Steroid-reducing Effects of Crisaborole
NCT03832010
9/14/2020

Date: September 14, 2020
Principal Investigator: Anna Grossberg
Application No.: IRB00178631

If you are using Epic for this study, fax a copy of the signed consent form to 410-367-7382.

Patient I.D. Plate

PARENT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: Proof of concept investigation of the steroid-reducing effects of crisaborole in children

Application No.: IRB00178631

Sponsor: Pfizer, Inc.

Principal Investigator: Anna Grossberg, MD
Rubinstein Bldg Suite 2107
200 N Wolfe St, Baltimore, MD 21287
Tel: 410-955-2049; 410-502-7546 (research program)
Fax: 410-614-9804

1. What you should know about this study:

- You are being asked to allow your child to join a research study. This consent form explains the research study and your child's part in the study. Please read it carefully and take as much time as you need. Ask your study doctor or the study team to explain any words or information that you do not understand.
- Joining this study is voluntary. If you allow your child to join the study, you can change your mind later. There will be no penalty or loss of benefits if you decide not to allow your child to continue the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to allow your child to participate.
- If we think your child's participation in this study may affect your child's clinical care, information about your child's study participation will be included in your child's medical record, which is used throughout Johns Hopkins. Doctors outside of Johns Hopkins may not have access to this information. You can ask the research team to send this information to any of your child's doctors.
- When Johns Hopkins is used in this consent form, it includes The Johns Hopkins University, The Johns Hopkins Hospital, Johns Hopkins Bayview Medical Center, Howard County General Hospital, Johns Hopkins Community Physicians, Suburban Hospital, Sibley Memorial Hospital and All Children's Hospital.
- Biospecimens (urine) will be collected in this study. Most biospecimens contain DNA, which is the genetic code for each person.
- A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

- If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.
- During this study, you will not have access to certain medical information and test results collected for study purposes. If an emergency occurs while your child is in the study, medical information needed for your child's treatment can be made available to your study physician and other physicians who treat your child. When the study is completed, all the information in your child's medical record will be available to you.

2. Why is this research being done?

This research is being done to find out whether using a non-steroid topical medication called crisaborole, reduces topical steroid usage in children with atopic dermatitis (eczema).

Atopic dermatitis is a chronic skin condition which affects many children. Topical steroids are used to treat children with atopic dermatitis. There are side effects associated with topical steroid use including but not limited to skin thinning, skin color change, and skin irritation. Fear of steroids and their side effects often leads parents to avoid their use. If children with atopic dermatitis are not getting enough medication for their skin condition, their condition may flare as a result.

There is a class of topical medications called calcineurin inhibitors (tacrolimus and pimecrolimus are examples of this class) which is also approved for treatment of atopic dermatitis. This class of medication is not in the same category as topical steroids and is associated with different side effects. Therefore, this class of medication is considered an alternative to steroids and is often used on sensitive areas of the body such as the face. However, this class of topical medication has a black box warning which lists serious side effects as determined by the Food and Drug Administration (FDA) regarding rare cases of malignancy. Concern for this risk can limit the use of these medications.

Crisaborole is in a different category of medication from topical steroids and topical calcineurin inhibitors. It is a topical phosphodiesterase inhibitor. Crisaborole has fewer side effects than topical steroids and does not have an associated black box warning. Crisaborole is approved by the FDA for the treatment of atopic dermatitis. It is not known whether crisaborole can be an effective steroid-reducing medication for children with atopic dermatitis.

Children 2 to 17 years old with mild-moderate atopic dermatitis may join this study.

How many children will be in this study?

Sixty children will be enrolled in this study at Johns Hopkins.

3. What will happen if you allow your child to join this study?

If you agree to allow your child to be in this study, we will ask you to allow your child to do the following things:

Study summary

In this study, your child will be randomized to one of three groups: the crisaborole group, placebo (vehicle) group, or control group.

Randomization is like drawing numbers from a hat. You and your child will not be informed which group your child belongs to, this is called "blinding". Study doctors will also not be informed which group your child belongs to, unless if necessary in the management of any problems that arise during the study.

