Across 2 Seasons	10	54	**81.5%** (63.3, 91.6)
Without High Risk Conditions	**Season 1**	0	7	**100%** (30.6, 100)
	Season 2	1	13	**92.3%** (48.8, 99.8)
	Across 2 Seasons	1	20	**95.0%** (68.7, 99.9)
With ≥ 1 High Risk Condition	**Season 1**	2	11	**81.8%** (16.7, 98.0)
	Season 2	7	23	**69.6%** (26.7, 89.0)
	Across 2 Seasons	9	34	**73.5%** (43.6, 88.8)



Prespecified High Risk Condition: Heart Disease, Lung Disease, Diabetes, Liver Disease, Renal Disease, Current Tobacco Use

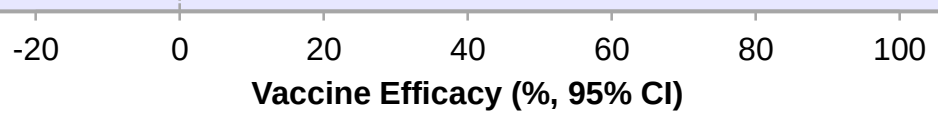
1. Munjal I. A bivalent RSVpreF vaccine to protect against infant illness through immunization of pregnant individuals and older adults via direct immunization. Presentation at World Vaccine Congress, April 1-4, 2024

Renoir

Primary endpoint:
RSV-LRTI with ≥3 symptoms

Consistent Efficacy was Observed Across RSV **Subgroup A and B**

RSV-LRTI with ≥ 3 Symptoms		Number of Events		Vaccine Efficacy (95% CI)
		RSVpreF	Placebo	
Overall	**Season 1**	2	18	**88.9%** (53.6, 98.7)
	Season 2	8	36	**77.8%** (51.4, 91.1)
	Across 2 Seasons	10	54	**81.5%** (63.3, 91.6)
RSV-A	**Season 1**	1	5	**80.0%** (-78.7, 99.6)
	Season 2	5	26	**80.8%** (49.1, 94.2)
	Across 2 Seasons	6	31	**80.6%** (52.9, 93.4)
RSV-B	**Season 1**	1	12	**91.7%** (43.7, 99.8)
	Season 2	2	10	**80.0%** (6.1, 97.9)
	Across 2 Seasons	3	22	**86.4%** (54.6, 97.4)



1. 95% CI; 2. One S1 case and one S2 case (both in the placebo group) and one S2 case in RSVpreF group were based on local testing without RSV subgroup. One S2 case in placebo group had both A and B subgroups.
LRTD = lower respiratory tract disease; RSV, respiratory syncytial virus; VE, vaccine efficacy.

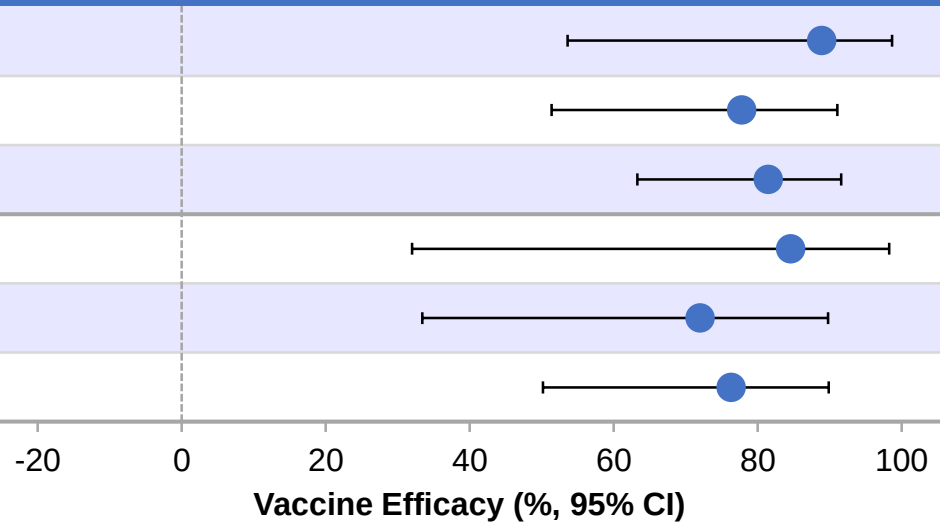
Renoir

1. Munjal I. A bivalent RSVpreF vaccine to protect against infant illness through immunization of pregnant individuals and older adults via direct immunization. Presentation at World Vaccine Congress, April 1-4, 2024

Primary endpoint:
RSV-LRTI with ≥3 symptoms

Vaccine Efficacy Observed in **Medically Attended Visits** Similar to Overall Vaccine Efficacy

RSV-LRTI with ≥ 3 Symptoms		Number of Events		Vaccine Efficacy (95% CI)
		RSVpreF	Placebo	
Overall	**Season 1**	2	18	**88.9%** (53.6, 98.7)
	Season 2	8	36	**77.8%** (51.4, 91.1)
	Across 2 Seasons	10	54	**81.5%** (63.3, 91.6)
Medically Attended	**Season 1**	2	13	**84.6%** (32.0, 98.3)
	Season 2	7	25	**72.0%** (33.4, 89.8)
	Across 2 Seasons	9	38	**76.3%** (50.2, 89.9)



1. Munjal I. A bivalent RSVpreF vaccine to protect against infant illness through immunization of pregnant individuals and older adults via direct immunization. Presentation at World Vaccine Congress, April 1-4, 2024

Pfizer Announces Positive Top-Line Data for Full Season Two Efficacy of ABRYSVO® for RSV in Older Adults

ABRYSVO, a bivalent vaccine, maintained consistently high protective efficacy for both RSV A and RSV B disease through two seasons after a single dose.

ABRYSVO efficacy was 77.8% against RSV lower respiratory tract disease with three or more symptoms in a second full RSV season in adults 60 years of age or older.

February 29, 2024 08:00 AM Eastern Standard Time

NEW YORK--(BUSINESS WIRE)--Pfizer Inc. (NYSE: PFE) today announced top-line ABRYSVO vaccine efficacy and safety data for respiratory syncytial virus (RSV) in adults 60 years of age and older following a second season in the Northern and Southern Hemispheres from the ongoing pivotal Phase 3 clinical trial (NCT05035212) RENOIR (RSV vaccine Efficacy study iN Older adults Immunized against RSV disease). Vaccine efficacy against RSV-associated lower respiratory tract disease (LRTD), defined by three or more symptoms, after disease surveillance in season two was 77.8% (95.0% CI: 51.4, 91.1); vaccine efficacy following season one was 88.9% (95.0% CI: 53.6%, 98.7%) , which demonstrates durable efficacy after two seasons.

Conclusiones

RSVpreF (Abrysvo®)

Demostró un perfil de **seguridad** general **favorable**

Siguió siendo **eficaz** en la prevención de la ETRI asociada al VRS
hasta el final de la temporada 1 y en la **temporada 2**

Se puede **coadministrar** con la vacuna frente a la influenza de **alta carga** y **adyuvada**

High Risk
Substudy A

MONeT: Inclusion Criteria and Objectives

A Study to Assess the Safety, Tolerability, and Immunogenicity of RSVpreF in Adults at High Risk of Severe RSV Disease (Study C3671023)

Inclusion Criteria	• Adults with stable chronic pulmonary (including asthma), cardiovascular (excluding isolated hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus) • Residents of nursing homes and other long-term care facilities
Primary Safety Outcome	• Local reactions and systemic events within 7 days after each vaccination • AEs and SAEs through 6 months • Newly diagnosed chronic medical conditions

Immunogenicity Outcome	**Primary – Neutralizing titers (NT) measured as:**
	• Geometric Mean Titer ratio
	  • Estimated by the ratio of the GMT for RSV A and RSV B serum NTs in MONET to that in RENOIR
	• Difference in Seroreponse (≥4-fold rise from baseline) Rate
	  • Measured by difference in rate of RSV A and RSV B serum NTs at 1 month after vaccination between MONET and RENOIR
	Secondary – Neutralizing titers measured as:
	• GMT for RSV A and RSV B in study population at day 1 and 1 month after vaccination
	• GMFR of NTs for RSV A and RSV B at day 1 and 1 month after vaccination

Study Details | A Study to Assess the Safety, Tolerability, and Immunogenicity of RSVpreF in Adults at High Risk of Severe RSV Disease | ClinicalTrials.gov

Adapted from clincialtrial.gov For Reactive Use Only. AE=adverse event; SAE=serious adverse event; GMT=geometric mean titer; GMFR=geometric mean fold rise.

Safety in Adults 18–59 Years Has Been Demonstrated in 7 Clinical Studies

Licensure in 18–59 Years of Age Will Be Based on Satisfactory Safety and Immunogenicity Compared to RSVPreF in Adults ≥ 60 Years

Totality of Safety Data to Support Licensure in Adults ≥18 to 59 Years	
1	**Study 1001 (n=98):** Phase 1/2 Dose Ranging
2	**Human Challenge (n=35):** Safety and Efficacy of 120µg without Adjuvant
3	**Study 1014 (n=745):** Lot Consistency
4	**Study 1004 (n=282):** Non-pregnant Concomitant Tdap
5	**Study 1003 (n=115):** Pregnant Women, Safety, Early Efficacy
6	**Study 1008 (n=3689):** Pregnant Women, Safety, Pivotal Efficacy
7	**Study 1023 (n=453):** (MONeT) Immunogenicity & Safety

Monet

>5,400 Adults Aged 18-59 Years of Age

Presented at ACIP meeting. 26 Junio 2024. Available at ACIP June 26-28, 2024 Presentation Slides | Immunization Practices | CDC

Demographics Between Vaccine and Placebo Recipients

	RSVPreF 120 µg (N = 453); n (%)	Placebo (N = 225); n (%)	Total (N = 678); n (%)
Sex			
Male	193 (42.6)	73 (32.4)	266 (39.2)
Female	260 (57.4)	152 (67.6)	412 (60.8)
Race			
White	312 (68.9)	152 (67.6)	464 (68.4)
Black or African American	106 (23.4)	57 (25.3)	163 (24.0)
Asian	24 (5.3)	9 (4.0)	33 (4.9)
Ethnicity			
Hispanic/Latino	102 (22.5)	48 (21.3)	150 (22.1)
Non-Hispanic/non-Latino	348 (76.8)	175 (77.8)	523 (77.1)
Age at Vaccination			
18-49 Years	**240 (53.0)**	**113 (50.2)**	**353 (52.1)**
50-59 Years	**213 (47.0)**	**112 (49.8)**	**325 (47.9)**
Mean (SD)	46.8 (9.9)	46.4 (10.5)	46.7 (10.1)

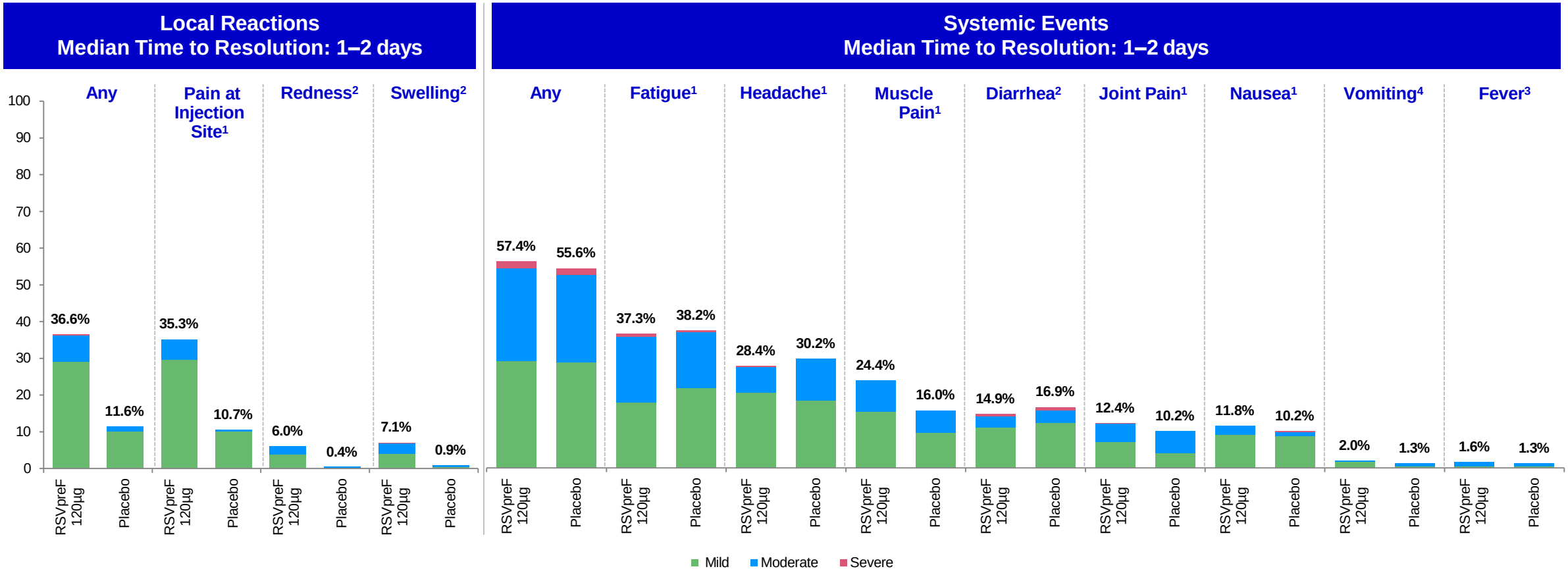
	RSVPreF 120 µg (N = 453); n (%)	Placebo (N = 225); n (%)	Total (N = 678); n (%)
With At Least 1 Prespecified Medical Condition*	**453 (100.0)**	**223 (99.1)**	**676 (99.7)**
Chronic Pulmonary Conditions	**239 (52.8)**	**116 (51.6)**	**355 (52.4)**
COPD	25 (5.5)	11 (4.9)	36 (5.3)
Asthma	198 (43.7)	88 (39.1)	286 (42.2)
Cardiovascular Conditions	**38 (8.4)**	**16 (7.1)**	**54 (8.0)**
CHF	9 (2.0)	3 (1.3)	12 (1.8)
CAD	19 (4.2)	4 (1.8)	23 (3.4)
Diabetes	**189 (41.7)**	**101 (44.9)**	**290 (42.8)**
Other	**139 (30.7)**	**68 (30.2)**	**207 (30.5)**
Liver Disease	20 (4.4)	13 (5.8)	33 (4.9)
Renal Disease	17 (3.8)	4 (1.8)	21 (3.1)
Neurologic Disease	16 (3.5)	1 (0.4)	17 (2.5)
Tobacco Use			
Current Tobacco Use	78 (17.2)	39 (17.3)	117 (17.3)

* Participants with multiple comorbidities are represented more than once

1. Clinicaltrials.gov NCT05842967 2. Pfizer Data on File

Presented at ACIP meeting. 26 Junio 2024. Available at ACIP June 26-28, 2024 Presentation Slides | Immunization Practices | CDC

Solicited Local/Systemic Reactions & Systemic Events Were Mild to Moderate and Resolved Quickly in Participants 18–59 Years



1. Severity definition: mild = no interference with daily activity; moderate = some interference with daily activity; severe = prevents daily activity
2. Severity definition: mild = >2-5 cm, moderate = >5-10 cm; severe = >10 cm

RSVPreF N = 451; placebo N = 225

1. Severity definition: mild = no interference with daily activity; moderate = some interference with daily activity; severe = prevents daily activity
2. Severity definition: mild = 2-3 loose stools in 24h; moderate = 4-5 loose stools in 24h; severe = 6 or more loose stools in 24h
3. Severity definition: mild 38.0°C-38.4 °C; moderate >38.4°C-38.9 °C; severe >38.9°C-40.0 °C; grade 4 >40.0 °C
4. Severity definition: mild = 1-2 time(s) in 24h; moderate = >2 times in 24h; severe = requires intravenous hydration

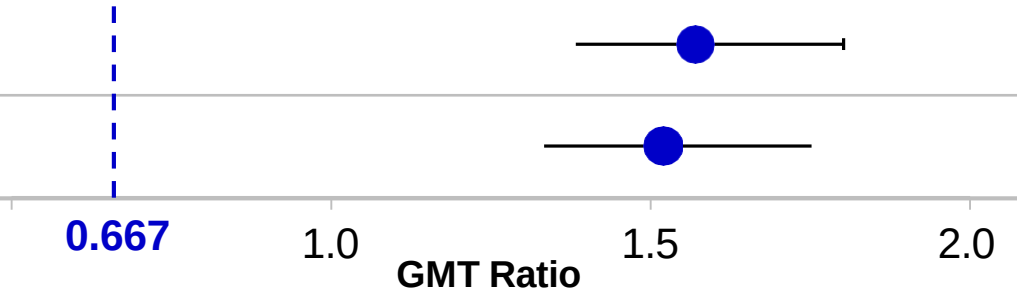
RSVPreF N = 451: Placebo N = 225

1. Clinicaltrials.gov NCT05842967 2. Pfizer Data on File

Presented at ACIP meeting. 26 Junio 2024. Available at ACIP June 26-28, 2024 Presentation Slides | Immunization Practices | CDC

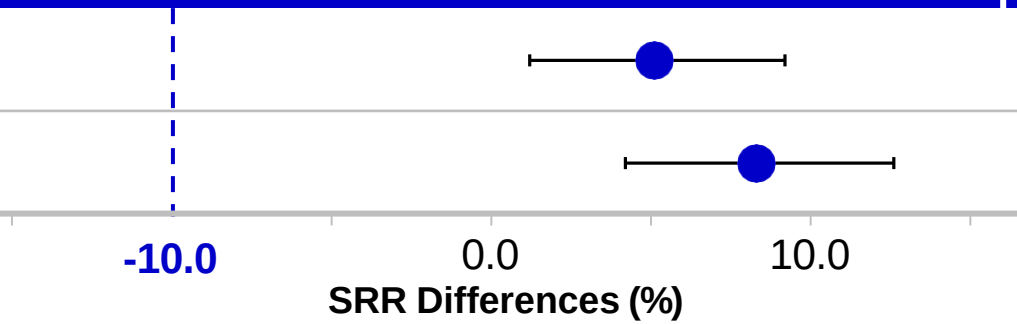
Non-Inferiority Met for All Four Co-Primary Endpoints

