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Summary

Background To evaluate the acceptance and safety of the treatment of newborns with nirsevimab (a long-acting monoclonal antibody designed to prevent respiratory syncytial virus infections) during the first season of implementation.

Methods A longitudinal, prospective, single-centre cohort study was conducted from September 18th, 2023, to January 23rd, 2024 at Lille University Hospital (Lille, France). All newborns admitted to the hospital's maternity department during the study period and whose parents agreed to participate in the study were included. Parents were asked to state whether or not they agreed for their infant to receive nirsevimab. The occurrence of adverse events (AEs) 2 h after nirsevimab treatment and 7, 14 and 30 days after discharge was documented by the mother. The primary endpoint was the nirsevimab treatment acceptance rate. The secondary endpoints were the variables associated with the acceptance of nirsevimab, the reasons for accepting or refusing nirsevimab, and the treatment's real-life safety, relative to a non-treated control group of newborns.

Findings Of the 1730 infants born in the hospital during the study period, 477 met all the inclusion criteria and were enrolled. The nirsevimab acceptance rate [95% confidence interval] was 91.6% [89.1%–94.2%]. In a multivariable analysis, the mother's age, lower parity and having a partner in work were significantly associated with nirsevimab acceptance. The most common reason for accepting treatment was "to protect my baby", and the most common reason for refusing treatment was the lack of long-term data on nirsevimab. The nirsevimab and control groups did not differ significantly in terms of the types and frequencies of AEs. At least one serious AE was reported for 9.4% of the infants in the nirsevimab group and for 10.3% in the control group. None of the serious AEs were considered to be related to nirsevimab treatment.

Interpretation The nirsevimab acceptance rate for newborns in the maternity unit was high during the first season of implementation. The safety profile was very good, with no significant differences between the nirsevimab group and the control group.

Funding None.

Keywords: Acceptance; Newborn; Nirsevimab; Respiratory syncytial virus; Safety

Introduction

Respiratory syncytial virus (RSV) is the world's leading cause of (i) lower respiratory tract infections in infants and (ii) hospital admissions and deaths due to these infections in infants under the age of one; the problem is especially severe in limited-resource countries.[1–3] Although deaths due to RSV are rare in high-resource countries, the pathogen typically causes annual

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Research in context

Evidence before this study

We searched PubMed database, from June 26, 2020 (date of the first study that mentioned nirsevimab) to January 23, 2024 (end of our study period), using only the terms "nirsevimab". Of the 97 references identified, only five were randomized clinical trials, from pivotal studies. Most of the other published studies focused on nirsevimab efficacy, medico-economic impact and implementation strategies. Although the safety of the treatment was considered in each of the pivotal clinical trials, the number of children included at birth in these studies was limited, with half of the children aged between 0 and 3 months and the other half aged 3 months or more. None of the 97 references identified evaluated the acceptance of nirsevimab; particularly when proposed at birth. To date, there were no published data designed to assess the acceptance of this new treatment, which is proposed at birth and requires an intramuscular injection, to prevent what is—in high-resource countries, at least—an essentially non-lethal disease.

Added value of this study

This is the first prospective, longitudinal, study conducted at the maternity department to assess the acceptance and safety of nirsevimab proposed at birth. Our results demonstrate a very high acceptance rate, identify significant variables associated with nirsevimab acceptance in multivariable analysis and reasons for acceptance or for refusal of nirsevimab. The safety profile of this preventive treatment administered at birth was good, with very few adverse events up until 30 days after injection. With the exception of more regurgitations 30 days after discharge in the nirsevimab group, other adverse events were similarly frequent in the nirsevimab and control groups.

Implications of all the available evidence

During the first season of immunization in France, the acceptance rate of nirsevimab (a novel treatment that requires an intramuscular injection in a newborn for the prevention of a disease that is frequent but non-fatal in Europe) was very high. Nirsevimab tolerance was good. However, some parents may refuse this treatment and expose their babies to a greater risk of respiratory syncytial virus infections and complications. The good safety of nirsevimab administered at birth and the identification of variables associated with acceptance and refusal of nirsevimab are data that could be used by doctors with parents reluctant to accept this preventive treatment after birth.

epidemics of bronchiolitis and thus triggers consultations with physicians, emergency department visits, hospital admissions (with admission to an intensive care unit in 20% of cases), and healthcare system saturation.[4–6]

Infants are especially vulnerable to RSV for several reasons, including anatomic factors and inability to produce an effective, lasting immune response.[7,8] About 90% of children will be infected with RSV before the age of two.[9] Even though premature infants and infants with chronic cardiac and lung diseases are most at risk of severe bronchiolitis,[10] the majority of hospital admissions concern healthy infants born at term.[9]

As a long-acting, IgG1κ-neutralizing, recombinant human monoclonal antibody against the RSV F protein, nirsevimab provides passive immunity without requiring the child's immune system to produce a response. A single, intramuscular injection of nirsevimab should protect the recipient throughout the epidemic season. Pivotal clinical trials have evidenced this preventive treatment's association with significantly lower hospital admission rates for RSV infections, severe RSV infections, and lower respiratory tract infections of all types.[11–15] No serious adverse events (AEs) were reported.[14–16] This preventive treatment received European marketing authorization in 2023 for administration to infants under the age of 24 months at the beginning of the epidemic season.[17,18]

Although nirsevimab is clinically safe and effective, parents may not necessarily agree to their infant being treated. Immunization hesitancy has increased worldwide[19]; for example, the level of acceptance of coronavirus disease-19 vaccines varied markedly from one European country to another.[20] To the best of our knowledge, there are currently no published research (i) designed to analyse the rate of acceptance of a new treatment given early in life to prevent what is—in high-resource countries, at least—an essentially non-lethal disease, and (ii) the criteria associated with this acceptance.

