ACTIV-6: COVID-19 Study of Repurposed Medications - Arm B (Fluvoxamine)

NCT05890586

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# Consent to Participate In a Research Study

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Jan 07, 2022

**TITLE:** ACTIV-6: COVID-19 Outpatient Randomized Trial to Evaluate Efficacy of Repurposed Medications

**PROTOCOL NO.:** None
IRB Protocol #20211467

**SPONSOR:** Duke Clinical Research Institute

<<CF-Main Header Block - Investigator>>
**STUDY-RELATED PHONE NUMBER(S):** <<CF-Main User Defined #1>>
[24 hour number is required]

**SPONSOR VERSION:** 5.0

You are being invited to participate in **ACTIV-6: COVID-19 Outpatient Randomized Trial to Evaluate Efficacy of Repurposed Medications**. About 15,000 participants from around 280 sites across the United States will be involved. The study is funded by The National Center for Advancing Translational Sciences (NCATS), a division of The National Institutes of Health (NIH). Duke Clinical Research Institute (DCRI) is the clinical coordinating center and Vanderbilt University Medical Center (VUMC) is the data coordinating center for this study. Please consider the following information in making your decision.

## STUDY SUMMARY

You are being asked to participate in this study because you have been diagnosed with the SARS-CoV-2 virus, you currently have some symptoms of COVID-19, the disease caused by the virus, and you are at least 30 years old. As part of this study, you will be given either a study medication or a placebo to see what types of effects the study medication or the placebo may have on your ability to get better and recover from the infection. You may benefit, but there is no guarantee. Others may benefit from the information learned.

Currently, the FDA has granted Emergency Use Authorization (EUA) to some monoclonal antibodies as a treatment for those diagnosed with COVID-19 who are having mild to moderate


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symptoms and are at risk of developing more severe COVID-19. You and your regular healthcare provider should discuss if this option may be right for you. You can receive a monoclonal antibody and enter the study, this is your choice and participation in the study is voluntary.

Your participation in the study will last about 3 months (90 days). All study visits can be remote (not in person). You will complete some surveys online or by phone if you do not have access to a computer/tablet/smart phone or internet. You may be asked to come in for an in-person visit if the research study team feels this is in your best interest. The surveys will ask you about your symptoms, general health, any medications you are currently taking and about any new or worsening medical problems you may be experiencing.

This study will compare multiple study medications and placebo. Placebo is a product that will look like the study medication, but it is inactive (does not contain any study medication). Researchers use placebo so they can find out if the study medication does anything for a participant's health. The study medication or placebo you will receive depends on when you enter the study and which study medications the study doctor determines are appropriate for you, based on your other medications and medical conditions. At your first visit, you will be assigned to receive study medication or placebo. The assignment is done by randomization (a process like pulling numbers from a hat). Neither you nor the study team will know if you are receiving study medication or placebo.

While participating in this research, you will continue to receive standard of care (care you would have received even if you were not participating in this study) as directed by your regular health care provider.

The potential side effects and risks are dependent on the drug chosen, but can include aches, rash, and serious allergic reactions.

More information about the ACTIV-6 study is provided below. If you are interested, please continue to read. If there is anything in this form you do not understand, please ask questions.



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## INTRODUCTION

### Why am I being asked to take part in this study?

You are being asked to participate in this study because you have had a recent COVID-19 test that is positive for the COVID-19 virus, you are exhibiting some mild to moderate symptoms of COVID-19, and you are at least 30 years of age.

### Why is this study being done?

Researchers would like to evaluate whether medications that are already approved by the FDA for other diseases might also work for COVID-19. This study is testing this in people with mild to moderate COVID-19 who do not require hospitalization. Use of these drugs for this study is considered "investigational." Investigational means these study medications or placebo are being researched for their effect on COVID-19. They are not approved by the FDA as treatment for COVID-19, but they are approved by the FDA for some other conditions.

## VOLUNTARY PARTICIPATION/ POTENTIAL BENEFITS

### Can I say no if I don't want to participate?

Yes, you do not have to take part. Your participation is voluntary. You can continue to get your usual health care even if you are not in this study.

### Will there be any benefit to others or me?

We do not know if you will benefit from taking part in this study. Your participation may help doctors learn more about possible medications that could help treat COVID-19. The information learned from this study may benefit others in the future.

## WHAT YOU CAN EXPECT IF YOU DECIDE TO PARTICIPATE

### How long will I be in this study?

Your participation will last about 90 days (3 months).

### Who will be my doctor on this study?



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Once you are enrolled in the study, you will continue under the care of your local (regular) health care provider. This healthcare provider should be your contact for all medical decisions and health-related questions. We may need to contact your health care provider during the time you are on study and afterwards.