GMR RSV A & B (Comparison: 18–59y High Risk to ≥60y)	**GMR** (95% CI)
Model Adjusted* GMR RSV-A	1.57 (1.396, 1.759)
Model Adjusted* GMR RSV-B	1.52 (1.333, 1.725)



Both Primary Endpoints Met Non-inferiority (CI LB >0.667)

Seroresponse Rate RSV A & B (Comparison: 18–59y High Risk to ≥60y)	**SRR Difference*** (95% CI)
SRR Difference RSV-A	5.1 (1.2, 9.2)
SRR Difference RSV-B	8.3 (4.2,12.6)



Both Primary Endpoints Met Non-inferiority (CI LB > -10%)

Abbreviations: GMR = geometric mean ratio; SRR=seroresponse rate
*Analysis of covariance model used as per protocol with sex and baseline titer (in logarithm scale) adjusted

1. Clinicaltrials.gov NCT05842967 2. Pfizer Data on File

Press Release Issued on 9 April: MONeT Study in Adults 18-59 at high risk for RSV Disease

Pfizer Press release | Vaccines | Vaccines

Pfizer Announces Positive Top-Line Results from Phase 3 Study of ABRYSVO® in Adults Aged 18 to 59 at Increased Risk for RSV Disease

Tuesday, April 09, 2024 - 06:45am

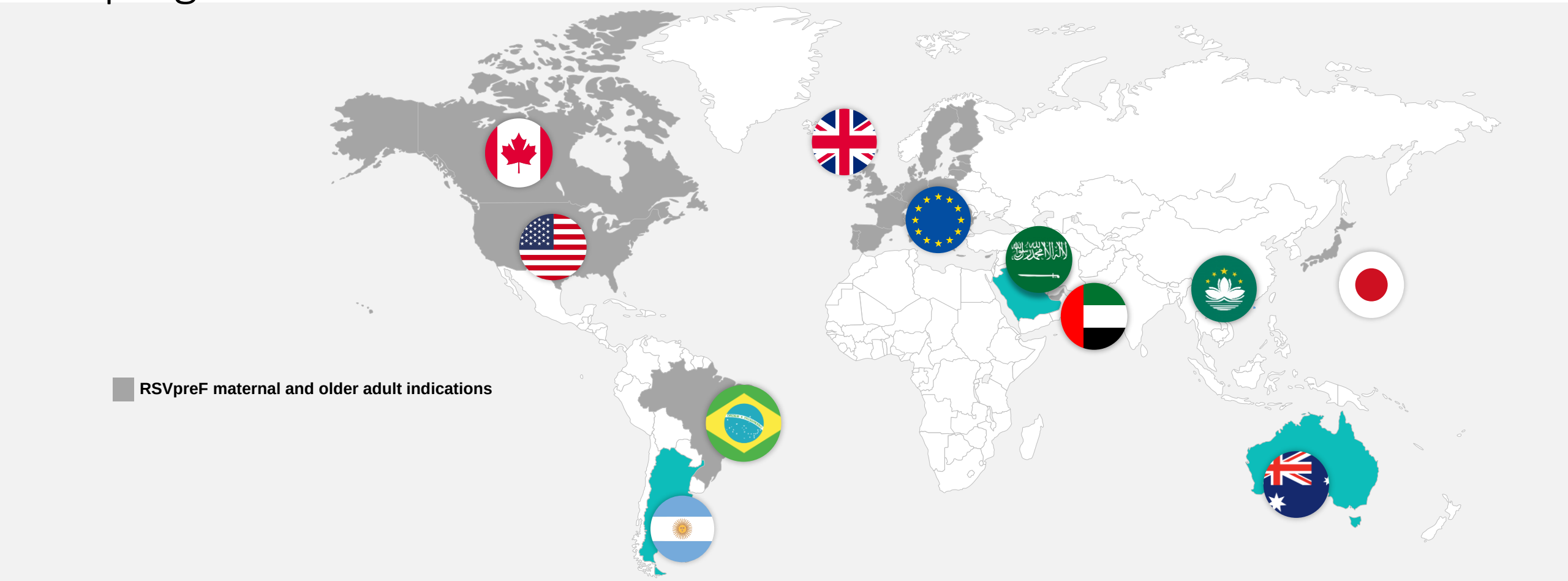
- *ABRYSVO met its trial primary endpoints in adults aged 18 to 59 with an increased respiratory syncytial virus (RSV) disease risk. The vaccine was well-tolerated and demonstrated an immune response non-inferior to adults aged 60 years and older*
- *Pfizer intends to submit these findings to regulatory agencies to seek approval of ABRYSVO in adults 18 to 59 years of age*

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced positive top-line immunogenicity and safety data from the ongoing pivotal Phase 3 clinical trial (NCT05842967) **MONeT** (RSV I**M**munizati**ON** Study for Adul**T**s at Higher Risk of Severe Illness),evaluating a single dose of ABRYSVO versus placebo in adults 18 to 59 years of age at risk of developing severe respiratory syncytial virus (RSV)-associated lower respiratory tract disease (LRTD).

- The study evaluated the safety, tolerability, and immunogenicity of ABRYSVO compared to placebo in adults 18-59 years of age at increased risk for severe RSV disease.
- All co-primary endpoints were met (non-inferiority criteria achieved)
- No safety concerns identified

Pfizer Announces Positive Top-Line Results from Phase 3 Study of ABRYSVO® in Adults Aged 18 to 59 at Increased Risk for RSV Disease | Pfizer. Accessed July 3rd, 2024

RSVpreF vaccine has been licensed globally for use in 2 populations: older adults, and infants via immunization of pregnant individuals*

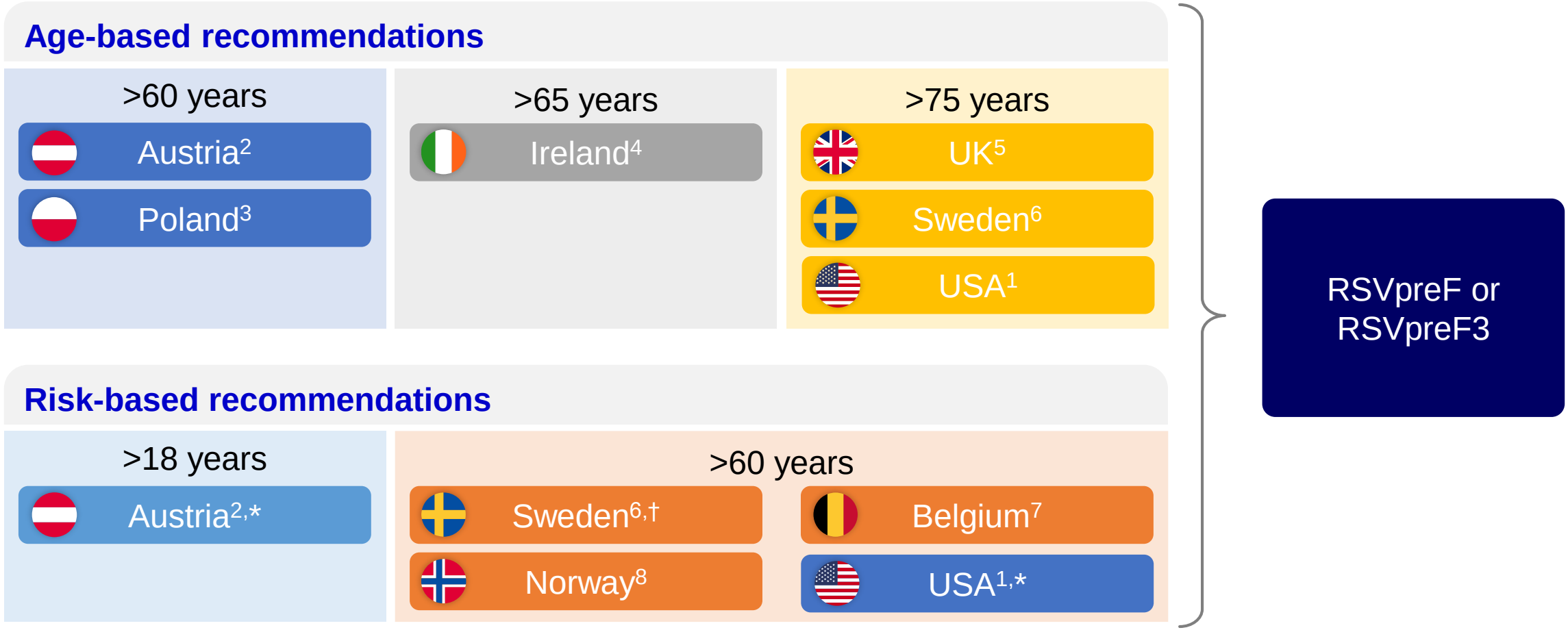


*As of April 2024

preF, prefusion F; RSV, respiratory syncytial virus

Maternal and older adult indications: USA: ABRYSVO (Respiratory Syncytial Virus Vaccine) Prescribing Information; EU: ABRYSVO Summary of Product Characteristics; Canada: ABRYSVO Product Monograph; UK: Abrysvo powder and solvent for solution for injection. Summary of Product Characteristics; Argentina: ANMAT autorizó la vacuna para personas gestantes contra el virus sincicial respiratorio; Japan Recombinant RS virus vaccine (pmda.go.jp); Macau: 澳門特區藥品 | 澳門特別行政區政府 藥物監督管理局 (isaf.gov.mo); Australia: Australian Product Information - ABRYSVO® (Recombinant Respiratory Syncytial Virus {Prefusion F Protein) Vaccine; Brazil: Anvisa registra vacina para prevenção de bronquiolite em bebês - Agência Nacional de Vigilância Sanitária; Saudi Arabia: Drugs List | Saudi Food and Drug Authority (sfda.gov.sa); United Arab Emirates: Registered Medical Product Directory | Services | Ministry of... (mohap.gov.ae). All URLs accessed April 2024

National RSV vaccination recommendations **for older adults**



*; 60-74 years + risk factors

preF, prefusion F; RSV, respiratory syncytial virus

1. ACIP June 26-28, 2024 Presentation Slides | Immunization Practices | CDC; 2. Impfplan Österreich 3. Vaccination schedule for the elderly - Szczepienia.Info (pzh.gov.pl); 4. Recommendations for passive immunisation and vaccination against respiratory syncytial in infants, children and older adults 5. Introduction of new NHS vaccination programmes against respiratory syncytial virus (RSV) - GOV.UK (www.gov.uk) 6. Vaccination mot RS-virus 7. Vaccination against RSV (adults) 8. RSV-vaksine - veileder for helsepersonell All URLs accessed July 3rd, 2024

Professional medical societies recognize RSV as a vaccine-preventable disease in vulnerable populations*

Older adults

Neumo Experts Prevention (NEP) Group[1] Position Paper

- *"… RSV vaccines should be part of the adult immunization program, and **an age-based strategy should be preferred over targeting high-risk groups**"*
- NEP recommends vaccination for adults aged **≥60 years**, especially those with chronic pulmonary disease, chronic cardiovascular disease, extreme obesity, neurologic impairment, kidney disease, diabetes, immunosuppression, or institutionalized status

Global Initiative for Chronic Obstructive Lung Disease (GOLD)[2] 2024 Report

- *The US CDC Advisory Committee on Immunization Practices (ACIP) and the European Commission recommend use of the available RSV vaccines for individuals aged **≥60 years***
- RSV vaccine added to recommended routine vaccination schedule list for individuals with stable COPD

German associations[3,†]

- *Vulnerable groups should be offered RSV vaccination in addition to influenza, COVID-19, and pneumococcal vaccination when appropriate*

RSV vaccine is recommended for:

- Adults aged **≥60 years**
- Adults of **any age** with severe pulmonary or cardiovascular pre-existing conditions
- Adults of **any age** with significant immune compromise

American Diabetes Association 2024 Standards of Care in Diabetes[4]

- *RSV vaccines are highly recommended for older adults aged >60 years with diabetes*

Italian Board of Scientific Societies for the Vaccination Calendar for Life[5]

- Recommended vaccination against RSV to all adults aged >75 years, due to the high risk of comorbidities or underlying conditions, and to those aged 60–75 years in high-risk groups

*As of April 2024; †Include DGP (Deutsche Gesellschaft für Pneumologie), DGI (Deutsche Gesellschaft für Infektiologie e.V.), DGIM (Deutsche Gesellschaft für Innere Medizin), DGHO (Deutsche Gesellschaft für Hämatologie und Medizinische Onkologie), DGG (Deutsche Gesellschaft für Geriatrie), PEG (Paul-Ehrlich-Gesellschaft für Infektionstherapie), CAPNETZ (Community Acquired Pneumonia Competence Network), DZL (Deutsches Zentrum für Lungenforschung), DZIF (Deutsches Zentrum für Infektionsforschung), Deutsche Atemwegsliga, and Deutsche Lungenstiftung

COPD, chronic obstructive pulmonary disease; RSV, respiratory syncytial virus

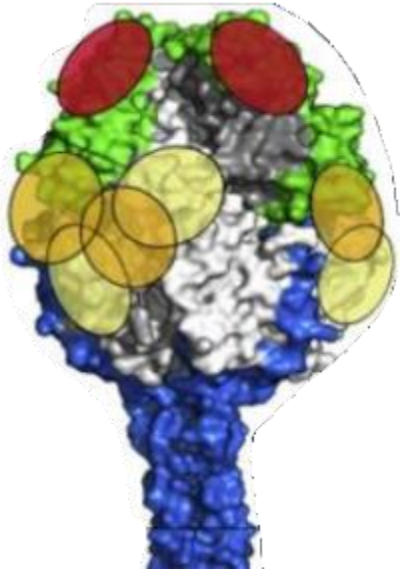
1. Redondo E et al. Arch Bronconeumol 2024;60:161-170; 2. 2024 GOLD Report [Accessed April 2024]; 3. Addo M et al. Infection 2024;52:285-288; 4. American Diabetes Association Professional Practice Committee. Diabetes Care 2024:47;S52-S76; 5. Raccomandazioni del Board del Calendario per la Vita sulla vaccinazione contro Virus Respiratorio Sinciziale (VRS o RSV) nella popolazione anziana e negli adulti a rischio [Accessed April 2024]

El virus respiratorio sincitial (VRS) y la vacuna RSVPreF3 OA de GSK para adultos mayores

Arexvy

AREXVY, la vacuna de GSK para adultos mayores frente al VRS

La combinación del antígeno RSVPreF3 (120 µg) y el adyuvante AS01E está específicamente diseñada para inducir robustas respuestas celulares y humorales para proteger a los adultos mayores y con comorbilidades



El antígeno RSVPreF3 está diseñado para mantener preferentemente la conformación prefusión e inducir anticuerpos neutralizantes para potenciar la inhibición de la replicación viral[1,2]

El sistema adyuvante AS01E potencia la respuesta immune celular y restablece los niveles de linfocitos T CD4+ específicos frente a RSVPreF3 en adultos mayores[2]

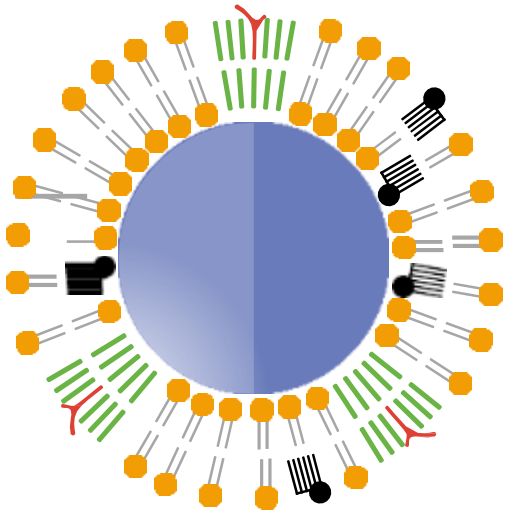


Image of F protein reproduced from Graham BS *et al. Curr Opin Immunol* 2015;35:30–38, Copyright 2015, with permission from Elsevier.

