

Bristol Vaccine Centre
Tel: 0117 342 0160 / harmonie-study@bristol.ac.uk

PARENT / LEGAL GUARDIAN INFORMATION SHEET

HARMONIE Little Lungs ABC Study

(Antibody Boost in Children)

Study to Prevent Respiratory Infection in Infants

including bronchiolitis, pneumonia and other chest infections often caused by the
Respiratory Syncytial Virus

Protocol Title:

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

Sponsor: Sanofi Pasteur - 14 Espace Henry Vallée, 69007 Lyon, France

Dear Parent(s),

We would like to invite you and your baby to take part in a research study to look at how strongly babies can be protected from serious illness due to RSV infection (Respiratory Syncytial Virus) by giving them a single dose of antibodies. This is a common virus. Most children have this virus before age 2 years. It can infect the respiratory tract and lungs, causing breathing or feeding problems especially in younger babies. In many babies, this is mild illness with cough or cold symptoms, fever, or wheezing, and they may be cared for at home. For some babies it causes serious lung infections such as pneumonia and bronchiolitis, which may require admission to hospital or intensive care. 2% of all babies are admitted to hospital. One in six of all children admitted to hospital and one in ten children admitted to intensive care are due to this virus.

Nirsevimab is an antibody injection developed in the laboratory by Sanofi and Astra Zeneca. These antibodies enable the baby's immunity to respond quickly to RSV and help prevent severe infection. Over 3000 babies have already been given nirsevimab and were monitored closely in clinical trials. These trials have shown that nirsevimab has a good safety profile in babies, and helped to protect them from needing medical care including hospitalisation. This study aims to provide more information about the effect of the antibody in helping to prevent babies needing to be hospitalised due to RSV.

Please read this parent / legal guardian information sheet and discuss any questions with the research doctor or nurse before you choose whether or not your baby may take part. Participation in the study is your choice. Your decision will not affect your baby's usual NHS care.

Take all the time you need to make your decision and please read the additional Parent-Guardian Information sheet for full details on this study.

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Is my baby eligible to take part?

All babies born at 29 weeks gestational age or more and below 12 months of age may be able to take part. To make sure this study is appropriate for your baby the team will ask you for information about their health, any allergies, and other medications. Babies with certain health conditions affecting their immunity or ability of their blood to clot may not be eligible to take part (more details are in the additional parent / legal guardian information sheet). Please discuss any questions or concerns you may have with the study team.

Babies can join the trial if they have not yet been through an RSV season and therefore are less likely to have developed natural immunity. RSV is usually spread during winter months by close contact with someone who is infected, especially if they sneeze or cough, producing droplets containing the virus.

What treatment is available for babies with RSV Infection?

There are no medicines to specifically treat an RSV infection. Supportive medical care aims to help with difficulties feeding, for example with a feeding tube, high temperatures with paracetamol / calpol, and breathing difficulties with oxygen or ventilation in Intensive Care.

What other preventive therapies are there?

There are no widely available preventive therapies for RSV infection (other than covering coughs and sneezes, handwashing and avoiding contact with others with symptoms).

Palivizumab is an injection of antibodies and has been given to a small number of babies in the NHS for over 20 years to help protect them against this virus. Palivizumab is an injection given every month to the baby. It is available to babies at very high risk of severe respiratory.

How is nirsevimab given to the baby?

Nirsevimab is given as a single injection in the thigh muscle, *like routine vaccinations*. Some babies in the study do not receive any injection but are equally valuable to this research as they allow us to compare how effective nirsevimab is at helping to prevent hospitalisations caused by RSV.

Where will the study be taking place?

In the UK parents may take part at participating NHS Sites including GP Practices, Maternity, Paediatric or General Hospitals. A total of 28,860 babies from birth to 12 months of age are planned to take part in the UK, France or Germany.

What will taking part involve for me and my baby?

If you choose to participate, you and your baby will be asked to attend one study appointment, which may be at a clinic, hospital, or at home. All other routine follow up will be by electronic diary (eDiary) or a phone call.

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One-off Study Appointment

We will check your baby is eligible to take part, then you will be invited to sign a consent form. We will collect information including:

- your contact details including email and telephone number
- your baby's name, gestational age at birth, date of birth, sex, weight, post code and NHS number.
- any medical conditions your baby has, current or previous medications, and any vaccines they have received. We will review your baby's medical records and records created during the study.