While participating in this research, you will continue to receive standard of care (care you would have received even if you were not participating in this study) as directed by your regular health care provider. Your regular health care provider will inform you of any changes to your care, based on your participation in this study.

## What is involved in this study?

A member of the research study team will tell you about the study and ask you questions about your health and medications. Because this study does not have in-person visits, you will communicate with the study team online or by phone. Once you receive and start taking the study medication or placebo, you will be asked to complete a survey, either online or by telephone if you are not able to use the internet. The survey will ask you about your general health and well-being, any new symptoms you have, or changes to your health. The survey will let us know how you are doing. If you do not fill out the online survey, we will follow up with you to check on how you are doing. If you need help completing the surveys, the study team can assist you. If you report you are hospitalized during the study, go to an urgent care center, or visit an emergency department, we may review your medical record to get information about your health status and the hospitalization or emergency visit. You will be asked to sign a medical record release for this purpose. The signed medical record release form is required for your participation in this study.

If you decide to participate and you are a good fit for the study, the information below describes in more detail what will happen during the study.



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## Personal Information

As part of this study, we will ask you to provide the following information:

- Your date of birth so we can confirm your age.
- Your phone number, email address, and cell phone so we can contact you to see how you are doing and to be sure you are doing all of the things needed for the study. Tell your study team if your contact information changes while you are participating. It's important that we know the address where you are staying so we can send you your study medication to the correct place.
- We will ask you to sign a medical release form to access your medical records so we can review your positive COVID-19 test result and any hospitalizations that occurred while you are participating in the study.
- Contact information for a trusted person that you know (family member or friend) so we can contact them if we cannot reach you. These people may give us some information about your health if you are unable to do so.
- A list of all your medicines (prescription and non-prescription).

## BASELINE (SCREENING) VISIT

When you are first thinking about being in the study, you will either complete an online form or talk to someone from the study team, typically on the telephone. The purpose of this visit is to check your interest in participating and to confirm that you can participate in the study. We will tell you about the study, how we will follow you, and you will be asked to provide your consent to participate. At this visit, we will also:

- Ask you to provide a clear photograph of your positive COVID-19 test result
- Ask you to provide identifying personal information such as home address, email, phone number, and a trusted person that you know (family or friend)
- Ask questions about your health, including potential for pregnancy and contraceptive use, and about any medications you are currently taking
- Complete online surveys about your health, mood, and COVID-19 symptoms you may be experiencing



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- Confirm that you can get the study medication or placebo shipped to your home. It is not possible to ship study medication or placebo to a post office box.
- Assign you to the study medication or placebo

After the study team speaks with you and evaluates your health and medical information, there may be reasons you are unable to participate in this study. These reasons will be explained to you.

## Study Medication Assignment

You will be randomized to receive study medication or placebo. Randomization means whether you receive study medication or placebo. Randomization will be determined by chance (like pulling numbers from a hat). As the number of drugs being tested increases, so does the chance you will be randomized to an active drug instead of placebo dependent upon which study arm(s) you choose. Neither you, your study doctor, nor the staff at the study site will know to which group you have been assigned, but we can quickly find out if there is ever a need to know for your safety and/or well-being.

Study medication or placebo will be shipped directly to your home. To ensure study medication arrives on schedule, it is important to the let the study team know if your address changes. You must provide a street address so we can make sure the study medication or placebo gets to you. **It is not possible to ship to a PO Box.**

You will be provided instructions about how to take the medication. To ensure study medication or placebo is taken as directed, and at the required intervals, you will be provided additional information about how to record taking study medication or placebo each day.

## INTERVENTION PERIOD (DAYS 1-14)

There may be a brief period between your consent to be in the study and the study medication or placebo arriving at your address. Once the study medication or placebo arrives at your address, the following events will occur:

Day 1:

- Receipt of study medication or placebo
- Study medication self-administration (you take study medication or placebo as directed)



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- Provide information about your general health and well-being, including potential for pregnancy and contraceptive use
- Provide information about any new or worsening symptoms
- Provide information about any medical care you have received or any new medications you are taking

Days 2-14:

- Take study medication as directed
- Complete a daily survey to confirm you took your study medication or placebo and to tell us about your health and well-being, including potential for pregnancy and contraceptive use, any medical care you have received, and any new medications you are taking.
- We ask that you report symptoms each day until each symptom resolves (must be resolved at least 3 days in a row). Symptom reporting will begin once you start taking the study medication and ending 28 days later.
- On Days 3, 7, and 14 only: Collect reading from the oxygen monitor you received from the study
- On Days 7 and 14 only: Provide information about your mood and quality of life, and your ability to perform normal tasks at home and your overall health
- You will stop taking study medication or placebo, per prescribing instructions
- On Day 14, a member of the study team will call to check in and evaluate your current health and ask you about any new medications you may be taking. We ask that you **please make every effort to keep this remote visit appointment. It is important for the study team to evaluate you throughout the study**

## FOLLOW-UP PERIOD (DAYS 15 -28)

The following events will occur during the Follow-Up Period, after you have finished taking the study medication or placebo.