1. Graham BS *et al. Curr Opin Immunol* 2015;35:30–38; 2. Leroux-Roels I, et al. J Infect Dis. 2022:jiac327.

Descripción general del desarrollo clínico

Fase I/II

Estudio RSV OA=ADJ-002[1]

Adultos jóvenes y adultos mayores, de 18-40 años o de 60-80 años

Primer ensayo clínico en el ser humano

Seguridad, inmunogenicidad, formulación y selección de la dosis

Estudio RSV OA=ADJ-003[2]

Adultos japoneses de 60-80 años

Seguridad, reactogenicidad e inmunogenicidad

Fase IIb

Estudio RSV OA=ADJ-011[3]

(ampliación del estudio 002)

Adultos ≥60 años

Persistencia, seguridad e inmunogenicidad de una dosis de recuerdo

Estudio RSV OA=ADJ-023[4]

Adultos inmunodeprimidos ≥50 años (receptores de trasplante de pulmón y de riñón)

Seguridad e inmunogenicidad

Fase III

Estudio AReSVi-006[5]

Adultos ≥60 años

Estudio de eficacia fundamental

Estudio AReSVi-004[6]

Adultos ≥60 años

Seguridad, reactogenicidad, inmunogenicidad, persistencia y revacunación

Estudio RSV OA=ADJ-009[7]

Adultos ≥60 años

Consistencia entre lotes

Estudio RSV OA=ADJ-018[8]

Adultos 50-59 años frente a ≥60 años

Seguridad, reactogenicidad e inmunogenicidad

Estudio RSV OA=ADJ-007[9]

Adultos ≥60 años

Seguridad, reactogenicidad e inmunogenicidad cuando se coadministra junto con FLU-QIV

Estudio RSV OA=ADJ-008[10]

Adultos ≥65 años

Seguridad, reactogenicidad e inmunogenicidad cuando se coadministra junto con FLU-QIV-HD

Estudio RSV OA=ADJ-017[11]

Adultos ≥65 años

Seguridad, reactogenicidad e inmunogenicidad cuando se coadministra junto con FLU-aQIV

Estudio RSV OA=ADJ-019[12]

Adultos mayores ≥60 años

Seguridad, reactogenicidad, inmunogenicidad cuando se coadministra con PCV20

Estudio RSV OA=ADJ-020[13]

Adultos ≥50 años

Seguridad, reactogenicidad, inmunogenicidad cuando se coadministra con la vacuna HZ/su en adultos

- Completado
- En curso

Estudios epidemiológicos

Estudio Epi RSV OA 022

Estudio Epi RSV OA 029

FLU-aQIV: vacuna tetravalente adyuvada frente a la gripe; FLU-QIV: vacuna tetravalente frente a la gripe; FLU-QIV-HD: vacuna tetravalente de dosis alta frente a la gripe; HZ/su, subunidad recombinante del herpes zóster; PCV20, vacuna antineumocócica conjugada 20-valente

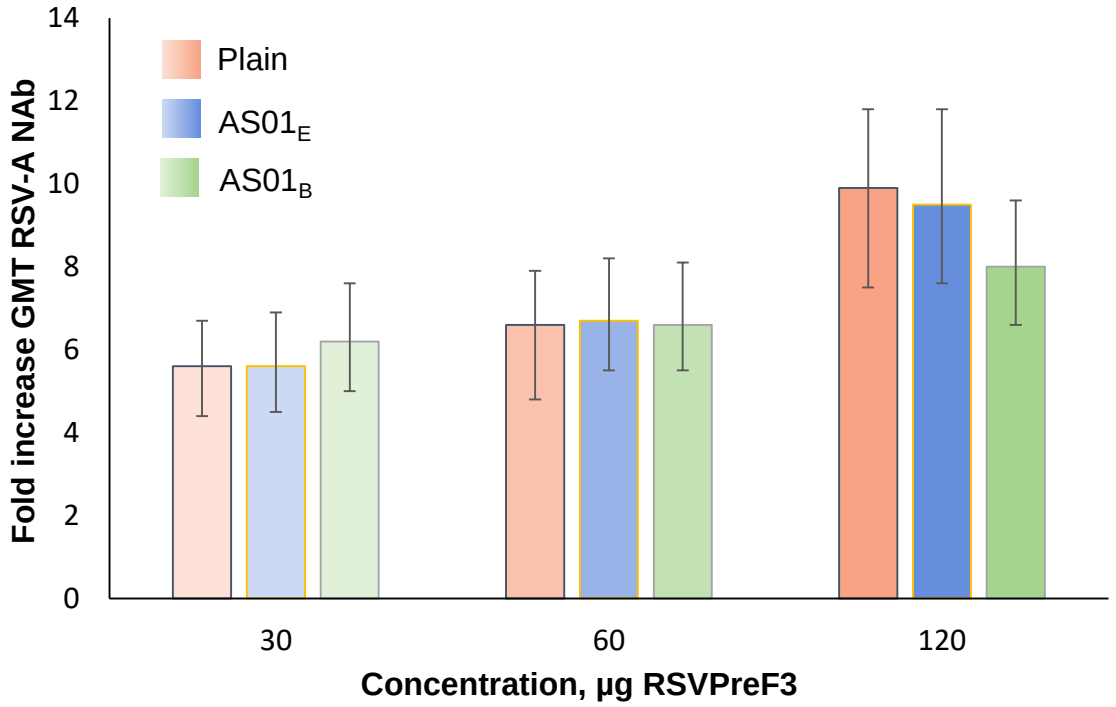
1. ClinicalTrials.gov, 2023. NCT03814590. https://www.clinicaltrials.gov/study/NCT03814590; 2. ClinicalTrials.gov, 2023. NCT04090658. https://www.clinicaltrials.gov/study/NCT04090658; 3. ClinicalTrials.gov, 2023. NCT04657198. https://www.clinicaltrials.gov/study/NCT04657198; 4. ClinicalTrials.gov, 2023. NCT05921903. https://www.clinicaltrials.gov/study/NCT05921903; 5. ClinicalTrials.gov, 2023. NCT04886596. https://www.clinicaltrials.gov/study/NCT04886596; 6. ClinicalTrials.gov, 2023. NCT04732871. https://www.clinicaltrials.gov/study/NCT04732871 ; 7. ClinicalTrials.gov, 2023. NCT05059301. https://www.clinicaltrials.gov/study/NCT05059301 ; 8. ClinicalTrials.gov, 2023. NCT05590403. https://www.clinicaltrials.gov/study/NCT05590403 ; 9. ClinicalTrials.gov, 2023. NCT04841577. https://www.clinicaltrials.gov/study/NCT04841577 ; 10. ClinicalTrials.gov, 2023. NCT05559476. https://www.clinicaltrials.gov/study/NCT05559476 ; 11. ClinicalTrials.gov, 2023. NCT05568797. https://www.clinicaltrials.gov/study/NCT05568797 ; 12. ClinicalTrials.gov, 2023. NCT05879107. https://www.clinicaltrials.gov/study/NCT05879107 ; 13. ClinicalTrials.gov, 2023. NCT05966090. https://www.clinicaltrials.gov/study/NCT05966090 . Todas las URLs consultadas en septiembre de 2023.

Inmunogenicidad después de 1 dosis de una vacuna con RSVPreF3 (estudio fase II)

Las formulaciones de la vacuna RSVPreF3 inducen una respuesta humoral y celular robusta

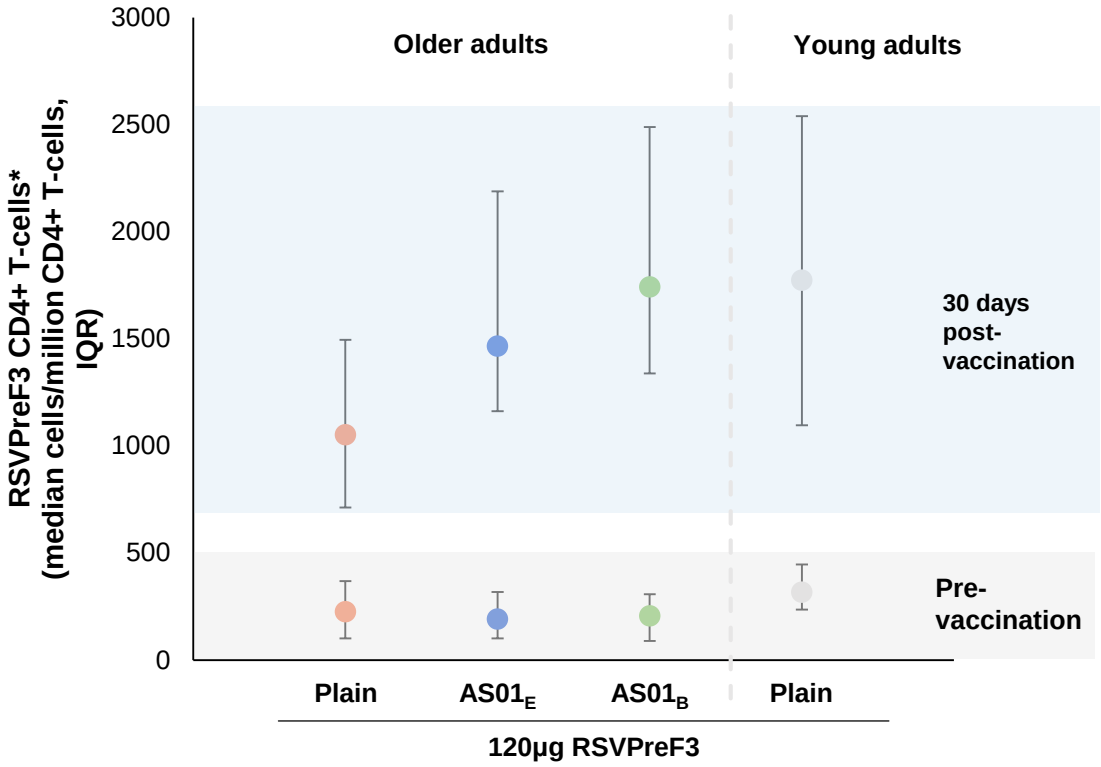
Respuesta de anticuerpos

Aumento de casi 10 veces los títulos de anticuerpos neutralizantes específicos frente al VRS-A (RSV-A NAb) con la formulación de RSVPreF3 120 µg 30 días después de la vacunación vs. prevacunación[1]



Respuesta de linfocitos T

El adyuvante AS01E potenció la respuesta T CD4+ específica frente a RSVPreF3 en adultos mayores a niveles similares al de los adultos jóvenes[2]



Los gráficos se han creado de forma independiente para GSK a partir de los datos originales

* Con expresión de al menos dos marcadores entre IL-2, CD40L, TNFα e IFNγ

AS01: sistema adyuvante 01; CD: cúmulo de diferenciación; GMT: media geométrica de los títulos; IFN: interferón; IL: interleucina; IQR: rango intercuartílico; NAb: anticuerpos neutralizantes; TNF: factor de necrosis tumoral

1. Leroux-Roels I et al. J Infect Dis. 2023;227:761–772; 2. Study Results, ClinicalTrials.gov, 2020. NCT03814590. https://clinicaltrials.gov/ct2/show/NCT03814590 (consultado en septiembre de 2023)

Seguridad y reactogenicidad después de una dosis

La vacuna fue bien tolerada; no se identificaron problemas de seguridad después de evaluar distintas formulaciones [1]

Las diferentes formulaciones de la vacuna RSVPreF3[1]

- No se reportaron AAs graves o mortales
- La frecuencia de AAs, AAGs y pIMDs fue similar entre los distintos grupos
- No se relacionó ningun AA con ninguna formulación de la vacuna

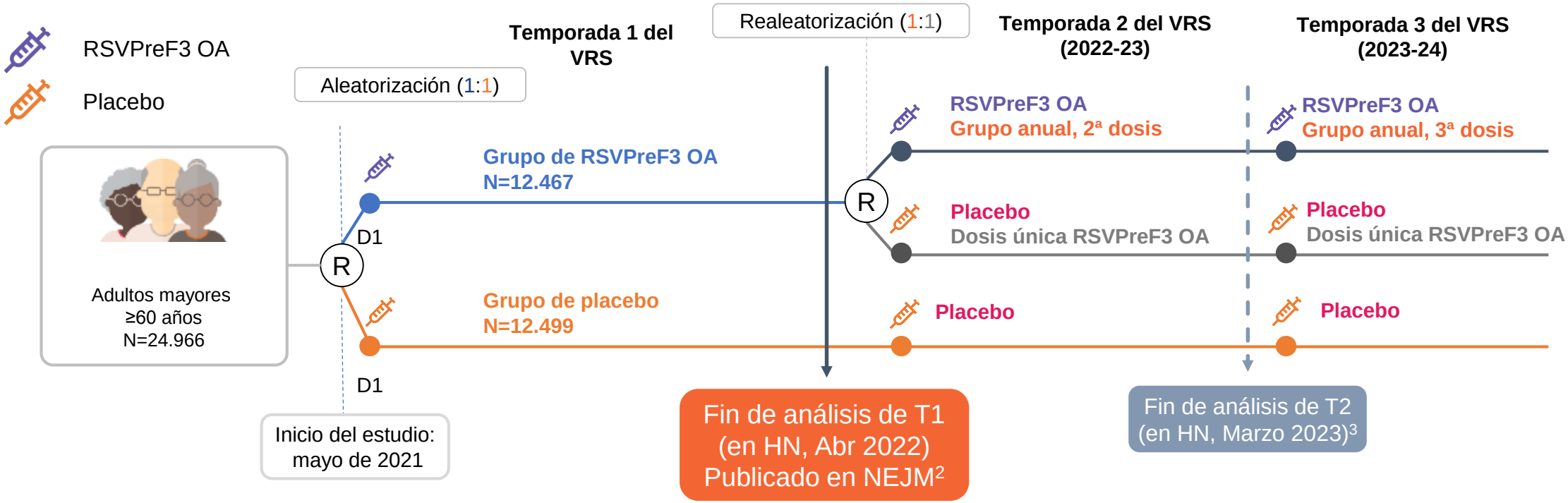
- Los AA notificados con mayor frecuencia fueron los siguientes:[1]
  - Dolor en el lugar de la inyección
  - Cansancio
  - Cefalea
- Las tasas de AA fueron superiores en los adultos mayores tras recibir las formulaciones $AS01_B$ adyuvadas en comparación con otras formulaciones[1]

Los resultados fueron consistentes con el perfil de seguridad clínico establecido para las vacunas adyuvadas[2]

* Resultados de seguridad/reactogenicidad hasta 1 mes después de la dosis 1. AA: acontecimiento adverso; AS01: sistema de adyuvantes 01; OA: adultos mayores; AAG: acontecimiento adverso grave. 1. Tica J *et al Open Forum Infect Dis* 2020;7:S187–188, https://doi.org/10.1093/ofid/ofaa439.429 (accessed May 2022); 2. Leroux-Roels G *et al. Clin Immunol* 2016;169:16–27

Diseño del estudio de fase III AReSVi-006[1–3]

Estudio de eficacia aleatorizado, controlado con placebo, observador ciego, multinacional



Objetivo primario: Demostrar la eficacia de una dosis de la vacuna RSVPreF3 OA para la prevención de la enfermedad del tracto respiratorio inferior (ETRI*) por VRS en adultos ≥60 años durante una temporada de VRS

Todos los casos de ETRI por VRS fueron confirmados por un comité externo independiente.

Figura adaptada con permiso de Ison MG *et al.* A respiratory syncytial virus (RSV) prefusion F protein candidate vaccine (RSVPreF3 OA) is efficacious in adults ≥60 years of age (YOA). Presentado en IDWeek, 19–23 de octubre de 2022, Washington, DC, EE.UU.
*confirmado por RT-PCR; †ETRI definido como ≥2 síntomas/signos respiratorios del tracto inferior durante ≥24 horas, incluyendo ≥1 signo respiratorio del tracto inferior O ≥3 síntomas respiratorios del tracto inferior durante ≥24 horas.
D, día; ETRI, enfermedad del tracto respiratorio inferior; HN, hemisferio norte; RT-PCR, reacción en cadena de la polimerasa con transcriptasa reversa; T, temporada
1. ClinicalTrials.gov, 2022. NCT04886596. https://clinicaltrials.gov/ct2/show/NCT04886596; 2. Papi A *et al. N Engl J Med* 2023;388(7):595–608; 3. GSK 2023. GSK's RSVPreF3 OA Vaccine (AREXVY). Presentado en ACIP, 21 de junio de 2023 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Adults-Friedland-508.pdf URLs consultadas en julio de 2023

Las características demográficas estuvieron equilibradas entre los diferentes grupos del estudio[1]

RSVPreF3 OA (N=12,467)		Characteristics	Placebo (N=12,499)	
69,5 años		**Edad media**	69,6 años	
n	**%**	**Grupo de edad**	**%**	**n**
12.467	100,0%	≥60 años	100,0%	12.499
6.963	55,9%	60-69 años	55,8%	6.980
4.487	36,0%	70-79 años	35,9%	4.491
1.017	8,2%	≥80 años	8,2%	1.028
n	**%**	**Sexo**	**%**	**n**
6.488	52,0%	Mujer	51,4%	6.427
5.979	48,0%	Hombre	48,6%	6.072
n	**%**	**Raza**	**%**	**n**
9.887	79,3%	Blanco	79,5%	9.932
1.064	8,5%	Negro o afroamericano	8,8%	1.101
953	7,6%	Asiático	7,6%	956
563	4,5%	Otra*	4,1%	510
n	**%**	**Estado de fragilidad †**	**%**	**n**
189	1,5%	Frágil	1,4%	177
4.793	38,4%	Prefrágil	38,3%	4.781
n	**%**	**Comorbilidad de interés Ω**	**%**	**n**
4.937	39,6%	≥1 comorbilidad de interés preexistente	38,9%	4.864
2.496	20,0%	≥1 enfermedad cardiorrespiratoria	19,4%	2.422
3.200	25,7%	≥1 enfermedad endocrina metabólica	25,9%	3.236
2.504	20.1%	≥2 comorbilidades de interés preexistentes	19.5%	2.434
805	6.5%	≥3 comorbilidades de interés preexistentes	6.6%	827

Alrededor del 39% de los participantes de cada grupo tenían ≥1 comorbilidad preexistente de interés asociada con un mayor riesgo de enfermedad grave por VRS Ω

La figura se creó de forma independiente para GSK a partir de los datos originales.
*Incluye nativos americanos, nativos de Alaska, nativos de Hawai y otros isleños del Pacífico; †evaluado por una prueba de velocidad de marcha; ΩEPOC, asma, cualquier enfermedad respiratoria/pulmonar crónica, diabetes tipo 1 o tipo 2, insuficiencia cardíaca crónica, enfermedad hepática o renal avanzada. EPOC, enfermedad pulmonar obstructiva crónica; 1. Papi A *et al. N Engl J Med* 2023;388(7):595–608; 2. Feldman RG *et al. Clin Infect Dis* 2023:ciad471. doi: 10.1093/cid/ciad471 Epub ahead of print.

Definiciones de casos de AReSVi-006[1,2]

IRA
≥2 síntomas o signos respiratorios
O
≥1 síntoma o signo respiratorio y 1 síntoma o signo sistémico durante al menos 24 horas

Síntomas o signos sistémicos

- Fiebre/febrícula
- Cansancio
- Dolores corporales
- Jaqueca
- Disminución del apetito

Síntomas o signos respiratorios

Síntomas o signos de las vías respiratorias superiores

- Congestión nasal
- Dolor de garganta

Síntomas respiratorios de las vías inferiores

- Esputo
- Tos
- Disnea

Signos respiratorios de las vías inferiores

- Sibilancia
- Crepitacioness/roncus
- Taquipnea
- Hipoxemia
- Suplemento de O_2

ETRI*
≥2 síntomas o signos de las vías respiratorias inferiores (≥1 signo)
O
≥3 síntomas respiratorios de las vías inferiores durante al menos 24 horas

Síntomas respiratorios de las vías inferiores

- Esputo
- Tos
- Disnea

Signos respiratorios de las vías inferiores

- Sibilancia
- Crepitacioness/roncus
- Taquipnea
- Hipoxemia
- Suplemento de O_2

ETRI* grave
≥2 signos respiratorios de las vías inferiores
O
episodio que impide las actividades normales y cotidianas

Signos respiratorios de las vías inferiores

- Sibilancia
- Crepitacioness/roncus
- Taquipnea
- Hipoxemia
- Suplemento de O_2

Figura reproducida de GSK, 2023. Presentación en la reunión del ACIP, 21 de junio de 2023
*Definición de casos del USPI
IRA, infección respiratoria aguda; ETRI, enfermedad del tracto respiratorio inferior; USPI, información de prescripción de EE. UU.
1. GSK 2023. GSK's RSVPreF3 OA Vaccine (AREXVY). Presentado en ACIP, 21 de junio de 2023 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Adults-Friedland-508.pdf Consultado en julio de 2023; 2. Papi A *et al. N Engl J Med* 2023;388(7):595–608.