Depending on your child's assignment, you will be asked to apply crisaborole, placebo, or control product according to study instructions. A placebo is an inactive substance that looks like the study drug but contains no active drug. The control product is Aquaphor, which is a skin moisturizer that does not contain active drug.

The three study groups are:
1. Crisaborole: crisaborole (blinded) plus topical steroid and Aquaphor
2. Vehicle group: crisaborole vehicle (blinded) plus topical steroid and Aquaphor
3. Control group: Aquaphor (blinded) plus topical steroid and Aquaphor

For each study group, you will be asked to apply moisturizer (Aquaphor) and topical steroid according to study instructions as part of standard care. Your child will have their skin examined and photographed. You and your child will be asked to complete questionnaires. You will be asked to track steroid usage in a diary. You and your child will be asked to return for follow-up visits. You will be asked to bring all study product tubes to follow-up visits to have them weighed. This is a 3 month study which requires 3 on-site visits. If you feel that this study would take too much time, or you would not be able to follow the instructions provided, you should not agree for your child to join the study.

The following sections will describe all the study visits and the procedures to be performed.

Screening/Consent
First, your child will have a Screening Visit to determine if your child qualifies to participate in this study.

- Your child's medical, surgical and medication history will be reviewed.
- Your child's skin will be examined.
- If your child is female and has experienced menstruation, your child will be asked to undergo urine pregnancy testing. Results of the pregnancy testing will be provided to you and your child. If you or your child do not want this to happen, you/your child should reconsider the decision to participate in the study.

Baseline/Day 0
If, based on the results of the screening procedures, your child qualifies to participate in the study, your child will be randomized to one of three groups: crisaborole, vehicle, or control.
At this study visit, the following will be obtained/performed:

- A study doctor will examine your child's skin and determine the severity of their atopic dermatitis using a standardized clinical scale.
- Responses to questionnaires from you and your child.
- Study products (crisaborole, crisaborole vehicle, topical steroid and Aquaphor will be dispensed by the research pharmacy according to your child's group assignment.
- Review instructions on how to use the study products. Using Aquaphor, topical steroid, and/or crisaborole are part of standard clinical care for atopic dermatitis.
- Provide copies of steroid usage diary and review how to complete this during the study.
- If your child is currently using a topical calcineurin inhibitor (tacrolimus or pimecrolimus), your child will be asked to undergo a 2 week wash out period during which the calcineurin inhibitor is discontinued.
- Standardized photographs of your child. Although the study team will take measures to de-identify these photographs (without showing the face or other identifying features), we cannot guarantee that your child will not be recognizable. You should know that:

- You may request that the photographs be stopped at any time.
- If you agree to allow the photographs and then change your mind, you may request that the imaging be destroyed. If the imaging has had all identifiers removed, we may not be able to do this.
- These photographs will be used for the purposes of this research and will not be published for any other reason.

Day 30*
*Depending on scheduling convenience for you and your child, this visit may not take place on exactly day 30 after starting the study (plus up to 10 days). At this study visit, the following will be obtained/performed:

- A study doctor will examine your child's skin and determine the severity of their atopic dermatitis using a standardized clinical scale.
- Responses to questionnaires from you and your child.
- Review instructions on how to use study products.
- Obtain completed steroid usage diary entries.
- Record weights of study product tubes.
- Refills of study products (crisaborole, vehicle, topical steroids and Aquaphor will be dispensed as needed by the research pharmacy according to your child's group assignment.
- Standardized photographs of your child.
- Record all adverse events experienced by your child.

Day 90**
**Depending on scheduling convenience for you and your child, this visit may not take place on exactly day 90 (plus up to 10 days) after starting the study.

- This visit will be identical to Day 30 Visit procedures.

Early Withdrawal from the Study
If you decide to stop your child's participation in the study early, you should inform the study staff as soon as possible.