Days 15-28:

- If you are still experiencing symptoms, then we will continue to ask you about your health each day. We will stop asking you these questions when you have had no symptoms for at least three days.



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Day 21:

- You will continue to report your symptoms. and will continue to ask you about your health each day. We will stop asking you these questions when you have had no symptoms for at least three days (in a row).

Day 28:

- Remote assessment/visit (Day 28) – A member of the study team will call to check in and evaluate your current health and ask you about any new medications you may be taking. We ask that you **please make every effort to keep this remote visit appointment. It is important for the study team to evaluate you throughout the study**
- You will also be asked to complete surveys about your Quality of Life, overall health and well-being, and your ability to perform normal tasks at home.
- You can stop reporting your symptoms if they have resolved for at least three days (in a row).

## FINAL VISIT (DAY 90)

The following events will occur around Day 90. This will be considered your final visit and your participation will end. There may be circumstances that could require us to continue to follow-up with you after this last visit. A member of the study team will provide you with this information. At this visit, the following events will occur:

- You will provide information about any medications you are currently taking
- Provide information about your general health, including pregnancy, and well-being
- Provide information about any new or worsening symptoms
- Fill out Quality of Life Survey , providing information about your mood, your ability to perform routine tasks and your overall health

## UNPLANNED STUDY VISIT

If you have any bad side effects while taking study medication or placebo, we may want to follow-up with you to get more information about the event. To do this, we may contact you for additional information and/or you may be asked to come in for a clinic visit. Your study doctor will provide information about what is needed and how you should proceed.



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## Online Surveys and Phone Calls

After your initial (Baseline) visit with the study team, we will ask you to complete brief surveys online or by phone to find out about your health, mood, medications and if you are taking your study medication. We will ask you to do these surveys throughout the study.

We ask that you provide your name and phone number so that the study organizers or your site may contact you. We will also ask you for the name and phone number of a person that you know and trust that can answer health questions about you if we are unable to reach you or you are unable to tell us yourself. This contact information is confidential and will only be available to representatives of the groups who are helping to organize this study - Duke Clinical Research Institute (DCRI) and Vanderbilt University Medical Center. Your site or DCRI may also contact your physician's office to obtain medical records to collect information about any care you have received if you have not been able to be contacted by phone.

If you miss any of your remote visits and/or are unable to complete your online surveys, the following will occur:

- Your site, or the DCRI Participant Research Operations (PRO), may contact you by phone or other methods
- These staff from your site, or the DCRI PRO will ask you questions that are on the online surveys.
- This phone interview should take about 15 minutes to complete.
- If we cannot reach you, or if you are unable to answer questions, we will contact your trusted friend or family member to answer questions on your behalf.
- Once enrollment is completed at your research study site, the site may close. If so, then all study questions can be answered by the DCRI PRO. If you have any questions concerning the study during this time, you should call 833-385-1880. All your healthcare will continue to be performed by your personal healthcare provider

## Can I Stop Participating before the Study is Complete?

You can choose to not participate or stop participating at any time without penalty or loss of benefits or access to standard medical care (care you would have received if you were not



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participating in this research). If possible, we would like for you to stay in the study until it is complete to make sure the final study results are helpful to you and others who may get COVID-19.

If you are thinking about stopping, please let your study doctor know as soon as possible. Your study doctor can talk about options that might work for you to continue.

We will tell you if we learn anything new that might change your mind about being in the study. If you decide to stop participating, your usual medical care will not be affected.

If you decide to stop taking the surveys and study calls, we will follow you by reviewing your medical record.

If we lose contact with you, we will keep collecting information from your medical record to see how you are doing until the study is done.

Your participation in the study may be stopped by your study doctor at any time without your consent.

## HOW WILL MY CONFIDENTIALITY BE PROTECTED?

In all research, there is a possible risk of the loss of confidentiality, but we will do our best to keep your information secure.

This study will have a *Certificate of Confidentiality* issued by the National Institutes of Health (NIH). This certificate is to protect the identity of research participants. It means that doctors, researchers, and other staff involved in this study cannot be forced to provide identities of any participants in any legal proceeding. The certificate protects against the involuntary release of information about subjects collected during this research. However, you may choose to voluntarily disclose the protected information and this certificate does not prohibit such voluntary disclosure. Furthermore, the parties listed in the "Use of Health Information" section of this consent form may review our records under limited circumstances and this certificate does not prohibit such disclosure.