Una sola dosis de la vacuna RSVPreF3 OA es eficaz para prevenir la ETRI-VRS durante la primera temporada de VRS

AReSVi-006 Temporada 1

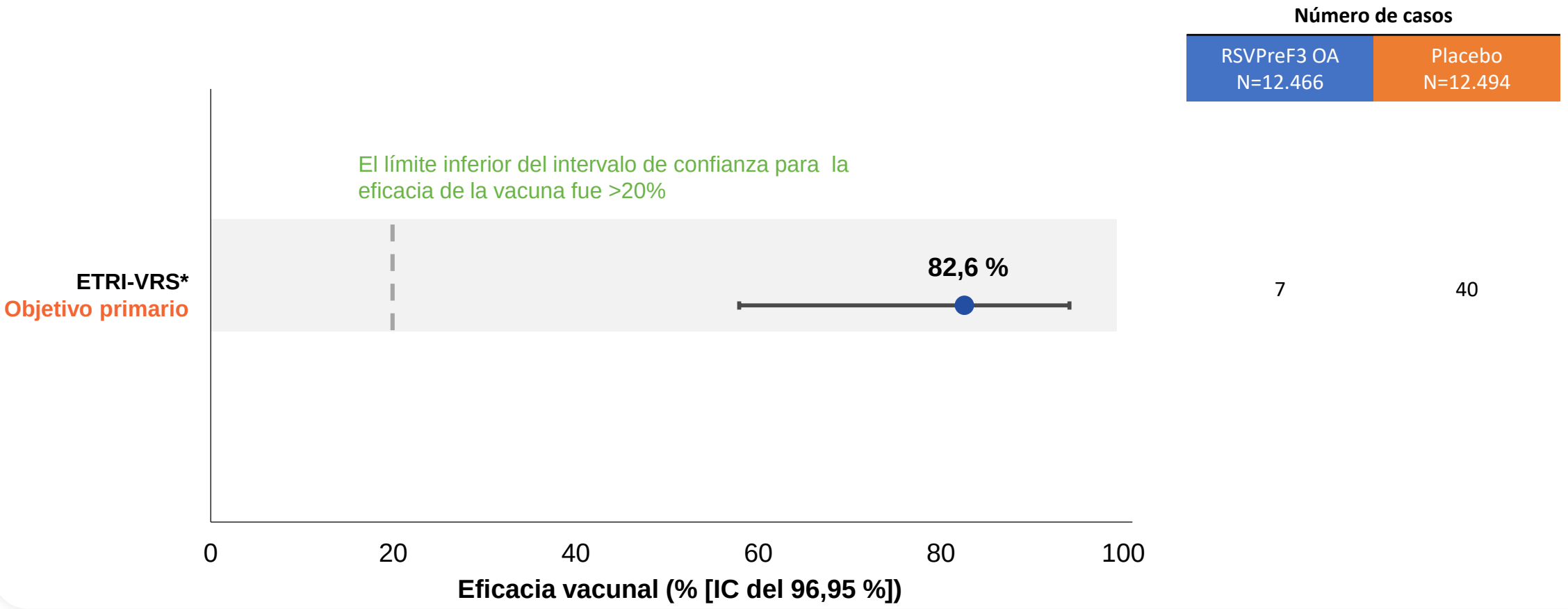


Figura adaptada con permiso de Ison MG *et al*. Una vacuna candidata de proteína F prefusión frente al virus respiratorio sincitial (VRS) (RSVPreF3 OA) es eficaz en adultos ≥60 años. Presentada en IDWeek, 19-23 de octubre de 2022, Washington, D. C., EE. UU.

* La ETRI se definió como ≥2 síntomas/signos del tracto respiratorio inferior durante ≥24 horas, incluidos ≥1 signo del tracto respiratorio inferior O ≥3 síntomas del tracto respiratorio inferior durante ≥24 horas; todos los casos de VRS se confirmaron mediante RT-PCR

IC: intervalo de confianza; LI: límite inferior; ETRI: enfermedad del tracto respiratorio inferior; RT-PCR: reacción de polimerasa en cadena con transcriptasa inversa

Papi A *et al. N Engl J Med* 2023;388(7):595–608

Eficacia alta y consistente en los distintos estadíos de la enfermedad asociada al VRS

AReSVi-006 Temporada 1

Temporada 1

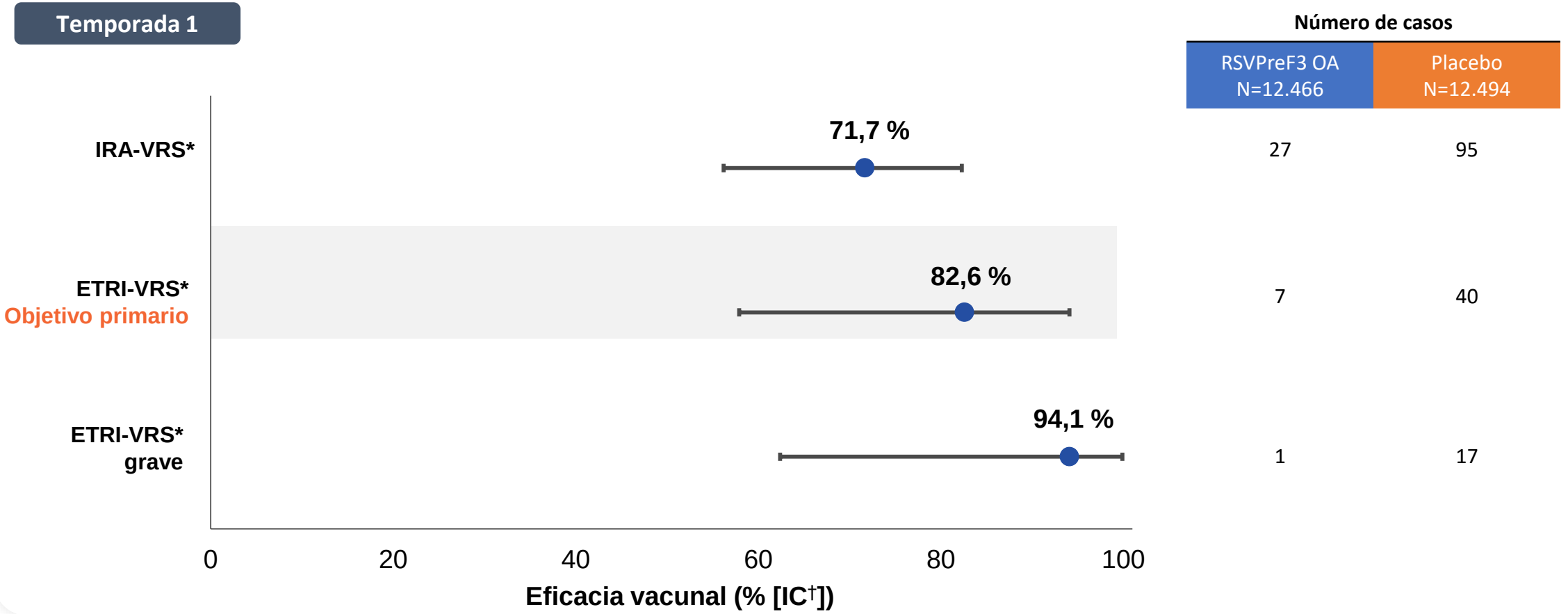


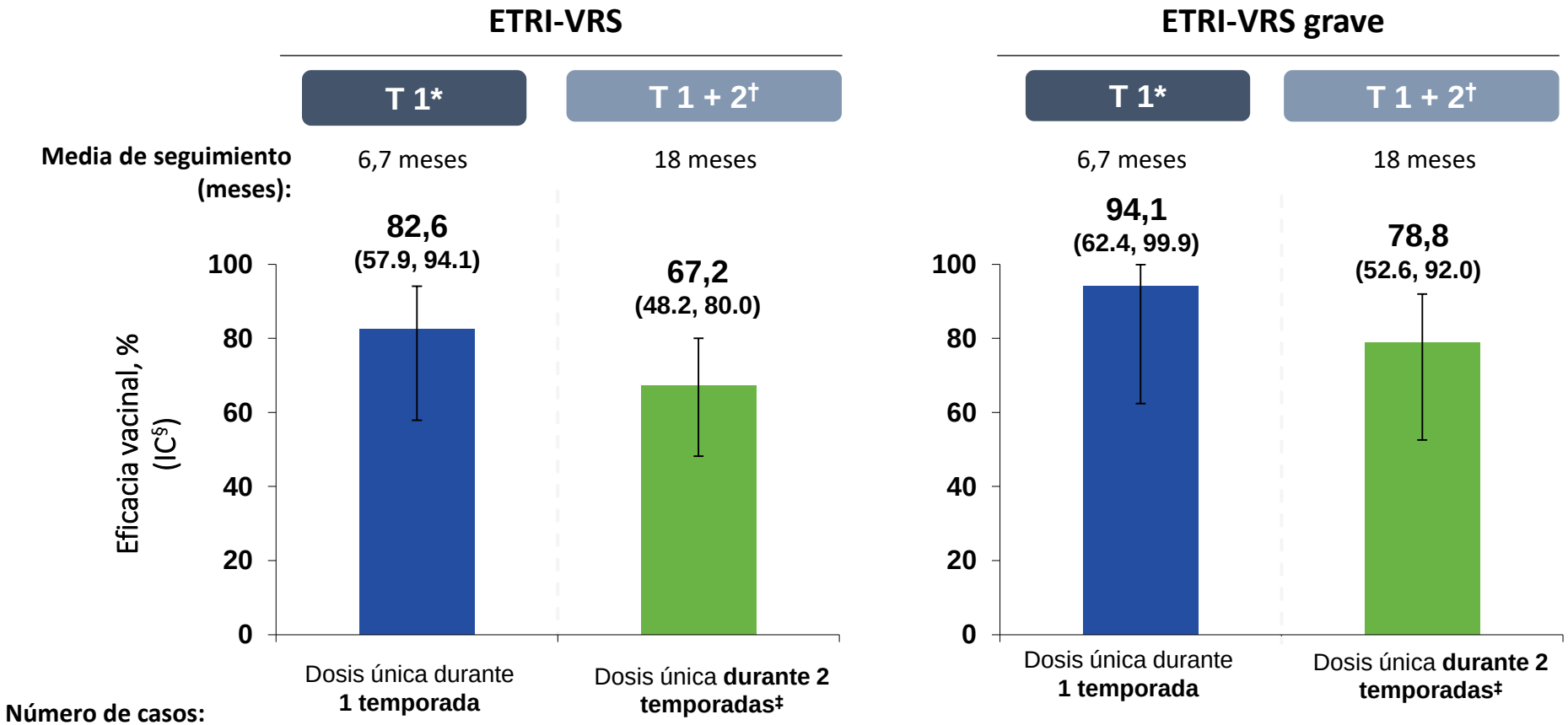
Figura adaptada con permiso de Ison MG *et al*. Una vacuna candidata de proteína F prefusión frente al virus respiratorio sincitial (VRS) (RSVPreF3 OA) es eficaz en adultos ≥60 años. Presentada en IDWeek, 19-23 de octubre de 2022, Washington, D. C., EE. UU.

* La IRA se definió como ≥2 síntomas/signos del tracto respiratorio durante ≥24 horas o ≥1 síntoma/signo del tracto respiratorio + 1 síntoma/signo sistémico durante ≥24 horas. La ETRI se definió como ≥2 síntomas/signos del tracto respiratorio inferior durante ≥24 horas, incluidos ≥1 signo del tracto respiratorio inferior o ≥3 síntomas del tracto respiratorio inferior durante ≥24 horas. La ETRI grave se definió como ETRI con ≥2 signos del tracto respiratorio inferior o un episodio de ETRI considerado grave por el investigador. Todos los casos de VRS se confirmaron mediante RT-PCR; †IC del 96,95 % para el criterio principal de valoración, del 95 % para todos los criterios secundarios de valoración

IRA: infección respiratoria aguda; IC: intervalo de confianza; ETRI: enfermedad del tracto respiratorio inferior; RT-PCR: reacción de polimerasa en cadena con transcriptasa inversa

Papi A et al. N Engl J Med 2023;388(7):595–608

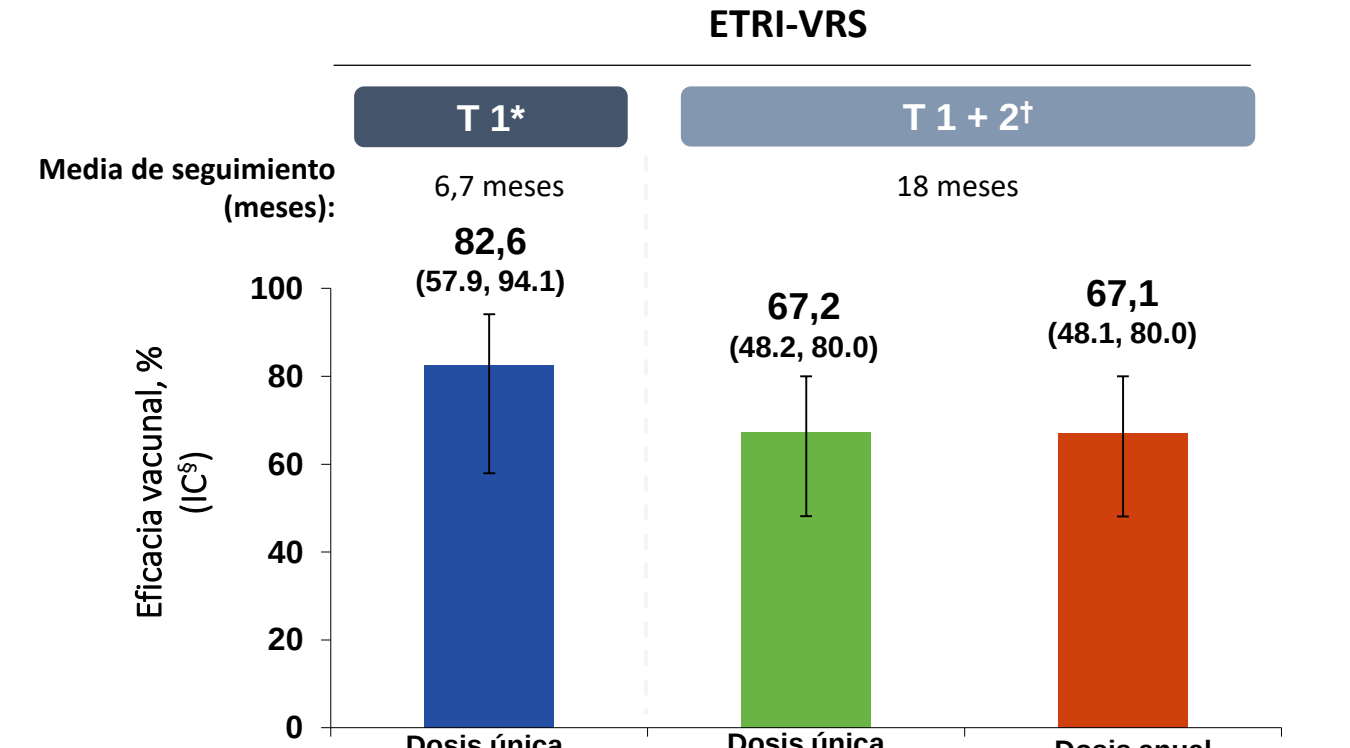
Una dosis de Arexvy confiere una eficacia duradera frente a la ETRI-VRS y la ETRI-VRS grave durante **al menos dos temporadas**[1]



Número de casos:	ETRI-VRS: T 1* (6,7 meses)	ETRI-VRS: T 1 + 2† (18 meses)	ETRI-VRS grave: T 1* (6,7 meses)	ETRI-VRS grave: T 1 + 2† (18 meses)
RSVPreF3 OA	**7** / 12,466	**30** / 12,469	**1** / 12,466	**7** / 12,469
Placebo	**40** / 12,494	**139** / 12,498	**17** / 12,494	**48** / 12,498

Las figuras se crearon independientemente para GSK a partir de los datos originales.
Conjunto expuesto modificado. *Hasta el final de la temporada 1 en el hemisferio norte (análisis de abril de 2022). †Desde 15 días después de la dosis 1 hasta el final de la temporada 2 en el hemisferio norte (análisis de marzo de 2023). ‡La EV se estima utilizando un modelo de regresión de Poisson ajustado según la edad, la región y la temporada.[2]; §IC del 96,95 % para la EV en la temporada 1, IC del 97,5 % en la temporada 1 + 2
IC: intervalo de confianza; ETRI: enfermedad del tracto respiratorio inferior; T: temporada; EV, eficacia de la vacuna
1. GSK 2023. GSK's RSVPreF3 OA Vaccine (AREXVY). Presentado en ACIP, 21 de junio de 2023 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Adults-Friedland-508.pdf; 2. GSK Press release, https://www.gsk.com/en-gb/media/press-releases/gsk-shares-positive-data-for-arexvy-its-respiratory-syncytial-virus-older-adult-vaccine-indicating-protection-over-two-rsv-seasons/#:~:text=Cumulative%20efficacy%20over%20two%20seasons,benefit%20for%20the%20overall%20population. URLs consultados en julio de 2023

La revacunación después de 12 meses parece no conferir un beneficio adicional de eficacia contra ETRI-VRS para la población general; los datos futuros informarán del momento óptimo de la revacunación[1]

