UNIVERSITÄTSmedizin. MAINZ

Frühjahrs-Tagung der PEG
Beyond COVID, what else, what's next?

DIENSTAG, 4. APRIL 2023

Beginn	Ende	Moderator / Referent	Themenblock / Vortrag
08:30	**10:30**	**Christian Bogdan, Erlangen Mathias Pletz, Jena**	**Impfungen – Neue Empfehlungen und Präparate**
08:30	09:00	*Christian Bogdan, Erlangen*	Aktuelle STIKO Empfehlungen (einschließlich COVID-19-Impfung)
09:00	09:30	*Mathias Pletz, Jena*	Neue Pneumokokkenimpfstoffe – wird alles einfacher?
09:30	10:00	*Markus Knuf, Worms*	Nirsevimab – nur für Risikogruppen?
10:00	10:30	*Kerstin Kling, Berlin*	Impfungen in der Reisemedizin: Neues zur Tollwut-, Gelbfieber- und Dengue-Prophylaxe
10:30	**11:00**	**Kaffeepause**	
11:00	**11:30**	**Mathias Pletz, Jena**	**Preisverleihung Wolfgang-Stille-Preis (Wissenschaftspreis)**
11:30	**12:30**	**NN**	**Integriertes Symposium Neue antivirale Therapieoptionen**
11:30	12:00	*NN*	Update Neueinführungen
12:00	12:30	*NN*	Update COVID-19
12:30	**13:30**	**Mittagspause**	
13:30	**15:00**	**Florian Thalhammer, Wien; Beatrice Grabein, München**	**Update Fokusspezifische Therapie**
13:30	14:00	*Werner Albrich, St. Gallen*	Pneumonie
14:00	14:30	*Christian Eckmann, Hann. Münden*	Intraabdominelle Infektionen
14:30	15:00	*Stefan Hagel, Jena*	Endokarditis und Cardiac Device Infections
15:00	**15:30**	**Kaffeepause**	
15:30	**16:30**	**Franziska Layer-Nicolaou, Wernigerode**	**Integriertes Symposium Management von Infektionen mit MRE Pfizer Pharma GmbH**
15:30	16:00	*Béatrice Grabein, München*	Neue Therapieoptionen bei MRGN - IDSA vs. ESCMID Leitlinie
16:00	16:30	*Holger Rohde, Hamburg*	Diagnostic Stewardship bei MRE
16:30	**16:45**	**Christian Bogdan, Erlangen**	**Résumé / Ausblick / Schlusswort / Verabschiedung**

Nirsevimab – nur für Riskogruppen?

Frühjahrstagung der PEG
04.04.2023, Bonn

Univ.-Prof. Dr. med. Markus Knuf
Klinik für Kinder- und Jugendmedizin, Worms
Tuberöse Sklerose-Zentrum, Worms

Pädiatrische Infektiologie, Universitätsmedizin Mainz
Pädiatrische Intensivmedizin, Universitätsmedizin Mainz

Interessenkonflikt

- LKP und PI bei klinischen Studien.
- Beratertätigkeit für GSK, Pfizer, Baxter, Novartis, Astra Zeneca, MedImmune, SPMSD/Sanofi Pasteur, MSD, Jansen, Takeda, GW-Pharma/Jazz-Pharma, Desitin, BioNTech, Milupa, Infectopharm, Plusultrapharrma u. a.
- Präsentationen während Industrie-Symposien.
- die o. g. Tätigkeiten nehme ich als **Dienstaufgabe** wahr
- Ich erhalte **persönlich keine Honorare** von pharmazeutischen Unternehmen.
- Es besteht diesbezüglich auch **keine Zielvereinbarung** mit meinem Dienstherrn.

Arbeitsgemeinschaft Influenza

ROBERT KOCH INSTITUT

ARE-Wochenbericht

Aktuelles zu akuten respiratorischen Erkrankungen

Buda S, Dürrwald R, Biere B, Reiche J, Buchholz U, Tolksdorf K, Schilling J, Goerlitz L, Streib V, Preuß U, Prahm K, Haas W und die AGI-Studiengruppe*

klinikum worms

ARE-Konsultationsindex nach Alter

Kalenderwoche 5 (30.1.

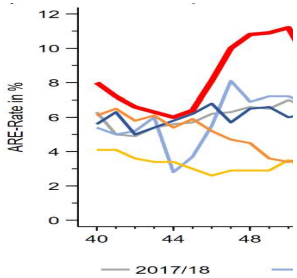
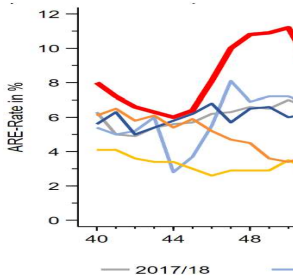


Abb. 1: Vergleich der für die E
2017/18 bis 2022/23



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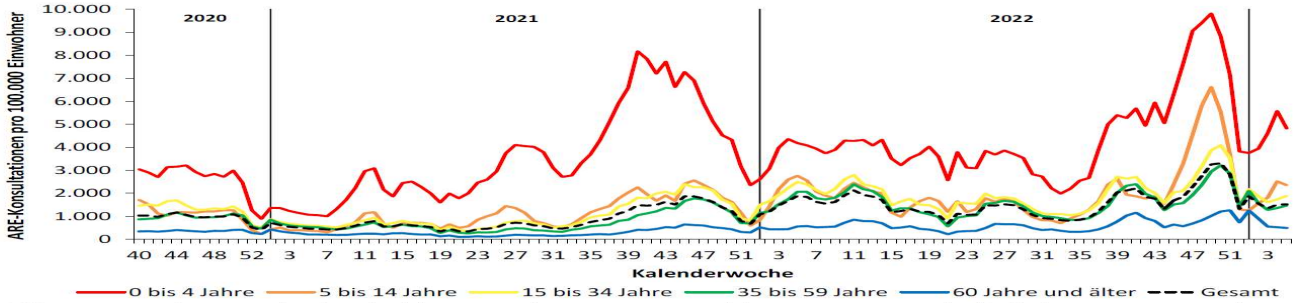
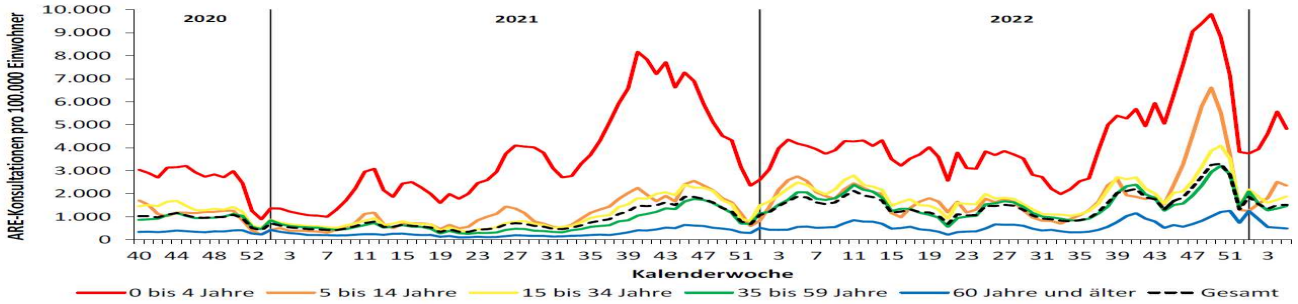


Abb. 3: Werte der Konsultationsinzidenz von der 40. KW 2020 bis zur 5. KW 2023 in fünf Altersgruppen und gesamt in Deutschland pro 100.000 Einwohner in der jeweiligen Altersgruppe. Der senkrechte Strich markiert jeweils die 1. KW des Jahres.



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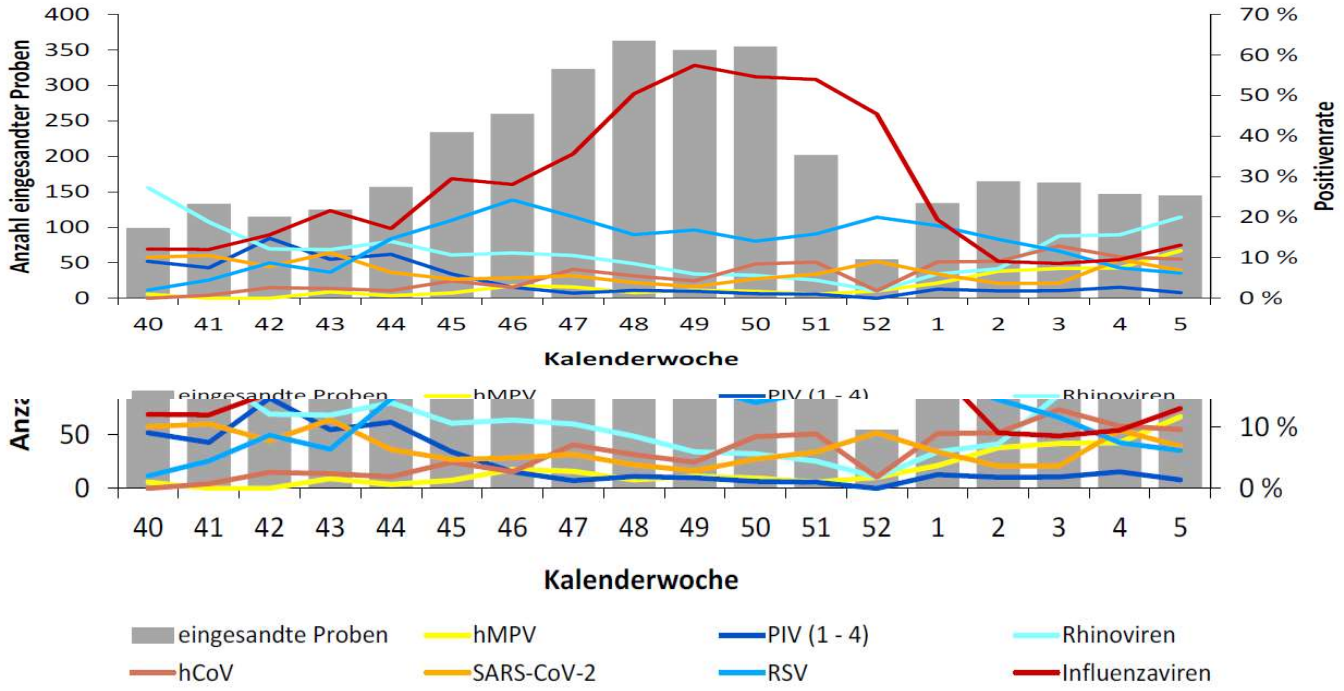

Abb. 4: Anteil der Nachweise für Influenzaviren, hCoV, SARS-CoV-2, RSV, hMPV, PIV und Rhinoviren (Positivenraten; rechte y-Achse) an allen im Rahmen des Sentinels eingesandten Proben (linke y-Achse, graue Balken) von der 40. KW 2022 bis zur 5. KW 2023.