Thus, the primary objective of the present real-life study was to evaluate the acceptance of nirsevimab at birth. The secondary objectives were to identify reasons why the parents agreed to (or refused) this preventive treatment for their newborn and to evaluate the treatment's safety in newborns.

Methods

Study design

We conducted a prospective, longitudinal, single-centre study in the maternity department at Lille University Hospital (Lille, France) from September 18th, 2023, to January 23rd, 2024. The study reporting complied with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

The French national nirsevimab immunization program started in September 2023, and 230,000 doses were made available by the government.[21] With approximately 62,000 births per month in France[22] and despite the prioritization of maternity units, supply shortages soon occurred. In the present study, recruitment stopped when nirsevimab was no longer available in our maternity department. At the time of the study, maternal RSV vaccination had not been implemented in France.

Ethics

The research protocol was approved by an independent ethics committee (Comité de protection des personnes *Ile de France III,* Paris France; reference: 2023-A01890-45, dated September 18th, 2023). The study database was registered with the French National Data Protection Commission (*Commission nationale de l'informatique et des libertés* (Paris, France)), DEC24-198. As needed for such observational study, a signed non-opposition form was obtained from all participants.

Participants

All healthy newborns admitted to Lille University Hospital's maternity department during the study period were eligible for inclusion. The infants had to have a gestational age of more than 34 weeks and/or a birthweight of more than 1800 g to stay in a maternity unit. The following inclusion criteria were applied to the infants' parents, regardless of whether or not they had agreed for their infant to be treated: a good understanding of the French language, social security coverage, and a means of communication (telephone or e-mail) enabling follow-up.

Infants were excluded if they were born outside the study period, birthed anonymously, or were under legal guardianship or trusteeship. Parents were excluded if they refused to participate in the study or if they were under legal guardianship or trusteeship. Hereafter, the term "parents" should be understood to mean both parents or the mother alone with authority to provide consent.

Outcomes and definitions

The primary endpoint was the nirsevimab acceptance rate, defined as the proportion of infants whose parents agreed to the treatment. The secondary endpoints were the parents' reasons for accepting or refusing treatment and the real-life safety of nirsevimab (defined as the incidence of AEs in the 2 h and the 7, 14 and 30 days following treatment).

In line with the French legislation, an AE was defined as an untoward medical occurrence after exposure to a medicine but that was not necessarily caused by the said medicine. A serious AE (SAE) was defined as an AE that results in death, is life-threatening, requires hospital admission or prolongation of existing hospital admission, results in persistent or significant disability or incapacity, or is a birth defect. The AEs were graded according to the Common Terminology Criteria for Adverse Events (version 5.0).[23] Lastly, the incidence of allergic conditions (including wheezing episodes, allergic rhinitis, allergic conjunctivitis, and eczema) was documented.

Study process

During the first clinical examination of the newborn by a paediatrician or paediatric resident (in the first 24 h of the stay in the maternity ward), the parents were given verbal information about bronchiolitis caused by RSV and about preventive treatment with nirsevimab. A leaflet containing this information was also given to the family. During the stay in the maternity department, the parents had to decide whether or not they wished their infant to be treated with nirsevimab. If the parents agreed, a single intramuscular dose of nirsevimab 50 mg was prescribed by a paediatrician and administered after the first 24 h of life and before discharge, at a time when the newborn was breastfeeding or bottle feeding. To ensure traceability, the nirsevimab batch number was noted in the "Other vaccinations" section of the family health booklet.

After the parents had been given information about RSV and nirsevimab and agreed (or not) for their infant(s) to be treated, they were invited to participate in the study. The infants were included in the study at the time of discharge, regardless of whether or not the parents had agreed to the nirsevimab treatment. In our safety analysis, newborns who were not treated with nirsevimab were considered to be controls. After the paediatrician or paediatric resident had given the parents information about the study, the parents gave their written consent to use of their personal data. In the presence of an investigator, the parents then filled out a questionnaire (Supplementary Material S1) on the treatment's acceptance and gave their contact details for the study follow-up. The follow-up consisted of online questionnaires completed at home about the safety of nirsevimab within 2 h after injection (only for infants having received nirsevimab) and then 7, 14 and 30 days after discharge, for all infants included in the study. The questionnaires were based on the secure LimeSurvey application. A leaflet containing quick response codes linking to the follow-up questionnaires was given to the parents on discharge. We attributed an inclusion number to each patient, in order to anonymize the data collected. On days 7, 14 and 30 after the nirsevimab injection, each included infant's parents received a mobile phone text message with a link to the LimeSurvey questionnaire. The inclusion number was given in the text message sent on day 7. The parents were chased up by phone if they had not completed the questionnaire on time, and the investigators posed the various questions directly over the phone.