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We will keep your personal information secure in the data system. You will be assigned a unique code that will be the link between you and your study information. This process keeps your health information and study results separate from your other personal information. Your personal information will be kept securely and will not be made available to anyone except for reasons described in this consent form, such as for shipping the study medication to you.

## Receiving Information from Your Medical Record

We will review your medical record while you are in the study. This information may include any medical visits or hospital, or emergency room visits you had during the study. We may also collect information about medicines, lab results, and other information that we determine may be useful to the study. Reviewing your medical, pharmacy, and laboratory records will help us understand your health status while you are participating in this study.

## ALTERNATIVES

### What other choices are there?

One alternative to study treatment are monoclonal antibodies. Monoclonal antibodies are man-made proteins that can help your body fight off COVID-19 and reduce the risk of severe disease and hospitalization. Currently, three monoclonal antibody (mAb) products have received Emergency Use Authorizations (EUA) from the Food and Drug Administration (FDA) for the treatment of mild to moderate COVID-19 in non-hospitalized patients with confirmed COVID-19. Monoclonal antibodies are currently offered to those who are at high risk for progressing to severe disease and/or hospitalization. If you are interested in receiving monoclonal antibodies you should discuss this with your regular healthcare provider. They will decide if this option is right for you. You may receive a mAb and still participate in the study. This is your choice.

Your other choice is not to participate in the study. Your usual medical care will continue whether or not you participate in this study.



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## RESULTS AND STUDY PROGRESS

### Will I be told the results of the research?

You will be notified if we find any new information that may affect your willingness to continue participating in this study.

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.

The set of information used to decide the results may be made available to other researchers. This includes survey results and other health information collected from all study participants. Identifying information like your name, date of birth, home address, phone number, or email address will not be included in this information set. You will be assigned a unique code that will be the link between you and your study information.

Results of the research may also be published. If results are published, they will not contain any information that is specific to you. Once the study is complete, there may be an opportunity to share the results of this research. If this occurs, you will be notified about how to access these results.

## POSSIBLE RISKS AND DISCOMFORTS

A team of health experts called the Independent Data Monitoring Committee will regularly monitor the safety of study participants and the progress of the study overall. The committee can stop and hold a study if they have concerns about safety.

### What risks can I expect from taking part in this study?

Possible side effects associated with the study medication or placebo are listed at the end of this document and are dependent on which study medication you get. You will indicate your willingness to participate in each study arm (arm means which study medication you will receive). Each arm will contain study medication or placebo and you will be randomized to receive either study medication or placebo.



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It is important to notify the study team of any new or worsening problems you may experience while on this study. There may be unknown risks from participation.

There is also the slight risk of loss of confidentiality. Every effort will be made to protect your information, as described later in this form.

## PAYMENT AND COSTS

### Will I be paid for being in this study?

You will receive one payment for your participation in the study. You will receive up to a $100 gift card upon completion of the study. The study team will determine when your participation is complete and will provide details regarding this payment. Your email and protected health information (PHI) may be shared with individuals and/or companies involved in processing payments. <<CF-Main Payment for Part. Paragraph>>
<<CF-Main Financial Disclosure>>

### Are there costs to me for being in this study?

The study medication or placebo will be provided to you free of charge. Study medication or placebo will only be provided according to the schedule described in this consent. Study medication or placebo will not be provided past your final study visit. You may keep the oxygen monitor provided by the study. You or your insurance provider will be billed for any medical care that you would receive whether or not you are part of this study.

## USE OF HEALTH INFORMATION FOR RESEARCH

### What is Protected Health Information (PHI)?

The PHI collected for this research study includes your name, address, phone number, email address, date of birth, and relevant health information like your medications and medical conditions.


### Will my PHI remain private?

We will make every effort to keep your PHI safe. We will store records in a locked cabinet or office or on a password-protected computer. Your identity and your PHI will not be shared outside of this study unless it is required to protect your safety, the safety of others, or if you give us approval to share it.



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## Who will have access to or receive my PHI?

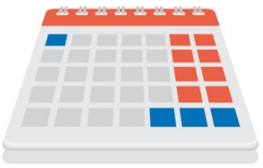
Your PHI may be given to others only if needed for reasons that are part of carrying out the study, such as determining the results of the study, making sure the study is being done correctly, and providing required reports.