Respiratorisches-Synzytial-Virus (RSV) und Erkrankung

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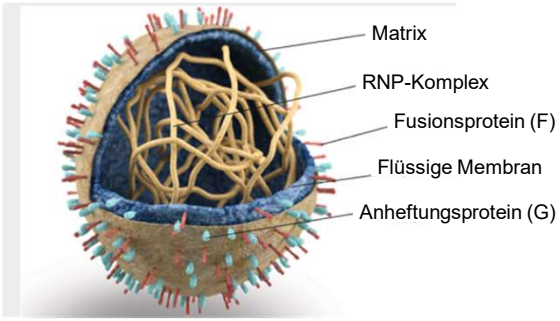
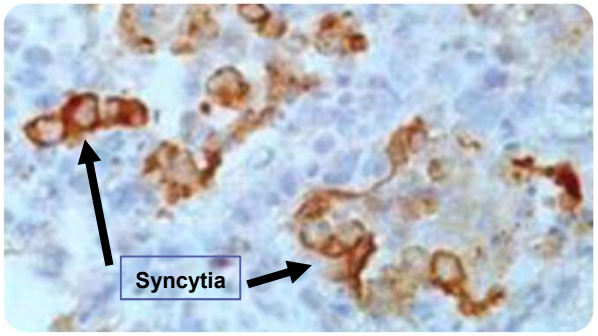
Respiratorische-Synzytial-Virus (RSV): „Steckbrief“





- **Familie der Paramyxoviren[1]**
- **120-300 nm großes umhülltes Virus,[2] negative Einzelstrang-RNA[1]**
- **zwei Hauptstämme: A und B[1-3]**
- **zwei Oberflächen-Glykoproteine:**
  - G (Anheftungsprotein) - determiniert A- oder B-Stamm
  - F (Fusionsprotein) – Angriffspunkt für Impfstoffe/Antikörper
- **RSV dringt in die Epithelzellen der Atemwege ein und verursacht Entzündungen, Ödeme, Synzyzienbildung und -ablösung[1,4]**

1. Collins PL, Crowe JE, Jr. Fields Virology. 5th ed (vol. 1). Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins;2007:1601–1646;
2. Walsh EE, *et al. J Infect Dis.* 1997;175(4):814–820; 3. Mufson MA, *et al. J Gen Virol.* 1985;66 (10):2111–2124; 4. Welliver TP, *et al. J Infect Dis.* 2007;195(8):1126–1136.

RSV-Infektionen: Variables klinisches Spektrum

Leicht → **Schwer**

Infektion der oberen Atemwege[1]

Niesen
Verstopfte Nase/Rhinorrhoe
Trockener Husten
Mittelohrentzündung

Nicht-respiratorische Symptome

Fieber und / oder
Schüttelfrost,
Schlafstörungen,
verminderter Appetit,
Reizbarkeit und Lethargie

Infektion der unteren Atemwege (LTRI) : Bronchiolitis / Pneumonie[1,2]

Keuchen / Atembeschwerden
Husten
Tachypnoe
Zyanose
Hypoxämie

RSV-Spektrum: von klinisch unbedeutenden bis zu lebensbedrohlichen Atemwegsinfektionen

1. Smith DK, Seales S, Budzik C. Am Fam Physician. 2017;95(2):94–99;
2. Perez-Yarza EG, et al. Pediatr Infect Dis J. 2007;26(8):733–739.

n = 1.554

Klinische Symptome bei stationären Kindern < 2 Jahre und RSV

Signs and symptoms at admission					
Cough	348 (89)	406 (83)	177 (95)	389 (81)	1320 (85)
Congested/runny nose	335 (85)	349 (71)	163 (87)	300 (62)	1147 (74)
Shortness of breath/respiratory distress	248 (63)	292 (59)	159 (85)	336 (70)	1035 (67)
Fever/chills	246 (63)	303 (62)	125 (67)	256 (53)	930 (60)
Tachypnea[d]	234 (60)	203 (41)	136 (73)	309 (64)	882 (57)
Inability to eat, poor feeding	242 (62)	241 (49)	158 (84)	131 (27)	772 (50)
Vomiting	183 (47)	141 (29)	87 (47)	131 (27)	542 (35)
Wheezing	123 (31)	95 (19)	83 (44)	122 (25)	423 (27)
Hypoxemia[e]	99 (25)	28 (6)	62 (33)	177 (37)	366 (24)
Diarrhea	79 (20)	56 (11)	45 (24)	59 (12)	239 (15)
Lethargy	87 (22)	23 (5)	62 (33)	42 (9)	214 (14)
Dehydration	49 (12)	1 (0)	43 (23)	28 (6)	121 (8)
Cyanosis	29 (7)	28 (6)	23 (12)	14 (3)	94 (6)
Ear infection	12 (3)	1 (0)	27 (14)	22 (5)	62 (4)
Decreased vocalization or stridor	10 (3)	7 (1)	9 (5)	4 (1)	30 (2)
Seizures	11 (3)	6 (0)	2 (1)	6 (1)	25 (2)
Hypothermia	4 (1)	1 (0)	2 (1)	0 (0)	7 (0)
Time from symptom onset to admission, days					
≤2	110 (28)	218 (44)	42 (22)	199 (41)	569 (37)
3- 00204	150 (38)	146 (30)	64 (34)	162 (34)	522 (34)
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J Pediatric Infect Dis Soc. 2020 Nov 10;9(5):587-595. doi: 10.1093/jpids/piz087.

Table 1. Continued

Characteristic	California N = 393 n (%)	Georgia N = 491 n (%)	Oregon N = 187 n (%)	Minnesota N = 483 n (%)	Total N = 1554 n (%)
≥5	128 (33)	113 (23)	79 (42)	115 (24)	435 (28)
Severity measures					
ICU admission	72 (18)	223 (45)	58 (31)	63 (13)	416 (27)
ICU LOS, median (IQR), days	4 (2,7)	4 (3,7)	4 (3,8)	5 (3,8)	4 (3,7)
Mechanical ventilation	9 (2)	46 (9)	10 (5)	28 (6)	93 (6)
Death	0 (0)	4 (1)	0 (0)	1 (0)	5 (0)
Hospital LOS (median/IQR), days	3 (2, 4)	4 (2, 6)	3 (2, 5)	3 (2, 5)	3 (2, 5)
Bacterial infection					
Tested for bacteria [f]	165 (42)	258 (53)	76 (41)	199 (41)	698 (45)
Bacteria confirmation from those tested [f]	9/165 (5)	14/258 (5)	6/76 (8)	14/199 (7)	43/698 (6)
Viral codetection					
Tested for other viruses [g]	330 (84)	480 (98)	122 (65)	456 (94)	1388 (89)
Coinfection with other virus, confirmation from those tested	23/330 (7)	94/480 (20)	8/122 (7)	19/456 (4)	144/1388 (10)

Abbreviations: ICU, intensive care unit; IQR, interquartile range; LOS, length of stay.
[a] Other category includes Asian/Pacific Islander, American Indian or Alaska Native, or multiracial, non-Hispanic.
[f] By any culture type.
[g] Test type not known.
[b] Prematurity defined as neonates born at <37 weeks of gestation.
[c] Other conditions include drug exposure, congenital malformations, small for gestational age, all remaining conditions <10 observations.
[d] Tachypnea definition: if 0–5 months and relative risk >55; if 6–11 months and relative risk >50; if 12–23 months and relative risk >46.
[e] Hypoxemia definition: minimum oxygen saturation <90%.

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„Outcome“ während Hospitalisation wegen RSV

Table 2. Frequency of Children Aged <2 Years With Severe Respiratory Syncytial Virus–Associated Outcomes During Hospitalization, Influenza Hospitalization Surveillance Network, October 2014–April 2015

Age Group, months	Intensive Care Unit Admission, if Hospitalized		Mechanical Ventilation, if Hospitalized		Death, if Hospitalized	
	% (95% CI[a])	n/n	% (95% CI[a])	n/n	% (95% CI[a])	n/n
0–2	35 (23–48)	(217/614)	11 (6–15)	(65/614)	0.3 (0–0)	(2/614)
3–5	25 (11–41)	(65/262)	3 (0–6)	(8/262)	0.4 (0–0)	(1/262)
6–11	18 (5–30)	(53/300)	3 (0–5)	(9/300)	0.7 (0–2)	(2/300)
12–23	21 (10–30)	(81/378)	3 (0–5)	(11/378)	…-	(0/378)

Abbreviation: CI, confidence interval.
aThe95% confidence intervals were adjusted by site.

J Pediatric Infect Dis Soc. 2020 Nov 10;9(5):587-595. doi: 10.1093/jpids/piz087.

Hospitalisation je 100.000 Kinder wegen RSV

Table 3. Estimates of Respiratory Syncytial Virus Disease Burden in Rates per 100 000 Children and Total Counts per Age Group, Influenza Hospitalization Surveillance Network, October 2014–April 2015

Hospitalizations	Age Group, months	Rate (95% CI[a])	Number (95% CI[a])
	0–2	1970 (1787–2177)	25 940 (23 527–28 667)
	3–5	897 (761–1073)	11 803 (10 016–14 128)
	6–11	531 (459–624)	6988 (6039–8210)
	12–23	358 (317–405)	14 132 (12 517–15 988)
	<24	687 (627–758)	54 237 (49 509–59 867)

Counts are extrapolation of rates to US population.

Abbreviation: CI, confidence interval.

[a]The 95% confidence intervals were adjusted by bootstrapping the number of hospitalizations and the detection multiplier, accounting for variability of testing and test sensitivities by site.

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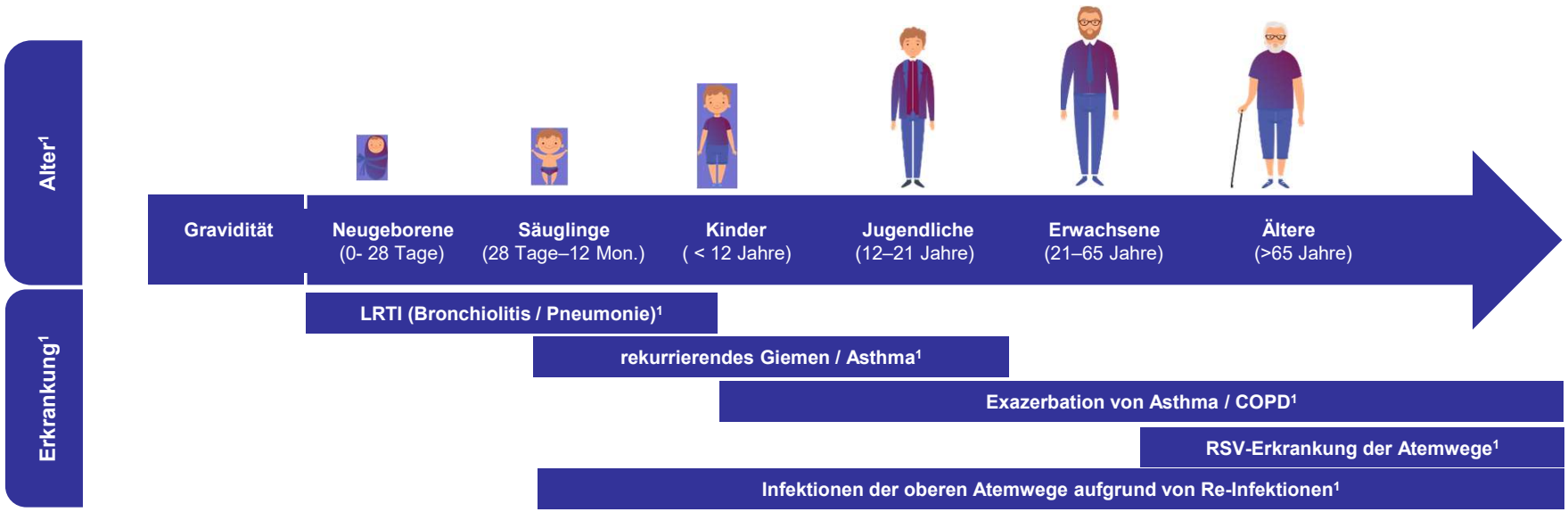
RSV – altersabhängiger Verlauf der Infektion[1,2]



LRTI: lower respiratory tract infection; COPD, chronic obstructive pulmonary disease;