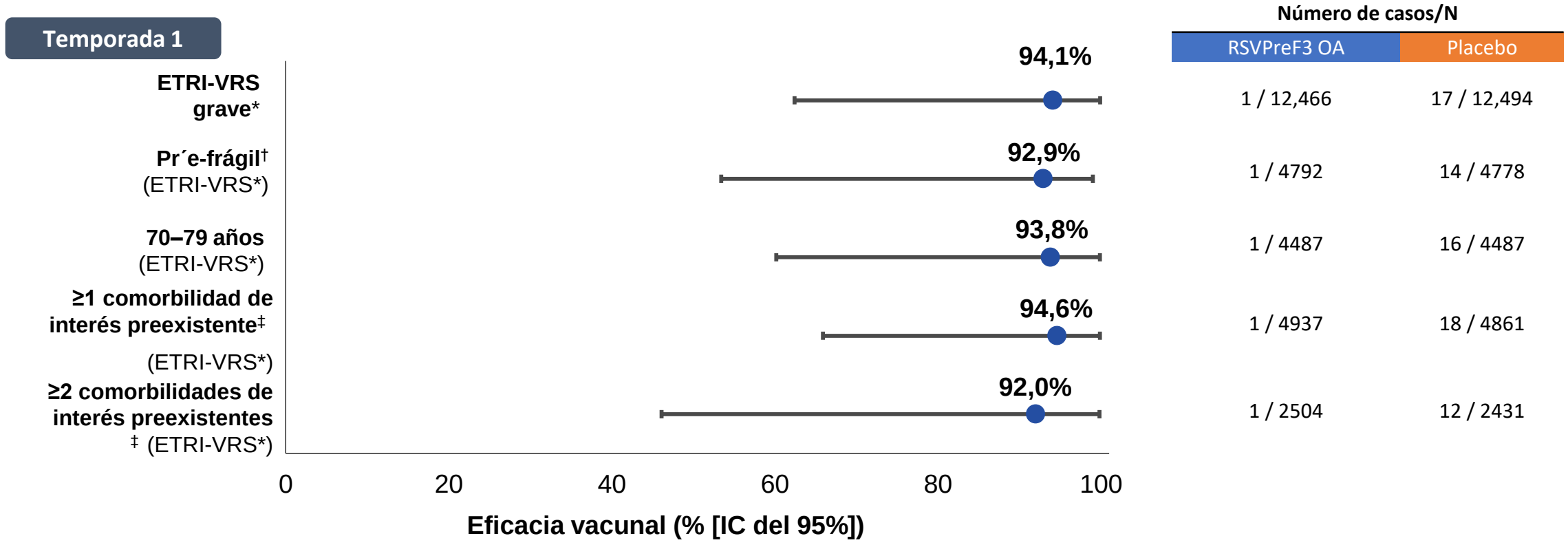


Número de casos:	Dosis única durante una temporada	Dosis única durante dos temporadas‡	Dosis anual (2 dosis espaciadas ~12 meses)‡
RSVPreF3 OA	**7** / 12,466	**30** / 12,469	**30** / 12,469
Placebo	**40** / 12,494	**139** / 12,498	**139** / 12,498

La figura se creó de forma independiente para GSK a partir de los datos originales.
Conjunto expuesto modificado. *Hasta el final de la temporada 1 en el hemisferio norte (análisis de abril de 2022). †Desde 15 días después de la dosis 1 hasta el final de la temporada 2 en el hemisferio norte (análisis de marzo de 2023). ‡La EV se estima utilizando un modelo de regresión de Poisson ajustado según la edad, la región y la temporada.[2]; §IC del 96,95% para la EV en la temporada 1, IC del 97,5% para la temporada 1 + 2. IC, intervalo de confianza; ETRI, enfermedad de´l tracto respiratorio inferior; EV, eficacia de la vacuna; T, temporada

1. GSK 2023. GSK's RSVPreF3 OA Vaccine (AREXVY). Presentado en ACIP, 21 de junio de 2023 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Adults-Friedland-508.pdf; 2. GSK Press release, https://www.gsk.com/en-gb/media/press-releases/gsk-shares-positive-data-for-arexvy-its-respiratory-syncytial-virus-older-adult-vaccine-indicating-protection-over-two-rsv-seasons/#:~:text=Cumulative%20efficacy%20over%20two%20seasons,benefit%20for%20the%20overall%20population. URLs consultados en julio de 2023

Eficacia alta y consistente frente a la enfermedad grave asociada al VRS en adultos mayores con mayor riesgo[1,2]

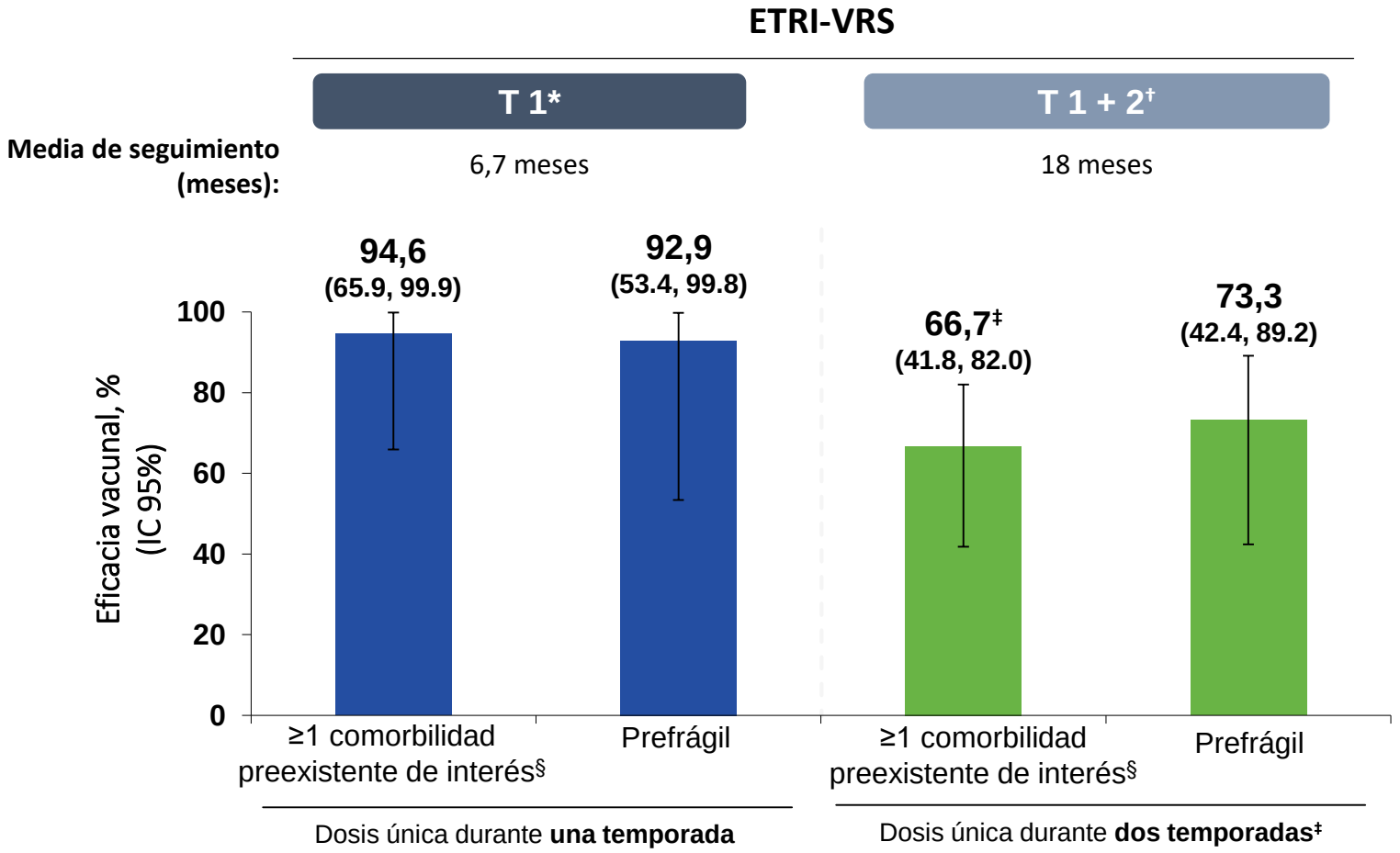


Debido a que se observaron muy pocos casos en adultos de 80 años o más y en los considerados frágiles, no podemos llegar a ninguna conclusión sobre la EV

Figura adaptada con permiso de Ison MG *et al*. Una vacuna candidata de proteína F prefusión frente al virus respiratorio sincitial (VRS) (RSVPreF3 OA) es eficaz en adultos ≥60 años. Presentada en IDWeek, 19-23 de octubre de 2022, Washington, D. C., EE. UU. * La ETRI se definió como ≥2 síntomas/signos del tracto respiratorio inferior durante ≥24 horas, incluidos ≥1 signo del tracto respiratorio inferior o ≥3 síntomas del tracto respiratorio inferior durante ≥24 horas. La ETRI grave se definió como ETRI con ≥2 signos del tracto respiratorio inferior o un episodio de ETRI considerado grave por el investigador. Todos los casos de VRS se confirmaron mediante RT-PCR; †El estado debilitado se evaluó mediante la prueba de velocidad de la marcha; ‡EPOC, asma, cualquier enfermedad respiratoria o pulmonar crónica, diabetes tipo 1 o tipo 2, insuficiencia cardiaca congestiva, enfermedad hepática o renal avanzada. EPOC: enfermedad pulmonar obstructiva crónica; IC: intervalo de confianza; ETRI: enfermedad del tracto respiratorio inferior; RT-PCR: reacción de polimerasa en cadena con transcriptasa inversa; EV: eficacia vacunal

1. Papi A *et al. N Engl J Med* 2023;388(7):595–608; 3. Feldman RG *et al. Clin Infect Dis* 2023:ciad471. doi: 10.1093/cid/ciad471. Epub ahead of print.

Una dosis de Arexvy confiere eficacia duradera frente a la ETRI-VRS en poblaciones vulnerables al menos durante dos temporadas[1]



No se puede concluir la eficacia de la vacuna en participantes frágiles debido al bajo número de casos reunidos

La figura se creó de forma independiente para GSK a partir de los datos originales. Consulte las notas para conocer el número de acontecimientos.
*Hasta el final de la temporada 1 en el hemisferio norte (análisis de abril de 2022). †Desde 15 días después de la dosis 1 hasta el final de la temporada 2 en el hemisferio norte (análisis de marzo de 2023)). ‡La EV se estima utilizando un modelo de regresión de Poisson ajustado según la edad, la región y la temporada.[2]; §Las comorbilidades de interés incluyen enfermedad pulmonar obstructiva crónica, asma, cualquier enfermedad respiratoria o pulmonar crónica, insuficiencia cardíaca crónica (enfermedad cardiorrespiratoria), diabetes mellitus tipo 1 o tipo 2, enfermedad hepática o renal avanzada (enfermedad endocrina o metabólica).
IC, intervalo de confianza; ETRI, enfermedad del tracto respiratorio inferior

1. GSK 2023. GSK's RSVPreF3 OA Vaccine (AREXVY). Presentado en ACIP, 21 de junio de 2023 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Adults-Friedland-508.pdf; 2. GSK Press release, https://www.gsk.com/en-gb/media/press-releases/gsk-shares-positive-data-for-arexvy-its-respiratory-syncytial-virus-older-adult-vaccine-indicating-protection-over-two-rsv-seasons/#:~:text=Cumulative%20efficacy%20over%20two%20seasons,benefit%20for%20the%20overall%20population. URLs consultadas en julio de 2023

Una dosis de Arexvy demostró ser eficaz frente a la ETRI-VRS* en adultos mayores con ≥1 comorbilidad preexistente de interés†[1,2]

AReSVi-006 Temporada 1

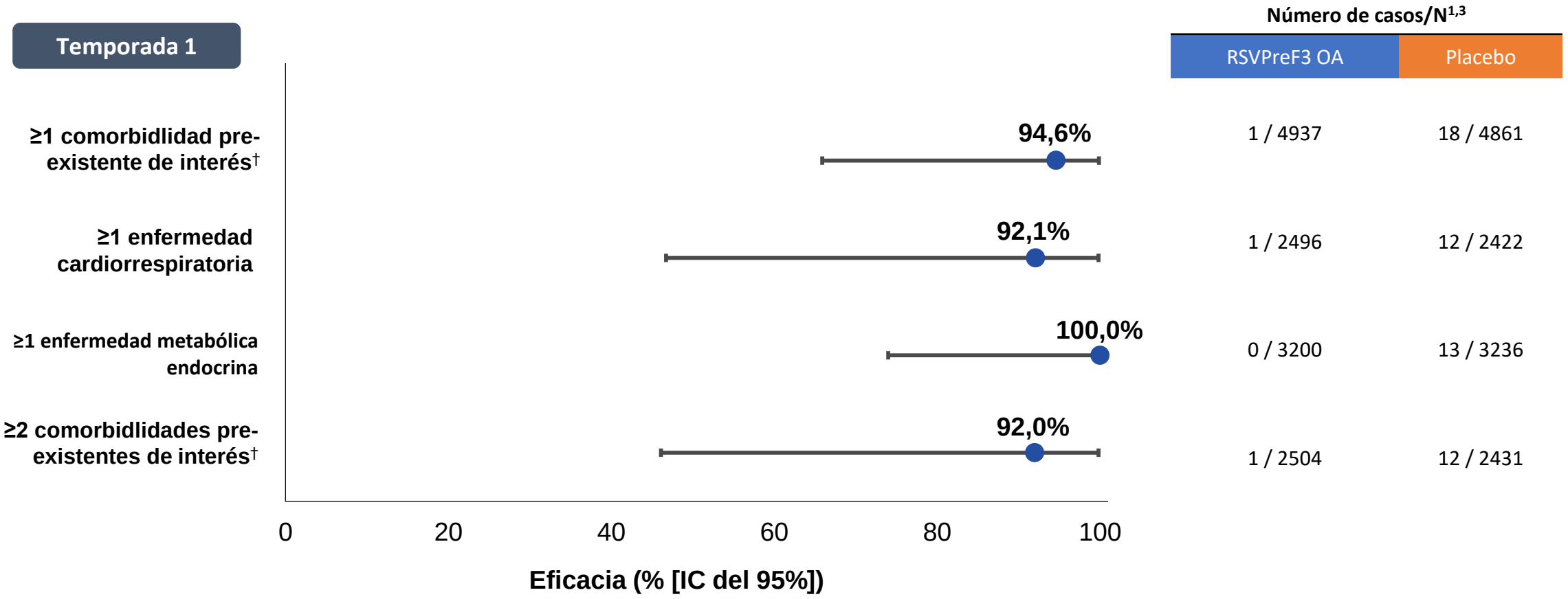


Figura adaptada de GSK RSVPreF3 Vaccine for Respiratory Syncytial Virus (RSV) in Older Adults presentado en el Comité Asesor de Vacunas y productos biológicos relacionados, 1 de marzo, 2023. https://www.fda.gov/media/165649/download (accedido septiembre 2023)

*ETRI definido como ≥2 síntomas/signos de las vías respiratorias inferiores durante ≥24 horas, incluido ≥1 signo de las vías respiratorias inferiores, o ≥3 síntomas de las vías respiratorias inferiores durante ≥24 horas. Todos los casos de RSV confirmados por RT-PCR; †EPOC, asma, cualquier enfermedad respiratoria/pulmonar crónica, diabetes tipo 1 o tipo 2, insuficiencia cardíaca congestiva, enfermedad hepática o renal avanzada

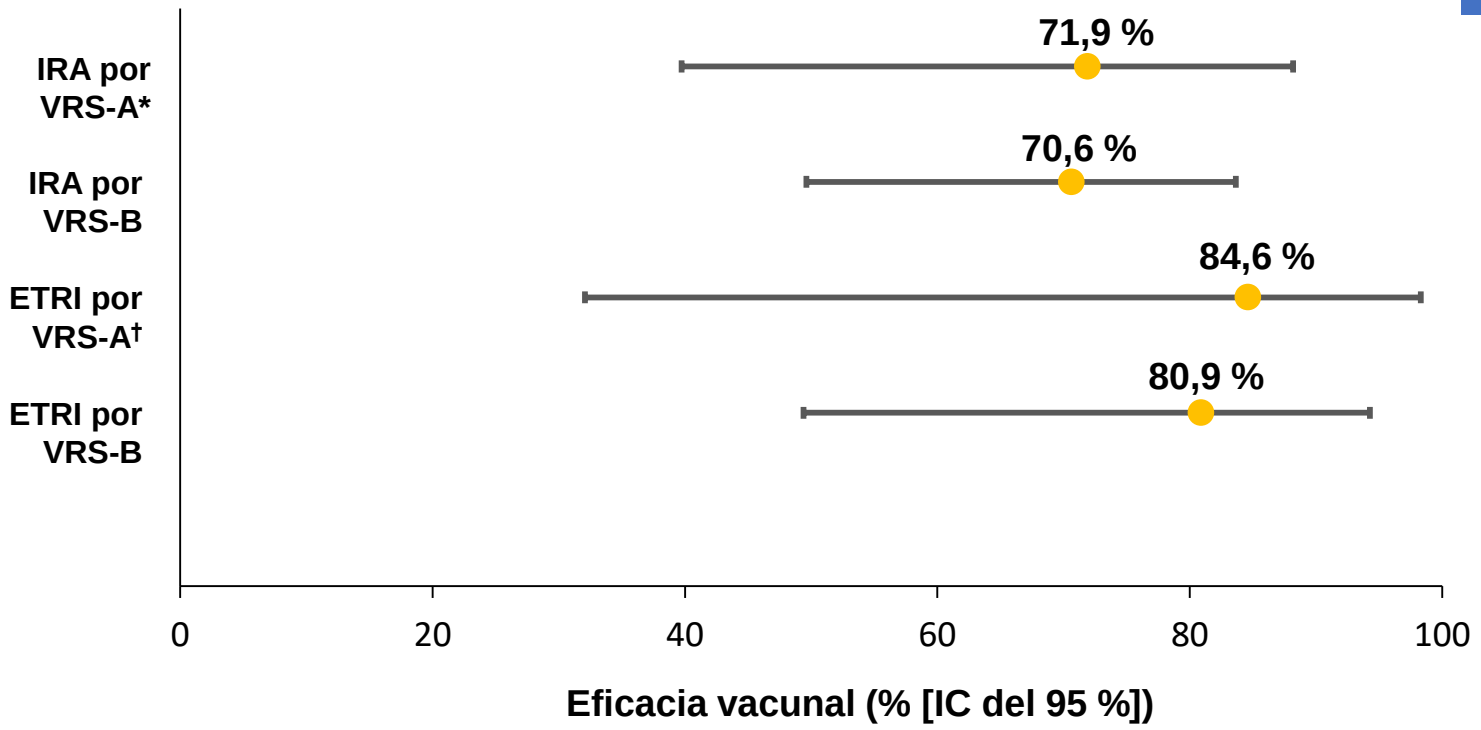
EPOC: Enfermedad Pulmonar Obstructiva Crónica; IC: interval de confianza; ETRI: enfermedad del tracto respiratorio inferior; RT-PCR, reacción de polimerasa en cadena con transcriptasa inversa