Study data

The initial study questionnaire was administered in the maternity department and gathered the following information: the mother's contact details for follow-up (phone number and e-mail address), demographic data (the mother's age, parity, marital status, educational level, professional activity (dichotomized as "in work" or "not in work", for the purposes of our analysis), the number of children, the family medical history (notably any history of allergy in the infant's mother, other parent or siblings; previous bronchiolitis or hospital admission of close family members for bronchiolitis; and antenatal knowledge of bronchiolitis), clinical data (the mother's pain scale score when filling out the questionnaire, spontaneous pregnancy vs. medically assisted reproduction, the term of the pregnancy, the birth weight, the infant's sex based on newborn's visible external anatomy, breastfeeding or bottle feeding, the partner's presence at the birth and during the first night, smoking during pregnancy, and passive smoking). The last question in the questionnaire addressed the reasons for accepting or refusing nirsevimab treatment; to avoid influencing the parents' answer, the question was open-ended.

The follow-up questionnaires (Supplementary Material S2) were designed to detect AEs within the 2 h following the injection of nirsevimab and at 7, 14 and 30 days after discharge. The questionnaires covered systemic AEs (crying, regurgitation, colic, vomiting, anaemia, cough, blocked nose, runny nose, seizures, malaise, fever, bronchiolitis, skin rash, mycoses, impaired intestinal transit, eating disorders, abnormal breathing, or otitis media) or, for those who received nirsevimab only, local AEs (pain, oedema, redness at the injection site, induration at the injection site, or a change in the colour of the leg). The questionnaire also included items on signs of anaphylaxis (facial oedema, abnormal breathing, a skin rash, vomiting, or diarrhoea) and whether or not these signs had prompted hospital admission or a consultation with a physician (Supplementary Material S2). The signs listed in the questionnaire were based on the AEs reported in the nirsevimab safety studies.[11–14,16]

Sample size and statistical analyses

Based on an average of 450 births per month in Lille University Hospital's maternity department, we expected 2250 births to occur during the 5-month study inclusion period covering the entire RSV season. We assumed that 50% of the parents would agree to participate in the study and thus estimated that up to 1125 children could be included in the study.[24] This planned number would have enabled us to estimate the nirsevimab treatment acceptance rate with a precision of ±3% or less. The precision was calculated as half of the 95% confidence interval (CI); for an acceptance rate of 50%, the expected 95% CI was from 47.1% to 52.9%.

Data for continuous variables were expressed as the mean (standard deviation), and data for categorical variables were expressed as the frequency. The nirsevimab treatment acceptance rate and its 95% CI were estimated in a binomial approximation. The nirsevimab and control groups were compared in a t-test or the Mann–Whitney U test (depending on the data distribution) for continuous variables, or a chi-squared test or Fisher's exact test (as appropriate) for categorical variables. Factor associated with treatment acceptance in a univariate analysis ($p < 0.10$) were added as candidate variables to the multivariable logistic regression model, using Firth's penalized-likelihood approach. Before we developed the multivariable model, we examined the absence of collinearity between the candidate predictors by calculating the variance inflation factors. In the event of collinearity, a clinical selection was made before inclusion in the multivariate model. Odds ratios [95% CIs] were derived as the effect size in logistic regression models, with the group refusing injection as the reference. Comparisons of the nirsevimab group and the control group with regard to AEs having occurred within 2 h of treatment or 7, 14 or 30 days after discharge were based on a chi-squared test or Fisher's exact test. All statistical tests were two-sided. The threshold for statistical significance was set to $p < 0.05$. Data were analysed using SAS software (version 9.4, SAS Institute Inc., Cary, NC, USA).

Role of the funding source

There was no specific funding for this research.

Results

Of the 1730 newborns admitted in Lille University Hospital's maternity department during the study period, 477 (28%) were enrolled in the study (437 in the nirsevimab group and 40 in the control group). On post-treatment day 30, the follow-up questionnaire was filled out for 270 participants in the nirsevimab group (62%) and 27 participants in the control group (68%) (Fig. 1). None of the children included in the control group received nirsevimab after discharge from the maternity hospital. The two groups were similar with regard to the newborns' baseline characteristics (Table 1). The newborns included in the study (n = 477) and those not included (n = 1253) did not differ significantly with regard to their baseline characteristics. The mothers of included infants and the mothers of non-included infants differed significantly with regard to gravidity, parity, and breastfeeding (Supplementary Material S3).