1. Openshaw PJM, *et al. Annu Rev Immunol.* 2017;35:501–532;
2. Shi T, *et al. Lancet.* 2017;390(10098):946–958; 3. Shi T, *et al. J Infect Dis.* 2020;222(Suppl. 7):S577–S583.
4. https://www.cdc.gov/ncbddd/childdevelopment/positiveparenting/index.html

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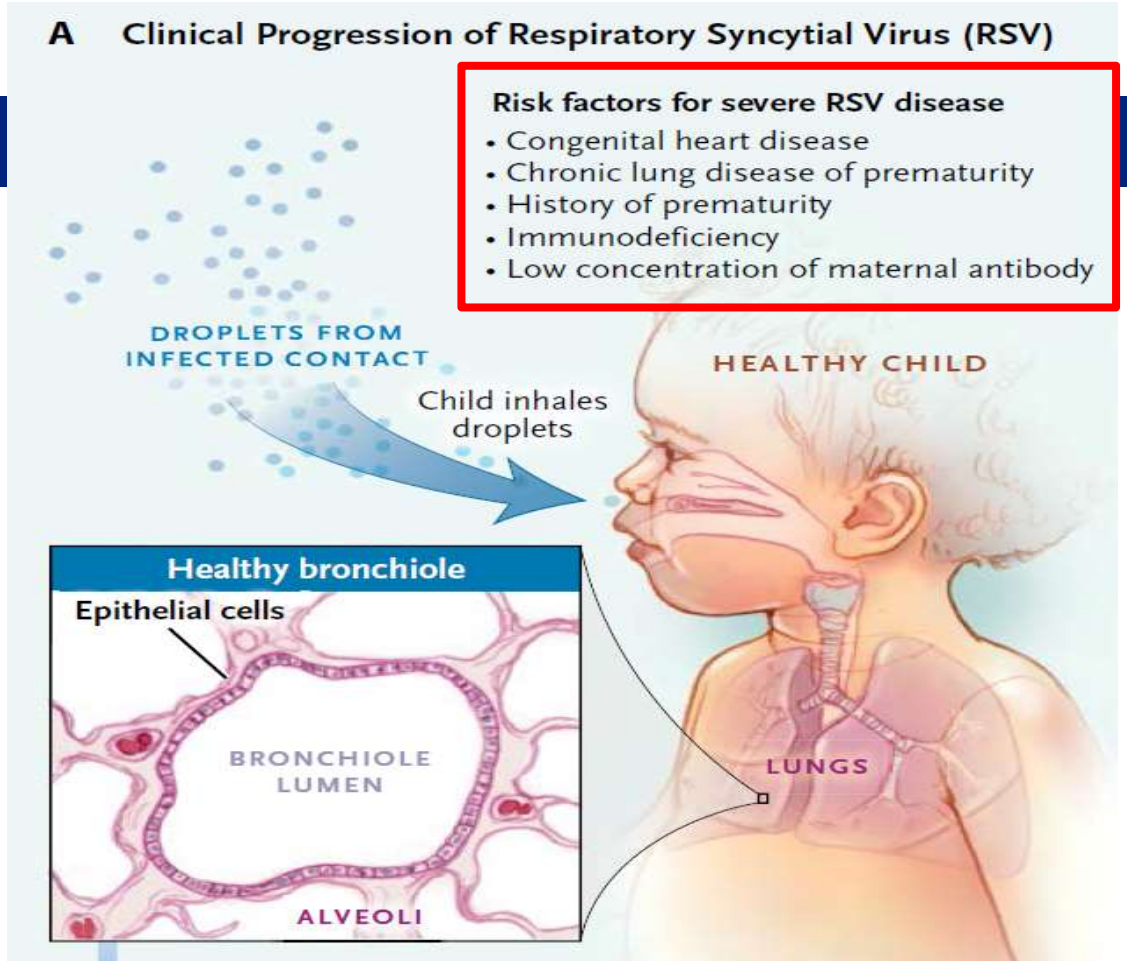
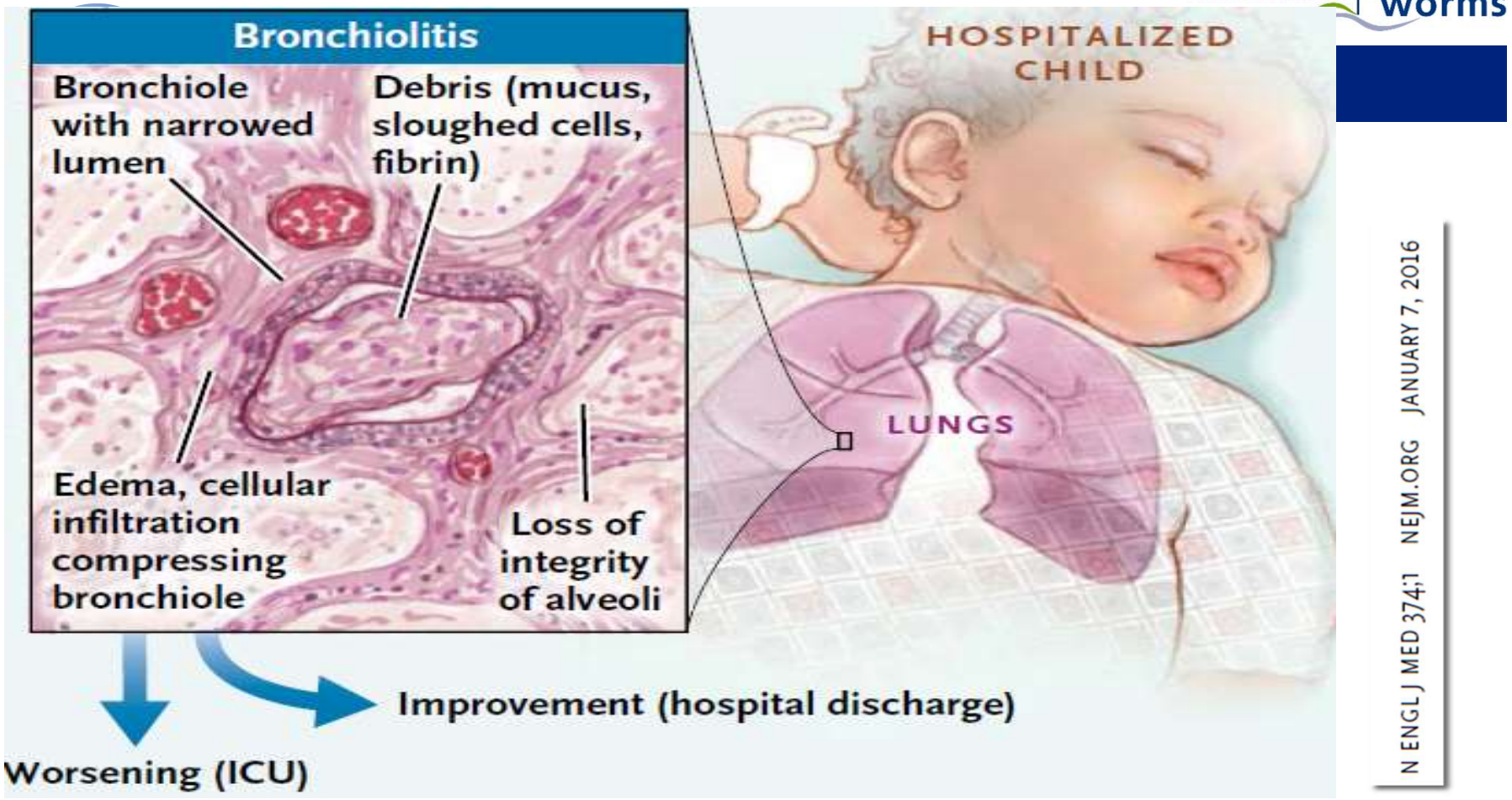


N ENGL J MED 374;1 NEJM.ORG JANUARY 7, 2016



N ENGL J MED 374;1 NEJM.ORG JANUARY 7, 2016

RSV – Risikofaktorenkonzept

–

Eur J Pediatr (2007) 166:1273–1283
DOI 10.1007/s00431-007-0426-y

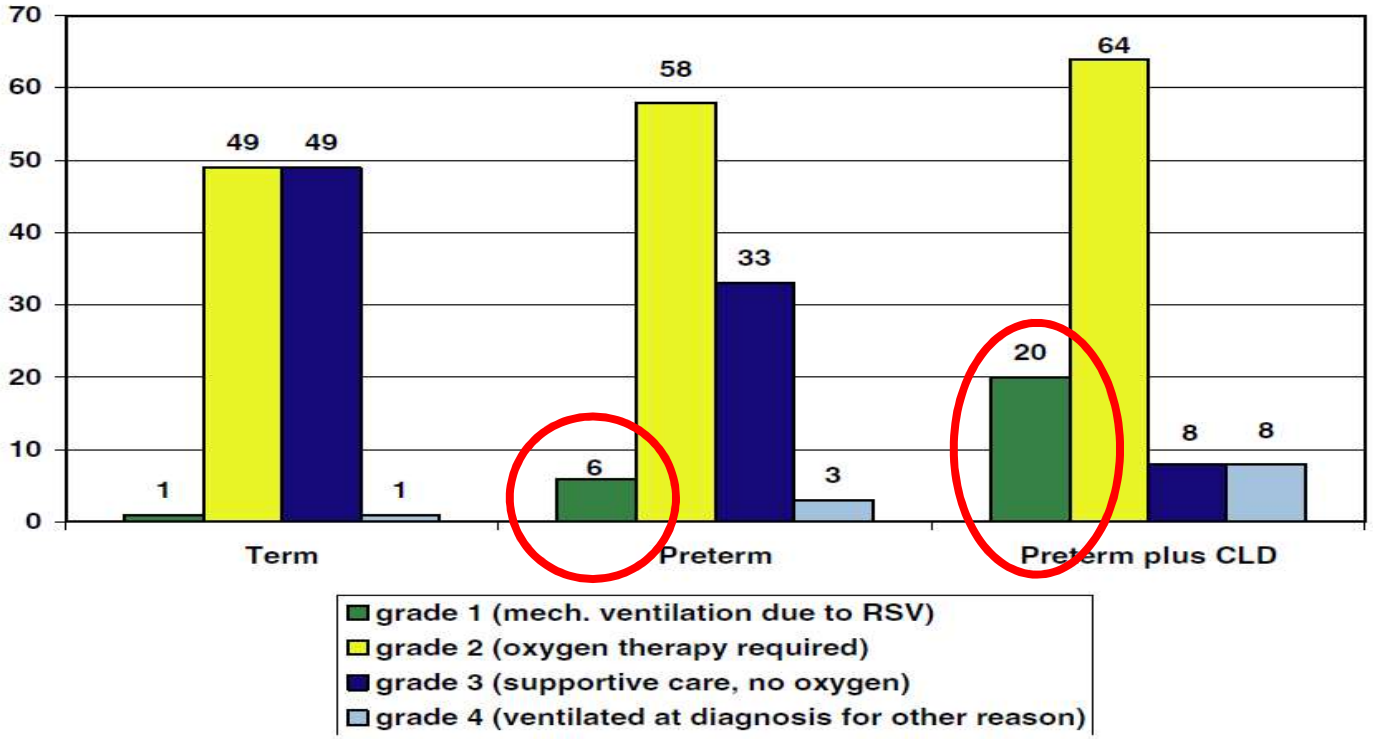
ORIGINAL PAPER

klinikum worms

Respiratory syncytial virus infection in 406 hospitalized premature infants: results from a prospective German multicentre database