1. GSK RSVPreF3 Vaccine for Respiratory Syncytial Virus (RSV) in Older Adults Presented at Vaccines and Related Biological Products Advisory Committee March 1, 2023. https://www.fda.gov/media/165649/download (accedido en septiembre de 2023); 2. Feldman RG e*t al. Clin Infect Dis* 2023:ciad471. doi: 10.1093/cid/ciad471. Epub ahead of print; 3. Papi A *et al. N Engl J Med* 2023;388(7):595–608

Una dosis de Arexvy es eficaz frente a la enfermedad asociada al VRS-A y al VRS-B

AReSVi-006 Temporada 1

Temporada 1



Número de casos

	RSVPreF3 OA N=12.466	Placebo N=12.494
IRA por VRS-A*	9	32
IRA por VRS-B	18	61
ETRI por VRS-A†	2	13
ETRI por VRS-B	5	26

2/3 de los casos de ETRI-VRS se asociaron con VRS-B

Figura adaptada con permiso Papi A *et al. N Engl J Med* 2023;388(7):595–608

* La IRA se definió como ≥2 síntomas/signos respiratorios durante ≥24 horas o ≥1 síntoma/signo respiratorio + 1 síntoma/signo sistémico durante ≥24 horas; † La ETRI se definió como ≥2 síntomas/signos del trato respiratorio inferior durante ≥24 horas, incluidos ≥1 signo del tracto respiratorio inferior O ≥3 síntomas del tracto respiratorio inferior durante ≥24 horas. Todos los casos de VRS se confirmaron mediante RT-PCR

IRA: infección respiratoria aguda; IC: intervalo de confianza; ETRI: enfermedad del tracto respiratorio inferior; RT-PCR: reacción de polimerasa en cadena con transcriptasa inversa

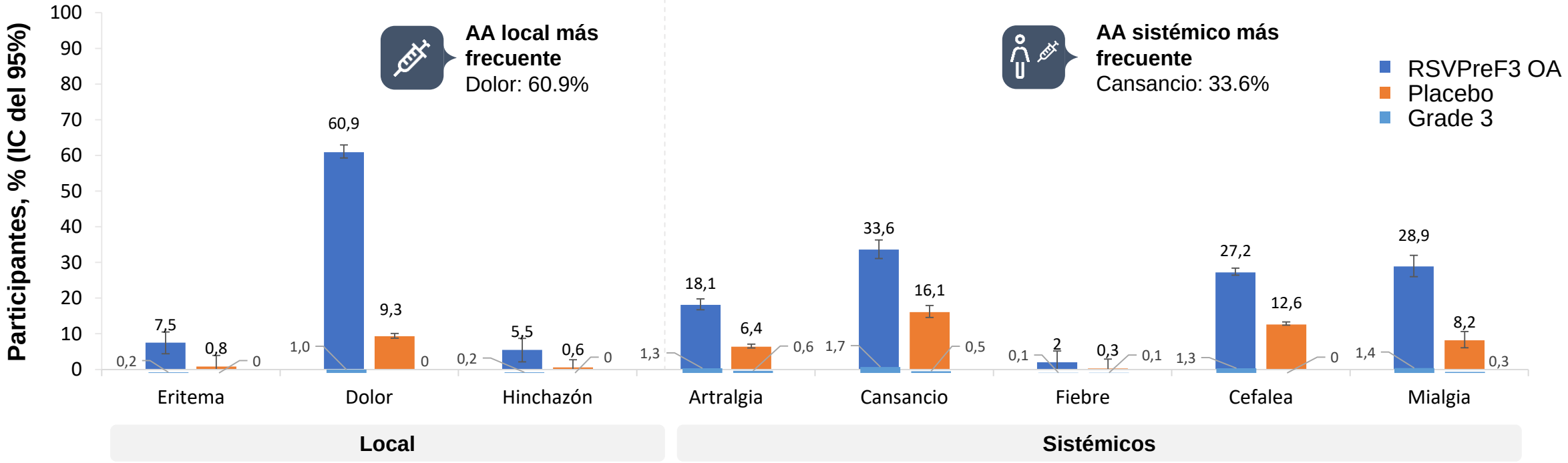
Papi A *et al. N Engl J Med* 2023;388(7):595–608

Arexvy fue bien tolerada[1,2]

La mayoría de los acontecimientos fueron pasajeros y de leves a moderados

AAs solicitados reportados durante los primeros 4 días tras la vacunación

Duración media (todos los AAs): 1–2 días



El perfil de reactogenicidad de una segunda dosis estuvo en línea con la primera dosis[3]

Grupo de seguridad solicitada (N=1757)
IC: intervalo de confianza; AA: acontecimiento adverso.

1. Papi A et al. N Engl J Med 2023;388(7):595–608; 3. GSK 2023. GSK's RSVPreF3 OA Vaccine (AREXVY). Presentado en ACIP, 21 de junio de 2023 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Adults-Friedland-508.pdf Consultado en julio de 2023

Resumen: Estudio AReSVi-006[1,2]

Eficacia

- El análisis de la primera temporada demostró que Arexvy confiere una eficacia alta y consistente frente a todo el espectro de la enfermedad por VRS, independientemente del subtipo de VRS en adultos ≥60 años de edad y con comorbilidades

Eficacia durante toda una temporada de VRS (basado en el análisis de la temporada 1):

82,6%	**94,1%**	**94,6%**	**93,8%**
ETRI-VRS (≥60 años)	ETRI-VRS grave (≥60 años)	ETRI-VRS (≥1 comorbilidad de interés*)	ETRI-VRS (70−79 años)

- Una dosis de Arexvy confiere una eficacia duradera frente a la ETRI-VRS durante al menos 2 temporadas completas de VRS, incluyendo la enfermedad grave en adultos con comorbilidades subyacentes y en edades avanzadas
- La revacunación después de 12 meses parece no conferir un beneficio adicional de eficacia frente a la ETRI-VRS. Los datos futuros informarán del momento óptimo de la revacunación

Seguridad

- Arexvy fue bien tolerada con un perfil de seguridad aceptable
- La mayoría de los AAs solicitados fueron de intensidad leve a moderada y transitorias
- El perfil de reactogenicidad y seguridad de una segunda dosis de Arexvy estuvo en línea con el de la primera dosis

*Incluye enfermedad pulmonar obstructiva crónica, asma, cualquier enfermedad respiratoria/pulmonar crónica, insuficiencia cardíaca crónica (cardiorrespiratoria), diabetes mellitus tipo 1 o tipo 2, enfermedad hepática o renal avanzada (endocrina o metabólica)

ETRI, enfermedad del tracto respiratorio inferior

1. Papi A *et al. N Engl J Med* 2023;388(7):595–608; 2. GSK 2023. GSK's RSVPreF3 OA Vaccine (AREXVY). Presentado en ACIP, 21 de junio de 2023 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Adults-Friedland-508.pdf Consultado en julio de 2023

Se cumplieron los criterios de valoración principales para FLU-QIV y AREXVY

Inmunogenicidad no inferior en la coadministración frente a la administración secuencial

Relación de GMTs de NAb frente a VRS y GMTs de HI entre el grupo control (administración secuencial) y el grupo de coadministración, 1 mes después de la vacunación[1,2]

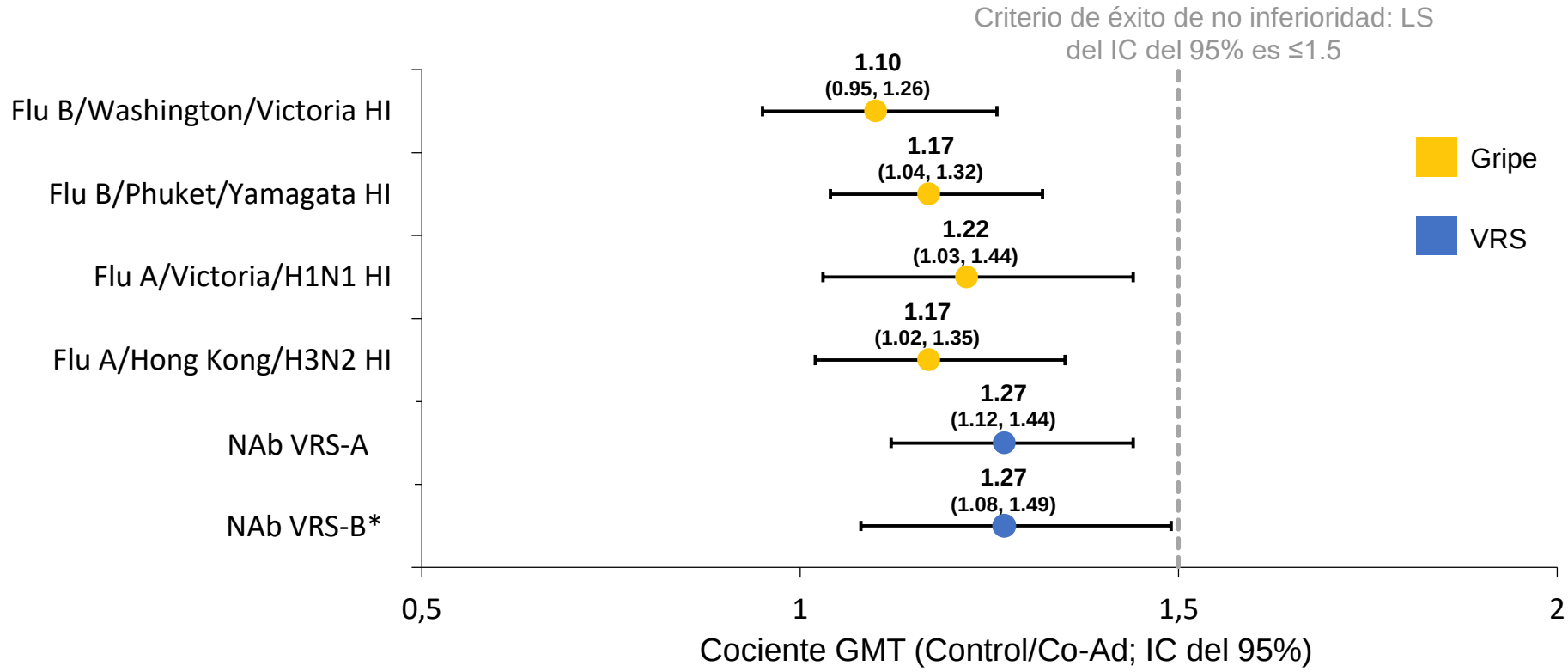


Figura adaptada con permiso de Chandler R *et al*. Immunogenicity, reactogenicity and safety of a respiratory syncytial virus prefusion F (RSVPreF3) candidate vaccine co-administered with the seasonal quadrivalent vaccine in older adults. Presentado en IDWeek, del 19 al 23 de octubre de 2022, Washington, DC, EE. UU.

*NAb VRS-B era un criterio de valoración descriptivo y secundario

IC: intervalo de confianza; Co-Ad, co-administración; FLU, vacuna antigripal; FLU-QIV, vacuna tetravalente contra la gripe; GMT, media geométrica de los títulos; HI, inhibición de la hemaglutinación; NAb, Anticuerpos neutralizantes; LS, límite superior. 1. Chandler R *et al*. Immunogenicity, reactogenicity and safety of a respiratory syncytial virus prefusion F (RSVPreF3) candidate vaccine co-administered with the seasonal quadrivalent vaccine in older adults. Presentado en IDWeek, del 19 al 23 de octubre de 2022, Washington, DC, USA; 2. GSK, 2022. Presentation at ACIP Meeting, October 20 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-10-19-20/02-RSV-Adults-Rizkalla-508.pdf (consultado en julio de 2023)

Co-administration of the adjuvanted respiratory syncytial virus (RSV) prefusion F protein vaccine (RSVPreF3 OA) with the adjuvanted recombinant zoster vaccine (RZV) in adults ≥50 years of age

Patrick Dennis,[1] Jean-Francois Roussy,[2] Anil K. Gupta,[3] Alexander Abitbol,[4] Naresh Aggarwal,[5] Naveen Garg,[6] Joseph G. Surber,[7] Theodore Lee,[8] Archana Jastorff,[9] Nadia Meyer,[9] Marie-Pierre David,[9] Hiwot Amare Hailemariam,[9] Caroline Portaels,[9] Catherine Gerard,[10] Amit Bhavsar,[9] on behalf of the RSV-020 study group

[1]DELRIGHT Research, New Orleans, Louisiana, USA; [2]DIEX Research, Quebec, Quebec, Canada; [3]Albion Finch Medical Center, Toronto, Ontario, Canada; [4]LMC Healthcare/Centricity Research, Toronto, Ontario, Canada; [5]Aggarwal and Associates, Brampton, Ontario, Canada; [6]Centricity Research, Pointe-Claire, Quebec, Canada; [7]Centricity Research, Talbotton, Columbus, Georgia, USA; [8]Headlands Research, Orlando, Florida, USA; [9]GSK, Wavre, Belgium; [10]GSK, Rixensart, Belgium

Background

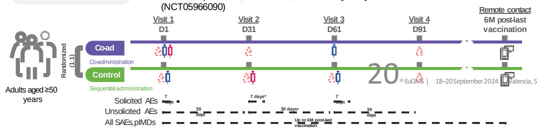
- Vaccines against RSV disease and herpes zoster are available and recommended in older adults.[1,2]
- Co-administration of vaccines could help protect older adults against diseases caused by both viruses, while improving convenience and vaccination coverage.[3]

Objectives

- **Primary:** To demonstrate the non-inferiority of the humoral immune responses to RSVPreF3 OA and RZV when co-administered compared to when administered alone (sequentially)
- **Secondary:** To evaluate reactogenicity and safety following co-administration and sequential administration of RSVPreF3 OA and RZV

Study design

Phase III, open-label, randomized, multi-country study (NCT05966090)

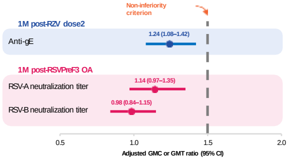


Non-inferiority criteria: upper limits of 95% confidence intervals (CIs) of anti-gE geometric mean concentration (GMC) ratio and RSV-A and RSV-B neutralization geometric mean titer (GMT) ratios (Control/Co-ad) at 1M post-RZV dose2 or 1M post-RSVPreF3 OA are ≤1.5

*AEs collected only after RSVPreF3 OA vaccination in the Control group. **D**, day; **M**, month; **AE**, adverse event; **SAE**, serious AE; **pIMD**, potential immune-mediated disease; **VZV**, varicella zoster virus; **gE**, glycoprotein E; **AS**, adjuvant system; **MPL**, monophosphoryl lipid A; **QS-21**, *Quillaja saponaria* Molina, fraction 21.

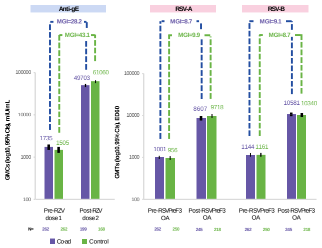
Results

- Overall, 530 participants (Co-ad: 265; Control: 265) were vaccinated. Baseline demographic characteristics were balanced between groups. The mean age ± standard deviation was 63.9±8.6 years in Co-ad and 63.9±8.7 in Control.
- Non-inferiority criteria for the humoral immune responses to RZV and RSVPreF3 OA were met.



N for anti-gE = 199 (Co-ad), 168 (Control); **N for RSV-A and RSV-B** = 237 (Co-ad), 218 (Control).

- Anti-gE antibody concentrations and RSV neutralization titers increased from pre- to post-vaccination in both groups.

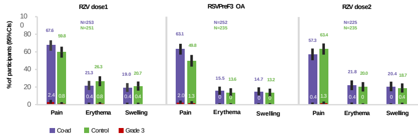


MGI (mean geometric increase) is the geometric mean of the within-participant ratios of the post-vaccination over the pre-vaccination titers or concentrations.

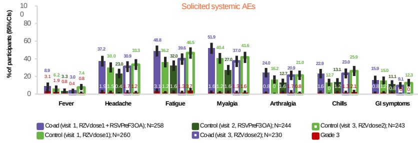
N, number of participants in the per-protocol analysis set; **mIU/mL**, milli international units per milliliter; **ED60**, estimated Dilution 60 (corresponds to the inverse of the interpolated serum dilution that yields a 60% reduction in the number of plaques compared to the virus control wells).

- Solicited administration-site AEs at either injection site were reported by 73.6% (Co-ad, post-RZV dose1+RSVPreF3 OA, N=258; Grade [Gr]3=3.9%), 60.4% (Control, post-RZV dose1, N=260; Gr3=1.9%) and 48.8% (Control, post-RSVPreF3 OA, N=244; Gr3=1.2%) of participants; overall, solicited systemic AEs were reported by 73.6% (Co-ad, post-RZV dose1+RSVPreF3 OA; Gr3=9.3%), 60.4% (Control, post-RZV dose1; Gr3=5.8%), and 49.2% (Control, post-RSVPreF3 OA; Gr3=3.7%) of participants.
- In both groups, the duration of solicited AEs was short and comparable, and the most frequently reported were pain at the injection site, fatigue, and myalgia.

Solicited administration-site AEs



Solicited systemic AEs



- Unsolicited AEs reporting rates were balanced between groups.
- Two participants reported pIMDs (Bell's palsy [Co-ad] after visit 1, considered causally related to vaccination by the investigator and resolved; gout [Control], not considered related to vaccination).
- No fatal SAEs, related SAEs, GBS, or ADEM were reported.

	Co-ad (N=265)	Control (N=265)
30 days post any vaccination, n (%)		
Any unsolicited AEs	61 (23.0)	79 (29.8)
Grade 3 unsolicited AEs	2 (0.8)	2 (0.8)
Up to data lock point*, n (%)		
SAEs	9 (3.4)	4 (1.5)
pIMDs	1 (0.4)	1 (0.4)
Related pIMDs	1 (0.4)	0 (0.0)

N, number of participants in the exposed set; **grade 3**, diameter >100 mm (erythema and swelling), temperature >39 °C (fever), prevented normal, everyday activities (all the other events); **n (%)**, number (percentage) of participants presenting ≥1 type of AE; **GI**, gastrointestinal; **GBS**, Guillain-Barré syndrome; **ADEM**, acute disseminated encephalomyelitis. *8 May 2024 (median follow-up time for both groups: 218 days); safety follow-up is ongoing and will collect information up to 6M post-last vaccination.

Conclusions

Co-administration of RSVPreF3 OA and RZV (both AS01-adjuvanted) demonstrated non-inferiority of humoral responses compared to sequential administration.