In the included population of newborns, the nirsevimab acceptance rate was 91.6% (95% CI: 89.1%–94.2%). The mother's age, the mother's educational level, lower parity, lower gravidity, the presence of other children at home, the partner's professional activity, and the antenatal receipt of information about nirsevimab

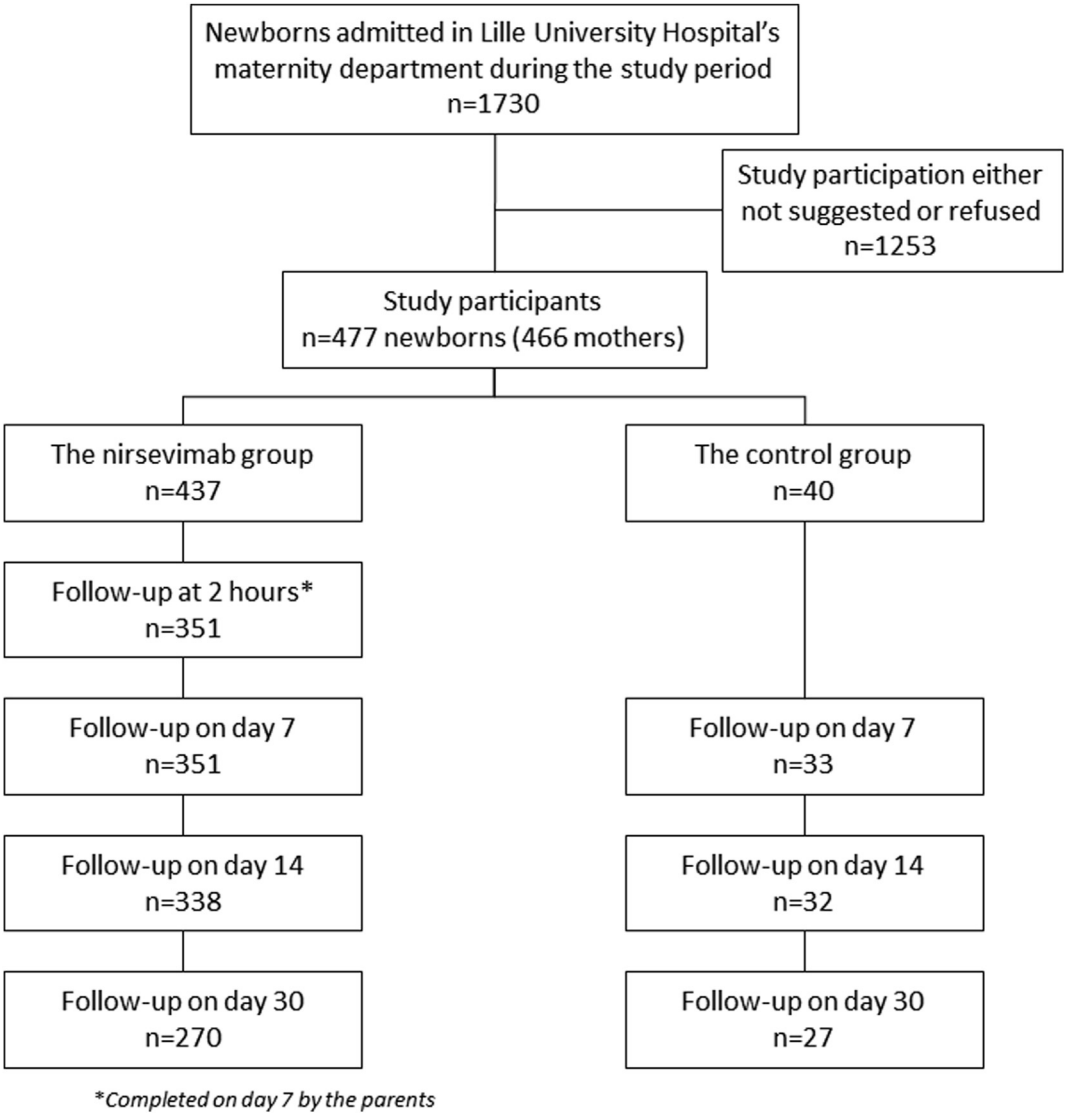

Fig. 1: Study flow chart.

were significantly associated with acceptance of nirsevimab treatment (Table 1). In a multivariable analysis, the variables associated with nirsevimab acceptance were older maternal age, lower parity, and having a partner in work (Table 2). The most common reason for accepting treatment was "to protect my baby", and the most common reason for refusing treatment was the lack of long-term data on nirsevimab (35%) (Table 3).

The nirsevimab and control groups did not differ significantly with regard to the types and frequencies of AEs. Two hours after the treatment, no SAEs were reported in the nirsevimab group (Table 4), and none of the infants needed to be examined by a physician because of the nirsevimab treatment. Most AEs were graded 1 or 2 for severity. At 2 h post-treatment, the most frequent AEs were pain (3.4%) and redness (1.7%). When analysing AEs on days 7, 14 and 30, the only significant intergroup differences concerned regurgitation on day 30; this was reported more frequently in the nirsevimab group (31%) than in the control group (8%) (Table 5). In the investigators' opinion, none of the reported SAEs were linked to the nirsevimab treatment.

In the nirsevimab group, there were fewer SAEs among newborns being breastfed than among newborns being bottle-fed (OR 0.4; [0.2–0.8]). Sex, prematurity, a birthweight below 2500 g, and a family history of allergy were not associated with the incidence of AEs in the nirsevimab group (Supplementary Material S4).