Arne Simon · Roland A. Ammann · Anja Wilkesmann · Anna M. Eis-Hübinger · Oliver Schildgen · Edda Weimann · Hans U. Peltner · Peter Seiffert ·

Fig. 2 Modified McIntosh Score (clinical severity grading) in prematurely born children (n=406) vs. children born at term (n=1,162) and in preterms with CLD (n=50) [in patients with RSV infection (1999–2005)] (proportions presented in %)



klinikum worms

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ORIGINAL PAPER

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Table 4 Results of uni- and multivariate logistic regression of clinical variables on course (complicated vs. not)

	Univariate logistic regression		Multivariate logistic regression	
Potential predictor	Odds ratio (95% CI)	*P*	Odds ratio (95% CI)	*P*
Prematurity	2.13 (1.64 to 2.77)	<0.001	1.71 (1.32 to 2.25)	<0.001
Born before gestational week 32	3.45 (2.14 to 5.79)	<0.001	n.s.	–
Born before gestational week 28	6.75 (2.43 to 26.03)	<0.001	n.s.	–
Birth weight <1,500 g	3.41 (2.09 to 5.79)	<0.001	n.s.	–
CLD_{plus}	44.61 (8.10 to infinity)	<0.001	25.03 (4.46 to infinity)	<0.001
Congenital heart disease	1.88 (1.24 to 2.93)	0.0022	n.s.	–

CLD = chronic lung disease of prematurity; CLD_{plus} = CLD with medical treatment in the last 6 months; n.s. = not significant

LL AWMF 048-012 - Überarbeitung 2017/2018 / Version 30.10.2018
Prophylaxe von schweren Erkrankungen durch Respiratory Syncytial Virus (RSV) bei Risikokindern

klinikum worms

publiziert bei: AWMF online – Das Portal der wissenschaftlichen Medizin

Leitlinie in Überarbeitung

DGPI – Deutsche Gesellschaft für Pädiatrische Infektiologie e.V.

AWMF-LL 048-012

Kernaussage 7: Palivizumab reduziert die RSV-bedingte Hospitalisierungsrate bei Frühgeborenen ≤ 35 +6 SSW bis zu einem Alter von 6 Monaten, bei Frühgeborenen ≤ 35 +6 SSW mit medikamentös behandelter chronischer Lungenerkrankung (BPD) bis zu einem Alter von 24 Monate und bei Kindern mit hämodynamisch relevanten Herzfehler bis zu einem Alter von 24 Monaten. In den Zulassungsstudien konnte eine Verhinderung schwerer letaler oder beatmungspflichtiger RSV-Erkrankungen nicht belegt werden. Palivizumab wird als weitgehend sicheres Medikament angesehen.

Kernaussage 13: Frühgeborene im Alter von ≤ 24 Lebensmonaten zum Beginn der RSV-Saison, die wegen mittelschwerer oder schwerer bronchopulmonaler Dysplasie/chronischer Lungenerkrankung in den letzten drei Monaten vor Beginn der RSV-Saison (Beginn frühestens Anfang November) mit Sauerstoff behandelt oder beatmet wurden, haben ein hohes Risiko, eine schwere RSV-Erkrankung (z.B. mit Hospitalisation) zu erleiden. Diese Kinder sollen eine Palivizumab-Prophylaxe erhalten.

Kernaussage 14: Frühgeborene mit einem Gestationsalter von ≤ 28+6 Schwangerschaftswochen im Alter von ≤ 6 Monaten zum Beginn der RSV-Saison haben ein mittleres Risiko, eine schwere RSV-Erkrankung (z.B. mit Hospitalisation) zu erleiden. Diese Kinder können eine Palivizumab-Prophylaxe erhalten.

Kernaussage 15: Frühgeborene mit einem Gestationsalter von 29+0 bis 34+6 Schwangerschaftswochen im Alter von ≤ 6 Monaten zum Beginn der RSV-Saison mit mindestens zwei der folgenden Risikofaktoren:

a) Entlassung aus der neonatologischen Primärversorgung direkt vor oder während der RSV-Saison,

b) Kinderkrippenbesuch oder Geschwister in externer Kinderbetreuung,

c) schwere neurologische Grunderkrankung.

Kernaussage 18: Kinder mit hämodynamisch relevanter Herzerkrankung - vor allem operations- bzw. interventionsbedürftige Herzfehler mit pulmonalarterieller Hypertonie, pulmonal-venöser Stauung oder Zyanose - sowie bei schwerer Herzinsuffizienz unter medikamentöser Therapie im Alter von < 6 Lebensmonaten zum Beginn der RSV-Saison haben ein hohes Risiko für eine schwere RSV-Erkrankung und sollen eine Palivizumab-Prophylaxe erhalten.

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Risikofaktoren

Frühgeburtlichkeit, Geburtsgewicht, Geschwister, Muttermilch, Soziodemographie

Risk factors for respiratory syncytial virus associated with acute lower respiratory infection in children under five years: Systematic review and meta–analysis

Ting Shi[1], Evelyn Balsells[1], Elizabeth Wastnedge[1], Rosalyn Singleton[2,3], Zeba A Rasmussen[4], Heather J Zar[5], Barbara A Rath[6], Shabir A Madhi[7,8,9], Stuart Campbell[11], Linda Cheyenne Vaccari[1], Lisa R Bulkow[2], Elizabeth D Thomas[4], Whitney Barnett[5], Christian Hoppe[6], Harry Campbell[1,10*], Harish Nair[1,11,12*]

Background Respiratory syncytial virus (RSV) is the most common pathogen identified in young children with acute lower respiratory infection (ALRI) as well as an important cause of hospital admission. The high incidence of RSV infection and its potential severe outcome make it important to identify and prioritise children who are at higher risk of developing RSV–associated ALRI. We aimed to identify risk factors for RSV–associated ALRI in young children.

Table 4. Meta–estimate of odds ratio for risk factors excluding studies with quality score ≤6.25 (ie, "low–quality")

Risk factor	Multivariable analysis		Multivariable and univariable analysis	
	No. of studies	Meta–estimate OR (95% confidence interval)	No. of studies	Meta–estimate OR (95% confidence interval)
Prematurity (gestational age <37 weeks)	2	–	7	1.96 (1.44–2.67)
Low birth weight	2	–	5	1.91 (1.45–2.53)
Being male	6	1.32 (1.24–1.40)	12	1.23 (1.13–1.33)
Siblings	6	1.53 (1.20–1.95)	11	1.60 (1.32–1.95)
Maternal smoking	4	1.34 (1.26–1.42)	7	1.36 (1.24–1.50)
History of atopy	1	–	5	1.47 (1.16–1.87)
Low parental education	4	1.23 (0.73–2.09)	6	1.40 (0.94–2.08)
Passive smoking	4	1.40 (0.65–3.00)	8	1.29 (0.96–1.73)
Daycare center attendance	2	–	3	1.61 (0.98–2.64)
Indoor air pollution	4	0.69 (0.35–1.37)	5	0.81 (0.42–1.57)
No breastfeeding	1	–	3	2.24 (1.56–3.20)
Crowding (>7 persons in household)	1	–	3	1.94 (1.29–2.93)

OR – odds ratio

Journal of the Pediatric Infectious Diseases Society

ORIGINAL ARTICLE

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Estimated Burden of Community-Onset Respiratory Syncytial Virus–Associated Hospitalizations Among Children Aged <2 Years in the United States, 2014–15

Carmen S. Arriola,[1] Lindsay Kim,[2] Gayle Langley,[2] Evan J. Anderson,[1,3] Kyle Openo,[4] Andrew M. Martin,[4] Ruth Lynfield,[5] Erica Bye,[6] Kathy Como-Sabetti,[5] Arthur Reingold,[4] Shua Chai,[4] Pam Daily,[6] Ann Thomas,[7] Courtney Crawford,[7] C. Reed,[1] S. Garg,[1] and Sandra S. Chaves[1]

[1]Influenza Division, Centers for Disease Control and Prevention, Atlanta, Georgia, USA; [2]Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA; [3]Departments of Medicine and Pediatrics, Emory University School of Medicine, Atlanta, Georgia, USA; [4]Georgia Emerging Infections Program, Atlanta Veterans Affairs Medical Center, Atlanta, Georgia, USA; [5]Minnesota Department of Health, St. Paul, Minnesota, USA; [6]California Emerging Infections Program, Oakland, California, USA; and [7]Oregon Public Health Division, Portland, Oregon

ristics of Respiratory Syncytial Virus Hospitalizations Among Children Aged <2 Years, by Study Site, 'k, October 2014–April 2015

	California N = 393 n (%)	Georgia N = 491 n (%)	Oregon N = 187 n (%)	Minnesota N = 483 n (%)	Total N = 1554 n (%)
	161 (41)	187 (38)	83 (44)	183 (38)	614 (40)
	53 (13)	73 (15)	38 (20)	98 (20)	262 (17)
	81 (21)	91 (19)	33 (18)	95 (20)	300 (19)
12–23	98 (25)	140 (29)	33 (18)	107 (22)	378 (24)
Sex					
Female	161 (41)	201 (41)	83 (44)	214 (44)	659 (42)
Race/Ethnicity					
Hispanic	172 (44)	101 (21)	47 (25)	40 (8)	360 (23)
White non-Hispanic	49 (12)	133 (27)	100 (53)	212 (44)	494 (32)
Black non-Hispanic	41 (10)	219 (45)	13 (7)	102 (21)	375 (24)
Other [a]	45 (11)	26 (5)	19 (10)	78 (16)	168 (11)
Missing data	86 (22)	12 (2)	8 (4)	51 (11)	157 (10)
Health insurance					
Public	283 (72)	361 (74)	126 (67)	166 (34)	936 (60)
Private	89 (23)	123 (25)	57 (30)	298 (62)	567 (36)
Both	14 (4)	2 (0)	4 (2)	17 (4)	37 (2)
None	4 (1)	2 (0)	0 (0)	2 (0)	8 (1)

Table 1. Demographic and Clinical Characteristics of Respiratory Syncytial Virus Hospitalizations Among Children Aged <2 Years, by Study Site, Influenza Hospitalization Surveillance Network, October 2014–April 2015

Characteristic	California N = 393 n (%)	Georgia N = 491 n (%)	Oregon N = 187 n (%)	Minnesota N = 483 n (%)	Total N = 1554 n (%)
Age group, months					
0–2	161 (41)	187 (38)	83 (44)	183 (38)	614 (40)
3–5	53 (13)	73 (15)	38 (20)	98 (20)	262 (17)
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J Pediatric Infect Dis Soc. 2020 Nov 10;9(5):587-595. doi: 10.1093/jpids/piz087.

Hospitalisation von Kindern < 2 Jahre und etwaige Risikofaktoren

Underlying condition					
No underlying condition or born premature	277 (70)	318 (65)	103 (55)	349 (72)	1047 (67)
Yes					
Prematurity[b]	66 (17)	81 (16)	30 (16)	80 (17)	257 (17)
Gestational age in weeks (min-max)	25–36	23–36	24–36	25–36	23–36
Asthma	24 (6)	38 (8)	8 (4)	16 (3)	86 (6)
Cardiovascular disease	14 (4)	25 (5)	21 (11)	15 (3)	75 (5)
Neurologic/neuromuscular disorders	16 (4)	30 (6)	14 (7)	17 (4)	76 (5)
Chronic lung disease	16 (4)	10 (2)	6 (3)	12 (2)	44 (3)
Abnormality of upper airway	4 (1)	6 (1)	10 (5)	10 (2)	30 (2)
Blood disease	3 (1)	7 (1)	3 (2)	4 (1)	17 (1)
Renal disorder	4 (1)	1 (0)	5 (3)	2 (0)	12 (1)
Immunocompromised condition	1 (0)	0 (0)	1 (1)	3 (1)	5 (0)
Chronic metabolic disease	1 (0)	1 (0)	0 (0)	2 (0)	4 (0)
Liver disease	0 (0)	1 (0)	1 (1)	1 (0)	3 (0)
Other conditions[c]	22 (6)	46 (9)	37 (20)	20 (4)	125 (8)

J Pediatric Infect Dis Soc. 2020 Nov 10;9(5):587-595. doi: 10.1093/jpids/piz087.