RSVPreF3 OA co-administered with RZV was generally well tolerated and had an acceptable reactogenicity/safety profile, with no clinically meaningful differences versus sequential administration.

References

1. Centers for Disease Control and Prevention. RSV vaccines for adults ages 60 and over. https://www.cdc.gov/rsv/vaccines/older-adults.html
2. Centers for Disease Control and Prevention. Shingles vaccination. https://www.cdc.gov/shingles/vaccines/index.html
3. Bonanni P et al. Hum Vaccin Immunother 2023; 19:2195786.

Trademark

Acknowledgments

Medical writing (Lucia Adina Truta), design and coordination support were provided by Akkodis Belgium c/o GSK.

Disclosures, RZV-020 study group

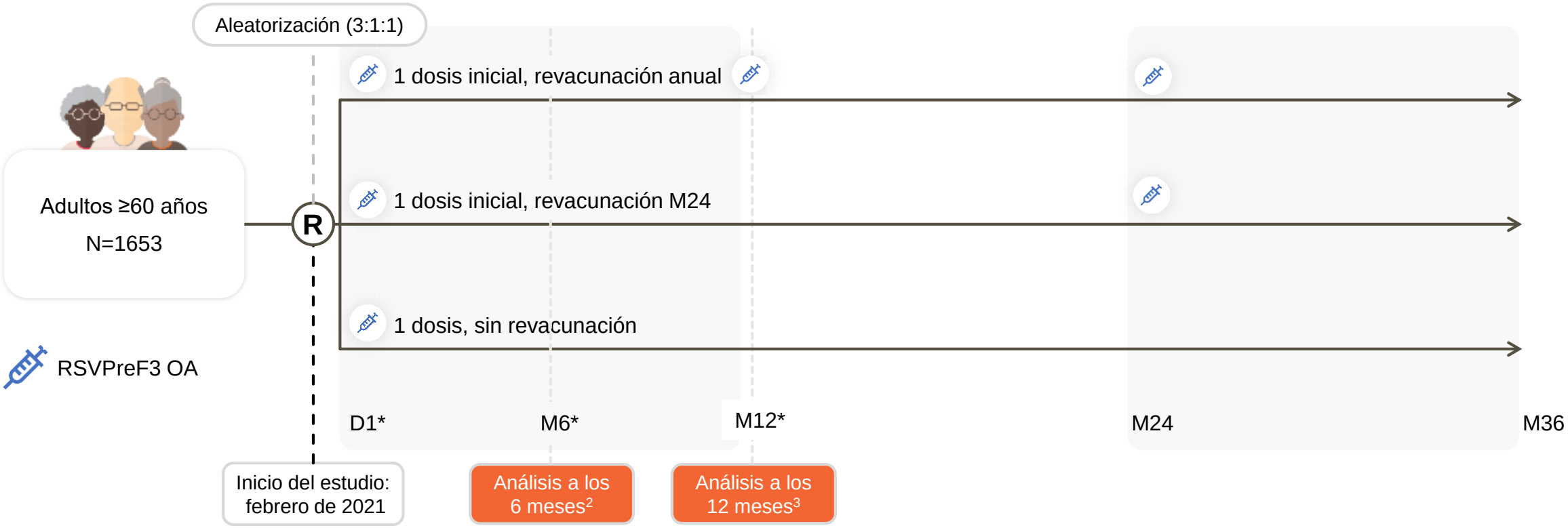
Funding

GSK

Presenter: Archana Jastorff, archana.m.jastorff@gsk.com

Diseño del estudio de fase III AReSVi-004[1–3]

Estudio abierto para el observador para evaluar la inmunogenicidad, la seguridad, la reactogenicidad y la persistencia de una sola dosis y de diferentes esquemas de revacunación



Objetivo primario: Evaluar la respuesta humoral 12 meses después de administrar una dosis en primovacunación *

Objectivos secundarios: Evaluar la respuesta humoral y celular (CMI†) 36 meses después de administrar una dosis en primovacunación y distintos esquemas de revacunación. También se evaluó la seguridad y reactogenicidad.

* El criterio principal de valoración es la media geométrica de los títulos de NAb (frente a VRS-A y VRS-B) el día 1 (antes de la vacunación), el D31, el M6 y el M12 después de la dosis 1; †CMI en cuanto a la frecuencia con que los linfocitos T $CD4^+$ o $CD8^+$ específicos frente a RSVPreF3 expresan al menos 2 marcadores de activación; CD: cúmulo de diferenciación; respuesta CMI: inmunidad mediada por células; D: día; M: mes; NAb: anticuerpo neutralizante; R, aleatorización

1. ClinicalTrials.gov. 2021. NCT04732871. https://clinicaltrials.gov/ct2/show/NCT04732871 (consultado en junio de 2023); 2. Schwarz TF *et al*. A candidate respiratory syncytial virus (RSV) prefusion F protein investigational vaccine (RSVPreF3 OA) is immunogenic when administered in adults ≥ 60 years of age: results at 6 months after vaccination. Presentado en IDWeek, octubre 19–23, 2022, Washington, DC, EE.UU.; 3. GSK, 2022. Presentación en la reunión del ACIP, 20 de octubre https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-10-19-20/02-RSV-Adults-Rizkalla-508.pdf (consultado en junio de 2023)

Autorización de comercialización de Arexvy

Indicaciones y contraindicaciones

EE.UU.[1]

Indicación:

Arexvy es una vacuna indicada para la inmunización activa para la prevención de la enfermedad del tracto respiratorio inferior (ETRI) causada por el virus respiratorio sincitial en individuos de 60 años de edad y mayores.

Contraindicación:

Antecedentes de reacción alérgica grave (por ejemplo, anafilaxia) a cualquier componente de la vacuna.

Unión Europea[2]

Indicación:

Arexvy está indicado para la inmunización activa para la prevención de la enfermedad del tracto respiratorio inferior (ETRI) causada por el virus respiratorio sincitial en adultos de 60 años y mayores.

El uso de esta vacuna debe estar de acuerdo con las recomendaciones oficiales.

Contraindicación:

Hipersensibilidad a los principios activos o a alguno de los excipientes.

Reino Unido[3]

Indicación:

Arexvy está indicado para la inmunización activa para la prevención de la enfermedad del tracto respiratorio inferior (ETRI) causada por el virus respiratorio sincitial en adultos de 60 años y mayores.

El uso de esta vacuna debe estar de acuerdo con las recomendaciones oficiales.

Contraindicación:

Hipersensibilidad a los principios activos o a alguno de los excipientes.

Canadá[4]

Indicación:

Arexvy, una vacuna contra el VRS, ha sido autorizada para su uso en Canadá para la prevención de la enfermedad del tracto respiratorio inferior causada por el VRS en adultos mayores de 60 años.

Contraindicación:

Hipersensibilidad a los principios activos o a alguno de los excipientes.

Japón[5]

Indicación:

El Ministerio de Salud, Trabajo y Bienestar ha aprobado Arexvy para la prevención de la enfermedad por VRS (virus respiratorio sincitial) para adultos de 60 años o más. El uso de esta vacuna debe estar de acuerdo con las recomendaciones oficiales.

Contraindicación:

Por confirmar

1. Food and Drug Administration (FDA), 2023. *Arexvy* Prescribing Information (PI). https://www.fda.gov/media/167805/download; 2. European Medicines Agency (EMA), 2023. Arexvy Summary of Product Characteristics (SmPC). https://www.ema.europa.eu/en/documents/product-information/arexvy-epar-product-information_en.pdf; 3. Medicines & Healthcare products Regulatory Agency (MHRA), 2023. *Arexvy* Summary of Product Characteristics. https://mhraproducts4853.blob.core.windows.net/docs/e3ae9af503f9e9824a7d1d40538536337caafaf8 4. Gobierno de Canadá. 2023. Respiratory syncytial virus (RSV): Canadian Immunization Guide. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/respiratory-syncytial-virus.html; 5. Comunicado de prensa de GSK del 25 de septiembre de 2023. https://www.gsk.com/en-gb/media/press-releases/japan-s-ministry-of-health-labour-and-welfare-approves-gsk-s-arexvy/; Todas las URLs consultadas en septiembre 2023.

Recomendaciones VRS

United States[1]

60+ Older Adults using shared clinical decision-making
(any RSV vaccine)

Ontario[7]

60+ Older Adults living in long-term care homes
(Arexvy)

Norway[5]

60+ Older Adults with underlying disease
(any RSV vaccine)

Sweden[6]

75+ All Older Adults
60+ with underlying disease

Poland[9]

60+ Older Adults
(any RSV vaccine)

United Kingdom[2]

75+ Older Adults
(any RSV vaccine)

Ireland[8]

65+ Older Adults
(any RSV vaccine)

Austria[3]

60+ Older Adults
18+ High Risk
(any RSV vaccine)

Belgium[4]

60+ Older Adults with underlying disease
(any RSV vaccine)

Países con recomendaciones para VRS

Melgar M, Britton A, Roper LE *et al.* Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023. *MMWR Morb Mortal Wkly Rep* 2023;72:793–801. doi: http://dx.doi.org/10.15585/mmwr.mm7229a4; 2. JCVI. Respiratory syncytial virus (RSV) immunisation programme: JCVI advice, 7 June 2023 - GOV.UK (www.gov.uk); 3. Bundesministerium. Impfplan Österreich. 2023. https://www.sozialministerium.at/dam/jcr:eb64732e-1747-400a-beeb-6d069f781182/Impfplan_%C3%96sterreich_2023_2024_Version1.0.pdf; 4. Superior Health Council. Vaccination Against Adults. 2023. https://www.health.belgium.be/sites/default/files/uploads/fields/fpshealth_theme_file/20230918_shc-9725_rsv_vaccination_adults_vweb_1.pdf; 5. PHI. RS-virusvaksine - veileder for helsepersonell. 2023. https://www.fhi.no/va/vaksinasjonsveilederen-for-helsepersonell/vaksiner-mot-de-enkelte-sykdommene/rs-virusvaksine/?term=. 6. Public Health Agency of Sweden. *Vaccination mot RS-virus — Folkhälsomyndigheten (folkhalsomyndigheten.se)*; 7. Ondatio Ministry of Health https://files.ontario.ca/moh-respiratory-syncytial-virus-fact-sheet-for-vaccine-recipients-v1.0-en-2023-10-25.pdf; 8. https://rcpi.access.preservica.com/uncategorized/IO_9275434a-99ff-44e5-b19c-04771ba2b1c0/; 9. https://dziennikmz.mz.gov.pl/DUM_MZ/2023/87/akt.pdf . URLs consultadas en septiembre 2023

Update on Moderna's RSV Vaccine, mRESVIA (mRNA-1345), in Adults ≥60 Years of Age

Advisory Committee on Immunization Practices (ACIP)

Rituparna Das, MD PhD

June 26, 2024

moderna

Licensure of mRESVIA, Moderna's RSV Vaccine (mRNA-1345) in United States

- FDA approval obtained May 31, 2024
- Indication/Presentation
  - For active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV) in adults 60 years of age and older
  - Single dose regimen
  - Prefilled syringe

Pivotal Safety and Efficacy Study Design

Study 301

Population

- Healthy adults including those with chronic, stable medical conditions, and/or frailty
- ≥ 60 years of age
- 22 countries (both Northern and Southern Hemisphere)

Regimen and follow-up

- Single-dose regimen (1:1 50 µg RSV vaccine or saline placebo)
- 24-month follow-up

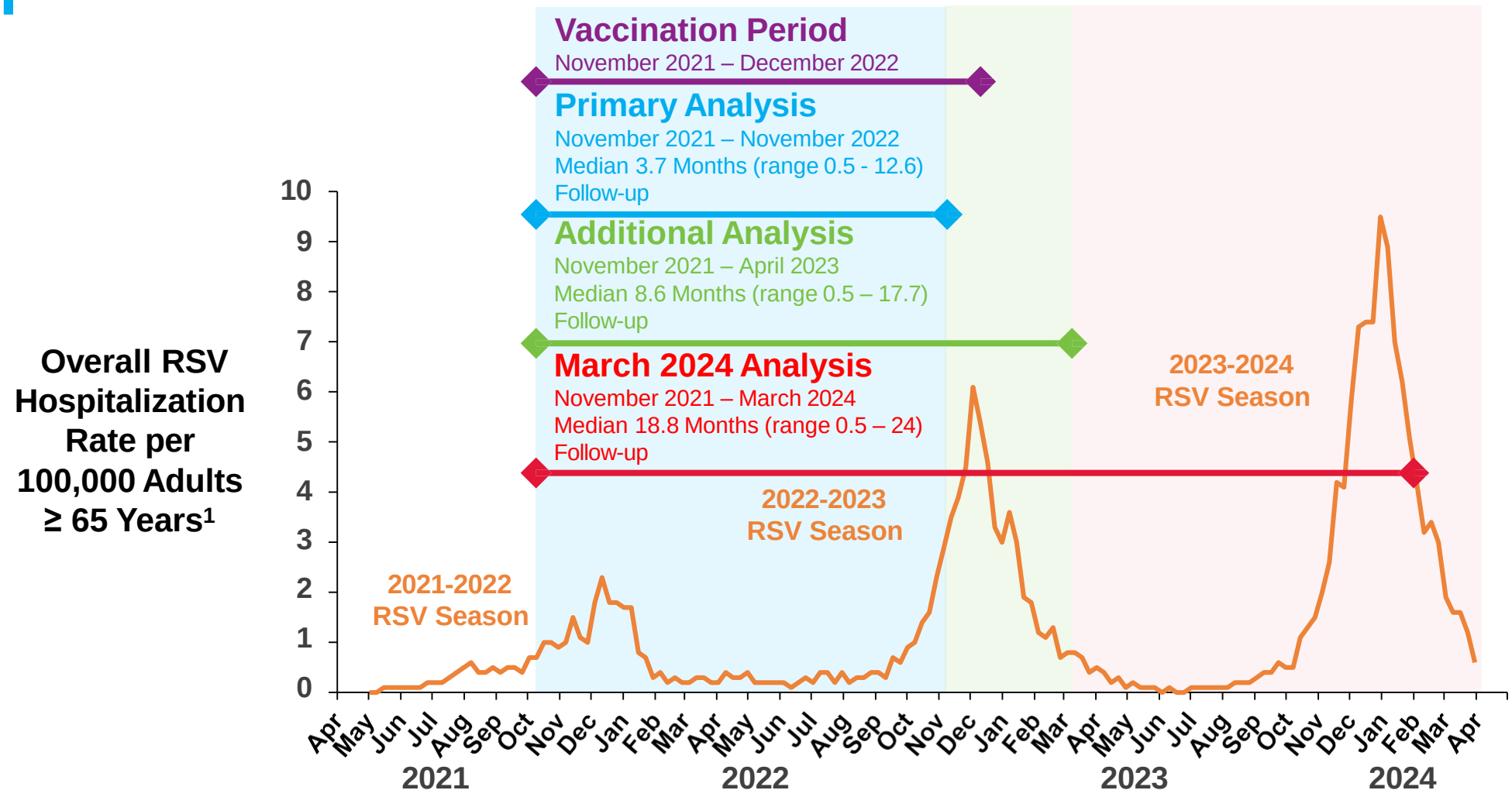
Stratified by

- Age (60 - 74 and ≥ 75 years)
- Presence or absence of congestive heart failure or chronic obstructive pulmonary disease

clinicaltrials.gov NCT05127434 https://clinicaltrials.gov/ct2/show/NCT05127434
Wilson et al *NEJM*, 2023.

Trial Analyses

US 2021-2023 RSV Hospitalization Rates (RSV-NET) in Adults ≥ 65 Years[1]



- RSV efficacy study conducted across 3 seasons
- >50% of participants enrolled in US
- **Primary Analysis:** Met success criteria
- **Additional Analysis:** >90% of participants followed for ≥ 6 months
- **March 2024 Analysis:** >90% of participants followed for ≥12 months

1. CDC. Respiratory Syncytial Virus Hospitalization Surveillance Network (RSV-NET). https://www.cdc.gov/respiratory-viruses/data-research/dashboard/most-impacted-hospitalizations.html

Timing of Vaccination and RSV Surveillance

Study 301

Vaccination

- COVID-19 pandemic precluded the assumption of standard RSV seasons
- Subjects vaccinated year-round for ~ 1 year (not limited to pre-RSV season)

Surveillance

- Active surveillance of >36,000 participants for RSV year-round (not limited to RSV seasons)
  - Included 2022/2023 and 2023/2024 high incidence RSV seasons[1]
    - Background rates in placebo recipients, 14 days - 24 months:
      - RSV-LRTD with ≥ 2 symptoms: 9.3 cases/1000 person years
      - RSV-LRTD with ≥ 3 symptoms: 3.7 cases/1000 person years
      - RSV-ARD: 16.4 cases/1000 person years
  - 683 confirmed RSV-ARD cases reported over 24 months

clinicaltrials.gov NCT05127434 https://clinicaltrials.gov/ct2/show/NCT05127434

1. CDC. Respiratory Syncytial Virus Hospitalization Surveillance Network (RSV-NET). https://www.cdc.gov/respiratory-viruses/data-research/dashboard/most-impacted-hospitalizations.html

Demographics of Study Participants

Study 301

Randomization Set Characteristic	RSV Vaccine (mRNA-1345) (N = 18,427)	Placebo (N = 18,387)
Median Age, years	**67**	**67**
Male, n (%)	9,410 (**51%**)	9,330 (**51%**)
Age Group, n (%)		
60 – 69 Years	11,437 (**62%**)	11,399 (**62%**)
70 – 79 Years	5,546 (**30%**)	5,534 (**30%**)
≥ 80 Years	1,444 (**8%**)	1,454 (**8%**)
Race/Ethnicity, n (%)		
White	11,311 (**61%**)	11,290 (**61%**)
Black or African American	2,204 (**12%**)	2,173 (**12%**)
Asian	2,151 (**12%**)	2,138 (**12%**)
Hispanic / Latino Ethnicity	6,117 (**33%**)	6,168 (**34%**)
Frailty Status (≥4 on Edmonton frail score)	3,862 (**21%**)	3,946 (**21%**)

Age, gender, race/ethnicity, and frailty status balanced between vaccine and placebo recipients
Race/ethnicity generally representative of US population