Subject Responsibilities
You and your child will have the following responsibilities during this study:

- Provide complete information about your child's medical history and current medical conditions.
- Talk to your study doctor before changing any of your child's medications.
- Your child cannot have been in another study with another investigational study drug within the last 30 days. Your child also cannot participate in another study while your child is enrolled in this study and during the following month after the end of this study.
- Come to study visits as scheduled.
- Follow study instructions for how to use the study products.
- Bring completed diary entries and medication tubes to follow-up visits.
- Promptly report any side effects or health problems your child is experiencing even if you don't think they are important or related to the study products or procedures.
- During the study, your child must not use any topical calcineurin inhibitor class medications (tacrolimus, pimecrolimus).
- Do not share the study products with anyone else.
- Tell the study staff if you wish for your child to stop taking part in the study.

- If you suspect that your child is pregnant, contact the study staff immediately.

How long will your child be in the study?
Your child will be in this study for 90 days.

4. What are the risks or discomforts of the study?

The risk of your child joining this study is that their atopic dermatitis may not be as well-controlled as compared with your child being under standard clinical care. If your child experiences any problems with their skin or adverse reactions to any study products or study procedures, you are advised to contact a study doctor about the issue as soon as possible.

Risks associated with study products:
Crisaborole: This can be associated with unlikely reactions of application site pain (4 out of 100 or 4%), allergic reactions and hives (less than 1 out of 100 or less than 1%).

Topical steroids: Topical steroids including hydrocortisone and triamcinolone which are used in this study may be associated with unlikely reactions of localized burning, itching, skin irritation, acne, allergic reaction, stretchmarks, hair follicle inflammation, excessive hair growth, skin color change, skin thinning, rash, skin infection, dry skin. Rare but serious side effects include hormonal abnormalities and abnormalities of laboratory results including changes in salt and sugar levels.

Vehicle: If your child is randomly assigned to the vehicle group, a placebo product will be used in place of crisaborole. There is an unlikely risk that your child will experience an allergic reaction to the ingredients in the vehicle product. There is a risk that your child's atopic dermatitis will get worse while using the vehicle product, which does not contain active medication to treat your child's atopic dermatitis.

Aquaphor: If your child is randomly assigned to the control group, Aquaphor will be used in place of crisaborole. There is an unlikely risk that your child will experience an allergic reaction to the ingredients in Aquaphor. There is a risk that your child's atopic dermatitis will get worse while using Aquaphor, which does not contain active medication to treat your child's atopic dermatitis.

Risks associated with the study procedures:
Urine pregnancy testing: If your child has experienced menstruation, your child will be asked to undergo urine pregnancy testing. No pain is expected to occur as a result of this study procedure. Your child may find the procedure stressful. You may find this study procedure inconvenient. There is a risk of you and your child discovering that your child is pregnant.

Photographs and physical exams: No pain is expected to occur as a result of these study procedures. All photographs taken during the study will only be identified by the study number, your child's study identification number, the visit number and/or date, and the photographed area. To protect your child's identity, photographs of the face will not be taken.

Wash-out period from topical calcineurin inhibitors: If your child is using a topical calcineurin inhibitor (tacrolimus, pimecrolimus) for their atopic dermatitis, your child will be asked to stop using the medication(s) for 2 weeks prior to beginning study protocols. Your child will be asked to not use the medication(s) for the entire duration of the study. There is a risk that your child's atopic dermatitis will flare after discontinuing the medication(s).

Confidentiality: There is an unlikely risk that information about your child may become known to people outside this study. Although every effort will be made to protect your child's confidentiality, there is still the possibility that information about your child may become known outside of this study.

Questionnaires: You and your child may get tired or bored when we are asking your or your child questions or to complete questionnaires. You/your child do not have to answer any question that you or your child do not want to answer.

There may be side effects and discomforts that are not yet known.

5. Are there risks related to pregnancy?

Any female child who has experienced menstruation is required to undergo urine pregnancy testing prior to beginning study participation. If your child becomes pregnant at any time during the study, they will be removed from the study. Results of pregnancy testing will be provided to you and your child. If you or your child do not wish to be tested for pregnancy, you or your child should decline to participate in this study. This research may hurt an embryo or fetus in ways we do not currently know.