Respiratory Syncytial Virus–Associated Hospitalizations Among Young Children: 2015–2016

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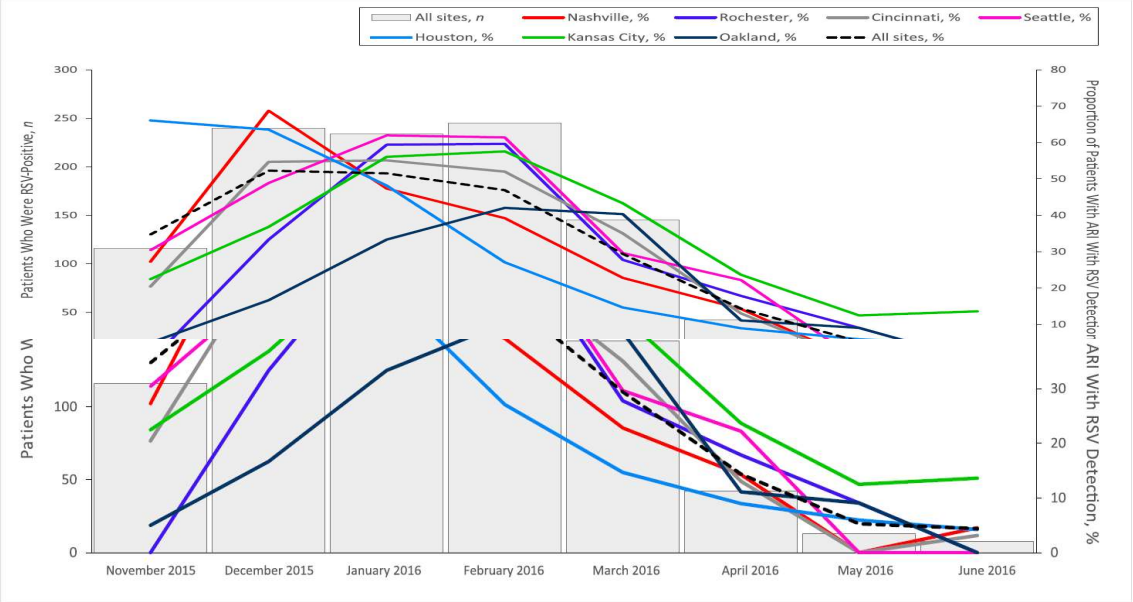

FIGURE 2
RSV-associated hospitalized children <5 years of age by enrollment date and site.

Hospitalisierung wgen ARI - Anteil RSV (

TABLE 1 Patient Demographics

Characteristic	RSV-Positive (n = 1043), n (%)[a]	RSV-Negative (n = 1926), n (%)[a]	P[b]
Sex			
Male	587 (56.3)	1140 (59.2)	.12
Female	456 (43.7)	786 (40.8)	—
Age, mo			
0–2	342 (32.8)	401 (20.8)	<.001
3–5	184 (17.6)	121 (6.3)	—
6–11	178 (17.1)	294 (15.3)	—
12–23	199 (19.1)	503 (26.1)	—
24–59	140 (13.4)	607 (31.5)	—

PEDIATRICS Volume 146, number 1, July 2020:e20193611

n = 2.969

TABLE 2 Patient History and Clinical Characteristics

Characteristic	RSV-Positive (n = 1043)	RSV-Negative (n = 1926)	P[a]
Any comorbid condition,[b] n (%)	217 (20.8)	714 (37.1)	<.001
Chronic lung disease	117 (11.2)	455 (23.6)	<.001
Congenital heart disease	46 (4.4)	106 (5.5)	.20
Neurologic and/or neuromuscular disease	43 (4.1)	118 (6.1)	.02
Immunocompromised condition	13 (1.2)	60 (3.1)	.002
History of prematurity (<37 wk),[c] n (%)	162 (17.9)	300 (22.7)	.006
Received palivizumab,[c] n (%)	21 (2.3)	95 (7.2)	<.001
Comorbid condition or history of prematurity, n (%)	339 (32.5)	892 (46.3)	<.001
Other children in household, n (%)			
<5 y old	454 (43.5)	717 (37.2)	<.001
5–17 y old	537 (51.5)	1066 (55.3)	.04
No other children	260 (24.9)	495 (25.7)	.64
Any household member is a smoker, n (%)	260 (24.9)	487 (25.3)	.83
History of breastfeeding, n (%)			
Any duration	825 (79.1)	1506 (78.2)	.57
Duration			
Never	215 (20.6)	410 (21.3)	<.001
<1 mo	225 (21.6)	342 (17.8)	—
1–6 mo	466 (44.7)	766 (39.8)	—
≥7 mo	127 (12.2)	376 (19.5)	—
Not specified	7 (0.7)	22 (1.1)	—

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PEDIATRICS Volume 146, number 1, July 2020:e20193611

n = 2.969

Hospitalisierung wegen RSV nach Gestationsalter und Lebensjahren

TABLE 3 RSV-Associated Hospitalized Children <2 Years of Age by Gestational Age and Age Group

Gestational Age at Birth	0–2 mo	3–5 mo	6–11 mo	12–23 mo	<24 mo
<29 wk, *n* (%)	0 (0)	2 (1)	6 (3)	11 (6)	19 (2)
29–31 wk, *n* (%)	2 (1)	3 (2)	8 (4)	5 (3)	18 (2)
32–34 wk, *n* (%)	14 (4)	16 (9)	11 (6)	9 (5)	50 (6)
35–36 wk, *n* (%)	34 (10)	18 (10)	12 (7)	6 (3)	70 (8)
≥37 wk, *n* (%)	288 (84)	144 (78)	141 (79)	164 (82)	737 (82)
Total,[a] *n*	342	184	178	199	903

[a] Includes 4 patients with an unknown history of prematurity and 5 patients with a history of prematurity with unknown gestational age.

Innerhalb der ersten 2 Lebensjahre erkranken überwiegend reife NG an RSV!

Infection (2022) 50:1587–1590
https://doi.org/10.1007/s15010-022-01889-6

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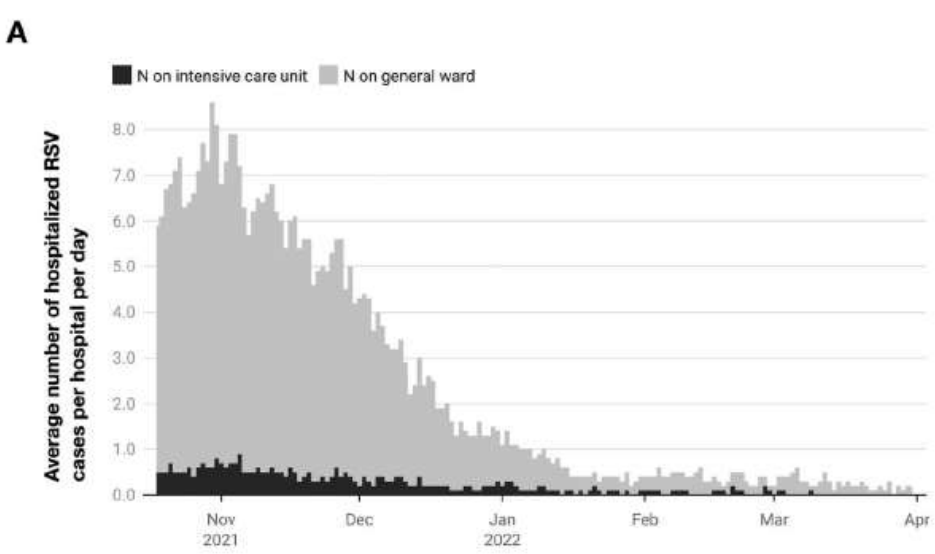
Aufnahme/Kinderklinik/Tag

BRIEF REPORT

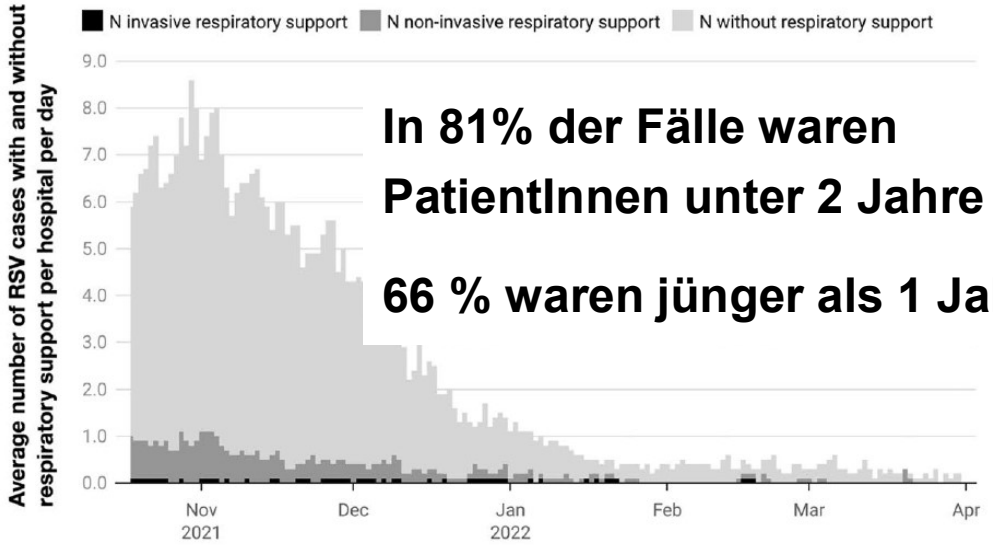
High burden of RSV hospitalizations in Germany 2021–2022

Tobias Tenenbaum[1] · Maren Doenhardt[2] · Natalie Diffloth[2] · Reinhard Berner[2] · Jakob P. Armann[2]



RSV-Fälle nach Behandlungsintensität und Alter

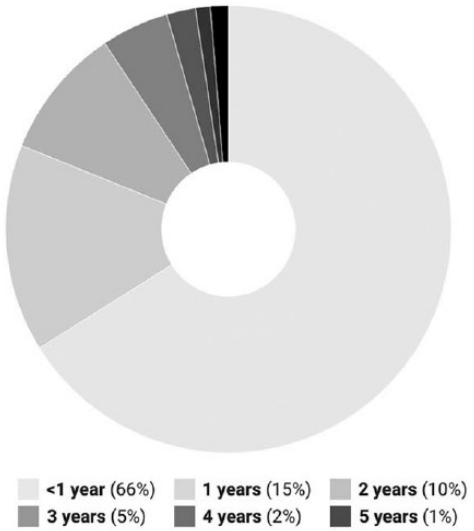
B



In 81% der Fälle waren PatientInnen unter 2 Jahre alt.

66 % waren jünger als 1 Jahr.

D



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RSV-Hospitalisierungsraten in der EU

Schätzungen zur Inzidenz von RSV-assoziierten ALRI* im Krankenhaus bei Kindern unter 5 Jahren

- globale Studien (passiv, krankenhausbasiert, stationär), jährliche Inzidenzraten von RSV-assoziierten ALRI* von 10-28/1.000 bei Kindern unter 1 Jahr in der EU
- Die Inzidenzraten aus passiven Studien könnten im Vergleich zu aktiven Studien unterschätzt werden.