March 8, 2024 data cutoff

Prespecified Comorbidities among Study Population

Study 301 – Randomization Set

Randomization Set	RSV Vaccine (mRNA-1345) (N = 18,427)	Placebo (N = 18,387)
≥1 Prespecified Comorbidity (%)	5,463 (30%)	5,357 (29%)
Chronic obstructive pulmonary disease (COPD)	1,097 (6%)	1,112 (6%)
Asthma	1,410 (8%)	1,365 (7%)
Chronic Respiratory Disease[1]	89 (0.5%)	84 (0.5%)
Diabetes	3,292 (18%)	3,207 (17%)
Congestive Heart Failure (CHF)	276 (2%)	268 (2%)
Advanced Liver Disease	49 (0.3%)	44 (0.2%)
Advanced Renal Disease	111 (0.6%)	127 (0.7%)

- **~30% of study participants with comorbidities**
- **Comorbidities balanced between vaccine and placebo recipients**

1. Chronic respiratory disease includes chronic pulmonary fibrosis (idiopathic and otherwise), restrictive lung disease, asbestosis, bronchiectasis, cystic fibrosis, pulmonary hypertension, sarcoidosis, and history of tuberculosis

March 8, 2024 data cutoff

Safety Data

Study 301

Safety Set – March 8, 2024 data cutoff

Based on median of 18.8 months of follow-up

Unsolicited Adverse Events Within 28 Days After Injection, Regardless of Relationship to Vaccine/Placebo

Study 301

Safety Set	RSV Vaccine (mRNA-1345) (N = 18,369)	Placebo (N = 18,316)
All, n (%)	3,823 **(21%)**	3,467 **(19%)**
Serious	126 **(0.7%)**	114 **(0.6%)**
Fatal	2 **(<0.1%)**	6 **(<0.1%)**
Medically-Attended	1,664 **(9%)**	1,587 **(9%)**
Leading to Study Discontinuation	2 **(<0.1%)**	11 **(<0.1%)**
Severe/≥ Grade 3	138 **(0.8%)**	138 **(0.8%)**
Non-Serious	3,697 **(20%)**	3,353 **(18%)**
Any Adverse Event of Special Interest (AESI)	3 **(<0.1%)**	9 **(<0.1%)**

No imbalances in any categories between vaccine and placebo recipients

March 8, 2024 data cutoff

Adverse Events of Special Interest (AESI)

Study 301

Safety Set

- **Neurological Disorders**
  - No cases of acute disseminated encephalomyelitis (ADEM)
  - No safety concern with Guillain-Barre syndrome (3 unrelated cases reported >500 days postinjection [1 vaccine, 2 placebo])
  - No imbalance observed for other neurological disorders including Bell's palsy/facial paralysis
- **Cardiac Events**
  - No imbalance observed in cardiac arrhythmias such as atrial fibrillation
  - No confirmed cases of:
    - Acute myocarditis in vaccine recipients
    - Acute pericarditis in vaccine recipients with onset < 42 days

March 8, 2024 data cutoff

Efficacy of mRNA-1345 Against RSV LRTD among Adults ≥ 60 Years

Study 301 – Primary and Additional Analyses

Per Protocol Analysis

Cases, n (%)	Primary Analysis (Case Driven)[1] *3.7 Months Median (range 0.5 - 12.6) Follow-up*			Additional Analysis[1] *8.6 Months Median (range 0.4 – 17.7) Follow-up*		
	RSV Vaccine (mRNA-1345) (N = 17,561)	**Placebo** (N = 17,503)	**Vaccine Efficacy** (%CI*)	**RSV Vaccine (mRNA-1345)** (N = 18,074)	**Placebo** (N = 18,010)	**Vaccine Efficacy** (% CI*)
RSV LRTD ≥ 2 symptoms	15 (0.09%)	70 (0.40%)	**78.7%** (62.8%, 87.9%)	48 (0.27%)	127 (0.71%)	**62.5%** (47.7%, 73.1%)
RSV LRTD ≥ 3 symptoms	5 (0.03%)	26 (0.15%)	**80.9%** (50.1%, 92.7%)	20 (0.11%)	51 (0.28%)	**61.1%** (34.7%, 76.8%)

- Vaccine protection continued through a high incidence RSV season (2022/2023)
- Lower bound of confidence interval continued to exceed 20%

1. US product insert mRESVIA

* For primary analysis, the alpha-adjusted 95.04% CI and 95.10% CI for RSV LRTD ≥ 2 symptoms and ≥ 3 symptoms are presented, respectively. For additional analysis, 95% CIs are presented.
Efficacy based on hazard ratios

Efficacy of mRNA-1345 Against RSV LRTD among Adults ≥ 60 Years - 18 Month Analysis

Study 301 - Per Protocol Set

March 2024 Analysis

	Cases, n (%)		
	RSV Vaccine (mRNA-1345) (N = 18,181)	**Placebo** (N = 18,132)	**Vaccine Efficacy (%) (95% CI)**
RSV LRTD ≥ 2 symptoms	113 (0.6%)	225 (1.2%)	**50.3%** (37.5%, 60.7%)
RSV LRTD ≥ 3 symptoms	46 (0.3%)	91 (0.5%)	**49.9%** (27.8%, 65.6%)

- Vaccine protection continued over a longer period through high incidence 2022/2023 and 2023/2024 RSV seasons
- Lower bound of the confidence interval continued to exceed 20%

March 8, 2024 data cutoff

Efficacy based on incidence rates adjusted for person-time.

Efficacy of mRNA-1345 Against Severe LRTD Among Adults ≥ 60 Years

Study 301 - Post Hoc Analysis/Per Protocol Set

	Vaccine Efficacy (95% CI)		
	Primary Analysis *3.7 Months Median (0.5 - 12.6) Follow-up*	**Additional Analysis** *8.6 Months Median (0.4 – 17.7) Follow-up*	**March 2024 Analysis,** *18 Month*
RSV-LRTD Associated Shortness of Breath[1,2]	**86.7%** (41.9%, 97.0%)	**74.6%** (50.7%, 86.9%)	**56.7%** (33.1%, 72.6%)

- Shortness of breath is a key driver of seeking a higher level of care[1,2]
- Vaccine is efficacious in preventing shortness of breath associated with RSV-LRTD
- Too few hospitalizations to assess vaccine efficacy

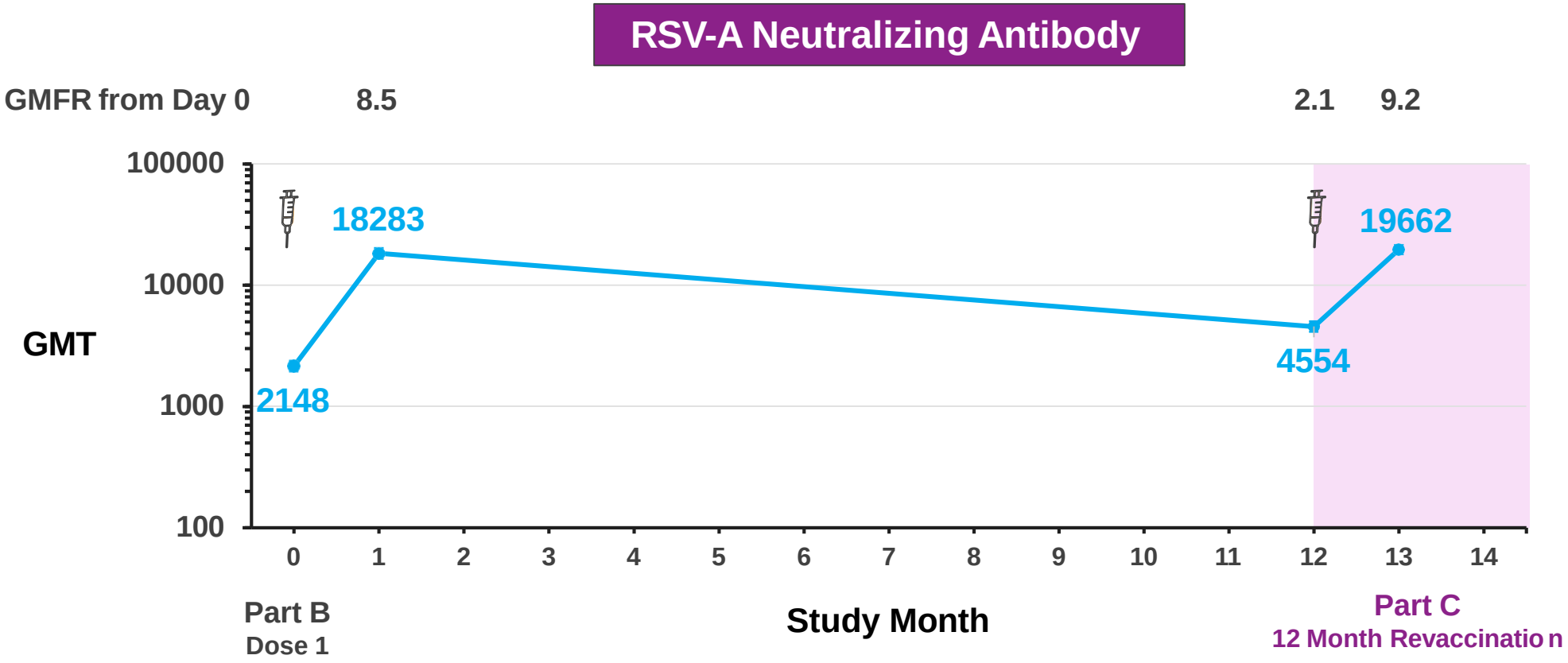
1. Falsey et al NEJM, 2005; 2. Panozzo et al ESWI, 2023

Persistence of RSV Antibody and Revaccination at 12 Months

Study 302

Durability of Neutralizing Antibody Responses Following Primary Dose and Revaccination at 12 Months with mRNA-1345

Study 302C – Adults ≥50 Years



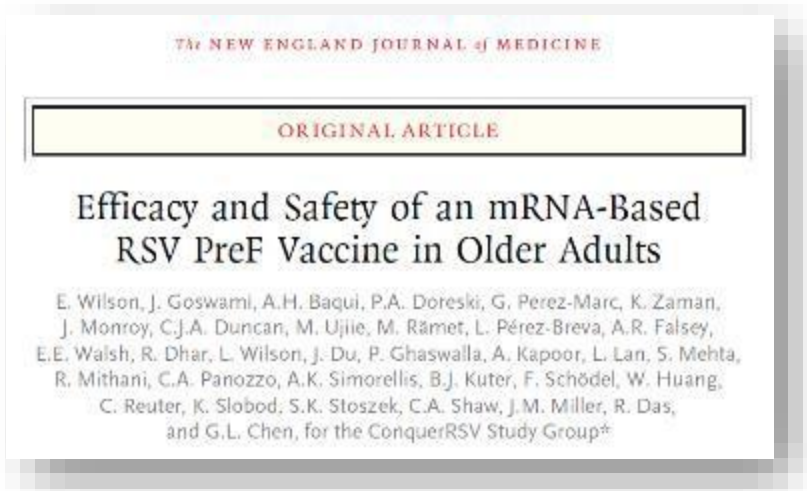
GMR of revaccination vs first dose:

- **RSV-A - 1.08 (0.99, 1.17)**
- **RSV-B - 0.91 (0.84, 0.99)**

Non-inferiority criteria met (LB of 95% CI of GMR > 0.667) for RSV-A and RSV-B

- RSV-A and RSV-B neutralizing antibodies detectable at 12 months post-vaccination
- Revaccination with mRNA-1345 as soon as 1 year after primary vaccination elicits responses similar to that following primary vaccination
- Revaccination met pre-specified non-inferiority success criteria

Vacunas VRS en desarrollo (RNAm-1345)



La eficacia fue del 68,4 % (IC 95 %, 50,9-79,7) frente a enfermedad respiratoria aguda asociada a VRS.

Table 2. Vaccine Efficacy against RSV-Associated Lower Respiratory Tract Disease with at Least Two or at Least Three Signs or Symptoms (Per-Protocol Efficacy Population).*

End Point	mRNA-1345		Placebo		Vaccine Efficacy (CI)†
	no. of participants	*no. of events*	*no. of participants*	*no. of events*	%
RSV-associated lower respiratory tract disease with ≥2 signs or symptoms‡					
Overall	17,572	9	17,516	55	83.7 (66.0 to 92.2)
RSV subtype					
RSV A	17,572	3	17,516	36	91.7 (73.0 to 97.4)
RSV B	17,572	6	17,516	19	68.5 (21.1 to 87.4)
Age group					
60–69 yr	11,168	8	11,118	33	76.0 (48.0 to 88.9)
70–79 yr	5,440	1	5,416	22	95.4 (65.9 to 99.4)
≥80 yr	964	0	982	0	NE (NE to NE)
RSV-associated lower respiratory tract disease with ≥3 signs or symptoms§					
Overall	17,572	3	17,516	17	82.4 (34.8 to 95.3)
RSV subtype					
RSV A	17,572	1	17,516	10	90.0 (22.0 to 98.7)
RSV B	17,572	2	17,516	7	71.5 (−37.0 to 94.1)
Age group					
60–69 yr	11,168	3	11,118	11	72.9 (2.8 to 92.4)
70–79 yr	5,440	0	5,416	6	100 (NE to 100)
≥80 yr	964	0	982	0	NE (NE to NE)

Wilson E et al. N Engl J Med 2023;389:2233-44 DOI: 10.1056/NEJMoa2307079

Resumen

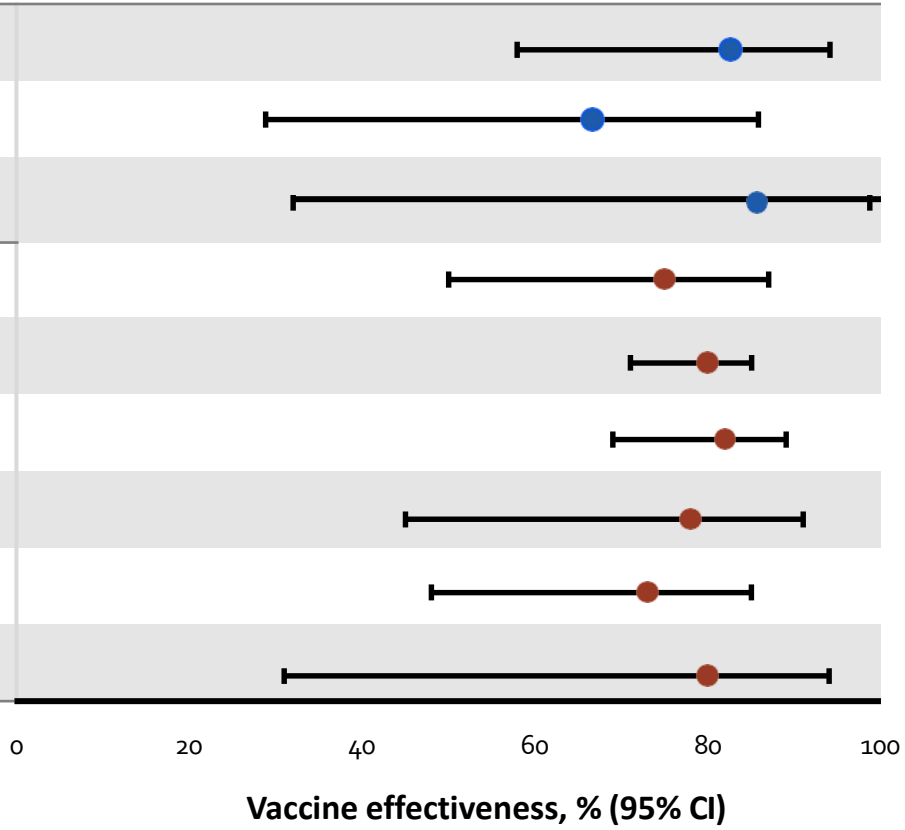
RSV Vaccine (mRNA-1345)

Safety	▪ Vacuna generalmente bien tolerada en >19.700 adultos ≥ 60 años vacunados con 50 µg de dosis autorizada ▪ Sin ADEM, sin casos de SGB relacionados con la vacuna ni otros problemas de seguridad
Efficacy	▪ Eficacia de ~19 meses de seguimiento ▪ Eficacia comparable en individuos ≥ 80 años, con ≥ 1 comorbilidad, y frágiles ▪ Se ha demostrado que previene la enfermedad grave por VRS basándose en el análisis de la dificultad respiratoria
Immunogenicity/ Revaccination	▪ Fuerte respuesta inmunitaria humoral y celular1 (ACIP Feb 2024) ▪ Anticuerpos neutralizantes detectables hasta 12 meses después de la vacunación ▪ La revacunación con ARNm-1345 un 1 año después de la vacunación primaria produce respuestas similares a las de la vacunación primaria ▪ Revacunación bien tolerada; sin problemas de seguridad
Concomitant Administration	▪ Se cumplen los criterios de inmunogenicidad preespecificados y no se observan problemas de seguridad con la administración concomitante de mRNA-1345 con vacunas estándar contra la gripe y COVID-19 (ACIP Feb 2024)

[1] Goswami et al, *JID*, 2024

Observational VE studies show RSV vaccines protect against severe RSV disease, similar to results from trials, although endpoints differ

Outcome	Analysis	Vaccine efficacy/effectiveness, % (95% CI)
Symptomatic, RSV-associated lower respiratory tract disease (LRTD)	GSK trial (≥2 or 3 sx LRTD, primary endpoint)†	83 (58–94)
	Pfizer trial (≥2 sx LRTI, co-primary endpoint)*	67 (29–86)
	Pfizer trial (≥3 sx LRTI, co-primary endpoint)*	86 (32–99)
RSV-associated hospitalization	IVY Network, adults ≥60 years§	75 (50–87)
	VISION, adults ≥60 years, immunocompetent	80 (71–85)
	VHA, adults ≥60 years§	82 (69–89)
	Medicare ESRD, otherwise immunocompetent, ≥65y	78 (45–91)
	VISION, immunocompromised	73 (48–85)
	Medicare ESRD, additional immunocompromise, ≥65y	80 (31–94)



Abbreviations: LRTI = lower respiratory tract infection; LRTD = lower respiratory tract disease; sx = symptoms or signs; y = years

† Papi A, et. al. Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults. *N Engl J Med*. 2023;388:595–608. See slide 44 for detailed definitions.

* Walsh E, et. al. Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults. *N Engl J Med*. 2023;388:1465–77. See slide 44 for detailed definitions.

§ Includes patients with immunocompromising conditions in the displayed VE estimate.

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Muchas gracias por vuestra atención