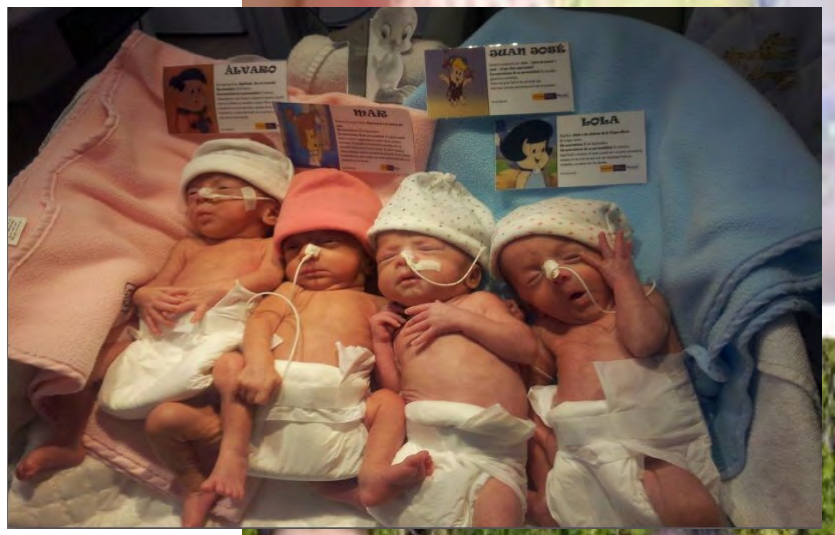
XXVII REUNIÓN

SEUP



Manuel Baca Jefe Servicio Pediatría y Neonatología
Hospital Quirónsalud Málaga;
Responsable del Grupo Pediátrico Uncibay

grupo pediátrico uncibay

CONFLICTO DE INTERESES

He realizado y realizo investigación y formación con,

Pfizer

gsk

AstraZeneca

MSD

SANOFI PASTEUR

moderna

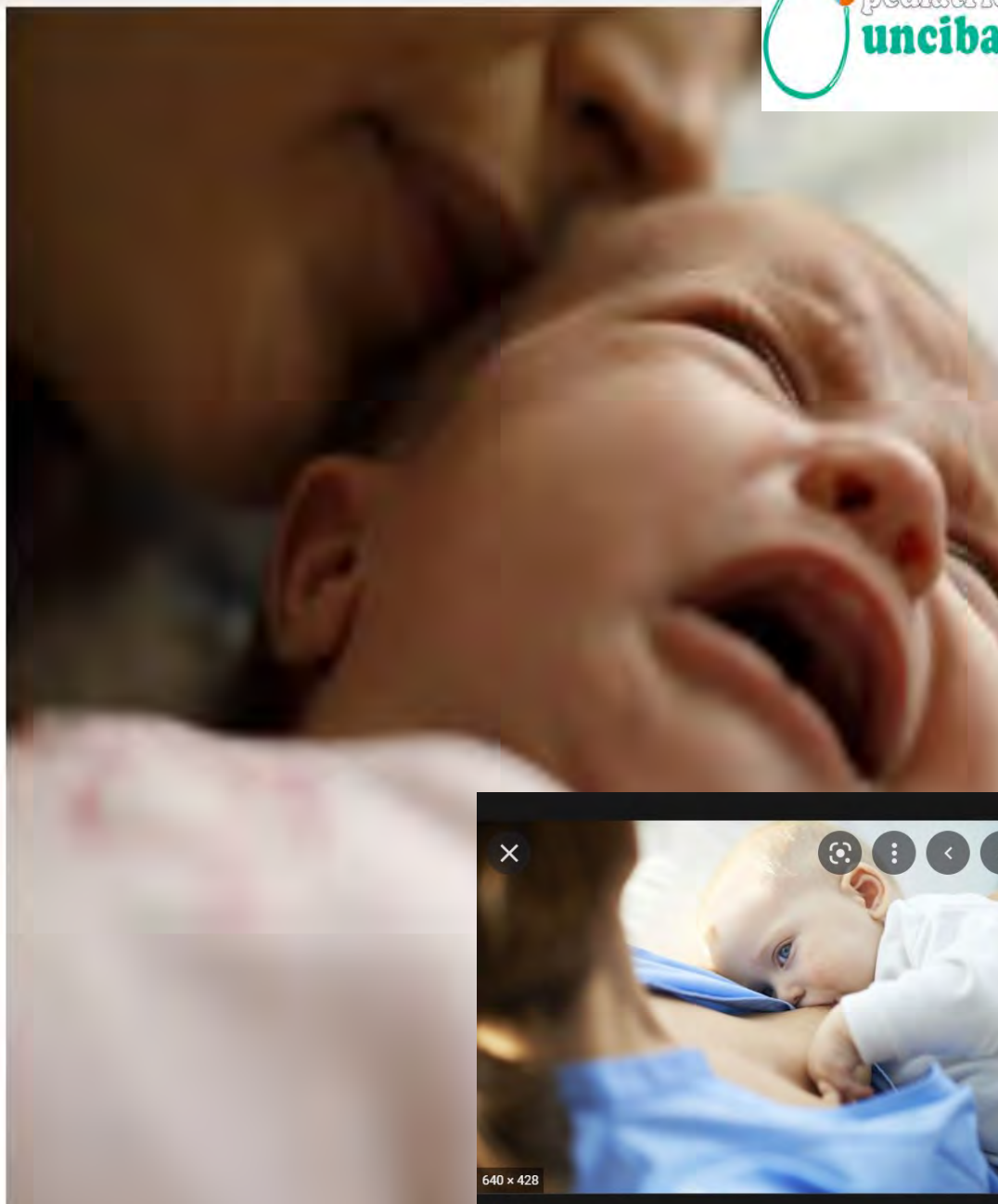
EL PAIS

Mamas & Papas

EL MÉDICO DE MI HIJ@ > | TRIBUNA

Como cada año, la bronquiolitis ya está aquí...

Intentaremos con este artículo aclarar algunos puntos para que quede claro a qué nos enfrentamos y qué herramientas médicas tenemos



MAT-ES-2301191 v1.0 – Mayo 2023

XXVII REUNIÓN SEUP

ABC SOCIEDAD

grupo pediátrico uncibay

Una epidemia de bronquiolitis más agresiva colapsa las UCIs pediátricas

- Cataluña se ha visto obligada a derivar pacientes a hospitales privados. L
  Aragón y Murcia

Navarra.com
LA INFORMACIÓN NO TIENE PRECIO

SALUD

El Gobierno se excusa en que subió la media de la bronquiolitis para justificar el traslado a niños fuera de Navarra

La falta de previsión operativa ha motivado que se prepare un refuerzo pediátrico para atender picos como el sufrido en estos meses.

“*Este año los primeros casos de bronquiolitis aguda por VRS se empezaron a atender en junio y julio. La principal inquietud es no saber cuándo se va a alcanzar el pico máximo de la epidemia, ni si la gravedad será mayor que en otras temporadas o cuántos meses confluirá esta epidemia con la gripe y la covid*”

LA VANGUARDIA

en este momento, hay días en los que no quedaban camas de UCI pediátrica en Cataluña, se nos llenaban y se hizo un esfuerzo por abrir más camas. La hospitalización está repleta. En Ohio, por ejemplo, han tenido que abrir un hospital de campaña para atender niños por culpa del VRS”.

El organismo de la UE recuerda que el VRS causa en la Europa comunitaria, más Gran Bretaña y Noruega unas 213.000 hospitalizaciones anuales en niños menores de cinco años y unas 158.000 de mayores de 65 años

https://www.alimente.elconfidencial.com ›

Para disponer de más camas de hospitalización, se están habilitando camas no pediátricas y suspendiendo cirugías programadas

Mibebeyyo.com - El Mundo

Alarma en Alemania e Italia por el colapso hospitalario debido a un gran brote de virus...

Libertad Digital

DIRECTO Marcador

grupo pediátrico uncibay

INICIO TECNOCIENCIA SALUD Pediatras alemanes alertan de un "colapso" hospitalario "nunca visto" por el VRS

Pediatras alemanes alertan de un "colapso" hospitalario "nunca visto" por el VRS

Alemania está experimentando una fuerte subida de los casos de VRS, un virus *desaparecido* el año pasado que resurge con fuerza.

Libertad Digital 04/11/2021 - 14:54

LA RAZÓN

Sociedad

por bronquiolitis

Los Centros para el Control y Prevención de Enfermedades de Estados Unidos, Europa y otras regiones ya están vigilando con cierta inquietud esta epidemia, que sigue presionando los hospitales

Según informa la Sociedad Española de Urgencias de Pediatría (SEUP)

LA BRONQUIOLITIS ALCANZA ESTAS SEMANAS EL PICO DE MÁXIMA INCIDENCIA EN ESPAÑA

- **Se prevé que la epidemia dure, al menos, 6 semanas más.**
- **Los pediatras de urgencias advierten que los servicios de urgencias se encuentran ya con máxima actividad y las plantas de hospitalización cerca del límite de su capacidad.**
- **En España se producen cada año alrededor de 100.000 episodios de bronqu menores de 2 años, siendo la principal causa de hospitalización en pediatría**

EL PAÍS

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Sociedad

EDUCACIÓN · MEDIO AMBIENTE · IGUALDAD · SANIDAD · CONSUMO · LAICISMO · COMUNICACIÓN

ENFERMEDADES RESPIRATORIAS >

El cóctel de covid, gripe y bronquiolitis que golpea Europa este invierno amenaza con poner bajo "grave presión" los sistemas de salud

rtve Noticias Televisión Radio Deportes Infantil RTVEPlay PlayRadio ElTiempo Playz

VerificaRTVE Mundial de balonmano Directos Radio 5 España Mundo Economía Cultura Ciencia RTVE Igualdad En tu comunidad

» Noticias » Ciencia y tecnología

La triple epidemia de COVID, gripe y bronquiolitis amenaza de nuevo al sistema sanitario

XXVII REUNIÓN SEUP

Limited Options for RSV Prophylaxis and Treatment

XXVII REUNIÓN SEUP

	Infants & Children			Adults	
	Preterm & High-Risk Newborns	Term Infants (<1 yrs of age)	Children (1-5 yrs of age)	High-Risk (E.g. COPD)	Elderly (>65 yrs of age)
Prophylaxis	Synagis® (Palivizumab)	none	none	none	none
Treatment	Virazole® (ribavirin)	Virazole® (ribavirin)	none	none	none

Approved Unmet Medical Need

[1] Villafana et al. Expert Rev Vaccines. 2017 16:1

El laboratorio titular de la autorización de comercialización de Synagis as Astrazeneca AB.
Virazole no está comercializado en España

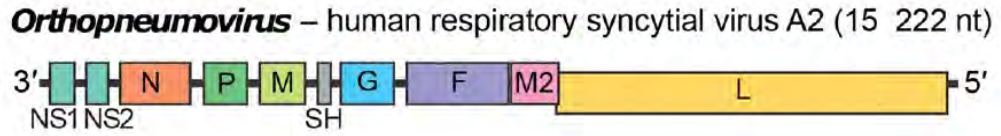
RSV is an enveloped negative-sense RNA virus

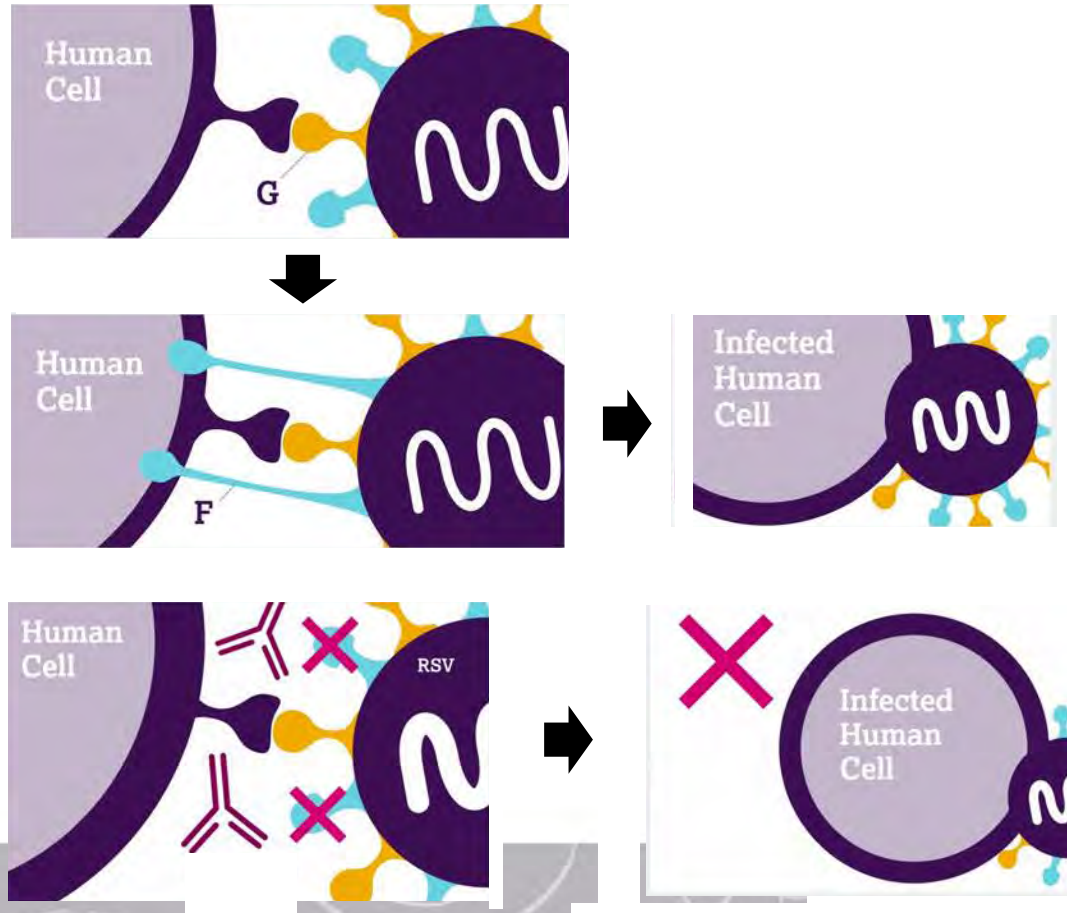
- Two distinct antigenic subtypes (**A and B**)

