Informed Consent Cover Page

Study Title: Randomized Controlled Trial of Budesonide + Surfactant versus Surfactant Alone in Extremely Preterm Infants ("The Budesonide in Babies (BiB) Trial")

NCT Number: NCT04545866

Informed Consent Document Date: May 15, 2020

Informed Consent Statement for:

Surfactant Plus Budesonide versus Surfactant Alone in Extremely Preterm Infants

Investigator

Location

Telephone

Protocol Title

Randomized Controlled Trial of Budesonide/Surfactant versus Surfactant Alone in Extremely Preterm Infants (The Budesonide in Babies (BIB) Trial)

General Information	We are asking you to allow your baby to take part in a research study. This research study is voluntary, meaning you do not have allow your baby to take part in it. We will describe the procedures, risks, and benefits further in the consent form.
Purpose	We commonly use a drug called surfactant to treat the underdeveloped lungs of a premature baby. The surfactant coats the inside of the lungs and helps babies to breathe easier. The purpose of this study is to find out if using a steroid called budesonide mixed together with the surfactant will help reduce chronic lung disease called bronchopulmonary dysplasia (BPD) better than giving the surfactant alone. We use both drugs commonly in premature babies.
Duration & Visits	Your baby will begin the study just after birth and will receive the study medication no more than two times during the first 50 hours. We will remain in touch with you after your baby is discharged from the hospital.
Overview of Procedures	If you decide to allow your baby to take part in the study, AND your baby's doctor has decided that your baby needs surfactant, a computer will assign your baby by chance to get surfactant alone or surfactant and budesonide together. We call this randomization. There is an equal chance to be assigned to either group.

	We will give the medication within 50 hours of birth. We will collect information from the medical record about your baby's hospitalization. We will collect additional information from the 2 year visit to our Newborn Follow Up Clinic.
Risks	**Risks of surfactant are:** • A temporary drop in heart rate or oxygen levels in the blood. • Blockage of breathing tube **Risks of surfactant and steroid combination are:** • A temporary drop in heart rate or oxygen levels in the blood • Blockage of breathing tube • Brief increase in blood sugar and/or blood pressure (this can happen with any steroid use) • There is a slight increased risk of a hole forming in the intestine (spontaneous intestinal perforation or SIP) when other steroids such as dexamethasone are given into a vein. Small studies have not shown this slight increase in risk when budesonide was given into the trachea, and this larger study will carefully monitor for an increased risk of SIP
Surfactant Benefits	For babies that receive the combination of steroid and surfactant together, there is a possible benefit of spending less time on a breathing machine (ventilator) or fewer days on added oxygen than babies that receive the surfactant alone. This may reduce the chance of developing chronic lung disease.
Alternatives	If you do not wish to allow your baby to be in this study, your baby will receive the usual care given in the hospital. This may include the use of surfactant and/or budesonide.

You are being asked to let your baby be in this study because he or she was born very prematurely and is at risk for complications of prematurity. Not all babies born this early survive, and some who do survive may develop serious medical problems related to the brain, lung, intestine, heart and blood vessels, eyes, and other organs. Premature babies may also have poor growth and neurodevelopmental (movement, behavior, and learning) problems. Whether or not you agree to have your baby be in this study will not change the medical problems associated with prematurity. Your baby's doctors have discussed extreme prematurity with you already and will keep you up to date on your baby's progress.

Your baby can be part of this study because he or she may be (or was) born before 29 weeks of pregnancy or weighs between 401 and 1000 grams (14 oz to 2 lbs, 2oz). Most babies born this early or small are given a drug called surfactant to help their lungs work better. Surfactant is usually given either right after birth or in the first 2 days. This study will look at whether giving another drug, budesonide, with the surfactant will reduce the chances of developing chronic lung disease-called bronchopulmonary dysplasia (BPD).

Before you decide whether or not to let your baby be in the study, it is important for you to know why this research is being done and what it means to be in the study. Please take time to read the following

information carefully, and talk about it with family, friends and others if you wish. It is very important that you ask us any questions you have about this research study.

This study is sponsored by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), which is part of the National Institutes of Health (NIH), and is being conducted at XXXXX by XXXXX <name of site and PI>.

What Is Bronchopulmonary Dysplasia?

Healthy lungs have tiny air sacs (called alveoli) that help oxygen get into our blood. The alveoli in very early premature babies are not mature. Many of these babies need to be on breathing machines (ventilators). Even though breathing machines can be life-saving, they can also cause lung damage, which can lead to a type of chronic lung disease called bronchopulmonary dysplasia (BPD).

To treat lungs that are not mature, a drug called surfactant is sometimes given through a tube in the baby's windpipe (trachea). Surfactant coats the inside of the lungs, which helps the baby breathe easier.