Variables	Control group (n = 40)	Nirsevimab group (n = 437)	p[a]
Mother's age, mean (SD)	30.0 (6.1)	31.2 (5.0)	0.02
Parity, mean (SD)	2.1 (1.2)	1.7 (0.9)	0.001
Gravidity, mean (SD)	2.5 (1.4)	2.0 (1.2)	0.02
Marital status: living with a partner, n (%)	39 (97.5)	421 (96.3)	1.00
Mother's educational level (baccalaureate or higher), n (%)	19 (47.5)	283 (64.8)	0.03
Mother's professional activity, n (%)	26 (70.3)	339 (77.6)	0.07
Partner's professional activity, n (%)	29 (78.4)	389 (89.0)	0.005
Spontaneous pregnancy, n (%)	37 (92.5)	388 (88.8)	0.60
Caesarean delivery, n (%)	9 (22.5)	80 (18.3)	0.51
Singleton pregnancy, n (%)	40 (100.0)	415 (95.0)	0.24
Partner present during childbirth, n (%)	36 (90.0)	410 (93.8)	0.32
Partner present on the first night, n (%)	23 (57.5)	311 (71.2)	0.07
Male sex, n (%)	19 (47.5)	239 (54.7)	0.38
Premature delivery, n (%)	1 (2.5)	37 (8.5)	0.35
Birthweight <2500 g, n (%)	2 (5.0)	36 (8.2)	0.76
Breastfeeding, n (%)	22 (55.0)	287 (65.7)	0.18
5-min Apgar score >6, n (%)	38 (95.0)	411 (94.1)	1.00
Transfer to a neonatal care unit, n (%)	2 (5.0)	9 (2.1)	0.23
Follow-up by a paediatrician or general practitioner, n (%)	34 (85.0)	373 (85.4)	0.95
Presence of other children at home, n (%)	32 (80.0)	238 (54.5)	0.002
History of maternal smoking, n (%)	7 (17.5)	50 (11.4)	0.30
Maternal smoking during pregnancy, n (%)	6 (15.0)	40 (9.2)	0.26
History of partner smoking, n (%)	13 (32.5)	99 (22.7)	0.14
History of allergy in the mother, n (%)	7 (17.5)	106 (24.3)	0.34
History of allergy in the partner, n (%)	3 (7.5)	86 (19.7)	0.06
History of allergy in the sibling, n (%)	8 (20.0)	61 (14.0)	0.30
Family history of bronchiolitis, n (%)	12 (30.0)	179 (41.0)	0.18
Antenatal knowledge of bronchiolitis, n (%)	35 (87.5)	405 (92.7)	0.22
Antenatal knowledge of nirsevimab, n (%)	13 (32.5)	240 (54.9)	0.007
Via a healthcare professional, n (%)	6 (15.0)	105 (24.0)	0.20
Via the media and social networks, n (%)	6 (15.0)	134 (30.7)	0.04
Via the family, n (%)	3 (7.5)	50 (11.4)	0.79

[a]Chi-squared test or Fisher's exact test.

Table 1: **Description of the study population, by treatment group.**

Variables	Adjusted OR	95% CI	p
Mother's age	1.1	1.1–1.2	<0.001
Parity[a]	0.3	0.1–0.6	0.003
Mother's professional activity[b]	1.3	0.6–2.7	0.52
Partner's professional activity	4.5	1.8–11.2	0.001
Partner present on the first night	1.5	0.7–3.1	0.34
History of allergy in the partner	2.7	0.8–8.8	0.11
Antenatal knowledge of nirsevimab	2.0	1.0–4.0	0.06

[a]Collinearity with gravidity and presence of other children at home. [b]Collinearity with Mother's educational level.

Table 2: **Multivariable analysis of variables associated with the acceptance of nirsevimab in univariate analysis with a p < 0.10 threshold.**

Discussion

The nirsevimab acceptance rate in our centre was very high (91.6%) during the first bronchiolitis season. In a multivariable analysis, the variables associated with nirsevimab acceptance were a higher maternal age, lower parity, and having a partner in work. No SAEs occurred within 2 h of nirsevimab injection. The nirsevimab group and the control group did not differ significantly in terms of the incidence of AEs reported in the 30 days post-treatment.