Your baby will then be randomly allocated to one of two groups – a process *known as randomisation*:

- **Nirsevimab Antibody Injection Group** will receive the study injection and temperature check.
- **No Antibody Injection Group** will not receive any injection at all

You and the study doctor/nurse will know whether your baby receives nirsevimab or not. Allocating babies to different groups allows researchers to compare without bias whether nirsevimab is more effective at preventing severe RSV illness and hospitalisation compared with the group that did not have an antibody injection and if there is any difference in side effects.

We do not require any blood sampling or other routine tests, other than a nasal swab if your child is hospitalised with a respiratory illness. This swab is usually normal practice for any baby admitted to hospital with a possible RSV infection. No other swabs (e.g. at home) are needed.

Follow Up by eDiary or Telephone

The study team will show you how to use the eDiary on your phone/tablet using the SnaploT app.

Fill in eDiary once a month for 6 months: we ask you to take a few minutes each month to routinely complete a few questions. You may connect to the eDiary any time over the study duration should you need to report any health events that may occur during the 12 months after the Study Visit. Please inform us if your baby has been unwell with any symptoms or treatments. A medical call centre set up for the study, or the local study team, may contact you (more than once if needed) to obtain any additional information for the study.

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If your child is very unwell or admitted to hospital for any reason from the time of your first visit until the end of the study 12 months later:

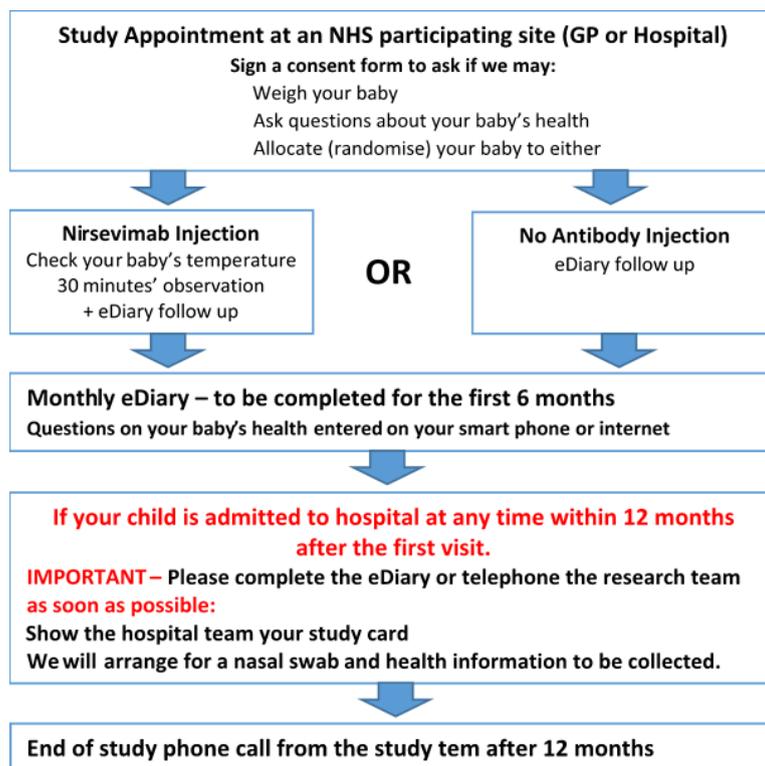
It is important to let the study team know as soon as possible

- To contact the team: please record this in your e-Diary (you can choose a convenient time for the study team to contact you). If possible, also phone the research team
The study team will ask questions about your child's health and related treatments.
- Study card: please show the hospital doctor or nurse the study card (paper card or on your phone) and ask them to contact us as soon as possible.
- Nasal swab: we will ask you if a doctor or nurse may then take a swab sample from inside your baby's nose to test for the RSV virus (this is often taken as part of standard care; therefore we will not need to take another one).

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Phone call at the End of the study after 12 months – the study team will contact you.

Participant's Flow chart



Potential study benefits:

If your baby is assigned to receive the Nirsevimab injection, they may have a reduced risk of severe infection and hospitalisation as found in previous studies of babies given Nirsevimab. However, there is no guarantee that all babies will be protected from severe RSV infection. We aim to learn more about this during this study.

If your baby does not receive the Nirsevimab injection, their risk of becoming infected with RSV will be the same as all other babies who don't receive any antibody injection.