We want to test whether giving a drug called budesonide with the surfactant will be even better at reducing these lung problems than surfactant alone. Budesonide is a steroid that is usually given by a mist the baby breathes in. Steroids help decrease the irritation, swelling and redness of the lung tissue which could cause lung damage. We use both drugs in premature babies.

Why is this study being done?

The main purpose of this study is to find out if using surfactant and budesonide together will help reduce chronic lung disease more often than giving surfactant alone.

How many babies will be in this study?

Approximately 1160 babies in the United States will join this study. ## babies from <site> will be part of the study.

What will happen if my baby is in this research?

When parents agree for their baby to be in this study, we will randomly assign their baby (like the flip of a coin) to one of two groups. The babies in one group will get surfactant alone. The babies in the other group will get the same surfactant mixed with budesonide. There is an equal chance of being in either group.

Your baby will begin the study soon after birth, sometimes in the delivery room right after birth. When the doctors decide your baby needs a dose of surfactant any time in the first 2 days after birth, we will give the drug(s) assigned to your baby's group, for up to two doses.

To get into the lungs, these drugs will be given through a tube in the windpipe (trachea). We will give the study drug(s) the same way for babies in each group.

Neither you nor your baby's doctors or nurses will know which group your baby is in.

If your baby needs more than two doses of surfactant in the first 2 days, or any doses after the first 2 days, the standard dose of the surfactant alone will be used.

All other parts of your baby's care will be the usual treatments for premature babies in the NICU.

What information will be collected?

We will collect information from your baby's medical records, such as test results, problems he or she has while in the hospital, and other drugs received. We will also collect information about the mother, such as age, years of education, marital status, race/ethnicity, type of insurance, and health issues during pregnancy.

If your baby is transferred to another hospital for care, we will continue to collect information from the medical record.

Follow-up

After your baby goes home from the hospital, he or she will be scheduled for routine follow-up exams in our clinic. The follow-up visit at which we will be collecting information for the study will be done when your baby is about 2 years old. The visit will take about two hours to do. During the visit, we will test your baby's movement, behavior, and development. We will provide a summary of the test results to you.

How long will my baby be in this study?

Your baby will begin the study just after birth and will remain in the study until the follow-up visit at 2 years of age.

Sometimes important information can be learned from seeing study participants when they are older than two years. This study does not include later follow-up right now, but if that changes we may contact you later about coming back for another follow-up visit.

What are the possible risks and discomforts from being in this research study?

Risks of Surfactant Alone

Your doctor has decided your baby will need to receive surfactant. The risk of receiving surfactant are:

- A temporary drop in heart rate or oxygen levels in the blood.
- Blockage of breathing tube

For babies to be eligible to participate in this study, the doctor has already made a decision to give surfactant.

Risks of Surfactant Plus Budesonide

The risks of getting surfactant and budesonide together are:

- A temporary drop in heart rate or oxygen levels in the blood
- Blockage of breathing tube
- Brief increase in blood sugar and/or blood pressure (this can happen with any steroid use)
- There is a slight increased risk of a hole forming in the intestine (spontaneous intestinal perforation or SIP) when other steroids such as dexamethasone are given into a vein. Small studies have not shown this slight increase in risk when budesonide was given into the trachea, and this larger study will carefully monitor for an increased risk of SIP.

Unknown Risks

There may be risks to being in this study that are not known to the researchers at this time. Some unknown risks may be learned during this study. If any new risks that might affect your

baby are learned while your baby is in this study, we will let you know about them.

Confidentiality

If your baby is in this study, there is a small risk of loss of confidentiality or privacy. Every effort will be made to keep your baby's information confidential.

What are the benefits of being in this study?

Benefits of Surfactant Alone

Since this is the treatment commonly used, there is no known additional benefit for this group, other than having additional medical personnel paying attention to your baby.

Benefits of Surfactant Plus Budesonide

Babies that receive the combination of budesonide and surfactant may spend less time on a breathing machine or fewer days on supplemental oxygen than babies that receive the surfactant alone. This may reduce the chance of developing lung damage and bronchopulmonary dysplasia.

Follow-up

Follow-up testing is a very important part of the study because it helps us understand how your baby is developing and may help us find problems early, so we may get the right care for your baby. It helps us learn more about the treatment being studied in this research and how it may affect the neurodevelopment of children born premature. There is currently not enough information to indicate if there will be a benefit or risk in terms of neurodevelopment.

It is possible there will be no benefit to your baby from joining this study, but information from this study may help other premature babies in the future.

Will my baby's medical information be kept private/confidential?

Any personal information about you or your baby that is collected during this study will be kept confidential under the law. A study number will be used to identify your baby. Only the study team at your hospital will know your baby's name. We will do everything we can to keep your and your baby's records confidential, but we cannot guarantee absolute confidentiality.