Glycoprotein (G) – mediates attachment to human epithelial airway cells

Fusion protein (F) – undergoes conformational change to promote fusion of viral and human cell membranes to all infection

F protein is the ***target*** of the neutralizing monoclonal antibody **Synagis® (palivizumab)**





[1] McLellan et al., Science 2013 340:1113;

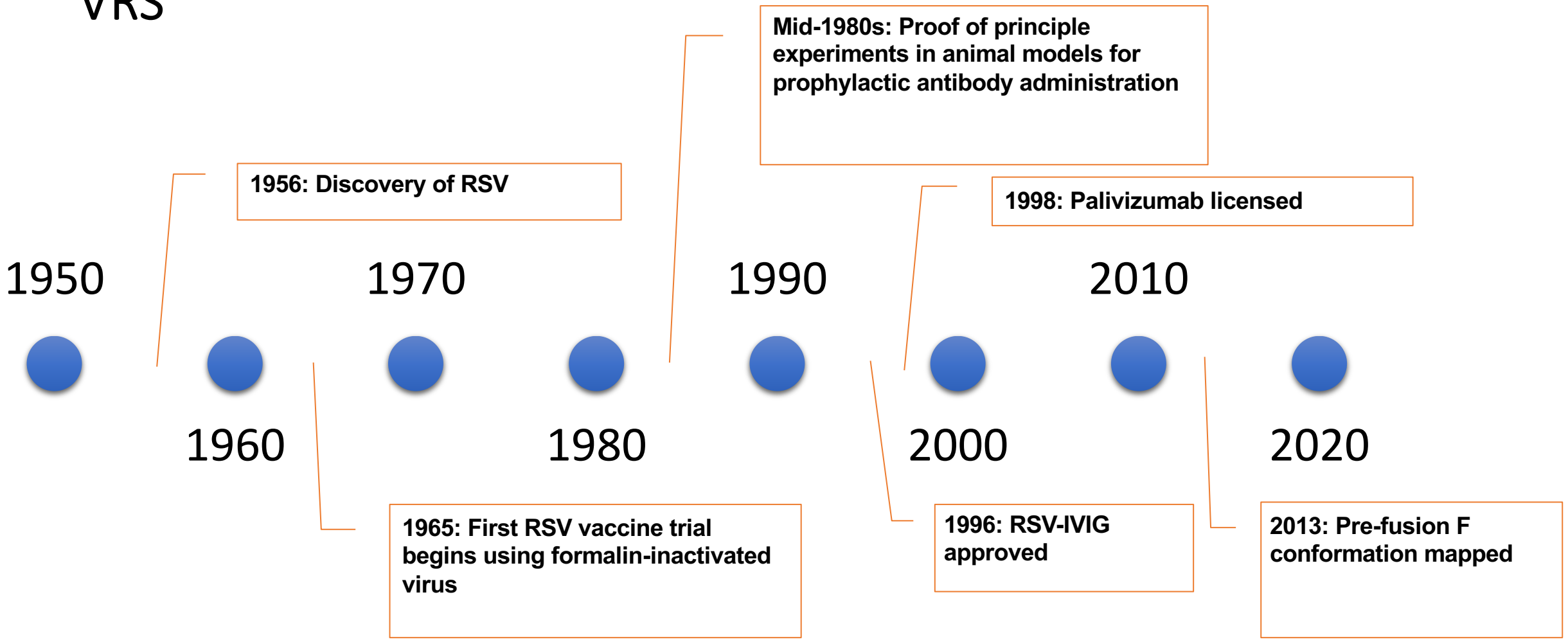
El desarrollo de la prevención VRS en lactantes es un gran reto

- Lactantes poseen una respuesta inmunitaria deficiente, sistema inmune inmaduro, frente al VRS
- Enfermedad grave por VRS se da principalmente en el primer año de vida (<6 meses)
- La inmunidad tras una infección natural es limitada
- Reinfecciones frecuentes
- Supresión de la respuesta inmune por AC maternos circulantes

.1 Mejias et alAnn Allergy Asthma Immunol,2020.

FDA U.S. FOOD & DRUG ADMINISTRATION	• Fast Track designation, Mar 2015 • Breakthrough Therapy designation, Feb 2019
EUROPEAN MEDICINES AGENCY SCIENCE MEDICINES HEALTH	• PRIME scheme, Jan 2019
AMED Japan Agency for Medical Research and Development (AMED)	• Designated a product of high priority, Feb 2019
Medicines & Healthcare products Regulatory Agency	• Promising Innovative Medicine, Jan 2021 (UK)
NATIONAL MEDICAL PRODUCTS ADMINISTRATION 国家药品监督管理局	• Breakthrough Therapy designation, Jan 2021 (China)

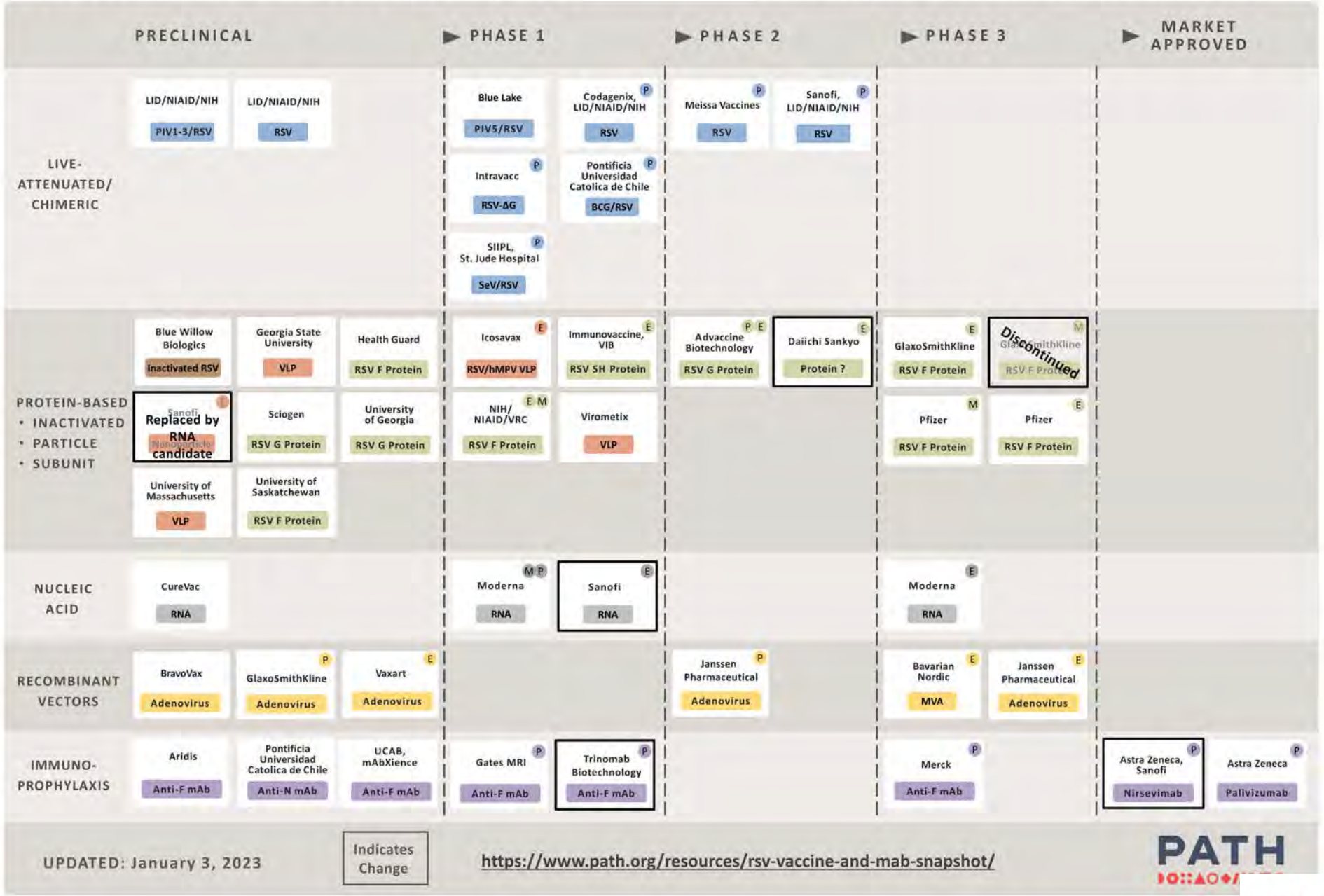
Eventos importantes en los últimos años en la Prevención VRS



Sande CJ. Implementation strategies for passive respiratory syncytial virus immunisation. Lancet Infect Dis 2021; 21(9): 1200-1.

RSV Vaccine and mAb Snapshot

TARGET INDICATION: (P) =PEDIATRIC (M) =MATERNAL (E) =ELDERLY



UPDATED: January 3, 2023

Indicates Change

https://www.path.org/resources/rsv-vaccine-and-mab-snapshot/

PATH

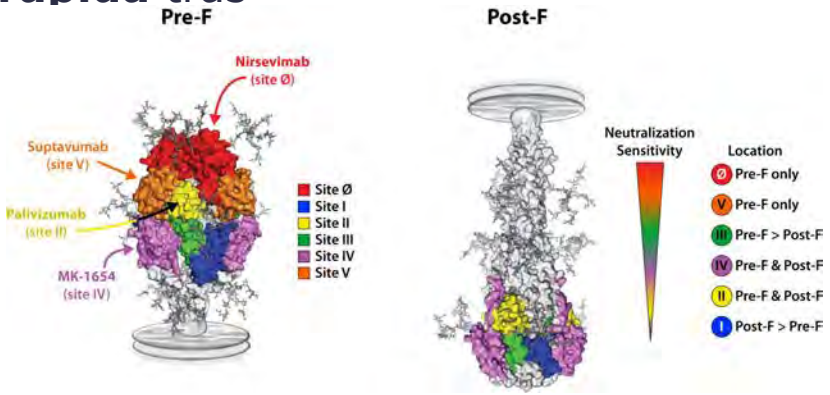
AC de acción prolongada : buscando la protección para todos los lactantes en su primera temporada de VRS

Tecnología

- AcM IgG1 completamente humano de alta potencia derivado de linfocitos B humanos
- YTE: tecnología de prolongación de semivida

Aspectos destacados de las posibles propiedades

- **Inmunización pasiva proporcionando protección directa y rápida** tras la administración
- Administración 1 dosis intramuscular
- Dosis fija IM (<5 kg, 50 mg; ≥5kg, 100 mg) / 2–8 °C



Criterio de valoración clínico y población diana

- prevención de infección de vías respiratoria inferiores por VRS
- Todos los lactantes (incluidos prematuros) que se exponen a su 1era temporada de VRS
- Niños con enfermedad pulmonar crónica/cardiopatía congénita en su 1era y 2da temporada de VRS

Referencia bibliográfica: Zhu Q, et al. Sci Transl Med. 2017;9(388).

NIRSEVIMAB HA SIDO APROBADO POR LA EMA Y ESTA PENDIENTE DE PRECIO Y REEMBOLSO EN ESPAÑA

Estrategias de prevención VRS

XXVII REUNIÓN SEUP

Lactantes < 6 meses

Protección enferm. grave
Stma Inmune inmaduro
Naive para VRS
Mala respuesta vacunas VRS

Anticuerpos Monoclonales

Embarazadas

Seguridad fetal
Transf. Ac placentarios
Inmunidad preexistente
(Ac neutralizantes)

Vacunas de subunidades
No vacunas vivas
No adjuvantes

INMUNIZACIÓN PASIVA

Niños > 6 meses

Mejor respuesta inmune
No naive para VRS
Transmisión enfermedad
Protección de rebaño

Vacunas vivas atenuadas
basadas en vectores virales

Ancianos (> 65 años)

Inmunosenescencia
Riesgo de enferm. graves
Patologías de base
Inmunidad preexistente
(infecciones previas por VRS)

Vacunas de subunidades con adjuvantes
No vacunas vivas

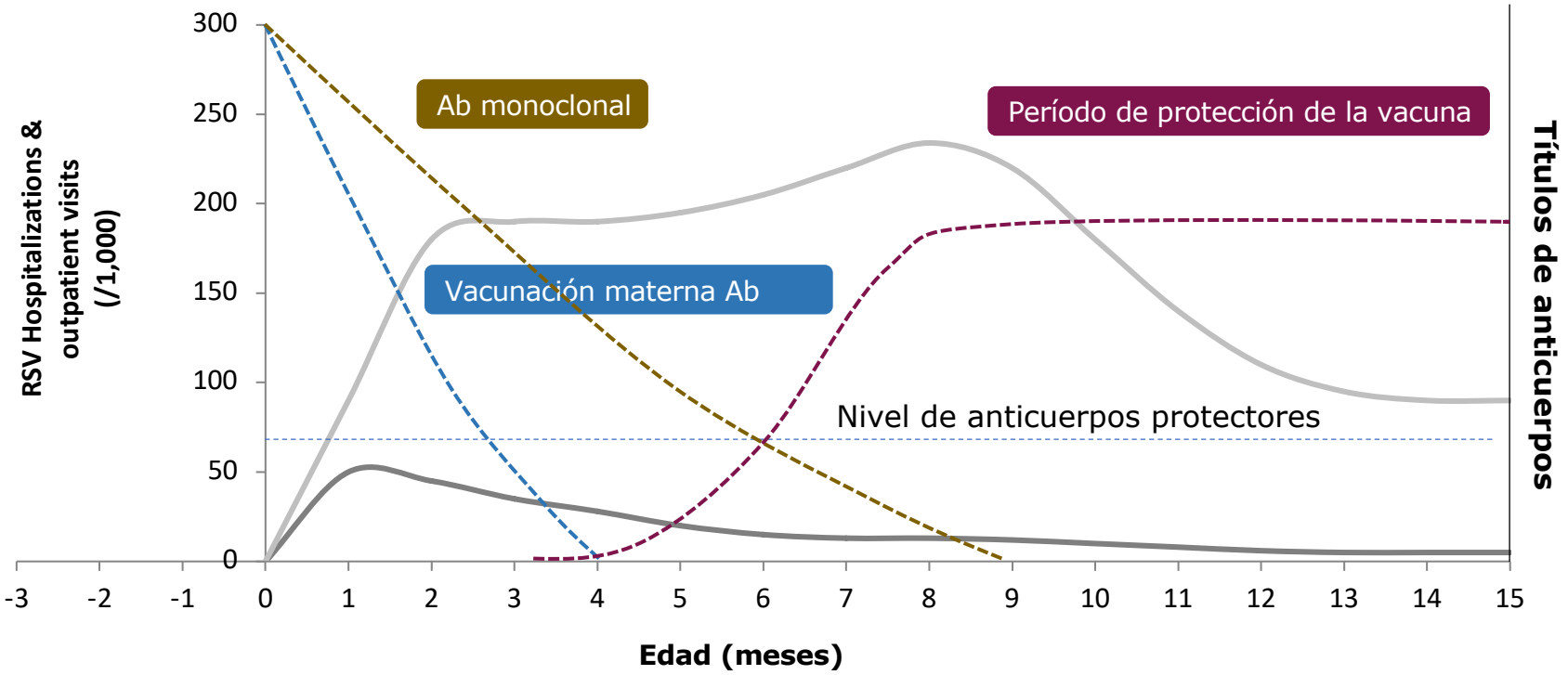
(Ensayos Fase III > 60 a)