6. Are there benefits to your child from being in the study?

There may or may not be a direct benefit to your child from being in this study. It is possible that your child's atopic dermatitis will get better, stay the same, or get worse. If your child takes part in this study, your child may help others in the future.

7. What are your options if you do not want your child to be in the study?

You do not have to allow your child to join this study.

If your child does not take part in the study, your child's care at Johns Hopkins will not be affected.

8. Will it cost you anything to allow your child to be in this study?

No. You will receive a separate Insurance and Research Participant Financial Responsibility Information Sheet (Sheet).

This Sheet will give you the following information:

- The procedures, tests, drugs or devices that are part of this research and that will be paid for by the study (no cost to you).

- The procedures, tests, drugs or devices that will be billed to you and/or your health insurer. If you have health insurance, you will be responsible for any co-pays or deductibles not covered by your insurance.

9. Will you or your child be paid if you allow your child to join this study?

You will be paid $100 after your child has completed the Day 0 visit, $100 after completing the Day 30 visit, and $100 after completing the Day 90 visit. There is a $100 bonus if your child completes the study. You will be compensated for parking costs. You will not receive compensation for visits your child has not completed. If you do not follow instructions appropriately for a visit (such as forgetting to bring the study drug or diary entries) the compensation will be reduced by 50% for the visit.

You may be required to provide your social security number to be paid for taking part in this study. Federal tax law requires that you report your research payments when you file your taxes. If your total

payments from Johns Hopkins exceed $600 per year, Johns Hopkins will report these payments to the Internal Revenue Service and you will receive a 1099-MISC form from us.

10. Can your child leave the study early?

- You can agree to allow your child to be in the study now and change your mind later.
- If you wish to end your child's participation, please tell us right away.
- Leaving this study early will not stop your child from getting regular medical care.
- If your child leaves the study early, Johns Hopkins may use or give out your child's health information that it already has, if the information is needed for this study or any follow-up activities.

11. Why might we take your child out of the study early?

Your child may be taken out of the study if:

- Staying in the study would be harmful to your child's health.
- Your child needs treatment not allowed in the study.
- You or your child fails to follow instructions.
- Your child becomes pregnant.
- The study is cancelled.
- There may be other reasons to take your child out of the study that we do not know at this time.
- If your child is taken out of the study early, Johns Hopkins may use or give out your child's health information that it already has if the information is needed for this study or any follow-up activities.

12. How will your child's privacy be protected?

We have rules to protect information about your child. Federal and state laws and the federal medical Privacy Rule also protect your child's privacy. By signing this form you provide your permission, called your "authorization," for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about your child. This includes things learned from the procedures described in this consent form. They may also collect other information including your child's name, address, date of birth, and information from your child's medical records (which may include information about HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

The research team will know your child's identity and that your child is in the research study. Other people at Johns Hopkins, particularly your doctors, may also see or give out your child's information. We make this information available to your child's doctors for your child's safety.

People outside of Johns Hopkins may need to see or receive your child's information for this study. Examples include government agencies (such as the Food and Drug Administration), safety monitors, other sites in the study and companies that sponsor the study.

If your child is in a cancer study that receives federal funding, the National Cancer Institute (NCI) now requires that we report identifiable information (such as, zip code) about your child's participation. You may contact the NCI if you have questions about how this information is used.

We cannot do this study without your authorization to use and give out your child's information. You do not have to give us this authorization. If you do not, then you may not join this study.

We will use and disclose your child's information only as described in this form and in our Notice of Privacy Practices; however, people outside Johns Hopkins who receive your child's information may not

be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your child's information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

The use and disclosure of your child's information has no time limit. You may revoke (cancel) your permission to use and disclose your child's information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and fax information are on page one of this consent form.

If you do cancel your authorization to use and disclose your child's information, your child's part in this study will end and no further information about your child will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

13. Will the study require any of your other health care providers to share your child's health information with the researchers of this study?

As a part of this study, the researchers may ask to see your child's health care records from her/his other health care providers.