The nirsevimab acceptance rate was very high for a novel treatment requiring an intramuscular injection in a newborn and for the prevention of a disease that is frequent but non-fatal in Europe. This might be due to the high quality of the prenatal information provided by healthcare workers, which was mentioned by the parents. It might also be linked to high awareness in the general public of the significant impact of the bronchiolitis epidemic during the previous season,[25] and the marketing of this new preventive treatment against RSV. As a reason for accepting nirsevimab, some parents mentioned that a relative had been affected by the disease or that they had heard about the burden of bronchiolitis in infants. This widespread acceptance of nirsevimab across France was not anticipated by the French health authorities; there were not enough doses of nirsevimab to cover the eligible population throughout the entire RSV season. Data on the first bronchiolitis season after the marketing authorization of nirsevimab are available for three other countries: Spain, Luxembourg, and the USA. The treatment rates were high, although these studies were not designed to analyse acceptance *per se* or the reasons for acceptance. The treatment rates reported for Spain's Galicia region (91.7% of the target population) and Navarro region (92%) are similar to our value.[26,27] In three other Spanish regions, the treatment rate ranged from 79% to 99%.[28] A nationwide study in Luxembourg found a mean treatment rate of 84% and highlighted variations from one maternity clinic to another (from 66% to 94%).[29] A prospective observational cohort study was performed in a region of Italy, with immunization between December 23rd, 2023 and February 15th, 2024, for children born after May 1st, 2023; the nirsevimab acceptance rate was 68.7% (369 out of 537).[30] A study in the state of Massachusetts sought to determine the nirsevimab acceptance rate during a period when the treatment was in short supply; a value of 47% was reported.[31] In the latter study, the variables associated with acceptance of nirsevimab treatment were a preferred language other than English, and medical complexity. The lower acceptance rate observed in Massachusetts may also be related to the introduction of the maternal vaccination against RSV at the same time in the USA.

Nirsevimab's safety was as good in our population of newborns as in the pivotal clinical trials.[11–15] No SAEs were reported in the first 2 h post-treatment. There was

no difference between the treatment and the control groups with regard to AEs reported 7, 14 and 30 days after treatment, with the exception of more regurgitation on day 30 in the nirsevimab group. This might be related to the way the newborns were fed; children in the nirsevimab group were significantly more likely to be breastfed than children in the control group. Nirsevimab was administered earlier in life in our study than in the pivotal clinical trials, in which half of the children were three or more months old.[12,13] However, the SAE rates in our treatment group (9.4%) and our control group (10.3%) did not differ significantly and were close to the values reported in the pivotal clinical trials in healthy late-preterm or term infants (6.8% in the nirsevimab-treated group and 7.3% in the control group) and preterm infants (11.2% in the nirsevimab-treated group and 16.9% in the control group).[12,13] Moreover, very few AEs were reported for newborns to whom nirsevimab was administered soon after birth in the 2023-24 studies.[26]

The main limitation of this prospective, longitudinal study was its single-centre design. However, this design facilitated the uniform provision of training for healthcare professionals and the uniform provision of information to parents; these were important factors in setting up our nirsevimab treatment programme. Indeed, the high quality of the information provided by health professionals was one of the reasons why the parents agreed to nirsevimab treatment. The quality of information provision would not necessarily have been reproducible in multiple investigating centres, which limits the generalization of these findings. Secondly, the number of children included was lower than expected; this might have been due to the limited availability of nirsevimab in France. During the study period, 1067 doses were available for 1730 births in the maternity department. Accordingly, the inclusion period was shortened from 5 months to 4 months. Moreover, fewer parents than expected (27.6%, rather than a ~50%) agreed to participate in the study. This is not unusual in studies requiring longitudinal follow-up of the patients.[24] And asking parents to participate in a study in the first few days after the emotional event of childbirth and with little time to think things over might have reduced the participation rate. The low economic status of some parents had no impact on the study participation rate, thanks to universal health coverage the state's provision of full health insurance coverage for the most deprived and the full payment of nirsevimab by the State during this first season.[21] Thirdly, the number of parents lost to follow-up increased over time, despite the use of new tools for longitudinal data collection (quick response codes, text messages, e-mail messages, etc.). The amount of data collected and the frequent recall might have prompted loss to follow-up. Nevertheless, the reply rate was still over 60% at 30 days post-injection, and ratio between the number of questionnaires from the treatment group and the number from the control group remained at around 10:1. Lastly, people who agreed to participate in the

Categories	Reasons given	n (%)
Reasons for accepting preventive treatment with nirsevimab	Protection of the baby against RSV	248 (56.4)
	Provision of antenatal information by healthcare professionals	157 (35.7)
	The high quality of the postnatal information received in the maternity department	150 (34.1)
	A lower likelihood of consultations or hospital admission	141 (32.0)
	A family history of bronchiolitis	77 (17.5)
	The likelihood of catching RSV from older children	56 (12.7)
	Information received via the media and social networks	54 (12.3)
	The newborn has risk factors	32 (7.3)
	Recommended by the family antenatally	31 (7.0)
Reasons for refusing preventive treatment with nirsevimab	A lack of long-term data on nirsevimab	14 (35.0)
	The need for an intramuscular injection	8 (20.0)
	Nirsevimab is not compulsory	6 (15.0)
	Doubt about nirsevimab's effectiveness	6 (15.0)
	Fear of side effects	5 (12.5)
	No family history of bronchiolitis	5 (12.5)
	No knowledge about bronchiolitis	4 (10.0)
	The infant has a disease	2 (5.0)