INMUNIZACIÓN ACTIVA

Mejias A et al. Ann Allergy Asthma Immunol 125 (2020) 36e46

grupo pediátrico uncibay

El reto de proteger al lactante frente al VRS



Visitas ambulatorias por VRS por edad (Hall et al., 2009)

Hospitalizaciones por VRS por edad (Stockman et al., 2012)

Títulos de Ab neutralizante activo con la vacuna

Títulos de Ab neutralizante pasivo de la inmunización materna

Ab neutralizante pasivo de inmunización con monoclonal de vida media extendida

Esposito S et al. Front Immunol 2022 April

MEDI8897 Phase 2b Pivotal Registration Study

A Phase 2b Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of MEDI8897, a Monoclonal Antibody with an Extended Half-Life Against Respiratory Syncytial Virus, in Healthy Preterm Infants

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 30, 2020 VOL. 383 NO. 5

Single-Dose Nirsevimab for Prevention of RSV in Preterm Infants

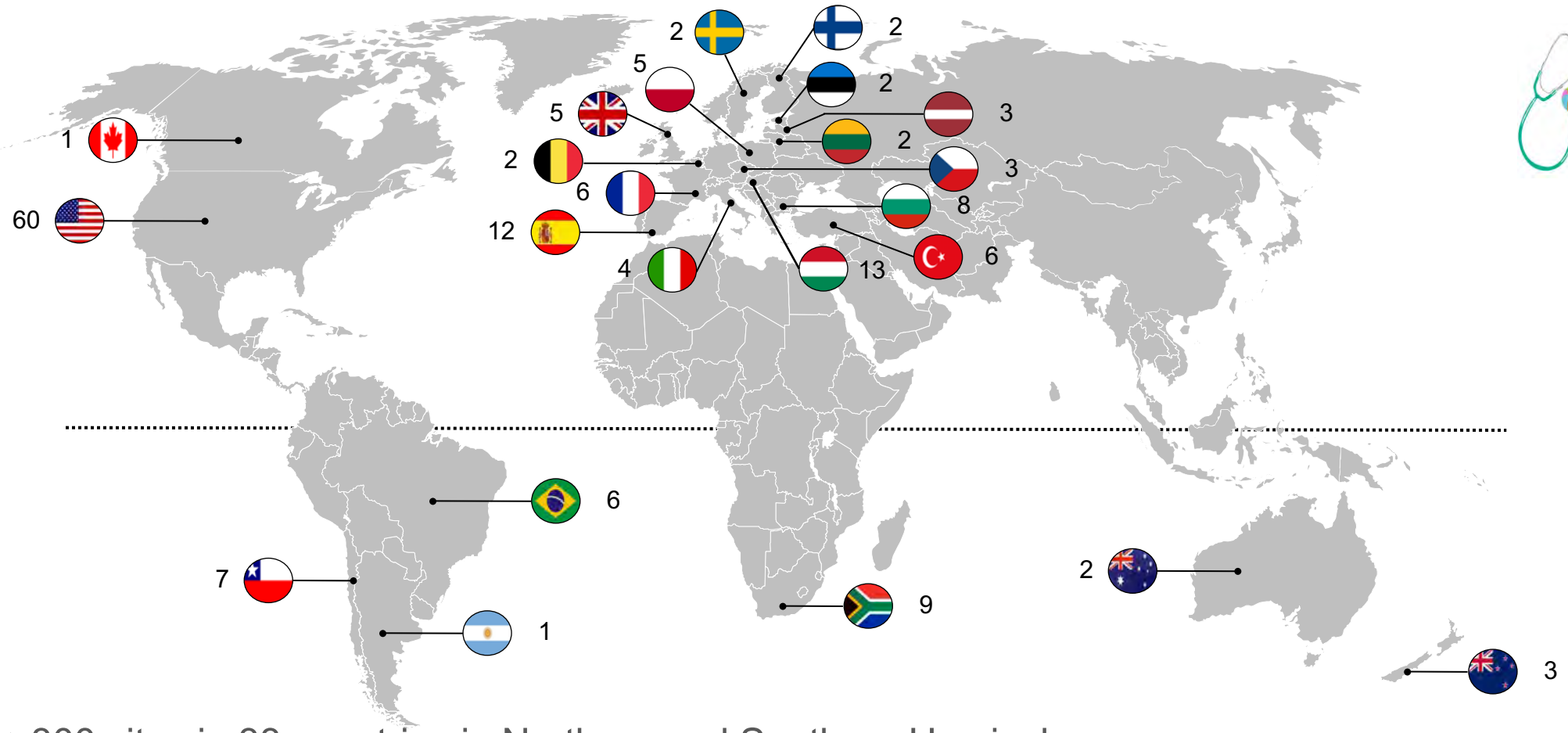
M. Pamela Griffin, M.D., Yuan Yuan, Ph.D., Therese Takas, B.S., Joseph B. Domachowske, M.D., Shabir A. Madhi, M.B., B.Ch., Ph.D., Paolo Manzoni, M.D., Ph.D., Eric A.F. Simões, M.D., Mark T. Esser, Ph.D., Anis A. Khan, Ph.D., Filip Dubovsky, M.D., Tonya Villafana, Ph.D., and John P. DeVincenzo, M.D., for the Nirsevimab Study Group*

NIRSEVIMAB HA SIDO APROBADO POR LA EMA Y ESTÁ PENDIENTE DE PRECIO Y REEMBOLSO EN ESPAÑA

grupo pediátrico uncibay

GEOGRAPHICAL DISTRIBUTION:

Randomized, Double-blind, Placebo-controlled Study to Evaluate the Safety and Efficacy of MEDI8897 Monoclonal Antibody, Extended Half-life against Respiratory Syncytial Virus,



- **Location:** >300 sites in 33 countries in Northern and Southern Hemispheres
  - Northern Hemisphere (Austria, Belgium, Bulgaria, Canada, Czech Republic, Estonia, Finland, France, Germany, Hungary, Israel, Italy, Japan, Latvia, Lithuania, Mexico, Poland, Republic of Korea, Russia, Spain, Sweden, Turkey, Ukraine, United Kingdom, and United States of America [USA])
  - Southern Hemisphere (Argentina, Australia, Brazil, Chile, Colombia, New Zealand, Panama, and South Africa).

20

Case definitions of increasing disease severity

See **Ron Dagan,[1] Laura L. Hammitt[2], Beatriz Seoane Nuñez[3], Manuel Baca Cots[4]**, et al, N Engl J Med 2022;386:837-46 for details

1. MA RSV LRTI: the infant should be presented for medical care and:

RSV positive	AND	Lower respiratory tract involvement	AND	Sign of severity
Positive by central laboratory RT-PCR assay		**At least one sign of:** • Rhonchi • Rales • Crackles • Wheeze		**At least one sign of:** • Increased respiratory rate* • Hypoxaemia† • Acute hypoxic or ventilatory failure • New onset apnoea • Nasal flaring • Retractions • Grunting • Dehydration

2. **Medically attended RSV LRTI with hospitalisation** corresponds to infants who met the primary case definition and were hospitalised
3. **Medically attended RSV LRTI (very severe)** corresponds to infants who were hospitalised and required supplemental oxygen or intravenous fluids

*Increased respiratory rate at rest (age <2 months, ≥60 breaths/min; age 2 to 6 months, ≥50 breaths/min; age >6 months to 2 years, ≥40 breaths/min)
†Hypoxemia (in room air - oxygen saturation <95% at altitudes ≤1800 meters or <92% at altitudes >1800 meters)
RT PCR, reverse transcriptase-polymerase chain reaction.

MAT-ES-2301191 v1.0 – Mayo 2023

Schedule of Evaluations – Day 1 to Day 511

Local Amendment – European Union

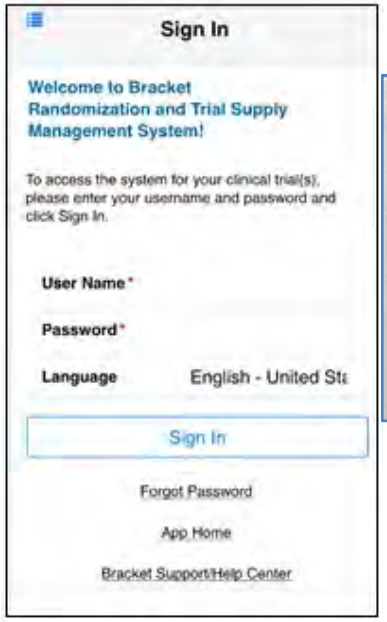
Visit Number	V2	TC	V3	V4	V5	V6	V7	Telephone Call			LRTI		Skin Reaction
Procedure / Study Day	**D1**	**D8 (± 2 days)**	**D15 (± 2 days)**	**D31 (± 5 days)**	**D91 (± 7 days)**	**D151 (± 7 days)**	**D361 (± 7 days)**	**D1-151 Q2W (± 5 days)**	**D152-361 monthly (± 5 days)**	**D362-511 Q2W (± 5 days)**	**D1-361 as needed**	**D362-511 as needed**	**D1-361 as needed**
Medical history update	X		X	X	X	X	X						
Physical examination	X		X	X	X	X	X						
Weight	X		X	X	X	X	X						
Vital signs	X		X	X	X	X	X						
Blood sample for PK, ADA	X		X (PK only)			X	X				X		
Assessment of AEs/SAEs	X	X	X	X	X	X	X	X	X		X		X
Assessment of AESIs and NOCDs	X	X	X	X	X	X	X	X	X		X		X
Concomitant medications	X	X	X	X	X	X	X	X	X		X		X
Verify eligibility criteria	X												
Randomization	X												
Investigational product administration	X												
Assessment of LRTI											X	X	
Nasal swab collection											X	X	
Assessment of skin reaction													X
Telephone contact		X						X	X	X (respiratory illness inquiry only)			
HRU and caregiver burden											X		

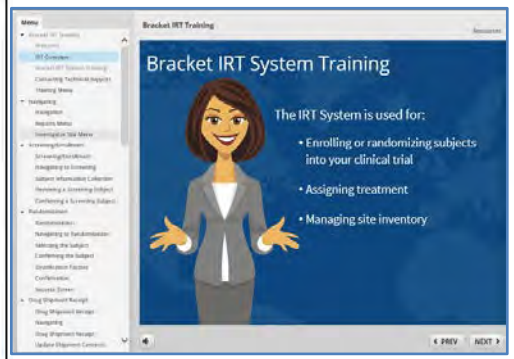
Bracket is now… SIGNANT HEALTH
Science. Technology. Service.™

XXVII REUNIÓN SEUP

Medimmune D5290C00004 MELODY
IXRS (Signant) System Site Training

IXRS (Signant) System Transactions





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Ensayo fase2b Nirsevimab– Placebo controlled 2:1 preterm 29-34 GA – 1 single i.m. dose 50 mg

End Points and Analyses	Nirsevimab (N=969)	Placebo (N=484)	Relative Difference (95% CI)	P Value
	number (percent)		%	
Medically attended RSV-associated lower respiratory tract infection				
Poisson regression with robust variance			70.1 (52.3–81.2)	<0.001
Observed events	25 (2.6)	46 (9.5)		
Participants with imputation of data†	24 (2.5)	11 (2.3)		
Cochran–Mantel–Haenszel test: observed events	25 (2.6)	46 (9.5)	72.9 (56.5–83.1)	<0.001
Hospitalization for RSV-associated lower respiratory tract infection				
Poisson regression with robust variance			78.4 (51.9–90.3)	<0.001
Observed events	8 (0.8)	20 (4.1)		
Participants with imputation of data†	24 (2.5)	11 (2.3)		
Cochran–Mantel–Haenszel test: observed events	8 (0.8)	20 (4.1)	80.0 (55.0–91.1)	<0.001