Some of those that may receive, use, or disclose your PHI are:

- ACTIV-6 researchers and staff including the NIH and Duke Clinical Research Institute (DCRI) and the Vanderbilt University Medical Center
- Researchers and staff at sites who are helping with the study
- Healthcare professionals affiliated with the study
- Healthcare providers who have provided your health services or treatment
- Pharmacy staff and representatives who will package and ship study medication
- Representatives of the institutional review board (IRB) sometimes called the "ethics board" <<CF-Main SMO Company 1>> <<CF-Main Affiliated IN Language 1>>
- Government health and regulatory agencies such as the FDA
- A team of health experts call the Independent Data Monitoring Committee who will regularly monitor the safety of study participants and the progress of the study overall

Your information may be shared with groups who are not listed above. The federal privacy rules may not apply to these groups; however, they have their own rules and codes to assure that all efforts, within reason, will be made to keep your PHI private.

## How long will you keep my PHI?



We will keep your health information and the consent form for as long as we need it, which will be for at least six (6) years. <<CF-Main User Defined #6>>This approval does not expire. Any research information entered into your medical record will be kept for as long as records are kept by the place where you receive your health care.

## Do I have to share my PHI with you?

If you do not agree to use of your PHI, you will not be able to enroll or continue in this study. We will stop collecting information about you, but information we have already collected will



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still be used. You can tell your study doctor by sending a letter to his/her address that you want to take away your approval to use your PHI. You can find his/her address below. If you decide to stop your participation in the study, you can send a request through the web portal.

## CONTACT INFORMATION

You will be provided a copy of your consent. Please refer to this consent if you have questions at any time during your participation on this study. The study team contact information is provided here:

| | |
|---|---|
| Study Site Name: | **[Site]** |
| Study Doctor Name: | **[Name/Credentials of Responsible PI at Site]** |
| Study Doctor Contact: | **[Number(s)] (24 hours)** |
| Study Doctor Address: | **[Address]** |
| | **[City, State, Zip]** |
| Study Coordinator Name (if applicable): | **[Name/Credentials of Alternate Point of Contact for the Study]** |
| Study Coordinator Contact (if applicable): | **[Number(s)] <<CF-Main Emerg. Phone Number>>** |

### Is there anyone I can call if I have questions or problems?

If you have questions, concerns, or complaints about your participation, or suffered an injury or physical issue caused by the study, please call your study doctor at the number listed above.

If you have questions, concerns, or complaints about study participation, you may contact the ACTIV-6 study hotline at (833)-385-1880.

Immediate necessary medical care is available at **[Site]**<<CF-Main User Defined #2>> if you are injured because of your participation in this study. However, there is no commitment by **[Site]<<CF-Main User Defined #2**, your physicians, Duke University (Duke Clinical Research Institute), or the NIH to provide monetary compensation or free medical care to you in the event of a study-related injury.



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**PREP**

Study related subject injury compensation will not be provided by Duke. The Public Readiness and Emergency Preparedness Declaration (PREP), was issued by the Department of Health and Human Services on March 10, 2020. This declaration may limit the legal rights of a subject participating in a COVID-19 clinical study that uses a drug, device or vaccine designed to treat, diagnose, cure or prevent COVID-19. This includes the Study medication. Subjects using the Study medication may have limits on their right to sue the manufacturers, the Study sponsor, healthcare providers and others for significant injuries and adverse reactions. Under some circumstances, compensation may still be available under the PREP Declaration for certain patients who sustain injuries. To find out more, go to https://www.hrsa.gov/cicp/about/index.html or call 1-855-266-2427.

If you have questions, concerns or complaints about the research, or information about your rights as a research subject, you should contact the WCG Institutional Review Board (IRB). The IRB is a group of people who review the research to protect your rights as a study participant. You can call the WCG IRB at toll free at 855-818-2289, or email at researchquestions@wcgirb.com.

## RISKS ASSOCIATED WITH IVERMECTIN AND PLACEBO

Any drug may have side effects. Because of this, it is important to notify the study team of any new or worsening conditions you may experience while taking study medication or placebo and after you finish taking the required dose of study medication or placebo. It is also important to tell the study team about any new or current medications you are taking.

Below are some possible, known risks associated with ivermectin and placebo. There may also be unknown risks from participation. **If you experience side effects such as difficulty breathing, wheezing, change in heart rate, nausea, vomiting and diarrhea, rash or hives shortly after taking ivermectin, you should seek medical attention right away, as these could be signs of a severe or life-threatening allergic reaction.**

The dose of ivermectin or placebo you receive is based on your weight at the time of study enrollment. This study is testing two different doses of ivermectin.