Taking part in the study will have no impact your baby's standard NHS health care. Both groups' contribution to the study is extremely valuable.

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Possible risk or discomfort from taking part in this study:

The study doctor and nurses are trained to take measures to limit any discomfort for your baby, and monitor and treat any reactions they may experience. By carefully monitoring more babies in this study the researchers will learn more about side effects, however previous Nirsevimab studies of babies receiving this injection provide information to show there is no significantly increased risk to the safety of the more than 3000 babies studied.

Nirsevimab injection may cause some pain, swelling, bruising, or hardening or redness at the injection site. Your child may get a rash or have a fever. These side effects are usually mild and last a short time and are similar to those from other vaccines routine they receive.

There is a rare risk your baby could have an allergic reaction, such as a rash, swelling of the lips or face, or difficulty breathing. The study staff are trained and equipped to deal with this unlikely event. If such a reaction occurs, it is usually almost immediately after the injection is given. Therefore, we ask you and your baby to remain at the place where the injection was given for 30 minutes to be monitored and we can provide immediate medical care if this is needed. Nirsevimab is given as an injection into the thigh muscle.

Your baby may experience some different side effects. Please ask the study doctor or nurse if you have any more questions about signs and symptoms of any potential side effects.

Will I receive any payments for taking part in the study?

Reasonable expenses will be reimbursed, for example study related travel (fuel, train/bus tickets and parking). You will need to bring in all receipts for the costs you have incurred related to this study and they will be paid back to you. If you have any questions regarding reimbursement for your expenses, please discuss with the study doctor or study staff.

You will not be paid for your baby to participate, but you will receive £75 to compensate for the cost of using your own mobile device or computer to complete the electronic consent, for reporting necessary study details and/or reporting any serious health problems during the study using the eDiary, and for responding to the monthly electronic contacts (up to 6 months after the initial Study Visit).

Please note you will not have to pay additional charges beyond those charged as standard by your mobile network provider to receive and send data, texts, and/or e-mails.

What if something goes wrong?

We will make every effort to ensure your child's safety and well-being during the study.

The Sponsor Sanofi has insurance to provide compensation in the unlikely event that any injury is caused by taking part in this study in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI). NHS indemnity operates in respect of the clinical treatment which may be provided if you needed to be admitted to hospital.

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What if I choose to stop my baby's participation in the study or if the study is stopped?

You may choose to end your baby's participation in the study at any time and do not need to give a reason. Please inform us, as the study team may recommend a final phone call to check on your baby's health. Any information already collected will be kept as initially planned unless you ask us to remove this. We would ask you to consent to allow us to continue to collect information from your baby's NHS records to find out if they attended a hospital.

If for any reason the study is stopped, we will inform you.

How will we use information about your baby and is it confidential?

We will keep all information about your baby safe and secure at your local trial site and a limited amount of data at the medical call centre. All personal identifiable data and contact details will be pseudo-anonymised by using a study number. You and your baby will not be identifiable in any publications or reports shared outside of this research study.

Some of this pseudo-anonymised information will be sent to other countries who are taking part in the trial for analysis. The local site will store identifiable data about you and your baby for a period of 25 years. Authorised research staff, the funder, and regulatory bodies who monitor/audit the study to ensure it is complying with research regulations may access the data.

Your baby's GP will be informed if you consent for your baby to take part in this study.

Where can you find out more about how your baby's information is used?

You can find out more about how we use your baby's information at:

- www.hra.nhs.uk/information-about-patients/
- www.hra.nhs.uk/patientdataandresearch

Study information and results

A description of this study will be available on <https://www.clinicaltrialsregister.eu> and <http://www.clinicaltrials.gov>. When this study is complete, a simple summary of the results will be prepared and you will be informed of where this may be found.

Additional information

You will also receive a second document called "Additional Parent Information" which has detailed information on this research study.

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Contact for questions about your rights

If you have any complaints about any part of the study, how it is being done, or any questions about your rights as a study participant, you may contact your local Patient Advice and Liaison Service (PALS). PALS is a confidential NHS service that can provide you with support that you may have regarding the care you receive as an NHS patient. Please refer to the separate Informed Consent Form for the contact details.

Research and Ethics Committee Review

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee (REC), who perform an independent review of research to protect your safety, rights, and wellbeing. This study has been reviewed and given favourable opinion by South Central - Berkshire Research Ethics Committee.

The Sponsor would like to thank you for taking your time to read this information sheet