Griffin P et al. NEJM 2020

NIRSEVIMAB HA SIDO APROBADO POR LA EMA Y ESTA PENDIENTE DE PRECIO Y REEMBOLSO EN ESPAÑA

Fase 3

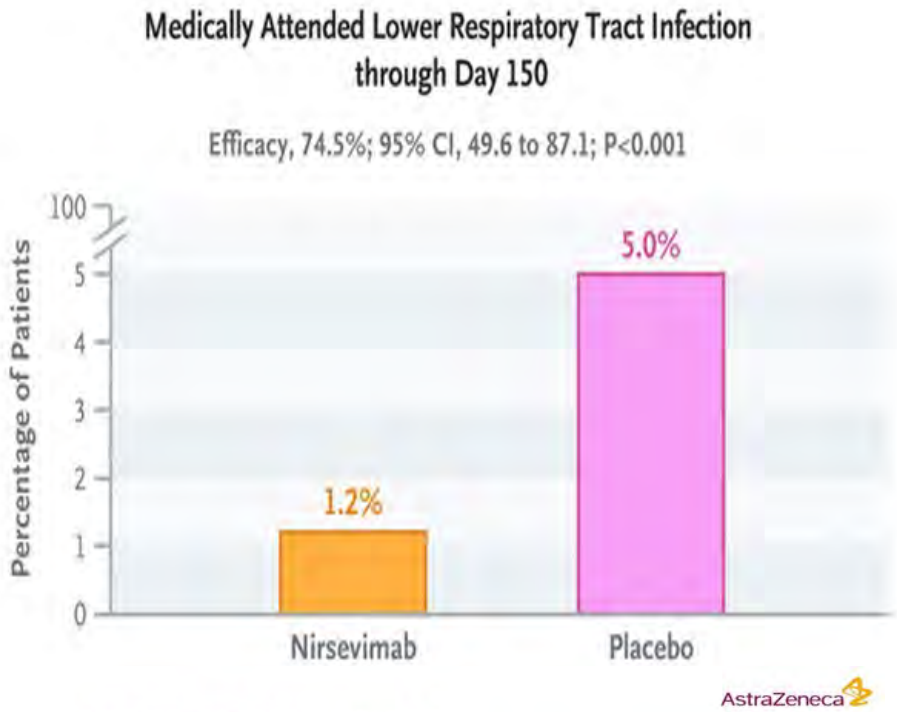
XXVII REUNIÓN SEUP

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants

Laura L. Hammitt, M.D., Ron Dagan, M.D., Yuan Yuan, Ph.D., Manuel Baca Cots, M.D., Miroslava Bosheva, M.D., Shabir A. Madhi, Ph.D., William J. Muller, Ph.D., Heather J. Zar, Ph.D., Dennis Brooks, M.D., Amy Grenham, M.Sc., Ulrika Wählby Hamrén, Ph.D., Vaishali S. Mankad, M.D., Pin Ren, Ph.D., Therese Takas, B.Sc., Michael E. Abram, Ph.D., Amanda Leach, M.R.C.P.C.H., M. Pamela Griffin, M.D., and Tonya Villafana, Ph.D., for the MELODY Study Group*



MEDI8897 (Nirsevimab)

Melody (D5290C00004) Study Protocol Overview

Ebube Onwasigwe, MD and Melissa Larick, Scientist for Clinical Research

Strictly Confidential
26 July 2021

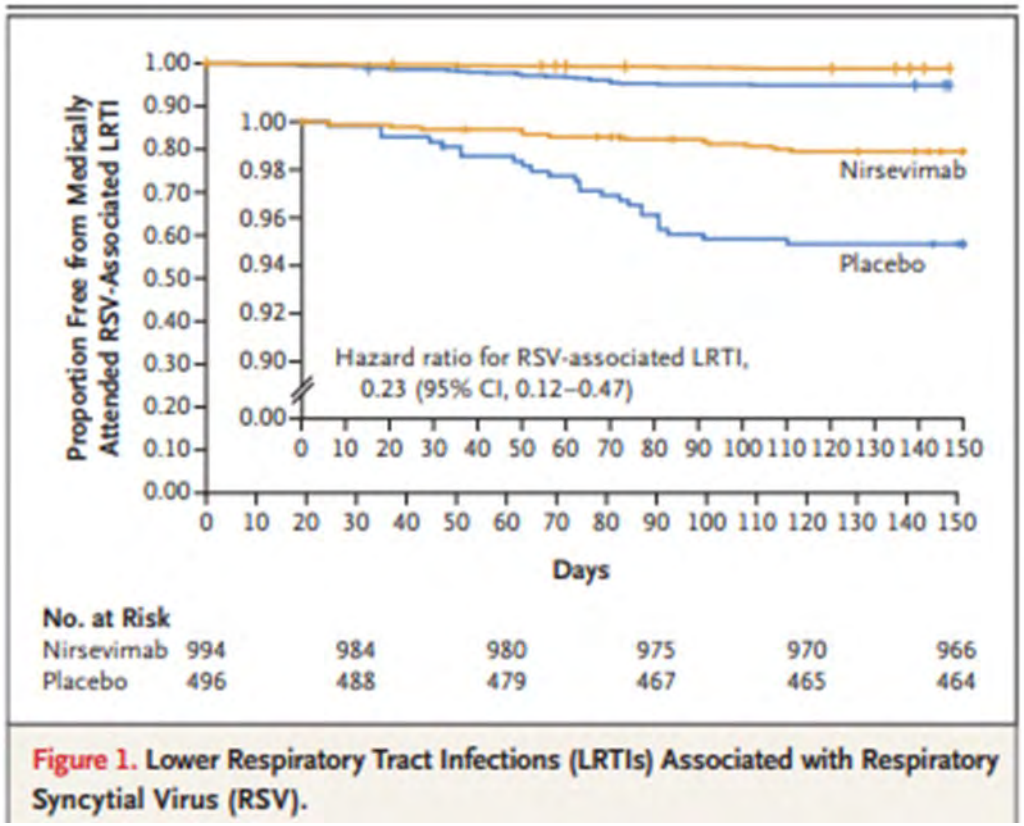


Figure 1. Lower Respiratory Tract Infections (LRTIs) Associated with Respiratory Syncytial Virus (RSV).

Hammit LL et al. Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants N Engl J Med 2022;386:837-46.DOI: 10.1056/NEJMoa2110275

Table 3. Outcomes through 150 Days after the Injection.*

Outcome	Nirsevimab (N=686)	Placebo (N=342)	Efficacy (95% CI)†	Cases Averted per 1000 Infants Treated (95% CI)‡	Number Needed to Treat (95% CI)§
	no. (%)				
Medically attended RSV-associated lower respiratory tract infection on any test result¶	17 (2.5)	37 (10.8)	77.0 (59.8 to 86.8)	83.4 (62.0 to 105.0)	12 (10 to 17)
Medically attended RSV-associated lower respiratory tract infection on central test result¶	15 (2.2)	33 (9.6)	77.2 (58.7 to 87.5)	74.7 (53.0 to 95.0)	14 (11 to 19)
Medically attended lower respiratory tract infection of any cause¶	60 (8.7)	62 (18.1)	51.5 (32.6 to 65.2)	93.6 (63.0 to 124.0)	11 (9 to 16)
Hospitalization for any respiratory illness due to RSV on any test result	9 (1.3)	11 (3.2)	59.0 (2.1 to 82.9)	19.0 (5.5 to 32.0)	53 (32 to 182)
Hospitalization for any respiratory illness due to RSV on central test result	7 (1.0)	9 (2.6)	61.1 (−3.7 to 85.4)	16.1 (4.5 to 28.0)	62 (36 to 223)
Hospitalization for any respiratory illness of any cause	16 (2.3)	14 (4.1)	42.8 (−15.8 to 71.7)	17.7 (2.0 to 33.0)	57 (31 to 500)

NIRSEVIMAB HA SIDO APROBADO POR LA EMA Y ESTA PENDIENTE DE PRECIO Y REEMBOLSO EN ESPAÑA

Hammit LL et al. Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants N Engl J Med 2022;386:837-46.DOI: 10.1056/NEJMoa2110275

Table 4. Adverse Events That Occurred through 360 Days after the Injection.*

Variable	Nirsevimab (N=987)	Placebo (N=491)	Total (N=1478)
		no. of participants (%)	
Any adverse event	863 (87.4)	426 (86.8)	1289 (87.2)
Considered to be related to the trial regimen	10 (1.0)	7 (1.4)	17 (1.2)
Occurred ≤1 day after the injection	18 (1.8)	3 (0.6)	21 (1.4)
Occurred ≤3 days after the injection	56 (5.7)	23 (4.7)	79 (5.3)
Occurred ≤7 days after the injection	132 (13.4)	63 (12.8)	195 (13.2)
Adverse event of grade ≥3 severity	36 (3.6)	21 (4.3)	57 (3.9)
Adverse event that resulted in death	3 (0.3)	0	3 (0.2)
Serious adverse event†	67 (6.8)	36 (7.3)	103 (7.0)
Considered to be related to the trial regimen	0	0	0
Adverse event of special interest‡	1 (0.1)	0	1 (0.1)
Adverse event related to Covid-19	7 (0.7)	7 (1.4)	14 (0.9)
Confirmed case of Covid-19§	6 (0.6)	6 (1.2)	12 (0.8)
Adverse event suspected to be related to Covid-19¶	1 (0.1)	1 (0.2)	2 (0.1)

NIRSEVIMAB HA SIDO APROBADO POR LA EMA Y ESTA PENDIENTE DE PRECIO Y REEMBOLSO EN ESPAÑA

Hammit LL et al. Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants N Engl J Med 2022;386:837-46.DOI: 10.1056/NEJMoa2110275

Nueva generación de anticuerpos monoclonales frente a VRS

1. Más potencia
2. Más duración: 1 dosis protege durante 5 meses
3. Protección INMEDIATA
4. Aplicación a TODOS los lactantes

Sparrow E et al. Vaccine 2022, Mazur et al. 2022

Autorizacion de comercialización de nirsevimab recomendado por la EMA el 16-sep-2022

Nirsevimab MAA accepted by EMA

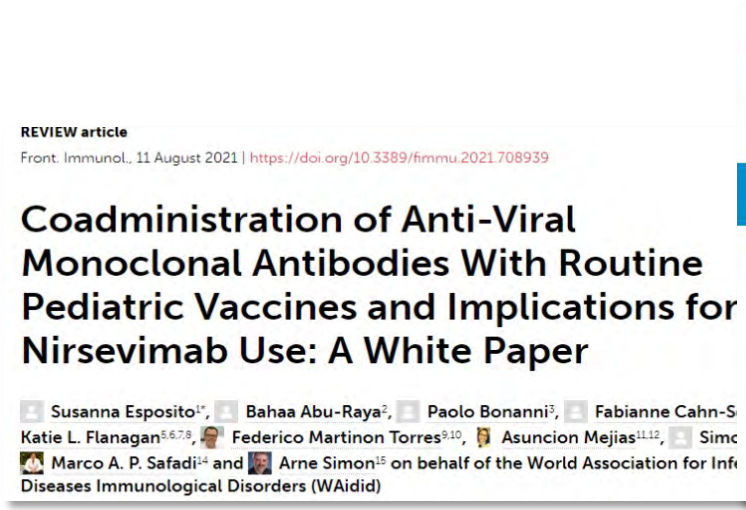
It is very exciting time to be part of MEDI program now when AZ's Marketing Authorization Application for Nirsevimab has been accepted under accelerated assessment procedure by European Medicines Agency (EMA), for the prevention of medically attended LRTI in all infants through their first RSV season. You can read more in this press release. Thank you everyone for doing your absolute best in order to bring this medica tion close

Recomendado para la prevención de VRS en TODOS, incluidos con patología de riesgo, los recién nacidos y lactantes durante su primera estación de VRS

NIRSEVIMAB HA SIDO APROBADO POR LA EMA Y ESTA PENDIENTE DE PRECIO Y REEMBOLSO EN ESPAÑA

Coadministración con vacunas pediátricas rutinarias

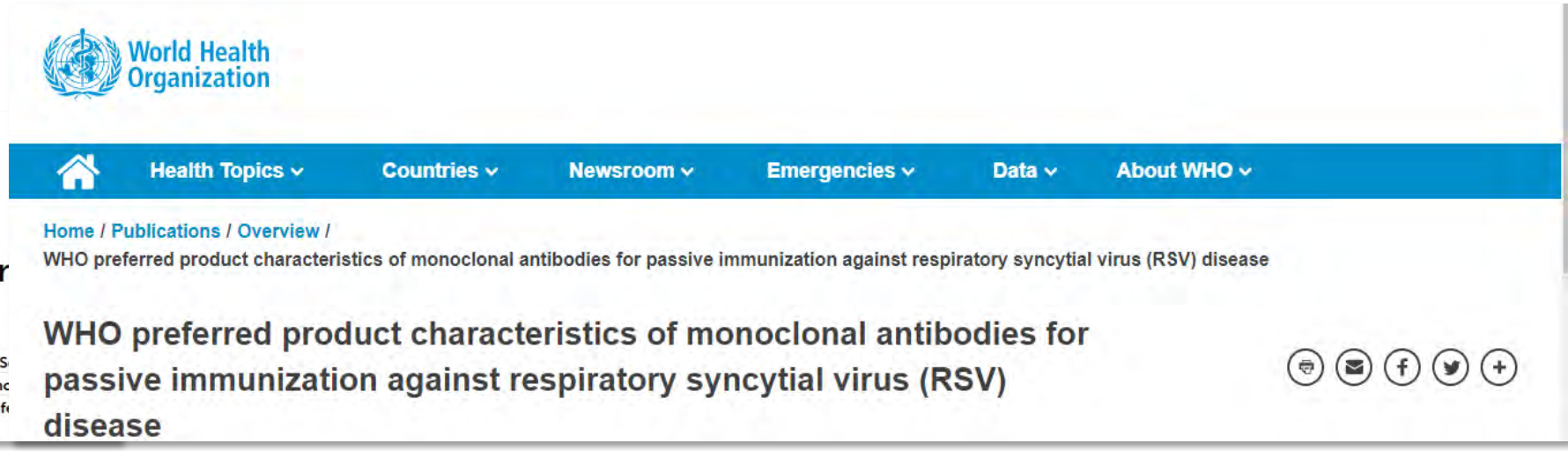
XXVII REUNIÓN SEUP


REVIEW article

Front. Immunol., 11 August 2021 | https://doi.org/10.3389/fimmu.2021.708939

Coadministration of Anti-Viral Monoclonal Antibodies With Routine Pediatric Vaccines and Implications for Nirsevimab Use: A White Paper

Susanna Esposito[1*], Bahaa Abu-Raya[2], Paolo Bonanni[3], Fabianne Cahn-S
Katie L. Flanagan[5,6,7,8], Federico Martinon Torres[9,10], Asuncion Mejias[11,12], Simo
Marco A. P. Safadi[14] and Arne Simon[15] on behalf of the World Association for Inf
Diseases Immunological Disorders (WAidid)


World Health Organization

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WHO preferred product characteristics of monoclonal antibodies for passive immunization against respiratory syncytial virus (RSV) disease

WHO preferred product characteristics of monoclonal antibodies for passive immunization against respiratory syncytial virus (RSV) disease

Desarrollado para administrarse como las estrategias de inmunización de rutina, que tienen coberturas de > 90%[1]. Sin necesidad de visitas adicionales, proporcionando protección a los niños nacidos dentro y fuera de la temporada[2,3]

1- Hill HA et al. MMWR Morb Mortal Wkly Rep 2019; 68: 913–918.
2-Rodriguez-Fernandez R et al. Pediatr Infect Dis J 2021
3-Esposito S et al. Frontiers in immunology 2021; 12, 708939.