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The most common (more likely) side effects of ivermectin or placebo are:

- Body aches and or joint pain
- Headache
- Dizziness
- Temporary vision changes (higher likelihood at the higher dose)
- Lymph node swelling and or tenderness (swollen glands) in armpits, groin or neck
- Fever
- Dry, itchy skin
- Raised, itchy rash or hives
- Generally feeling "under the weather" and or feeling tired

Rare (less likely) side effects of ivermectin or placebo are:

- Worsening of bronchial asthma
- Stevens-Johnson syndrome (a condition causing small and sometimes large patches of skin to blister and peel)
- Seizure
- Elevated bilirubin (liver enzymes)

## RISK OF PREGNANCY WHILE TAKING IVERMECTIN OR PLACEBO

- **For people capable of getting pregnant:**

The effects of Ivermectin on a developing pregnancy or breastfeeding infant are unknown. If you are pregnant or planning to become pregnant during the next 90 days and or are breast feeding, please inform the study team. You will be asked to complete a Pregnancy Reasonably Excluded Checklist.

If you are someone who could become pregnant (you have not had a hysterectomy and/or both tubes and/or both ovaries removed and/or you are not postmenopausal and over the age of 45) and you have a sexual partner who is able to conceive children (has not had a vasectomy with a negative post-surgery semen analysis), it will be important for you to practice effective



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birth control methods while taking study medication or placebo. Please ask the study team about acceptable methods.

Because no birth control method is 100% effective, you should notify your study doctor immediately if you think there is any chance you could be pregnant, even if you have had a recent negative pregnancy test. If you become pregnant, we may want to review your medical history before and after you give birth.

- **For people who can get someone pregnant:**

If you can conceive children and your partner is someone who could possibly become pregnant (they have not completed menopause and are over the age of 45 or have not had a hysterectomy and/or both tubes and/or both ovaries removed) you should practice effective birth control methods while taking study medication or placebo. If you have questions about what is considered effective birth control, please ask the study team.

You should not donate sperm for the duration of the study and for 30 days after the last dose of study medication.

If your partner becomes pregnant while you are taking ivermectin, it is important to notify the study team right away. They may want to review your partner's medical history during and after the birth.

☐ **Study participant agrees to participate in the ivermectin and placebo arm of this study**

☐ **Study participant does not agree to participate in the ivermectin and placebo arm of this study**



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## RISKS ASSOCIATED WITH FLUVOXAMINE MALEATE AND PLACEBO

Any drug may have side effects. Because of this, it is important to notify the study team of any new or worsening conditions you may experience while taking fluvoxamine or placebo and after you finish taking the required dose of fluvoxamine or placebo.

Because some drugs should not be taken with fluvoxamine or placebo, it is also important to **tell the study team about any new or current medications (prescription and non-prescription) that you are taking before you start taking fluvoxamine or placebo.**

Below are some possible, known risks associated with fluvoxamine and placebo. There may also be unknown risks from participation. **If you experience side effects such as difficulty breathing, wheezing, change in heart rate, nausea, vomiting and diarrhea, rash or hives shortly after taking fluvoxamine, you should seek medical attention right away, as these could be signs of a severe or life-threatening allergic reaction.**

The most common (more likely) side effects of fluvoxamine or placebo are:

- Nausea
- Somnolence (feeling drowsy, sleepy)
- Insomnia (hard to fall asleep and stay asleep)
- Asthenia (physical weakness, lack of energy)
- Nervousness
- Headache
- Dry mouth
- Dyspepsia (indigestion)
- Constipation
- Abnormal ejaculation
- Sweating
- Anorexia (loss of appetite, not eating)
- Tremor (uncontrolled quivering or trembling)
- Vomiting



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Rare (less likely) side effects of fluvoxamine or placebo are:

- Hematemesis (vomiting blood)
- Purpura (rash of purple spots under the skin caused by internal bleeding from small blood vessels)
- Hemoptysis (coughing up blood)
- Laryngismus (spasm of the larynx which can cause heavy or labored breathing)
- Hematospermia (blood in semen)
- Withdrawal syndrome (physical and mental symptoms that occur after stopping or reducing intake of a drug)

## RISK OF PREGNANCY WHILE TAKING FLUVOXAMINE MALEATE OR PLACEBO

- **For people capable of getting pregnant:**

The effects of fluvoxamine on a developing pregnancy or breastfeeding infant are unknown. If you are pregnant or planning to become pregnant during the next 90 days and or are breastfeeding, please inform the study team. You will be asked to complete a Pregnancy Reasonably Excluded Checklist.

If you are someone who could become pregnant (you have not had a hysterectomy and/or both tubes and/or both ovaries removed and/or you are not postmenopausal and over the age of 45) and you have a sexual partner who is able to conceive children (has not had a vasectomy with a negative post-surgery semen analysis), it will be important for you to practice effective birth control methods while taking study medication or placebo. Please ask the study team about acceptable methods.

Because no birth control method is 100% effective, you should notify your study doctor immediately if you think there is any chance you could be pregnant, even if you have had a recent negative pregnancy test. If you become pregnant, we may want to review your medical history before and after you give birth.