Land (Region)	Inzidenz der RSV-assoziierten ALRI (pro 1.000 Kinder pro Jahr)		
	Alter <1 Jahr	Alter <2 Jahre	Alter <5 Jahre
Spanien (Gipuzoka)	26	15	6
Deutschland (Kiel)	16	9	5
Deutschland (multizentrisch)	28	16	8
UK (Shropshire)	28	16	8
Schweden (N. Stockholm)	14	8	4
Österreich (S. Austria)	12	7	4
UK	28	16	8
Niederlande	10	6	3

*ALRI, acute lower respiratory infection

Nair HN, *et al. The Lancet.* 2010;375(9725):1545–1555.

RSV – Prophylaxe

–

Optionen zur Prophylaxe für Säuglinge[1]

Säuglinge und Kinder

	Frühgeborene und Hochrisiko-Neugeborene[a]	Termingeborene <1 Jahr	Kinder 1–5 Jahre
Prophylaxe	Palivizumab	Keine	Keine
Behandlung	Ribavirin zur Inhalation[b]	Ribavirin zur Inhalation[b2,3]	Keine

zugelassen

zugelassen in Einzelfällen, nicht routinemäßig empfohlen*

ohne Angebot

[a]Hochrisiko definiert als: Frühgeborene, die im Gestationsalter von ≤ 35 Wochen geboren wurden, Kinder mit chronischer Lungenerkrankung und Kinder mit hämodynamisch bedeutsamer angeborener Herzerkrankung ; [b]Zugelassen von FDA und von der EMA für einige EU Mitgliedsländer zur Behandlung einer RSV Infektion, aber nicht zum routinemäßigen Einsatz und ohne Empfehlung für den Einsatz bei allen Fällen; FDA, Food and Drug Administration.

1. Villafana T, *et al. Expert Rev Vaccines.* 2017;16(7):1–13. 2. https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-clinical-evaluation-medicinal-products-indicated-prophylaxis-treatment-respiratory_en.pdf 3. AAP : https://pediatrics.aappublications.org/content/118/4/1774

Respiratory syncytia
the vaccine and mon

Natalie I Mazur, Jonne Terstappen, Ranju Baral, A
Clare L Cutland, Linda Eckert, Daniel Feikin, Tiffan
Siddhivinayak Hirve, Keith P Klugman, Leyla Krag
Flor M Munoz, Patrick K Munywoki, Lawrence M
Charles Sande, Padmini Srikantiah, Naveen Thac
Maria Zambon, Louis Bont

Respiratory syncytial virus is the second

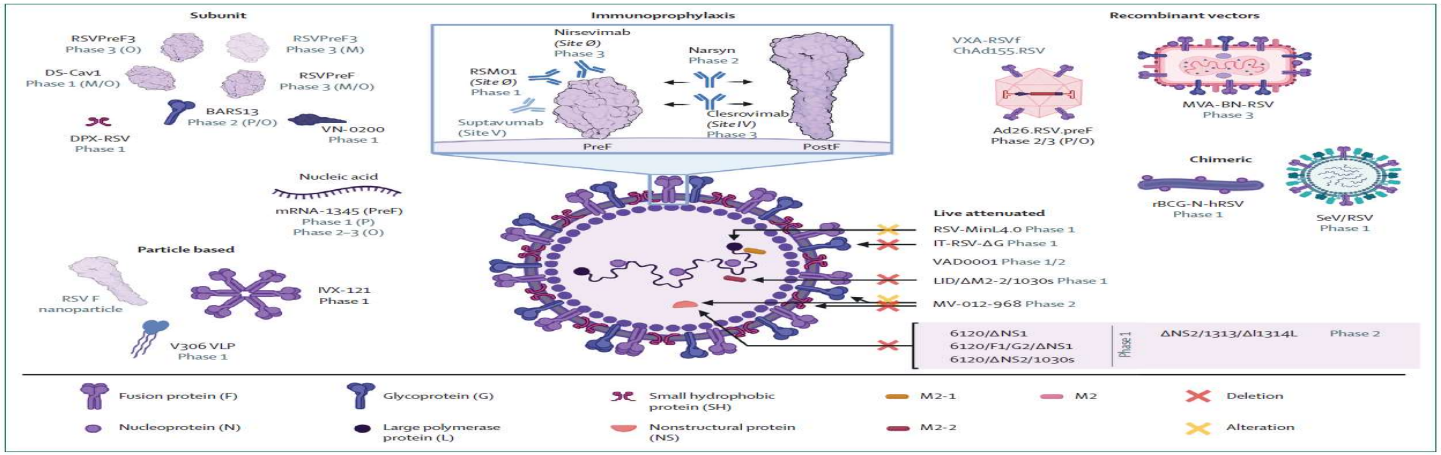
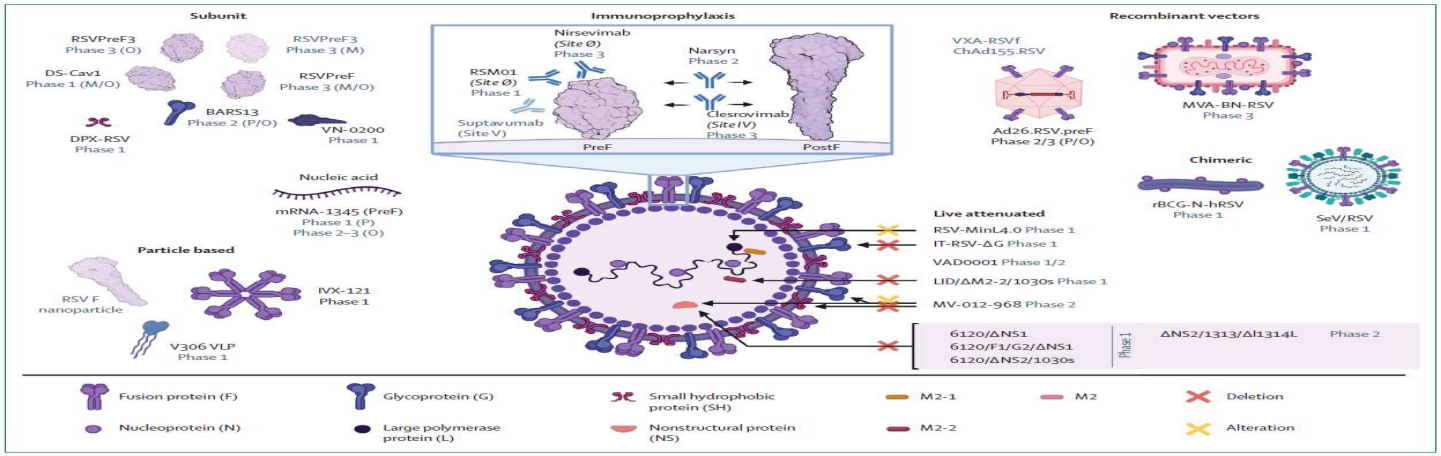


Figure 2: **Overview of vaccine candidates by preventive approach**
Pre-F protein was created with Protein Data Bank RCSB PDB 4MMU[28,29] and post-F protein was created with 3RRT.[30,31] Light grey indicates vaccine development halted or discontinued. RSV=respiratory syncytial virus. PreF=prefusion protein. PostF=postfusion protein. Ad=adenovirus. MVA=modified vaccinia Ankara virus. BCG=mycobacterium bovis. SeV=sendai virus.



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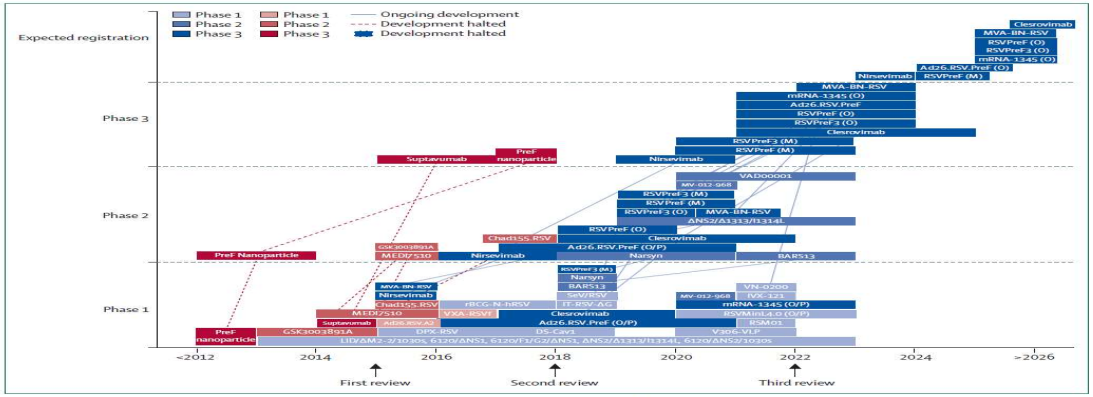

Figure 4: **Historical perspective of RSV vaccine and immunoprophylaxis development over the last 10 years and expected market access**
Candidates that are in ongoing development (blue) or no longer in development (red) are presented at the timing of the clinical trials rounded off to full years. The darkness of the colour represents the furthest development (phase 1, 2, or 3) of the candidate. Candidates with multiple clinical trials are connected with full or dotted lines to show the speed of development. Live attenuated viruses by the same manufacturer are summarised in one box as development of these candidates largely overlaps. The timing of current and previous RSV vaccine landscape reviews is shown at the bottom. RSV=respiratory syncytial virus. PreF=prefusion protein. The development of RSVPreF (M) was not discontinued but instead halted (dotted box). Expected registration was estimated by adding 1 year after published interim results, or if not available by adding 1 year to the estimated completion year published on ClinicalTrials.gov. In case of a phase 1/2 or 2/3 trial, the trial has only been placed in the furthest developed stage.

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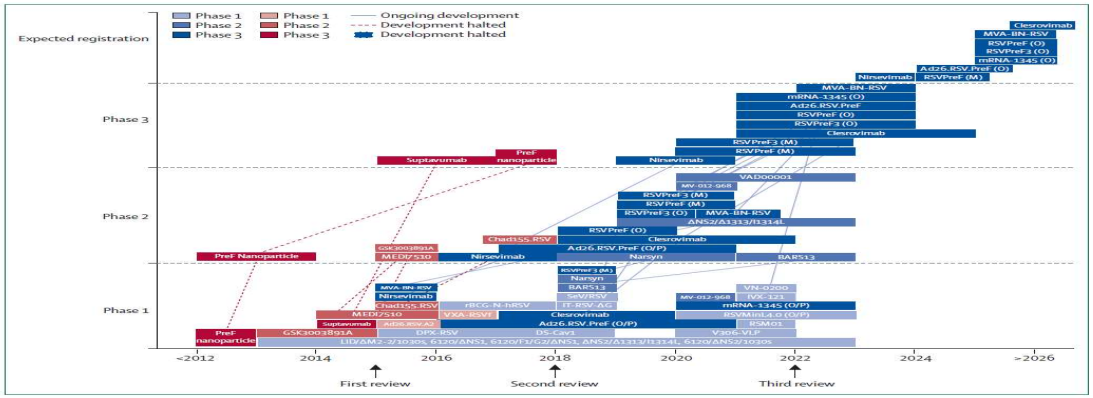
See Online for appendix

For **Vaccines for the World Conference** see https://www.resvinet.org/rsvvw21.html