NIRSEVIMAB HA SIDO APROBADO POR LA EMA Y ESTÁ PENDIENTE DE PRECIO Y REEMBOLSO EN ESPAÑA

Pooled Efficacy of Nirsevimab Against RSV Lower Respiratory Tract Infection in Preterm and Term Infants

Eric AF Simões[1], *Shabir A Madhi*[2], *Heather J Zar*[3], *Miroslava Bosheva*[4], *William J Muller*[5], *Therese Takas*[6], *Anna Berglind*[8], *M Pamela Griffin*[6], *Yuan Yuan*[6], *Ulrika Wählby Hamrén*[7], *Amanda Leach*[6], *Tonya Villafana*[6]

[1]Children's Hospital Colorado, Aurora, CO, USA; [2]South African Medical Research Council Vaccines and Infectious Diseases Analytics Research Unit, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; [3]Department of Paediatrics and Child Health, Red Cross Children's Hospital, and SA-MRC Unit on Child and Adolescent Health, University of Cape Town, South Africa; [4]University Multiprofile Hospital for Active Treatment Sv. Georgi Medical University, Plovdiv, Bulgaria; [5]Ann & Robert H. Lurie Children's Hospital of Chicago and Northwestern University Feinberg School of Medicine, IL, USA; [6]Vaccines and Immune Therapies, BioPharmaceuticals R&D, AstraZeneca, Gaithersburg, MD, USA; 7BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden

Congress Presentation: European Society for Pediatric Infectious Diseases Congress 2022, Athens, Greece

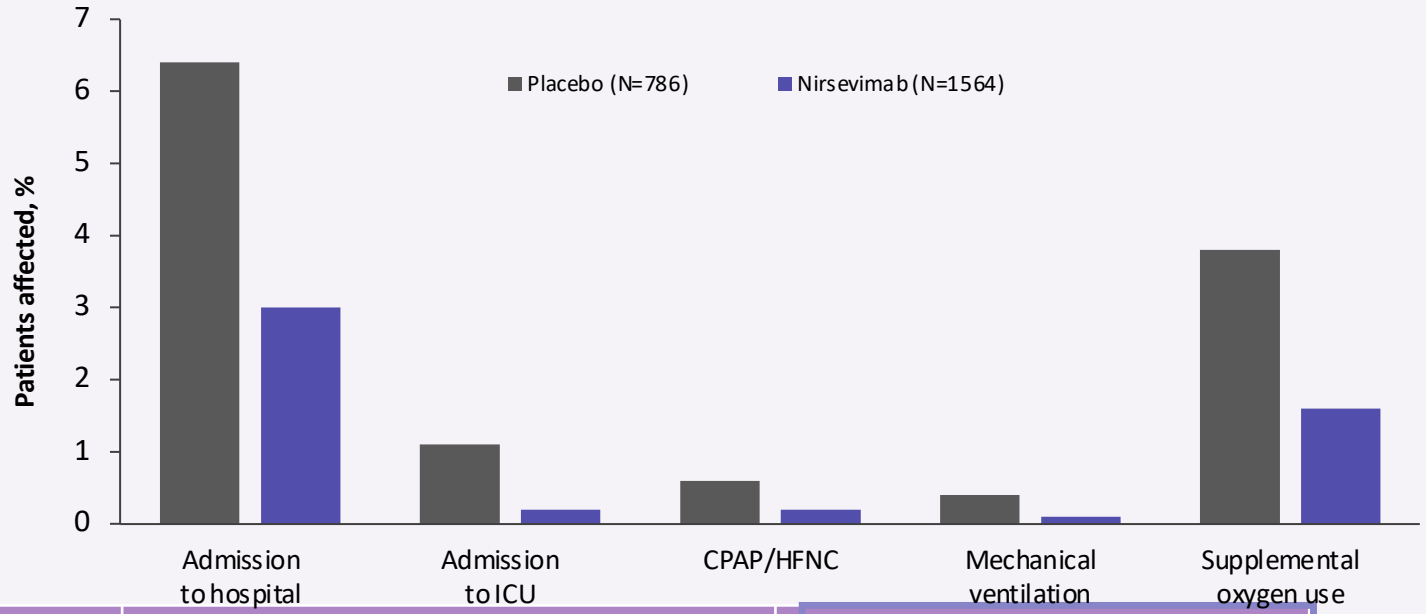
ESPID 2022 ATHENS & ONLINE 9-13 MAY

grupo pediátrico uncibay

NIRSEVIMAB HA SIDO APROBADO POR LA EMA Y ESTA PENDIENTE DE PRECIO Y REEMBOLSO EN ESPAÑA

Visitas ambulatorias y uso de antibióticos

(nirsevimab comparado con placebo)



	Placebo (N=786)	Nirsevimab (N=1564)	
	Events per 100 infants‡ (95% CI)	Events per 100 infants‡ (95% CI)	RRR† (95% CI)
Outpatient visits for all-cause MA LRTI	28.1 (23.5, 33.8)	16.3 (13.9, 19.3)	**41.9 (25.7, 54.6)**
Antibiotic course	34.6 (29.0, 41.2)	26.4 (22.8, 30.6)	**23.6 (3.8, 39.3)**

Simões EAF et al. The Lancet Child & Adolescent Health. 2023

XXVII REUNIÓN SEUP

ESPID 2023 LISBON & ONLINE 8 - 12 MAY

Nirsevimab efficacy against RSV lower respiratory tract infection in preterm and term infants by subtype: Pooled analysis of Phase 2b and Phase 3 MELODY trials

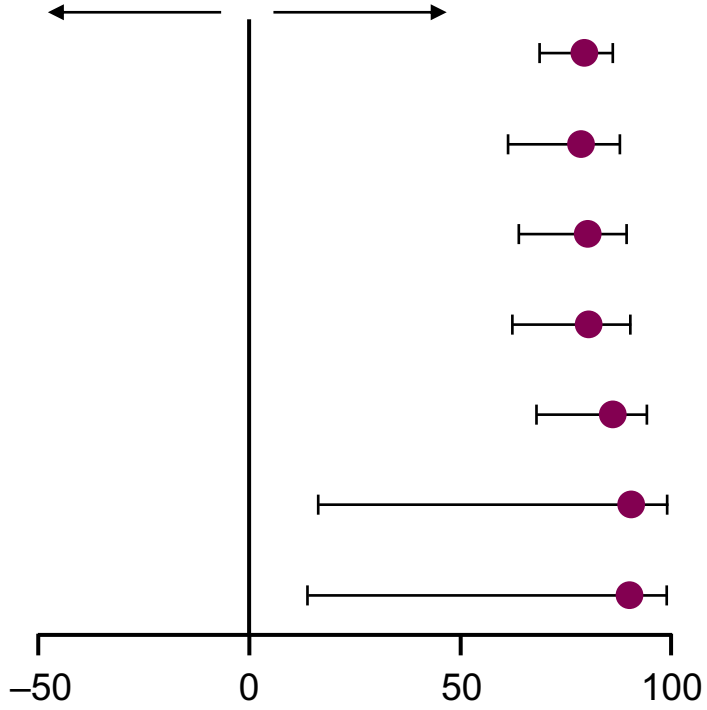
Shabir A. Madhi,[1] Amanda Leach,[2] Manuel Baca Cots,[3] Celeste Cummings,[4] Alexander Currie,[5] Ron Dagan,[6] Joseph B Domachowske,[7] Amy Grenham,[2] Laura L. Hammitt,[8] Ulrika Wählby-Hamrén,[9] Elizabeth J. Kelly,[2] Conrado Juan Llapur,[10] William J. Muller,[11] Jose M. Novoa,[12] Xavier Saez Llorens,[13] Eric A. F. Simões,[14] Therese Takas,[2] Tonya Villafana[2]

[1]South African Medical Research Council Vaccines and Infectious Diseases Analytics Research Unit, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; [2]Clinical Development, Biopharmaceuticals R&D, AstraZeneca, Gaithersburg, MD, USA; [3]Quirónsalud Málaga Hospital, Malaga, Spain; [4]Late Respiratory & Immunology, Biopharmaceuticals R&D, AstraZeneca, Durham, NC, USA; [5]Clinical Development, Vaccines and Immune Therapies, BioPharmaceuticals R&D, AstraZeneca, Cambridge, UK; [6]The Shraga Segal Department of Microbiology, Immunology and Genetics, Faculty of Health Sciences of the Ben-Gurion University of the Negev, Beer-Sheva, Israel; [7]State University of New York Upstate Medical University, Syracuse, NY, USA; [8]Department of International Health, Johns Hopkins University, Baltimore, MD, USA; [9]Clinical Pharmacology and Quantitative Pharmacology, AstraZeneca, Gothenburg, Sweden; [10]Hospital del Niño Jesús, San Miguel de Tucumán, Argentina; [11]Ann and Robert H. Lurie Children's Hospital of Chicago and Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [12]Hospital Padre Hurtado, Santiago, Chile; [13]Cevaxin Research Center, Panama City, Panama; [14]Children's Hospital Colorado, Aurora, CO, USA.

Presented at ESPID 2023, 8 – 12 May 2023

Robust efficacy favouring nirsevimab against MA RSV LRTI of different severities and RSV subtypes*

	Placebo (N=1293)	Nirsevimab (N=2579)	RRR (95% CI)
MA RSV LRTI	80 (6.2)	31 (1.2)	**79.0** (68.5, 86.1)
RSV subtype A	39 (3.0)	16 (0.6)	**78.1** (61.1, 87.7)
RSV subtype B	41 (3.2)	15 (0.6)	**80.0** (63.7, 89.0)
MA RSV LRTI requiring hospitalisation	33 (2.6)	12 (0.5)	**80.6** (62.3, 90.1)
Very severe MA RSV LRTI†	28 (2.2)	7 (0.3)	**86.2** (68.1, 94.0)
MA RSV LRTI requiring ICU admission	6 (0.5)	1 (0.04)	**90.1** (16.4, 98.8)
MA RSV LRTI requiring respiratory support	6 (0.5)	1 (0.04)	**89.8** (13.7, 98.8)



RRR and it's corresponding 95% CI and p-value were estimated based on Poisson regression with robust variance (including study code and stratification factors as covariates) obtained after missing data imputation. *For all participants who received the approved dose of nirsevimab (infants <5 kg, 50 mg; ≥5 kg, 100 mg). †Defined as those cases of hospitalisation for MA RSV LRTI that required supplemental O_2 or IV fluids. CI, confidence interval; ICU, intensive care unit; IV, intravenous; LRTI, lower respiratory tract infection; MA, medically attended; RRR, relative risk reduction; RSV, respiratory syncytial virus

Conclusions

- A pooled analysis of nirsevimab demonstrated 79.0% efficacy against the primary case definition of MA RSV LRTI in infants ≥29 wGA over 5 months
  - Similar efficacy was observed across RSV subtypes and different severities of disease, including cases requiring hospitalisation, very severe cases, and cases requiring ICU admission or additional respiratory support
  - The subgroup analysis show a high level of efficacy across subgroups that is consistent with the overall result

Nirsevimab for the prevention of RSV disease in healthy late-preterm and term infants: follow-up through second RSV season

Ron Dagan,[1] Laura L. Hammitt[2], Beatriz Seoane Nuñez[3], Manuel Baca Cots[4], Miroslava Bosheva[5], Shabir A. Madhi[6], William J. Muller[7], Heather J. Zar[8], Amy Grenham[9], Manish Shroff[10], Therese Takas[9], Vaishali S. Mankad[11], Amanda Leach[9] and Tonya Villafana[9] for the MELODY Study Group*

[1]Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel; [2]Department of International Health, Johns Hopkins University, Baltimore, USA; [3]Biometrics, Vaccines & Immune Therapies, BioPharmaceuticals R&D, AstraZeneca, Madrid, Spain; [4]Quirónsalud Málaga Hospital, Malaga, Spain; [5]University Multiprofile, Hospital for Active Treatment, St. George Medical University, Plovdiv, Bulgaria; [6]South African Medical Research Council Vaccines and Infectious Diseases Analytics Research Unit and African Leadership in Vaccinology Expertise, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; [7]Ann and Robert H. Lurie Children's Hospital of Chicago and Northwestern University Feinberg School of Medicine, Chicago, USA; [8]Department of Paediatrics and Child Health, Red Cross Children's Hospital, and the Medical Research Council Unit on Child and Adolescent Health, University of Cape Town, Cape Town, South Africa; [9]Vaccines & Immune Therapies, Biopharmaceuticals R&D, AstraZeneca, Gaithersburg, MD, USA; [10]Patient Safety, Chief Medical Office, R&D, AstraZeneca, Waltham, MA, USA; [11]Clinical Development, Vaccines and Immune Therapies, Biopharmaceuticals R&D, AstraZeneca, Durham, NC, USA

Presented at RSV 2022, 29 September – 2 October 2022

*See **Ron Dagan,[1] Laura L. Hammitt[2], Beatriz Seoane Nuñez[3], Manuel Baca Cots[4]**, et al, N Engl J Med 2022;386:837-46 for details

MAT-ES-2301191 v1.0 – Mayo 2023

NIRSEVIMAB HA SIDO APROBADO POR LA EMA Y ESTA PENDIENTE DE PRECIO Y REEMBOLSO EN ESPAÑA

A low incidence of RSV LRTI was observed during RSV season two with no hospitalised cases

Increasing severity

Definition, n (%)	RSV Season 1 (2019 – 2020): To Day 151		RSV Season 2 (2020 – 2021): Days 361 – 511	
	Placebo (n=496)	Nirsevimab (n=994)	Placebo (n=482)	Nirsevimab (n=964)
Medically attended RSV LRTI (protocol-defined)	25 (5.0)	12 (1.2)	2 (0.4)	7 (0.7)
Medically attended RSV LRTI with hospitalisation (protocol-defined)	8 (1.6)	6 (0.6)	0 (0.0)	0 (0.0)
Medically attended RSV LRTI (very severe)	7 (1.4)	5 (0.5)	0 (0.0)	0 (0.0)