Table 3: **Reasons for the acceptance or refusal of nirsevimab treatment.**

Adverse events	N	(%)
At least one adverse event[b]	21	(6.0)
Serious adverse events	0	(0.0)
Infant examined by a physician because of an adverse event	0	(0.0)
Systemic adverse events	6	(1.7)
None	347	(98.9)
Diarrhoea	2	(0.6)
Abnormal breathing	2	(0.6)
Skin rash	1	(0.3)
Other systemic adverse event[c]	1	(0.3)
Facial oedema	0	(0.0)
Vomiting	0	(0.0)
Local adverse events	20	(5.7)
None	334	(95.2)
Pain	12	(3.4)
Redness at the injection site	6	(1.7)
Induration at the injection site	1	(0.3)
Local oedema	0	(0.0)
Leg colour change	0	(0.0)
Other local adverse event[c]	1	(0.3)

[a]Completed on day 7 by the parents. [b]Number of infants concerned. A given infant may have had one or more adverse events. [c]The box had been ticked but the parents had not provided the details.

Table 4: **Safety of nirsevimab within 2 h of the injection (n = 351).**[a]

AEs	Day 7			Day 14			Day 30		
	Nirsevimab group n (%)	Control group n (%)	p	Nirsevimab group n (%)	Control group n (%)	p	Nirsevimab group n (%)	Control group n (%)	p
All AEs	173 (49.3)	18 (54.5)	0.56	192 (56.8)	20 (62.5)	0.53	155 (57.4)	11 (40.7)	0.10
SAEs	9 (2.6)	0 (0.0)	1.00	7 (2.1)	3 (9.0)	0.18	13 (4.8)	2 (7.4)	0.63
Cumulative AE	185 (52.7)	18 (54.5)	0.84	262 (73.3)	24 (72.7)	0.93	295 (84.3)	24 (75.0)	0.18
Cumulative SAE	9 (2.6)	0 (0.0)	1.00	15 (4.4)	2 (6.5)	0.64	26 (9.4)	3 (10.0)	1.00
Crying	11 (3.1)	3 (9.1)	0.10	19 (5.6)	2 (6.3)	0.70	14 (5.2)	2 (7.4)	0.65
Regurgitation	102 (29.1)	12 (36.4)	0.38	94 (27.8)	8 (25.0)	0.73	84 (31.1)	2 (7.4)	0.01
Colic	59 (16.8)	6 (18.2)	0.81	85 (25.1)	13 (40.6)	0.06	86 (31.9)	4 (14.8)	0.08
Vomiting	7 (2.0)	2 (6.1)	0.18	7 (2.1)	0 (0.0)	/	4 (1.5)	0 (0.0)	/
Anaemia	1 (0.3)	1 (3.0)	/	1 (0.3)	0 (0.0)	/	0 (0.0)	0 (0.0)	/
Runny nose	NA	NA	/	11 (3.6)	3 (9.4)	0.11	24 (8.9)	3 (11.1)	0.72
Blocked nose	40 (11.4)	1 (3.0)	0.23	51 (15.1)	4 (12.5)	1.00	47 (17.4)	4 (14.8)	1.00
Cough	40 (11.4)	1 (3.0)	0.23	15 (4.4)	3 (9.4)	0.20	25 (9.3)	2 (7.4)	1.00
Fever	0 (0.0)	0 (0.0)	/	3 (0.9)	0 (0.0)	/	5 (1.5)	0 (0.0)	/
Otitis media	NA	NA	/	0 (0.0)	0 (0.0)	/	1 (0.3)	0 (0.0)	/
Seizures/malaise	1 (0.3)	1 (3.0)	/	2 (0.6)	0 (0.0)	/	1 (0.4)	0 (0.0)	/
Bronchiolitis	1 (0.3)	0 (0.0)	/	2 (0.6)	1 (3.1)	/	3 (1.2)	1 (3.7)	/
Skin rashes & mycoses[a]	16 (4.6)	4 (12.1)	0.08	42 (12.4)	4 (12.5)	1.00	20 (11.1)	2 (7.4)	0.75
Constipation	27 (7.7)	6 (18.2)	0.05	31 (9.2)	5 (15.6)	0.22	19 (7.0)	2 (7.6)	1.00
Diarrhoea	NA	NA	/	11 (3.3)	0 (0.0)	0.61	5 (1.9)	1 (3.7)	/
Eating disorder	8 (2.3)	0 (0.0)	1.00	4 (1.2)	1 (3.1)	/	8 (3.0)	1 (3.7)	0.58
Abnormal breathing	5 (1.4)	0 (0.0)	/	8 (2.4)	2 (6.3)	0.21	14 (5.2)	0 (0.0)	0.62
Other[b]	1 (0.3)	0 (0.0)	/	11 (3.3)	0 (0.0)	0.61	6 (2.2)	2 (7.4)	0.16
Consultation with a physician	26 (7.4)	7 (21.2)	0.02	50 (14.8)	7 (21.9)	0.30	41 (15.2)	4 (14.8)	1.00
ED visit	5 (1.4)	0 (0.0)	/	3 (0.9)	1 (3.1)	/	9 (3.3)	1 (3.7)	1.00
Hospital admission	4 (1.1)	0 (0.0)	/	3 (0.9)	1 (3.1)	/	4 (1.5)	0 (0.0)	/
ICU admission	NA	NA	/	NA	NA	/	0 (0.0)	1 (3.7)	/

AE, adverse event; SAE, serious adverse event; ED, emergency department; ICU, intensive care unit; NA, Not available. [a]The skin rashes were neonatal acne (n = 40), buttock erythema (n = 3), or non-specified rashes. [b]Other: conjunctivitis (n = 7), COVID (n = 1), or not specified (n = 12).