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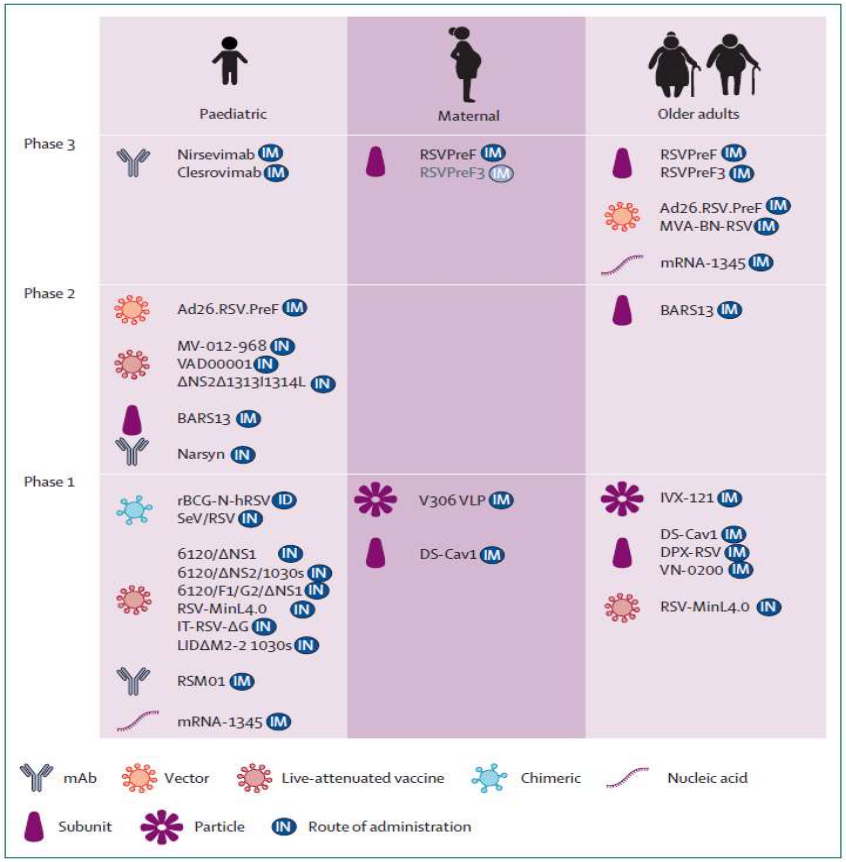

Figure 3: **RSV vaccine and monoclonal antibody agents by target population**
Vaccine candidates and monoclonal antibidies are categorised into three different target populations: paediatric, maternal, and older adults (aged >60 years) and clinical phase of development (ie, phase 1, 2, or 3). Different immunisation approaches are indicated by the key. Light grey text indicates development halted.
IM=intramuscular. IN=intranasal. ID=intradermal. RSV=respiratory syncytial virus. PreF=prefusion protein. PostF=postfusion protein.

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*

N Engl J Med 2022;386:837-46.
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rms

Table 1. Characteristics of the Participants at Baseline.*

Characteristic	Nirsevimab (N=994)	Placebo (N=496)	Total (N=1490)
	no. of participants/total no. (%)		
Age			
≤3.0 mo	577/994 (58.0)	285/496 (57.5)	862/1490 (57.9)
>3.0 to ≤6.0 mo	317/994 (31.9)	162/496 (32.7)	479/1490 (32.1)
>6.0 mo	100/994 (10.1)	49/496 (9.9)	149/1490 (10.0)
Gestational age			
≥35 to <37 wk	132/993 (13.3)	76/495 (15.4)	208/1488 (14.0)
≥37 wk	861/993 (86.7)	419/495 (84.6)	1280/1488 (86.0)
Female sex	464/994 (46.8)	257/496 (51.8)	721/1490 (48.4)
Weight			
<5 kg	403/992 (40.6)	192/496 (38.7)	595/1488 (40.0)
≥5 kg	589/992 (59.4)	304/496 (61.3)	893/1488 (60.0)
Race or ethnic group†			
American Indian or Alaska Native	57/991 (5.8)	26/496 (5.2)	83/1487 (5.6)
Asian	36/991 (3.6)	18/496 (3.6)	54/1487 (3.6)
Black	286/991 (28.9)	136/496 (27.4)	422/1487 (28.4)
Native Hawaiian or other Pacific Islander	6/991 (0.6)	5/496 (1.0)	11/1487 (0.7)
White	524/991 (52.9)	272/496 (54.8)	796/1487 (53.5)
Other or multiple categories	82/991 (8.3)	39/496 (7.9)	121/1487 (8.1)
Hemisphere of residence			
Northern	686/994 (69.0)	342/496 (69.0)	1028/1490 (69.0)
Southern	308/994 (31.0)	154/496 (31.0)	462/1490 (31.0)

* Data are for the intention-to-treat population.
† Race or ethnic group was reported by the parents or guardians. Each category includes participants whose parents or guardians selected only that category. "Other or multiple categories" includes participants whose parents or guardians indicated a category other than those listed or for whom more than one category was checked.

Table 2. Medically Attended Lower Respiratory Tract Infections and Hospitalizations Associated with Respiratory Syncytial Virus (RSV) through 150 Days after the Injection.*

End Point and Analysis	Nirsevimab (N=994)	Placebo (N=496)	Efficacy (95% CI)†	P Value
	no. (%)			
Medically attended RSV-associated lower respiratory tract infection			74.5 (49.6 to 87.1)	<0.001
Poisson regression with robust variance				
Observed events	12 (1.2)	25 (5.0)		
Participants with imputation of data‡	15 (1.5)	6 (1.2)		
Hospitalization for RSV-associated lower respiratory tract infection			62.1 (−8.6 to 86.8)	0.07
Poisson regression with robust variance				
Observed events	6 (0.6)	8 (1.6)		
Observed events	12 (1.2)	25 (5.0)		
Participants with imputation of data‡	15 (1.5)	6 (1.2)		
Hospitalization for RSV-associated lower respiratory tract infection			62.1 (−8.6 to 86.8)	0.07
Poisson regression with robust variance				
Observed events	6 (0.6)	8 (1.6)		
Participants with imputation of data‡	15 (1.5)	6 (1.2)		

* Data are for the intention-to-treat population.
† Efficacy was defined as the relative risk reduction (calculated as 1 minus the relative risk, where the relative risk was estimated with the use of a Poisson regression model with robust variance) in the nirsevimab group as compared with the placebo group and is expressed as a percentage.
‡ Data were imputed for participants who had no events and were not followed through 150 days after the injection.

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)	33.4 (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)

* Data are for participants in the northern hemisphere in the intention-to-treat population. Any test result refers to either the central reference test for the trial or a local test performed in the context of clinical care. Any respiratory illness included both upper and lower respiratory tract infections.

† Efficacy was defined as the relative risk reduction (calculated as 1 minus the relative risk, where the relative risk was estimated with the use of a Poisson regression model) in the nirsevimab group as compared with the placebo group and is expressed as a percentage. The efficacy and 95% confidence intervals were estimated on the basis of Poisson regression with robust variance with the use of only the term of trial-group assignment.

‡ The number of cases averted was calculated as the difference in the estimated number of cases between nirsevimab and placebo and expressed per 1000 infants treated. The 95% confidence intervals were estimated with the use of bootstrapping, with the 2.5 and 97.5 percentiles of 1000 replicates obtained by sampling participants, and were not adjusted for multiplicity.

§ The number needed to treat to avert one case of RSV-associated lower respiratory tract infection was calculated as the reciprocal of the difference in risk between the nirsevimab group and the placebo group.

¶ Included are medically attended lower respiratory tract infections, regardless of whether they met the criteria for the definition used for the primary end point.

Nirsevimab: A Development Program Conducted Across All Infants

	Term and Preterm Healthy Infants 29+ wGA		Infants Eligible to Receive Palivizumab
	Similar Study Design Across Complementary Populations		
	PHASE 3 Pivotal[1] MELODY STUDY (N ~ 3000)	PHASE 2b POC/Pivotal[2] (N ~ 1500)	PHASE 2/3 Pivotal[3] MEDLEY STUDY (N ~ 1500)
STUDY POPULATION	• **Infants ≥35 wGA** • Not eligible to receive palivizumab (AAP or other national/local guidelines)	• **Infants 29-<35 wGA** • Not eligible to receive palivizumab (AAP or other national/local guidelines)	• **Preterm Infants <35 wGA Infants with CLD/CHD** • Eligible to receive palivizumab (AAP or other national/local guidelines)
COMPARATOR STUDY POPULATION	**2:1 Nirsevimab: Placebo** • **Infants ≥35 wGA** • Not eligible to receive palivizumab (AAP or other national/local guidelines)	**2:1 Nirsevimab: Placebo** • **Infants 29-<35 wGA** • Not eligible to receive palivizumab (AAP or other national/local guidelines)	**2:1 Nirsevimab: Palivizumab** • **Preterm Infants <35 wGA Infants with CLD/CHD** • Eligible to receive palivizumab (AAP or other national/local guidelines)
COMPARATOR	**2:1 Nirsevimab: Placebo**	**2:1 Nirsevimab: Placebo**	**2:1 Nirsevimab: Palivizumab**
	Efficacy, Safety and PK		**Safety and PK (Efficacy via PK)**

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PK, pharmacokinetics.
1 Hammitt LL,et al N Engl J Med. 2022 Mar 3;386(9):837-846. **2.** Griffin MP, et al. N Engl J Med. 2020 Jul 30;383(5):415-425. **3.** Domachowske Joseph et al. N Engl J Med 2022 Mar 386:9, 892-894.

Nirsevimab for the prevention of RSV in all infants – CDC https://www.cdc.gov › 02-rsv-mat-ped-felter-508, PDF

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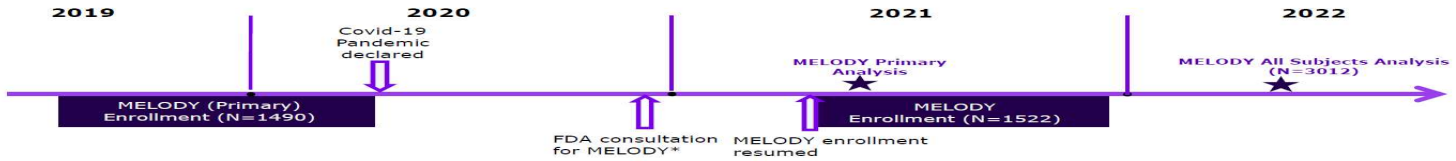
Impact of COVID-19 Pandemic on the Phase 3 MELODY Trial



Study enrollment and location

- Enrollment began 23 July 2019
- 150 sites (20 countries) in the Northern Hemisphere enrolled 1028 subjects in 2019 and experienced a typical RSV season
- 10 sites (in South Africa) in the Southern Hemisphere enrolled 462 subjects in early 2020

Situation and mitigation

- Onset of the COVID-19 pandemic in March 2020 led to several operational challenges leading to a pause in enrollment for MELODY
- No RSV cases occurred during the typical 2020 Southern Hemisphere
- After consultation with FDA, decision was made to analyze the primary endpoint after first 1490 enrolled (Primary).
- Study enrollment resumed in 2021.