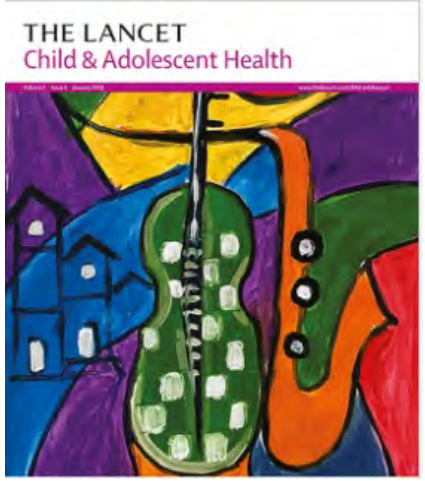
*See **Ron Dagan**,[1] **Laura L. Hammitt**[2], **Beatriz Seoane Nuñez**[3], **Manuel Baca Cots**[4], et al, N Engl J Med 2022;386:837-46 for details

Conclusions

In infants who received nirsevimab prior to their first RSV season, during the second RSV season there was:

- ***a low incidence of medically attended RSV LRTI***
- ***no cases of hospitalisation due to medically attended RSV LRTI***

*See **Ron Dagan**,[1] **Laura L. Hammitt**[2], **Beatriz Seoane Nuñez**[3], **Manuel Baca Cots**[4], et al, N Engl J Med 2022;386:837-46 for details



Efficacy of nirsevimab against respiratory syncytial virus lower respiratory tract infections in preterm and term infants, and pharmacokinetic extrapolation to infants with congenital heart disease and chronic lung disease: a pooled analysis of randomised controlled trials

Eric A F Simões, Shabir A Madhi, William J Muller, Victoria Atanasova, Miroslava Bosheva, Fernando Cabañas, Manuel Baca Cots, Joseph B Domachowske, Maria L Garcia-Garcia, Ineta Grantina, Kim A Nguyen, Heather J Zar, Anna Berglind, Celeste Cummings, M Pamela Griffin, Therese Takas, Yuan Yuan, Ulrika Wählby Hamrén, Amanda Leach, Tonya Villafana

www.thelancet.com/child-adolescent **Published online January 9, 2023** **https://doi.org/10.1016/S2352-4642(22)00321-2**

NIRSEVIMAB HA SIDO APROBADO POR LA EMA Y ESTA PENDIENTE DE PRECIO Y REEMBOLSO EN ESPAÑA

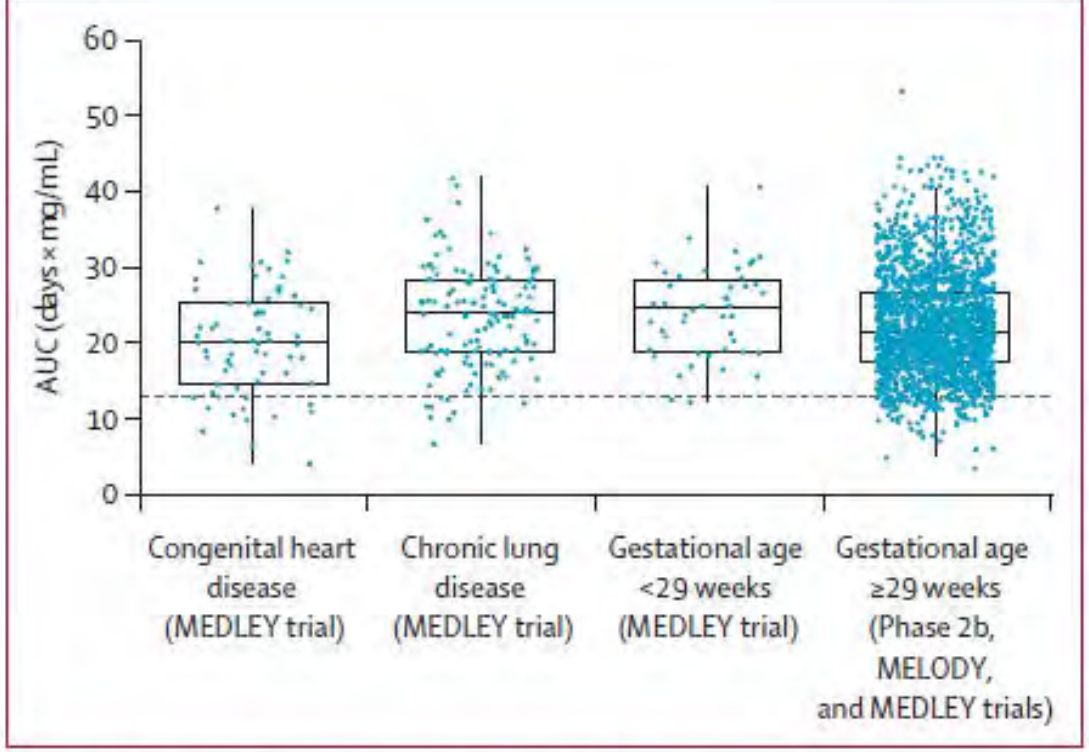


Figure 3: **Nirsevimab exposures across infant subgroups (as-treated population)**

	Placebo group (n=786)			Nirsevimab group (n=1564)			Relative risk reduction (95% CI)*
	Number of infants with ≥1 event	Number of events	Number of events per 100 infants (95% CI)	Number of infants with ≥1 event	Number of events	Number of events per 100 infants (95% CI)	
Any antibiotic prescription	157 (20%)	269	34·6 (29·0–41·2)	258 (16%)	409	26·4 (22·8–30·6)	23·6% (3·8–39·3)
Outpatient visits for LRTI	133 (17%)	219	28·1 (23·5–33·8)	171 (11%)	253	16·3 (13·9–19·3)	41·9% (25·7–54·6)

LRTI=lower respiratory tract infection. *Percentage reduction in number of events per 100 infants per RSV season (5 months) in the nirsevimab group versus the placebo group.

Table 3: **Outpatient visits per LRTI and antibiotic prescription for any cause up to 150 days post-dose (intention-to-treat population)**

Simões EAF et al. The Lancet Child & Adolescent Health. 2023

Nirsevimab vs Palivizumab en pretérmino, y enfermedad pulmonar o cardíaca crónica

Table 1. Adverse Events Occurring during Treatment through 360 Days after Administration of the First Dose of Nirsevimab in the As-Treated Population.*

Event	Preterm Cohort		CHD–CLD Cohort	
	Palivizumab (N=206)	Nirsevimab (N=406)	Palivizumab (N=98)	Nirsevimab (N=208)
	number of infants (percent)			
≥1 Adverse event	134 (65.0)	268 (66.0)	72 (73.5)	148 (71.2)
≥1 Treatment-related adverse event	4 (1.9)	6 (1.5)	2 (2.0)	4 (1.9)
≥1 Adverse event of grade ≥3 severity†	7 (3.4)	14 (3.4)	13 (13.3)	30 (14.4)
≥1 Treatment-related adverse event of grade ≥3 severity†	0	0	0	0
Any adverse event with outcome of death (grade 5 severity)†	0	2 (0.5)	1 (1.0)	3 (1.4)
≥1 Serious adverse event‡	11 (5.3)	28 (6.9)	20 (20.4)	40 (19.2)
≥1 Serious adverse event, grade ≥3 adverse event, or both†	11 (5.3)	28 (6.9)	21 (21.4)	45 (21.6)
≥1 Treatment-related serious adverse event	0	0	0	0
≥1 Adverse event of special interest§	0	1 (0.2)	0	1 (0.5)
≥1 Covid-19–related adverse event¶	1 (0.5)	8 (2.0)	1 (1.0)	2 (1.0)

At day 151, **serum level**s on nirsevimab were similar **in the two cohorts** and similar to those reported in the MELODY trial

The **antidrug– antibody response** at day 151 **was low** (occurring in 2 of 483 infants [0.4%] in the nirsevimab group and 9 of 251 infants in the palivizumab group [3.6%]).

In infants with CHD or CLD and in those born preterm, the **safety profile of nirsevimab was similar to that of palivizuma**

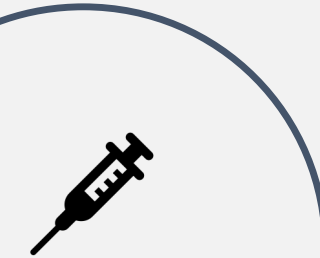
Domachowske J et al. NEJM 2022

Estrategias preventivas con anticuerpos monoclonales de acción prolongada

Lactantes nacidos durante la temporada de VRS

Posibilidad de administración inmediatamente después del nacimiento antes de las vacunas rutinarias

En la maternidad



1 dosis única intramuscular

Lactantes nacidos fuera de la temporada de VRS

Administración concomitante con vacunas rutinarias, para minimizar visitas, aprovechando las ya calendarizadas y aumentar la adherencia.

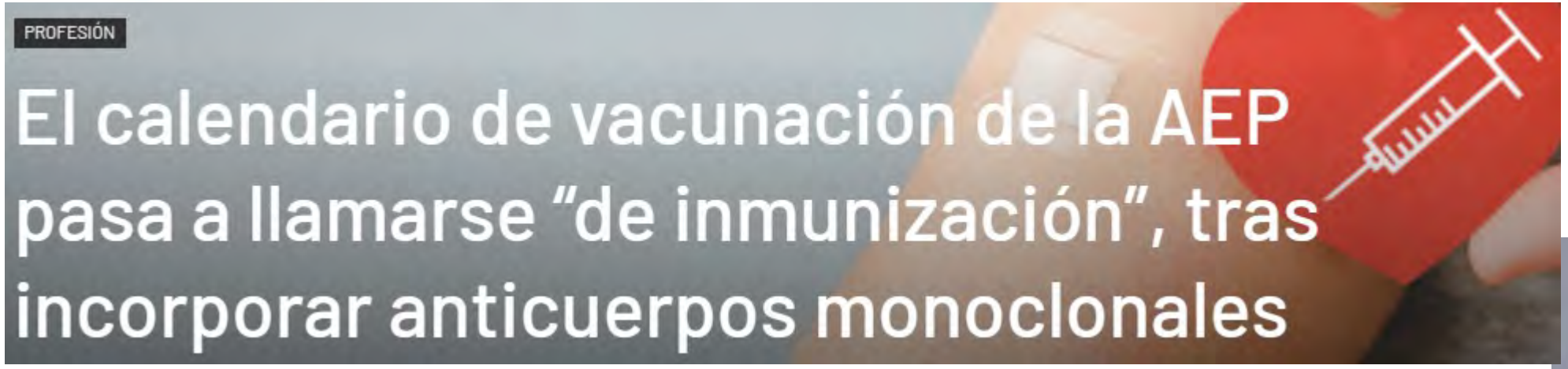
En AP
Rescate de niños
Concomitante con otras vacunas

NIRSEVIMAB HA SIDO APROBADO POR LA EMA Y ESTÁ PENDIENTE DE PRECIO Y REEMBOLSO EN ESPAÑA

R Esposito S, et al. Front Immunol. 2021;12:708939.

GACETA MÉDICA

grupo pediátrico uncibay



XXVII REUNIÓN SEUP

Instituto Nacional de Estadística

Todos los partos	
Todos los tiempos	420.290
Menos de 28 semanas	1.015
De 28 a 31 semanas	2.575
De 32 a 36 semanas	23.345
De 37 a 41 semanas	323.559
De 42 y más semanas	5.710

https://www.ine.es/jaxi/Datos.htm?path=/t20/e301/nacim/a2015/l0/&file=01011.px

Farmacia
HOSPITALARIA

Rangos de EG (semanas)	Temporada 12/13	Temporada 13/14
	Nº ingresos (%)	Nº ingresos (%)
≤28 +6 días	2 (1,20)	1 (0,65)
29 – 31 +6 días	2 (1,20)	4 (2.61)
32 – 34 +6 días	10 (5,99)	14 (9,15)
>35	153 (91,61)	134 (87,59)

XXVII REUNIÓN SEUP

Yolanda Hernández-Gago[1] , Marina Lombardero-Pin[1] , Casilda Ortega de la Cruz[2] , Pablo A Maciuniak[3] , Alicia Díez del Pino[1]
[1]Servicio de Farmacia del Complejo Hospitalario Universitario Insular Materno Infantil Canarias.

https://dx.doi.org/10.7399/fh.2017.41.2.10565

Calendario de inmunizaciones de la Asociación Española de Pediatría

2023

www.vacunasaep.org

VACUNA	Edad en meses						Edad en años				
	2	3	4	11	12	15	3-4	6	12	14	15-18
Hepatitis B[1]	HB		HB	HB							
Difteria, tétanos y tosferina[2]	DTPa		DTPa	DTPa				DTPa/ Tdpa	Tdpa		
Poliomielitis[3]	VPI		VPI	VPI				VPI			
Haemophilus influenzae tipo b[4]	Hib		Hib	Hib							
Neumococo[5]	VNC		VNC	VNC							
Rotavirus[6]	RV	RV	(RV)								
Meningococo B[7]	MenB		MenB		MenB						
Meningococos C y ACWY[8]			MenC		Men ACWY				Men ACWY		
Gripe[9]				Gripe (6 meses a 59 meses)							
Sarampión, rubeola y parotiditis[10]					SRP		SRP				
Varicela[11]						Var	Var/ SRPV				
SARS-CoV-2[12]								SARS-CoV-2 (a partir de 5 años)			
Virus del papiloma humano[13]									VPH		
Virus respiratorio sincitial[14]	AcVRS (hasta los 6 meses)										

Cambio del nombre del calendario. De vacunaciones a inmunizaciones, dado que entra en juego un anticuerpo monoclonal para prevenir la enfermedad por virus respiratorio sincitial (VRS).

(14) Virus respiratorio sincitial.- Se recomienda nirsevimab (anticuerpo anti-VRS) en todos los recién nacidos y lactantes menores de seis meses y su administración anual a niños menores de dos años con enfermedades subyacentes que aumenten el riesgo de infección grave por VRS.

laSexta

ESPAÑA SOCIEDAD PROGRAMAS DEPORTES INTERNACIONAL CIENCIA Y TECNOLOGÍA CULTURA SERIES VIRAL ECONOMÍA TIEMPO CÓMO

SALUD Y ENFERMEDADES Alimentación Ejercicio Psicología Sexualidad Bienestar

Pediatría

Así es nirsevimab, el primer fármaco protector contra el VRS (causante de bronquiolitis en niños)

Se trata del primer fármaco (un anticuerpo monoclonal) aprobado por la Comisión Europea que supone la primera y única opción de protección frente al virus respiratorio sincitial (VRS), muy frecuente en niños menores de dos años.