Table 5: **Adverse events in the nirsevimab and control groups on days 7, 14 and 30.**

study were probably more likely to accept the preventive treatment; this might have led to overestimation of the nirsevimab acceptance rate.

Since only 477 children could be included, the observed acceptance rate could be estimated with a precision of ±4.5% or less. No formal sample size calculation was performed in order to address the factors associated with nirsevimab treatment acceptance. We cannot therefore rule out having missed some differences, due to a lack of statistical power. In a *post hoc* power assessment, we calculated the smallest significant between-group difference (expressed as an OR) would have allowed us to obtain a power of 80% with our study sample (n = 477). With an acceptance rate of 90%, we could detect an OR of 1.5 per standard deviation increment in exposure factors (or OR of 0.7 for a protective effect). With our study sample size and the observed acceptance rate and despite our use of a penalized approach, we cannot rule out overfitting in the multivariate analysis.

The incidence of AEs appeared to be high: at least one AE was reported by day 30 for 85.8% of the infants in the nirsevimab group and for 73.3% of the infants in the control group. It is possible that participation in the study prompted parents to report AEs more diligently, as had been shown in the pivotal studies.[12,13] The reported AEs concerned symptoms that are frequent in the neonatal period. The design of the study did not allow further investigation into the reasons why regurgitation was more frequent in the nirsevimab group than in the control group. None of the AEs were considered to be related to the nirsevimab treatment, as was also observed in the pivotal studies.

Given that this was a real-life study with consecutive recruitment, included infants did not differ from non-included infants with regard to their characteristics and those of the parents. Hence, the participants were likely to be representative of the infants born in Lille University Hospital's maternity department.

Targeted information for young mothers, those with high parity and those whose partner is not in work might increase the acceptance rate. In our univariate analysis, antenatal provision of information (especially that given by health professionals or through the media) and knowledge of the disease caused by RSV appeared to be associated with the high nirsevimab acceptance

rate. The intensity of the bronchiolitis epidemic during the previous winter (2022–2023) and the significant media coverage of the impact on healthcare systems in Europe and North America might have contributed to the high nirsevimab acceptance rate observed here. A nirsevimab-induced decrease in the incidence of RSV infections might reduce pressure on the healthcare system and thus prompt less media coverage of bronchiolitis. As with other preventive treatments (such as non-mandatory vaccinations against influenza or rotavirus), lower media coverage might cause the nirsevimab acceptance rate to fall. Moreover, the recently developed option of vaccinating pregnant women for the prevention of RSV infections in infants[32,33] might also lead to a drop in the nirsevimab acceptance rate because it would avoid the infant having an intramuscular injection in the first few days of life.[34] In the future, it would be interesting to study potential changes over time in the nirsevimab acceptance rate.

Strains of RSV can mutate and develop resistance,[35] which is potentially linked to the selective pressure exerted by antibody treatment. Palivizumab-resistant strains appear to be rare.[36] Although palivizumab was administered to a small proportion of children, one study found RSV resistance to this therapeutic in 5.4% of treated individuals.[37] The widespread use of nirsevimab might foster the emergence of resistance and a reduction in effectiveness; in turn, this might be a barrier to the acceptance of preventive therapies. Further studies will need to assess the level of resistance to treatment and the consequences of nirsevimab use for exposure to and the impact of RSV infection during the subsequent epidemic seasons.

The treatment of newborns with long-acting antibodies appears to be acceptable and safe. The vaccine for pregnant women also represents a new strategy for preventing RSV infection in newborns. Both RSV vaccines appear to have an acceptable safety profile and are effective against severe RSV illness and hospitalisations. The decision to administer either a maternal RSV vaccine or an RSV monoclonal antibody in infants depends on a multitude of factors influenced by the specific context and situation in each country. Acceptability and access will be key factors in deciding which product to recommend and the implementation strategy.[38]

Contributors

All authors were involved in the conceptualization of the study. MLe and MG were responsible for statistical analyses. COdS, CT, LG and AE were responsible for data collection. MLa, CL, DD, TR and FD were responsible for study and team supervision. COdS, CT and FD wrote the initial draft of the manuscript. All authors read and approved the final version of the manuscript. All authors had full access to all the data in the study and accept responsibility for the decision to submit for publication. FD coordinated the revision process.

Data sharing statement

Data collected for the study will be made available to others after reasonable request to the corresponding author.

Declaration of interests

FD was member of a board expert about VRS for Sanofi-Pasteur and about vaccines in children for MSD. FD has been invited at the ESPID meeting by MSD in 2024 to present preliminary results of this research. MLa was member of a board expert about meningococcus for Sanofi-Pasteur. Other authors have no conflict of interest to declare in relation to this research.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102986.

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