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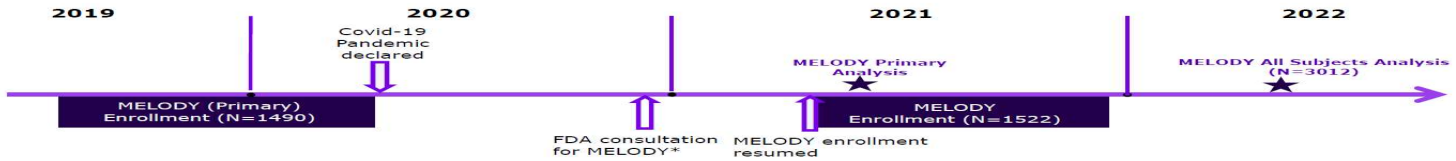
1. Hammitt LL et al. N Engl J Med 2022;386:837-46.
* EMA consultation in parallel

4

Impact of COVID-19 Pandemic on the Phase 3 MELODY Trial



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4

Nirsevimab for the prevention of RSV in all infants – CDC https://www.cdc.gov › 02-rsv-mat-ped-felter-508, PDF

Nirsevimab for the prevention of RSV in all infants – CDC https://www.cdc.gov › 02-rsv-mat-ped-felter-508, PDF

MELODY All Subjects – Efficacy through D151

Phase 3

Definition	Placebo (N=1003)		Nirsevimab (N=2009)		Efficacy	
	n	%	n	%	Efficacy	95% CI
MA RSV LRTI	54	5.4	24	1.2	**76.4**	62.3-85.2
MA RSV LRTI with hospitalization	20	2.0	9	0.4	**76.8**	49.4-89.4
MA RSV LRTI	54	5.4	24	1.2	**76.4**	62.3-85.2
MA RSV LRTI with hospitalization	20	2.0	9	0.4	**76.8**	49.4-89.4
MA RSV LRTI (very severe)	17	1.7	7	0.3	**78.6**	48.8-91.0

LRTI, lower respiratory tract infection; MA, medically attended; RSV, respiratory syncytial virus.
Very severe = hospitalization + requirement for supplemental oxygen and/or intravenous fluids

Nirsevimab for the prevention of RSV in all infants – CDC https://www.cdc.gov › 02-rsv-mat-ped-felter-508, PDF

Efficacy through D151

MELODY subjects N=3012
Ph 2b recommended dose subjects N=860

Definition	Placebo (N=1293)		Nirsevimab (N=2579)		Efficacy	
	n	%	n	%	Efficacy	95% CI
MA RSV LRTI	80	6.2	31	1.2	**79.0**	68.5-86.1
MA RSV LRTI with hospitalization	33	2.6	12	0.5	**80.6**	62.3-90.1
MA RSV LRTI (very severe)	28	2.2	7	0.3	**86.2**	68.1-94.0

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LRTI, lower respiratory tract infection; MA, medically attended; RSV, respiratory syncytial virus.
Very severe = hospitalization + requirement for supplemental oxygen and/or intravenous fluids

Pooled MELODY All Subjects AND Phase 2b Recommended Dose

Efficacy through D151

MELODY subjects N=3012
Ph 2b recommended dose subjects N=860

Definition	Placebo (N=1293)		Nirsevimab (N=2579)		Efficacy	
	n	%	n	%	Efficacy	95% CI
MA RSV LRTI	80	6.2	31	1.2	**79.0**	68.5-86.1
MA RSV LRTI with hospitalization	33	2.6	12	0.5	**80.6**	62.3-90.1
MA RSV LRTI (very severe)	28	2.2	7	0.3	**86.2**	68.1-94.0

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LRTI, lower respiratory tract infection; MA, medically attended; RSV, respiratory syncytial virus.
Very severe = hospitalization + requirement for supplemental oxygen and/or intravenous fluids

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*

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Table 1. Characteristics of the Participants at Baseline.*

Variable	Nirsevimab (N=969)	Placebo (N=484)
Hemisphere — no. (%)		
Northern	659 (68)	329 (68)
Southern	310 (32)	155 (32)
Age		
Mean — mo	3.29±2.22	3.28±2.31
Distribution — no. (%)		
≤3 mo	516 (53.3)	257 (53.1)
>3 to ≤6 mo	320 (33.0)	153 (31.6)
>6 mo	133 (13.7)	74 (15.3)
Gestational age		
Mean — wk	32.7±1.4	32.7±1.5
Distribution — no. (%)		
≥29 to ≤32 wk	363 (37.5)	185 (38.2)
>32 wk	606 (62.5)	299 (61.8)
Female sex — no. (%)	468 (48.3)	224 (46.3)
Weight — kg	4.60±1.92	4.51±1.96
Race or ethnic group — no./total no. (%)†		
American Indian or Alaska Native	0	1/484 (0.2)
Asian	5/968 (0.5)	10/484 (2.1)
Black	189/968 (19.5)	67/484 (13.8)
Native Hawaiian or other Pacific Islander	8/968 (0.8)	3/484 (0.6)
White	693/968 (71.6)	355/484 (73.3)
Other	61/968 (6.3)	43/484 (8.9)
Multiple categories	12/968 (1.2)	5/484 (1.0)
Sibling enrolled in trial — no. (%)	336 (34.7)	172 (35.5)

* Plus–minus values are means ±SD. Data are for the intention-to-treat population. Percentages may not total 100 because of rounding.
† Race and ethnic group were reported by the participants' parents or guardians. Race or ethnic group was not reported by one participant in the nirsevimab group.

Table 2. Medically Attended Lower Respiratory Tract Infection and Hospitalization Associated with Respiratory Syncytial Virus (RSV) through 150 Days after Dose.*

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)		
			(56.5–83.1)	
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

* Data are for the intention-to-treat population. The case definition for inclusion of the lower respiratory tract infection in the analysis of the end point required a positive result for RSV in a real-time, reverse-transcriptase–polymerase-chain-reaction assay performed at a central laboratory, a physical examination finding indicating involvement of the lower respiratory tract, and at least one indicator of clinical severity. CI denotes confidence interval.
† Data were imputed for participants who had no events and were not followed through 150 days after administration of the dose of nirsevimab or placebo.

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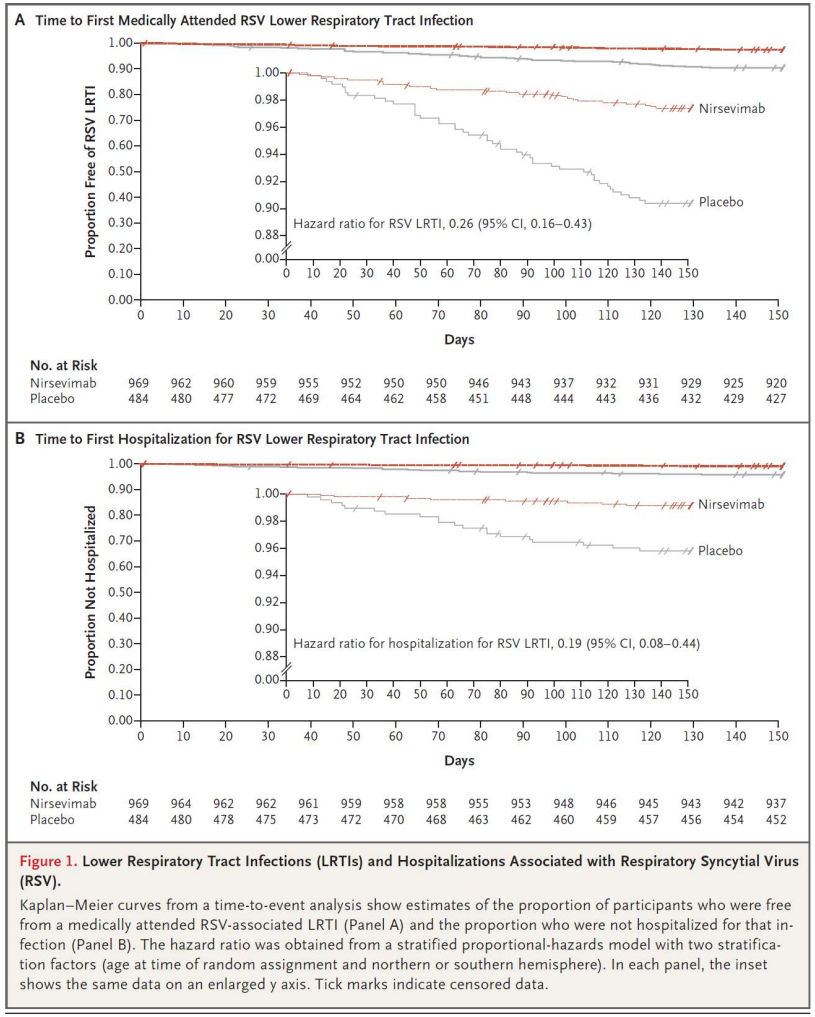

Figure 1. Lower Respiratory Tract Infections (LRTIs) and Hospitalizations Associated with Respiratory Syncytial Virus (RSV).

Kaplan–Meier curves from a time-to-event analysis show estimates of the proportion of participants who were free from a medically attended RSV-associated LRTI (Panel A) and the proportion who were not hospitalized for that infection (Panel B). The hazard ratio was obtained from a stratified proportional-hazards model with two stratification factors (age at time of random assignment and northern or southern hemisphere). In each panel, the inset shows the same data on an enlarged y axis. Tick marks indicate censored data.

	Placebo group (n=786)	Nirsevimab group (n=1564)	Relative risk reduction (95% CI)	p value
Medically attended RSV LRTI*	51 (6%)	19 (1%)	79·5% (65·9–87·7)	<0·0001
Hospital admission for medically attended RSV LRTI†	21 (3%)	9 (1%)	77·3% (50·3–89·7)	0·0002
Very severe RSV LRTI‡	18 (2%)	5 (<1%)	86·0% (62·5–94·8)	<0·0001
Medically attended LRTI of any cause‡§	149 (19%)	191 (12%)	35·4% (21·5–46·9)	<0·0001
Hospital admission for respiratory illness of any cause‡§	51 (6%)	57 (4%)	43·8% (18·8–61·1)	0·0022

95% CI) and p values were estimated on the basis of Poisson regression with robust variance
ns. LRTI=lower respiratory tract infection. RSV=respiratory syncytial virus. *The model included
group, and stratification factors (age at randomisation and hemisphere) as covariates obtained
after missing data imputation. †The model included study and treatment group as covariates
ined from PROC MIANALYZE after missing data imputation. ‡The model included treatment as
ll medically attended LRTIs according to the investigator's judgement, regardless of whether
teria for the definition of medically attended LRTI (appendix p 4).

Table 2: **Efficacy of nirsevimab weight-band dose on different case definitions of medically attended LRTI to 150 days post-dose (intention-to-treat population)**

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 I. 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

Summary

Background In a phase 2b trial and the phase 3 MELODY trial, nirsevimab, an extended half-life, monoclonal antibody against respiratory syncytial virus (RSV), protected healthy infants born preterm or at full term against medically attended RSV lower respiratory tract infection (LRTI). In the MEDLEY phase 2–3 trial in infants at higher risk for severe RSV infection, nirsevimab showed a similar safety profile to that of palivizumab. The aim of the current analysis was to assess the efficacy of nirsevimab using a weight-banded dosing regimen in infants born between

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S2352-4642(22)00323-2

Zusammenfassung

- RSV ist sehr häufige Ursache von tiefen Atemwegsinfektionen (LTRI) bei Säuglingen
- Erhebliche Morbidität (und Mortalität), kurz- und langfristige Komplikationen
- Mehrheit der wegen RSV hospitalisierten Säuglinge sind gesunde Säuglinge
- Keine kausale Therapie verfügbar
- **These:** Notwendigkeit, alle Säuglinge vor RSV zu schützen
- Passive und aktive Immunisierungsstrategien verfügbar bzw. in Entwicklung
- **Konzept:** Maternale Immunisierung
- Zu Beginn RSV-Saison: Monoklonale Antikörper nach der Geburt (**These:** für alle)
- Immunisierung des Kindes im höheren Lebensalter

VIELEN DANK FÜR IHRE AUFMERKSAMKEIT!

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