Your or your baby's personal information may be shared if required by law. Your and your baby's identity will not be shared in reports or publications about this study.

This research study has a confidentiality certificate that protects your baby's privacy. If a legal matter happens, researchers may not use anything that might identify your baby without your permission. The researcher may give information to authorities to prevent serious harm to you, your baby, or others.

You may give information to anyone you wish. If an insurer or employer learns that your baby is in a study and you agree to share study data with them, the researcher will do so. This means that you must also guard your baby's information.

Coded study information will be sent to the NICHD Neonatal Research Network's Data Coordinating Center, Research Triangle Institute (RTI) International, in Research Triangle Park, North Carolina. The University Institutional Review Board (IRB), Food and Drug Administration (FDA), and the Office of Human Research Protections (OHRP) may access these records.

Information from this research study will be kept by <Local Research Institution> and RTI International and may be shared for future research in accordance with the NIH Data Sharing Policy https://grants.nih.gov/grants/policy/data_sharing/ . Information released under this policy will not identify your baby or his/her participation in this research study.

A description of this study will be available on ClinicalTrials.gov, ID number NCT04545866, as required by U.S. Law. This website will not include information that can identify you or your baby. At most, the website will include a summary of the results of this study. You can search this website at any time.

<Insert Institution-specific HIPAA language, if applicable.>

What are the costs of being in this research study?

There will be no cost to you or your insurance for any test, treatment or visit that is done only for this study. The parts of your baby's care that would normally be done as standard treatment will be billed to you or your insurance company. The study will pay for all parts of your baby's care that are done only for the study.

Will I be paid for being in this research study?

There will be no payment to you or your baby for participation in this research study while in the hospital. *<If relevant, insert institution-specific local context re. travel reimbursement at the 22-26 month follow up visit and/or participation in multiple NICHD NRN studies that require this long-term follow up visit>*

What happens if my baby is injured as a result of being in this research study?

<If relevant, insert institution-specific compensation for injury language.>

Is being in this study voluntary?

Yes, being in this study is voluntary. If you decide to let your baby be in this study, you are still free to withdraw him/her at any time. You do not have to give a reason for changing your mind. If you do not let your baby join, or you decide to withdraw your baby from this study later, there will be no penalty or loss of benefits to which he/she is otherwise entitled.

If you do not let your baby be in the study, he/she will still receive all usual care that is available to him/her. This may include receiving the same treatments as in this study. Your choice will not affect the relationship you or your baby have with his/her doctor or other staff, or change the care that your baby receives.

<Describe any institution-specific withdrawal procedures.>

New Information

Sometimes new information becomes available during a research study that may influence your decision to let your baby be in the study. If this happens, the study team will tell you about it and talk with you about whether you want your baby to stay in the study. If you decide to withdraw your baby at that time, the research doctor will make arrangements for your baby's ongoing medical care. If you decide to let your baby stay in the study, you will be asked to sign an updated consent form.

Right of Investigator to Withdraw Participants

The investigator can withdraw your baby from the study without your approval. Possible reasons for withdrawal include new information that shows the risks of the study are greater than the benefits, or if your baby develops a severe problem that requires the study procedures to be stopped.

Who should I contact if I have questions or concerns about this study?

If you have any questions about the study or complaints or concerns during the study, you should contact the investigator (Dr. ___), the co-investigators (Drs. ___ or ___) or other study team members via the University Paging Operator: (xxx) xxx-xxxx, the University NICU (xxx-xxx-xxxx or the ____ NICU (xxx) xxx-xxxx, 24 hours a day. If you think your baby may have been injured from being in this study, you can contact the same people.

Institutional Review Board

Contact the Institutional Review Board (IRB) if you have questions regarding your baby's rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns which you do not feel you can discuss with the study team. The University IRB may be reached by phone at (xxx) xxx-xxxx or by e-mail at irb@xxxxx.edu.

We are always available to answer your questions. If you have any questions that come up during this study, please be sure to ask us.

STATEMENT OF CONSENT

I confirm that I have read this parental Informed Consent document and have been able to ask questions. I will be given a signed copy of this form to keep.

I agree to allow my baby to be in this research study <*insert if HIPAA authorization is bundled*> and authorize you to use and disclose health information about my baby for this study, as you have explained in this document.

_____

Baby's Name

_____

1st Parent/Guardian's Name

_____ _____

1st Parent/Guardian's Signature Date

_____

Relationship to Baby for 1st Parent/Guardian

<Insert 2nd Parent/Guardian line if necessary.>

_____

Name of Person Obtaining Authorization and Consent

_____ _____

Signature of Person Obtaining Authorization and Consent Date