14. What treatment costs will be paid if your child is injured in this study?

Johns Hopkins does not have a program to pay you if your child is hurt or has other bad results from being in the study. However, medical care at Johns Hopkins is open to your child as it is to all sick or injured people.

The costs for any treatment or hospital care you receive as the result of a study-related injury that are not covered by a health insurer will be billed to you.

By signing this form you and your child will not give up any rights you have to seek compensation for injury.

15. What other things should you know about this research study?

a. What is the Institutional Review Board (IRB) and how does it protect you?

The Johns Hopkins Medicine IRB is made up of:

- Doctors
- Nurses
- Ethicists
- Non-scientists
- and people from the local community.

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your child's rights as a participant or if you think you or your child have not been treated fairly. The IRB office number is 410-955-3008. You may also call this number for other questions, concerns or complaints about the research.

When the Johns Hopkins School of Medicine Institutional Review Board (IRB) reviews a study at another site, that site (institution) is solely responsible for the safe conduct of the study and for following the protocol approved by the Johns Hopkins IRB.

b. What do you do if you have questions about the study?
Call the principal investigator, Dr. Anna Grossberg at 410-955-2049. If you wish, you may contact the principal investigator by letter or by fax. The address and fax number are on page one of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-955-3008.

c. What should you do if your child injured or ill as a result of being in this study?
If you think your child is injured or ill because of this study, call Dr. Anna Grossberg at 410-955-2049 or our cutaneous translational research program (CTReP) at 410-502-7546 during regular office hours.

If your child has an urgent medical problem related to taking part in this study, call Dr. Anna Grossberg at 410-955-2049 or CTReP at 410-502-7546 during regular office hours, and 410-955-5000 after hours and on weekends, ask to speak to the Dermatology resident on-call.

d. What happens to Data and Biospecimens that are collected in the study?
Johns Hopkins and our research partners work to understand and cure diseases. The biospecimens and/or data your child provides are important to this effort.

If you allow your child to join this study, you should understand that you/your child will not own your child's biospecimens or data, and should researchers use them to create a new product or idea, you/your child will not benefit financially.

With appropriate protections for privacy, Johns Hopkins may share your child's biospecimens and information with our research sponsors and partners.

16. Assent Statement

This research study has been explained to my child in my presence in language my child can understand. He/she has been encouraged to ask questions about the study now and at any time in the future.

17. What does your signature on this consent form mean?

Your signature on this form means that:

- you understand the information given to you in this form
- you accept the provisions in the form
- you agree to allow your child to join the study

You and your child will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Signature of Parent	(Print Name)	Date/Time
Signature of Person Obtaining Consent	(Print Name)	Date/Time
Signature of Legally Authorized Representative (LAR) **For CHILD PARTICIPANT**	(Print Name)	Date/Time
Description of LAR's authority under Maryland Law to act as surrogate health care decision-maker for child research participant (for example, Legal Guardian; Court-ordered representative)		Date/Time
Signature of Child Participant (optional unless IRB required)	(Print Name)	Date/Time

I have received the separate Insurance and Research Participant Financial Responsibility Information Sheet.

Signature of Participant, LAR or Parent/Guardian	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO 410-367-7382; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

ONLY CONSENT FORMS THAT INCLUDE THE JOHNS HOPKINS MEDICINE LOGO CAN BE USED TO OBTAIN THE CONSENT OF RESEARCH PARTICIPANTS.

DOCUMENTATION OF PHYSICIAN/MID-LEVEL PROVIDER CONSENT

My signature below indicates that I have discussed the risks, benefits, and alternatives, answered any questions, and believe the participant is able to make an informed choice to join the study.

Signature of Physician/Mid-Level Provider (Print Name) Date/Time

Signature of Parent (Print Name) Date/Time

Signature of Legally Authorized Representative (LAR) (Print Name) Date/Time
For CHILD PARTICIPANT

Description of LAR's authority under state or applicable local law to act as surrogate health care decision-maker for child research participant (for example, Legal Guardian, court-ordered representative) Date/Time

Signature of Child Participant (optional unless IRB required) (Print Name) Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO 410-367-7382; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

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