Sanidad ›

CALENDARIO DE VACUNACIÓN

El calendario de vacunación infantil incorpora nirsevimab, la nueva arma contra la bronquiolitis

XXVII REUNIÓN SEUP

NIRSEVIMAB HA SIDO APROBADO POR LA EMA Y ESTÁ PENDIENTE DE PRECIO Y REEMBOLSO EN ESPAÑA

grupo pediátrico uncibay

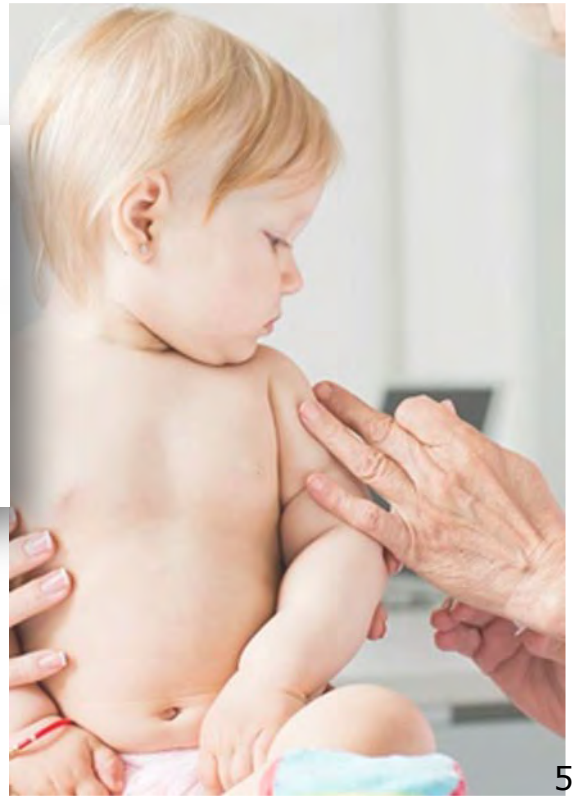
A Phase 3 randomized open-label study of nirsevimab (versus no intervention) in preventing hospitalizations due to respiratory syncytial virus (RSV) in infants (HARMONIE)

SB Drysdale, K Cathie, F Flamein, M Knuf, A Collins, H Hill, F Kaiser, R Cohen, C Felter, NC Vassilouthis, J Jin, M Bangert, S Royal, SN Faust and P Tissieres on behalf of the HARMONIE investigators.

O0082 / #1178

EFFICACY OF NIRSEVIMAB AGAINST RSV LOWER RESPIRATORY TRACT INFECTION HOSPITALIZATION IN INFANTS: PRELIMINARY DATA FROM THE HARMONIE PHASE 3B TRIAL

Oral Presentations Session
ORAL PRESENTATION SESSION 09: VACCINES



Resultados - **HARMONIE**

- **8.058 lactantes** aleatorizados
- **4016** (49,8%) recibieron Nirsevimab (1 en el grupo control)
- 8.026 siguieron el estudio (16 discontinuaron en cada grupo)

Objetivo	Nirsevimab (N=4.037)	No intervención (N=4.021)	Eficacia
Eficacia en IVRI-VRS hospitalización %	11 (0.3)	60 (1.5)	**83,21 %** (67,77-92,04)
Eficacia en IVRI-VRS hospitalitzades mayor gravedad %	5 (0.1)	19 (0.5)	**75,71%** (32,75-92,91)
Eficàcia en IVRI cualquier causa %	45 (1.1)	98 (2.4)	**58%** (39,69- 71,19)

El **perfil de seguridad** en este amplio estudio ha sido **favorable y consistente** con los datos ya presentados en los diferentes estudios pivotales

SB Drysdale, (2023, May 8–12). A Phase 3 randomized open-label study of nirsevimab (versus no intervention) in preventing hospitalizations due to respiratory syncytial virus (RSV) in infants (HARMONIE) [Oral presentation]. ESPID 2023: Lisbon, Portugal.

Key Conclusions

Nirsevimab efficacy in preventing RSV hospitalizations of **83.2%**

Nirsevimab efficacy in preventing severe RSV disease of **75.7%**

HARMONIE shows **58%** reduction in all-cause LRTI hospitalizations

HARMONIE has demonstrated the significant impact of nirsevimab on RSV LRTI, implemented in close to real life conditions, in an **all-infant** cohort

The safety profile of nirsevimab was consistent with data from previous trials

SB Drysdale, (2023, May 8–12). A Phase 3 randomized open-label study of nirsevimab (versus no intervention) in preventing hospitalizations due to respiratory syncytial virus (RSV) in infants (HARMONIE) [Oral presentation]. ESPID 2023: Lisbon, Portugal.

EL DERECHO A LA PROTECCION INDIVIDUAL del paciente siempre es valorable Y NOS LLEVARA A CAMBIAR ORIENTACIONES SANITARIAS.

XXVII REUNIÓN SEUP


INFORMACIÓN

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Paris desde 29€

La virulencia de la bronquiolitis llena de recién nacidos las unidades de cuidados intensivos

La UCI neonatal y pediátrica del Hospital General de Alicante está completa y en la de Sant Joan | sido ingresados seis bebés

grupo pediátrico uncibay

¡¡ MUCHAS GRACIAS POR SU ATENCIÓN!!

XXVII REUNIÓN SEUP

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TABLE 1. Incidence Rates Per 100 Infant-years for Medically Attended RSV Illness by Interval

	n	September to May Rate* (95% CI)	September to October Rate (95% CI)	November to March Rate† (95% CI)
RSV-related MAARI	287	42.5 (37.7–47.7)	4.8 (0.6–17.4)	60.9 (53.7–68.6)
RSV-related outpatient URI	112	15.4 (12.7–18.5)	2.4 (0.1–13.4)	22.3 (18.2–27.1)
RSV-related outpatient LRI	157	22.1 (18.8–25.8)	0.0 (0.0–8.9)	33.0 (27.9–38.8)
RSV-related ED visits	69	9.3 (7.3–11.8)	0.0 (0.0–8.9)	14.1 (10.8–17.9)
RSV-related hospitalization	57	7.7 (5.8–9.9)	0.0 (0.0–8.9)	11.8 (8.9–15.4)

Respiratory Syncytial Virus Disease in Preterm Infants in the US Born at 32–35 Weeks Gestation Not Receiving Immunoprophylaxis

The Pediatric Infectious Disease Journal • Volume 33, Number 6, June 2014

Sanidad
SOS de las urgencias pediátricas: la "pandemia" de bronquiolitis en bebés colapsa los hospitales

Sanidad ›

SANIDAD PÚBLICA

SOS de las urgencias pediátricas: la "pandemia" de bronquiolitis en bebés colapsa los hospitales

- La Sociedad Española de Urgencias Pediátricas (SEUP) muestra su "preocupación e incertidumbre por el incremento inesperado del volumen asistencial" por de casos de Virus Respiratorio Sincitial (VRS), muy contagioso.
- Los especialistas llevan días alertando de una epidemia triple: coronavirus, gripe y VRS y piden incorporar pruebas de detección rápida de los tres virus en los hospitales.
- En España, las infecciones por este virus originan entre 7.000 y 14.000 hospitalizaciones cada año.

LA RAZÓN
Cataluña

El fuerte rebrote de las infecciones respiratorias colapsa a los hospitales catalanes

El coronavirus se suma este año a la epidemia de bronquiolitis y los centros sanitarios vuelven a aplicar los protocolos de 2020

SINC
CIENCIA CONTADA EN ESPAÑOL

SALUD PÚBLICA

EL PAÍS

Sociedad

EDUCACIÓN · MEDIO AMBIENTE · IGUALDAD · SANIDAD · CONSUMO · LAICISMO · COMUNICACIÓN · ÚLTIMAS NOTICIAS

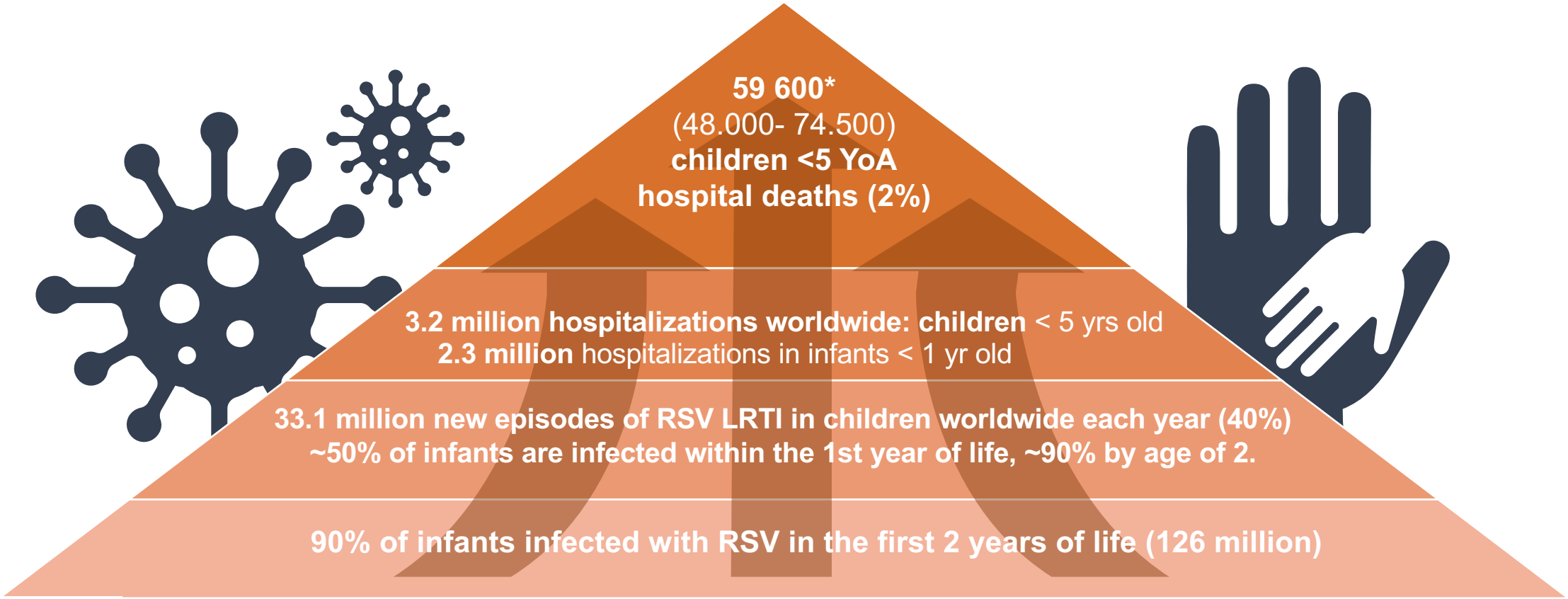
ENFERMEDADES RESPIRATORIAS >

El cóctel de covid, gripe y bronquiolitis que golpea Europa este invierno amenaza con poner bajo "grave presión" los sistemas de salud

El Centro Europeo de Control de Enfermedades advierte del riesgo ante un comienzo temprano de las epidemias de virus respiratorios

grupo pediátrico uncibay

RSV is the most common cause of Lower Respiratory Tract Infection (LRTI) in infants worldwide resulting in annual seasonal epidemics and serious disease or death in some young children



*118 200 deaths (combined hospital and community deaths)

[1] Shi et al., Lancet 2017 390:946; [2] Glenzen et al., Am J Dis Child 1986 140:543; Rha B et al. Pediatrics 2020.

El laboratorio titular de la autorización de comercialización de Synagis as Astrazeneca AB.
Virazole no está comercializado en España

Table 3. Outcomes through 150 Days after the Injection.*

Outcome	Nirsevimab (N = 686)	Placebo (N = 342)	Efficacy (95% CI)†	Cases Averted per 1000 Infants Treated (95% CI)‡	Number Needed to Treat (95% CI)§
	no. (%)				
Medically attended RSV-associated lower respiratory tract infection on any test result¶	17 (2.5)	37 (10.8)	77.0 (59.8 to 86.8)	83.4 (62.0 to 105.0)	12 (10 to 17)
Medically attended RSV-associated lower respiratory tract infection on central test result¶	15 (2.2)	33 (9.6)	77.2 (58.7 to 87.5)	74.7 (53.0 to 95.0)	14 (11 to 19)
Medically attended lower respiratory tract infection of any cause¶	60 (8.7)	62 (18.1)	51.5 (32.6 to 65.2)	93.6 (63.0 to 124.0)	11 (9 to 16)
Hospitalization for any respiratory illness due to RSV on any test result	9 (1.3)	11 (3.2)	59.0 (2.1 to 82.9)	19.0 (5.5 to 32.0)	53 (32 to 182)
Hospitalization for any respiratory illness due to RSV on central test result	7 (1.0)	9 (2.6)	61.1 (−3.7 to 85.4)	16.1 (4.5 to 28.0)	62 (36 to 223)
Hospitalization for any respiratory illness of any cause	16 (2.3)	14 (4.1)	42.8 (−15.8 to 71.7)	17.7 (2.0 to 33.0)	57 (31 to 500)

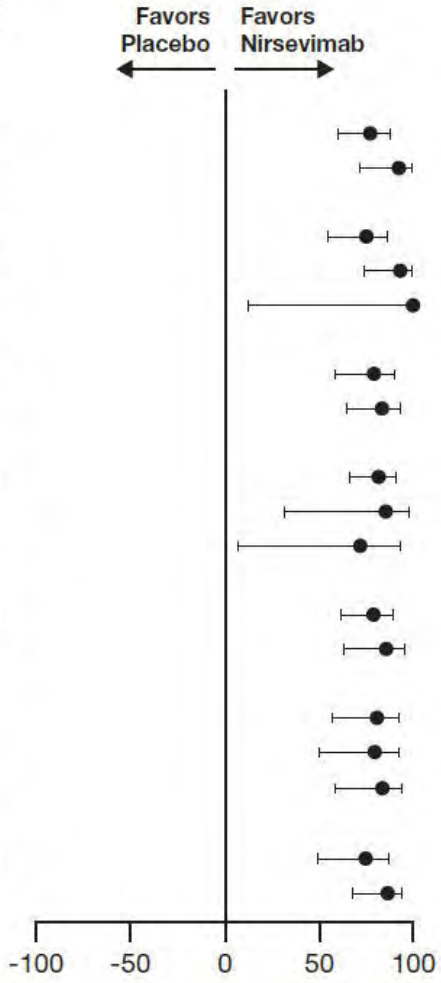
Table 4. Adverse Events That Occurred through 360 Days after the Injection.*