- **For people who can get someone pregnant:**

If you can conceive children and your partner is someone who could possibly become pregnant (they have not completed menopause and are over the age of 45 or have not had a hysterectomy and/or both tubes and/or both ovaries removed) you should practice effective



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birth control methods while taking study medication or placebo. If you have questions about what is considered effective birth control, please ask the study team.

You should not donate sperm for the duration of the study and for 30 days after the last dose of study medication.

If your partner becomes pregnant while you are taking fluvoxamine, it is important to notify the study team right away. They may want to review your partner's medical history during and after the birth.

☐ **Study participant agrees to participate in the fluvoxamine and placebo arm of this study**

☐ **Study participant does not agree to participate in the fluvoxamine and placebo arm of this study**

## RISKS ASSOCIATED WITH FLUTICASONE FUROATE INHALATION POWDER AND PLACEBO

Any drug may have side effects. Because of this, it is important to notify the study team of any new or worsening conditions you may experience while taking fluticasone or placebo and after you finish taking the required dose of fluticasone or placebo.

Because some drugs should not be taken with fluticasone or placebo, **it is also important to tell the study team about any new or current medications (prescription and non-prescription) that you are taking before you start taking fluticasone or placebo. Specifically, some medications can change the way the liver processes other medications- they are called CYP3A4 Inhibitors- and these medications may increase the amount of steroid that your body gets. Talk to the study team about all your medications and if any of your medications will change the way the steroid is processed. Monitor for signs of increased steroids in your body**



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**including difficulty sleeping; increased appetite, increased energy, restlessness; high blood sugar; or swelling in your legs or hands.**

There have been reports of serious reactions in patients with severe milk protein allergy after inhalation of other powder medications containing lactose; **therefore, it is important to also inform the study team if you have a severe milk protein allergy or are lactose intolerant.**

Below are some possible, known risks associated with fluticasone and placebo. There may also be unknown risks from participation. **If you experience side effects such as difficulty breathing, wheezing, change in heart rate, nausea, vomiting and diarrhea, rash or hives shortly after taking fluticasone, you should seek medical attention right away, as these could be signs of a severe or life-threatening allergic reaction.**

The most common (more likely) side effects of fluticasone or placebo are:

- Upper respiratory tract infection
- Nasopharyngitis (having a cold)
- Headache
- Bronchitis (inflammation of the mucous membrane in the bronchial tubes
- Influenza
- Sinusitis (inflammation of the sinuses)
- Oropharyngeal pain (pain in the throat)
- Pharyngitis (inflammation of the pharynx of the back of the throat)
- Back pain
- Dysphonia (difficulty in speaking due disorder of the mouth, tongue, throat, or vocal cords)
- Oral candidiasis (also known as oral thrush, caused by overgrowth of fungus Candida albicans on the lining of your mouth)
- Procedural pain (pain related to wound care)
- Rhinitis (runny nose)
- Throat irritation
- Abdominal pain
- Cough



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## RISK OF PREGNANCY WHILE TAKING FLUTICASONE FUROATE OR PLACEBO

- **For people capable of getting pregnant:**

The effects of fluticasone on a developing pregnancy or breastfeeding infant are unknown. If you are pregnant or planning to become pregnant during the next 90 days and or are breastfeeding, please inform the study team. You will be asked to complete a Pregnancy Reasonably Excluded Checklist.

If you are someone who could become pregnant (you have not had a hysterectomy and/or both tubes and/or both ovaries removed and/or you are not postmenopausal and over the age of 45) and you have a sexual partner who is able to conceive children (has not had a vasectomy with a negative post-surgery semen analysis), it will be important for you to practice effective birth control methods while taking study medication or placebo. Please ask the study team about acceptable methods.

Because no birth control method is 100% effective, you should notify your study doctor immediately if you think there is any chance you could be pregnant, even if you have had a recent negative pregnancy test. If you become pregnant, we may want to review your medical history before and after you give birth.

- **For people who can get someone pregnant:**

If you can conceive children and your partner is someone who could possibly become pregnant (they have not completed menopause and are over the age of 45 or have not had a hysterectomy and/or both tubes and/or both ovaries removed) you should practice effective birth control methods while taking study medication or placebo. If you have questions about what is considered effective birth control, please ask the study team.

You should not donate sperm for the duration of the study and for 30 days after the last dose of study medication.



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If your partner becomes pregnant while you are taking fluticasone, it is important to notify the study team right away. They may want to review your partner's medical history during and after the birth.

☐ **Study participant agrees to participate in the fluticasone and placebo arm of this study**

☐ **Study participant does not agree to participate in the fluticasone and placebo arm of this study**

## STATEMENT OF CONSENT

My signature below indicates that I have read and understood this consent form. I have had enough time and opportunity to think about the information, ask questions, and get my questions answered to my satisfaction. I understand that I am under no obligation to participate in this study, but I am willing to participate, and I am freely giving my consent to participate in the ACTIV-6 study.

A copy of this form will be given to you<<CF-Main California Bill of Rights>>.

## Participant:

**Print name:** _____

**Signature:** _____

**Date:** _____ **Time (24 hour clock)** _____



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## Study Doctor or Designee Who Obtained Consent:

**Print name:** _____

**Signature:** _____

**Date:** _____ **Time (24 hour clock)** _____



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**ACTIV-6** MEDICAL RECORDS RELEASE FORM
AUTHORIZATION FOR RELEASE OF PROTECTED HEALTH INFORMATION

I, **_____, birthdate __ __ __ /__ __ /__ __ __ __,** have signed a consent
*FIRST & LAST NAME, PRINTED* *month* *day* *yea*
form to participate in the **ACTIV- 6** study. For the purposes of the study, I give permission to the site study team, including personnel at the Duke Clinical Research Institute (DCRI), to collect medical information and billing information from any medical or healthcare facility I visit or at which I'm seen during my participation in the research.

The information I agree to have disclosed for the research includes:

- Medical bills (UB04 and/or Abstract Coding Summary)
- Hospital discharge summaries
- Reports from procedures, surgeries, laboratory tests, biopsies, radiologic images
- Results of autopsy
- Hospital patient discharge instructions
- Clinic notes/visits

This list represents the most information my site or DCRI could collect, but my site or DCRI will ask for the minimum necessary for research purposes and limited to specified dates of service.

By signing this form, I authorize the patient accounts and medical records departments at any medical or healthcare facility at which I am treated or evaluated to disclose medical information and billing information to the **ACTIV-6** study team at my site or DCRI.

I understand that, if I sign this form, I am still able to receive medical treatment that is not related to the study. I understand that I can revoke this authorization, at any time, by writing to the **ACTIV-6** study team at one of the addresses below. If I revoke the authorization, I understand information that was already shared will still be used for research purposes. Unless I revoke it earlier, this authorization will expire at the end of the research study. I understand that information used or disclosed by means of this authorization could be redisclosed and would no longer be protected under federal law. I will receive a copy of this authorization.



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_____ **DATE SIGNED** _____/_____/_____
*SIGNATURE* *MONTH* *DAY* *YEAR*

**********

**SITE OR DCRI PERSONNEL WILL COMPLETE THIS SECTION:**
For this research subject, please supply the information [indicated by a checked box below or, as indicated on the fax cover sheet]:

- ☐ Medical bills (UB04 and/or Abstract Coding Summary)
- ☐ Hospital discharge summaries
- ☐ Reports from procedures, surgeries, laboratory tests, biopsies, radiologic images
- ☐ Results of autopsy
- ☐ Hospital patient discharge instructions
- ☐ Clinic notes/visits
- ☐ History and physical form

**FOR DATE(S) OF SERVICE** [Or, as indicated on the fax cover sheet] _____

**Please mail or fax the information requested to:**

**Site:**
**By Mail:** [insert address)
**FAX Number**: [insert Fax number]

**DCRI:**
**By Mail:** Duke Clinical Research Institute, ATTN: ACTIV-6 Coordinating Center
300 West Morgan Street, Suite 800
Durham, NC 27701
**FAX Number**: TBD

<<CF-Main California HIPAA>>



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****For Sites in California****

**AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES**

**What information may be used and given to others?**
The study doctor will get your personal and medical information. For example:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits.

**Who may use and give out information about you?**
The study doctor and the study staff. [They may also share the research information with [enter SMO company name], an agent for the study doctor. delete if the site does not have an SMO]

**Who might get this information?**
The sponsor of this research. "Sponsor" means any persons or companies that are:

- working for or with the sponsor, or
- owned by the sponsor.

**Your information <u>may</u> be given to:**

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies in other countries,
- The institution where the research is being done,
- Governmental agencies to whom certain diseases (reportable diseases) must be reported, and
- Institutional Review Board (IRB)


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**Why will this information be used and/or given to others?**

- to do the research,
- to study the results, and
- to make sure that the research was done right.

If the results of this study are made public, information that identifies you will not be used.

**What if I decide not to give permission to use and give out my health information?**
Then you will not be able to be in this research study.

**May I review or copy my information?**
Yes, but only after the research is over.

**May I withdraw or revoke (cancel) my permission?**
This permission will be good until December 31, 2070.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

**Is my health information protected after it has been given to others?**
There is a risk that your information will be given to others without your permission.

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**Authorization:**
I have been given the information about the use and disclosure of my health information for this research study. My questions have been answered.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

**AUTHORIZATION SIGNATURE:**

_____ _____

**Signature of Subject** **Date**



Participant Initials: _____