Variable	Nirsevimab (N=987)	Placebo (N=491)	Total (N=1478)
		no. of participants (%)	
Any adverse event	863 (87.4)	426 (86.8)	1289 (87.2)
Considered to be related to the trial regimen	10 (1.0)	7 (1.4)	17 (1.2)
Occurred ≤1 day after the injection	18 (1.8)	3 (0.6)	21 (1.4)
Occurred ≤3 days after the injection	56 (5.7)	23 (4.7)	79 (5.3)
Occurred ≤7 days after the injection	132 (13.4)	63 (12.8)	195 (13.2)
Adverse event of grade ≥3 severity	36 (3.6)	21 (4.3)	57 (3.9)
Adverse event that resulted in death	3 (0.3)	0	3 (0.2)
Serious adverse event†	67 (6.8)	36 (7.3)	103 (7.0)
Considered to be related to the trial regimen	0	0	0
Adverse event of special interest‡	1 (0.1)	0	1 (0.1)
Adverse event related to Covid-19	7 (0.7)	7 (1.4)	14 (0.9)
Confirmed case of Covid-19§	6 (0.6)	6 (1.2)	12 (0.8)
Adverse event suspected to be related to Covid-19¶	1 (0.1)	1 (0.2)	2 (0.1)

Eficacia consistente frente a IVRI VRS MA subgrupos

aracteristic	Placebo (n=786)	Nirsevimab (n=1564)
ants per trial oposed se), n (%)		
Phase 2b <5 kg	290 (36.9)	570 (36.4)
MELODY	496 (63.1)	994 (63.6)
male, n (%)	397 (50.5)	736 (47.1)
e, median nths (range)	2.00 (0.03–10.97)	2.02 (0.03–11.10)
≤3.0 months, n (%)	531 (67.6)	1066 (68.2)
>3.0 to ≤6.0 months, n (%)	204 (26.0)	398 (25.4)
>6.0 months, n (%)	51 (6.5)	100 (6.4)
ight group on y 1, n (%)		
<5 kg	482 (61.3)	973 (62.3)
≥5 kg	304 (38.7)	589 (37.7)

Subgroup	Interaction p-value	Placebo (N = 786) Number of Infants	Placebo (N = 786) Observed Events	Nirsevimab (N = 1564) Number of Infants	Nirsevimab (N = 1564) Observed Events	RRR (95% CI)
Hemisphere	0.0998					
Northern Hemisphere		536	37 (6.9)	1086	17 (1.6)	77.3 (60.1, 87.5)
Southern Hemisphere		250	14 (5.6)	478	2 (0.4)	92.5 (71.2, 98.9)
Age at randomization	N/A					
⩽3.0 months		531	33 (6.2)	1066	17 (1.6)	74.3 (54.2, 86.0)
>3.0 months to ⩽6.0 months		204	15 (7.4)	398	2 (0.5)	93.1 (73.9, 98.9)
>6.0 months		51	3 (5.9)	100	0 (0.0)	100.0 (12.6, NE)
Sex	0.6285					
Male		389	25 (6.4)	828	11 (1.3)	79.3 (58.5, 90.2)
Female		397	26 (6.5)	736	8 (1.1)	83.4 (64.3, 92.9)
Race	0.7475					
White		478	37 (7.7)	919	13 (1.4)	81.7 (66.2, 90.6)
Black or African American		176	6 (3.4)	406	2 (0.5)	85.6 (31.7, 98.0)
Other		132	8 (6.1)	235	4 (1.7)	71.9 (7.1, 92.6)
Weight on Day 1	0.4860					
<5 kg		482	33 (6.8)	973	14 (1.4)	79.0 (61.2, 89.1)
⩾5 kg		304	18 (5.9)	589	5 (0.8)	85.7 (62.9, 95.2)
Region	0.9581					
North American		183	18 (9.8)	435	8 (1.8)	81.3 (57.6, 92.3)
Europe		290	16 (5.5)	548	6 (1.1)	80.2 (50.5, 92.9)
Rest of World		313	17 (5.4)	581	5 (0.9)	84.2 (58.7, 94.8)
Study Group	0.2851					
MELODY		496	25 (5.0)	994	12 (1.2)	74.5 (49.6, 87.1)
Phase 2b		290	26 (9.0)	570	7 (1.2)	86.2 (68.0, 94.0)



Gestational age group, n (%)		
≥29 to ≤32 weeks	116 (14.8)	219 (14.0)
>32 to <35 weeks	175 (22.3)	344 (22.0)
≥35 to <37 weeks	76 (9.7)	139 (8.9)
≥37 weeks	419 (53.3)	861 (55.1)
Race or ethnic group, n (%)		
American Indian or Alaska Native	26 (3.3)	57 (3.7)
Asian	24 (3.1)	39 (2.5)
Black or African American	176 (22.4)	406 (26.0)
Native Hawaiian or other Pacific Islander	8 (1.0)	12 (0.8)
White	478 (60.8)	919 (58.9)
Other	70 (8.9)	109 (7.0)
Multiple categories	4 (0.5)	18 (1.2)

RRR, relative risk reduction

Simões EAF et al. The Lancet Child & Adolescent Health. 2023

NIRSEVIMAB HA SIDO APROBADO POR LA EMA Y ESTA PENDIENTE DE PRECIO Y REEMBOLSO EN ESPAÑA

Conclusiones

- Nirsevimab es un nuevo anticuerpo de acción prolongada que protege frente al VRS con una dosis única
- Un análisis agrupado preespecificado demostró una eficacia del 79,5% frente a las infecciones del tracto respiratorio inferior (ITRI) atendidas médicamente:
  - Eficacia consistente entre diferentes grados de severidad de ITRI por VRS
  - Eficacia consistente entre subgrupos
  - Incluyendo ITRI medicamente atendidas y hospitalizados por todas las causas
- Beneficio asociado en la reducción de recursos hospitalarios, visitas ambulatorias y uso de antibioticos
  - Al año tras la administración, los niveles de NAb VRS fueron más elevados en los sujetos con nirsevimab en comparación con placebo incluso en los que han pasado infección medicamente atendida por VRS.
    - Esto sugiere un nivel de protección extendido mas allá de los 5 meses

European Medicines Agency. Ficha técnica o resumen de las características del producto: Beyfortus®2022

Nirsevimab vs Palivizumab en pretérmino, y enfermedad pulmonar o cardíaca crónica

Table 1. Adverse Events Occurring during Treatment through 360 Days after Administration of the First Dose of Nirsevimab in the As-Treated Population.*

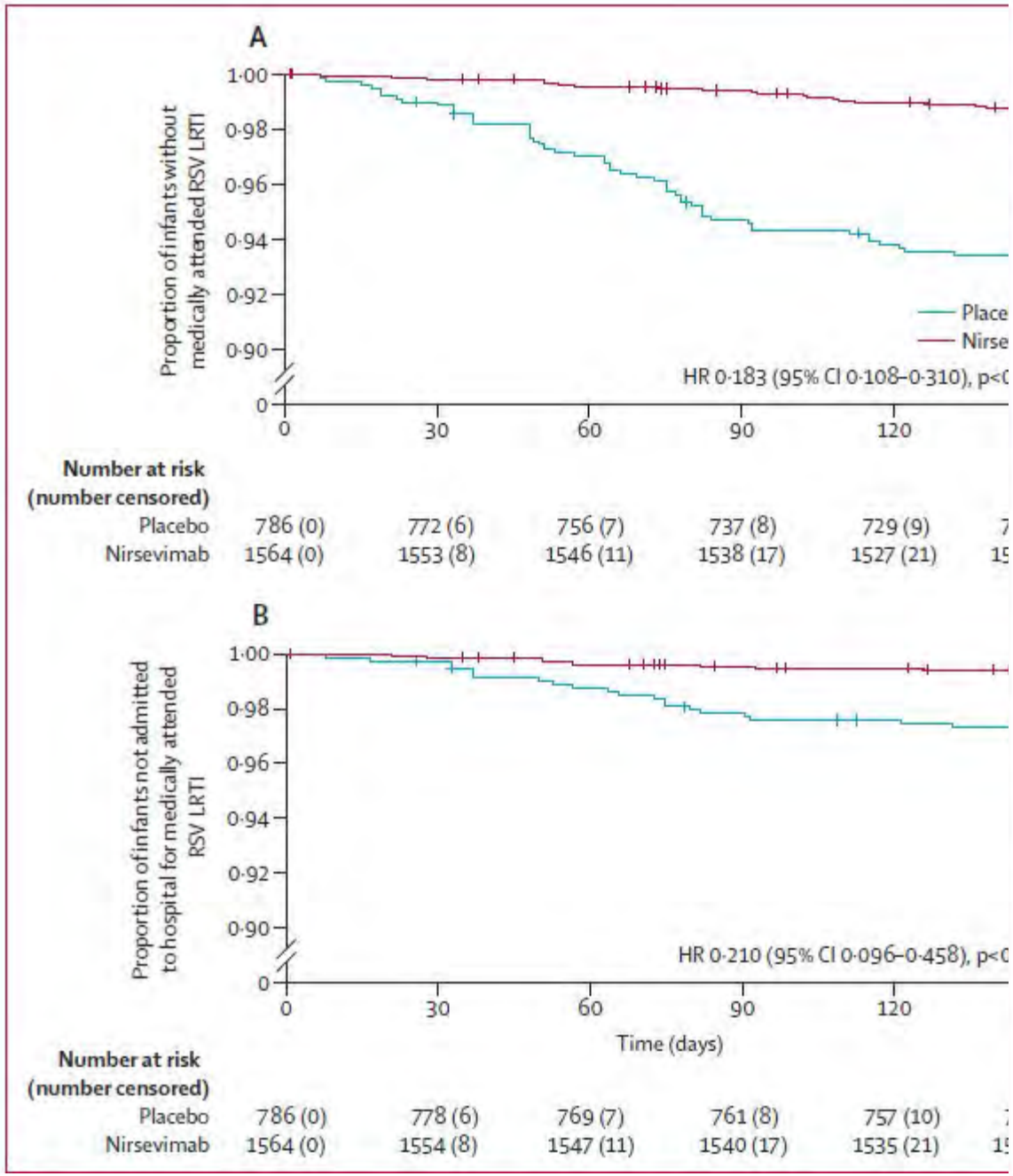
Event	Preterm Cohort		CHD–CLD Cohort	
	Palivizumab (N=206)	Nirsevimab (N=406)	Palivizumab (N=98)	Nirsevimab (N=208)
	number of infants (percent)			
≥1 Adverse event	134 (65.0)	268 (66.0)	72 (73.5)	148 (71.2)
≥1 Treatment-related adverse event	4 (1.9)	6 (1.5)	2 (2.0)	4 (1.9)
≥1 Adverse event of grade ≥3 severity†	7 (3.4)	14 (3.4)	13 (13.3)	30 (14.4)
≥1 Treatment-related adverse event of grade ≥3 severity†	0	0	0	0
Any adverse event with outcome of death (grade 5 severity)†	0	2 (0.5)	1 (1.0)	3 (1.4)
≥1 Serious adverse event‡	11 (5.3)	28 (6.9)	20 (20.4)	40 (19.2)
≥1 Serious adverse event, grade ≥3 adverse event, or both†	11 (5.3)	28 (6.9)	21 (21.4)	45 (21.6)
≥1 Treatment-related serious adverse event	0	0	0	0
≥1 Adverse event of special interest§	0	1 (0.2)	0	1 (0.5)
≥1 Covid-19–related adverse event¶	1 (0.5)	8 (2.0)	1 (1.0)	2 (1.0)

At day 151, **serum level**s on nirsevimab were similar **in the two cohorts** and similar to those reported in the MELODY trial

The **antidrug– antibody response** at day 151 **was low** (occurring in 2 of 483 infants [0.4%] in the nirsevimab group and 9 of 251 infants in the palivizumab group [3.6%]).

In infants with CHD or CLD and in those born preterm, the **safety profile of nirsevimab was similar to that of palivizuma**

Domachowske J et al. NEJM 2022



	Events, n/N (%)		RRR (95% CI)	$p_{interaction}$
	Placebo group	Nirsevimab group		
Overall	51/786 (6%)	19/1564 (1%)	79·5 (65·9–87·7)	NA
Hemisphere*				0·10
Northern	37/536 (7%)	17/1086 (2%)	77·3 (60·1–87·5)	
Southern	14/250 (6%)	2/478 (<1%)	92·5 (71·2–98·9)	
Age at randomisation, months*				NA
≤3·0	33/531 (6%)	17/1066 (2%)	74·3 (54·2–86·0)	
>3·0 to ≤6·0	15/204 (7%)	2/398 (1%)	93·1 (73·9–98·9)	
>6·0	3/51 (6%)	0/100 (0%)	100·0 (12·6–NE)	
Sex*				0·63
Male	25/389 (6%)	11/828 (1%)	79·3 (58·5–90·2)	
Female	26/397 (7%)	8/736 (1%)	83·4 (64·3–92·9)	
Ancestry*				0·75
White	37/478 (8%)	13/919 (1%)	81·7 (66·2–90·6)	
Black or African American	6/176 (3%)	2/406 (<1%)	85·6 (31·7–98·0)	
Other	8/132 (6%)	4/235 (2%)	71·9 (7·1–92·6)	
Weight on day 1, kg*				0·49
<5	33/482 (7%)	14/973 (1%)	79·0 (61·2–89·1)	
≥5	18/304 (6%)	5/589 (1%)	85·7 (62·9–95·2)	
Region*				0·96
North America	18/183 (10%)	8/435 (2%)	81·3 (57·6–92·3)	
Europe	16/290 (6%)	6/548 (1%)	80·2 (50·5–92·9)	
Rest of world	17/313 (5%)	5/581 (1%)	84·2 (58·7–94·8)	
Study group				0·29
MELODY†	25/496 (5%)	12/994 (1%)	74·5 (49·6–87·1)	
Phase 2b‡	26/290 (9%)	7/570 (1%)	86·2 (68·0–94·0)	

Figure 2: **Pooled subgroup analyses of medically attended RSV LRTIs through 150 days post-dose (intention-to-treat population)**