

**INFORMED CONSENT FORM
FOR STUDY DRUG LY3819253 (BAMLANIVIMAB)**

Sponsor / Study Title: National Institute of Allergy and Infectious Diseases /
“Adaptive Platform Treatment Trial for Outpatients with
COVID-19 (Adapt Out COVID)”

Protocol Number: ACTIV-2/A5401

**Principal Investigator:
(Study Doctor)**

[REDACTED]

Telephone:

[REDACTED]
[REDACTED]

[REDACTED]

[REDACTED]
[REDACTED]
[REDACTED]

Everything in the main study consent form you signed and dated before still applies to your participation unless otherwise noted in this form.

This form is for use in a research study that may involve participants who may or may not have the capacity to consent to take part in the study. When the participant cannot legally consent to take part, pronouns “you” and “your” should be read as referring to the participant rather than the person (legally authorized representative) who is signing and dating this form for the participant. In cases where the participant’s representative gives consent, the participant should be informed about the study to the extent possible given his/her understanding. During the course of the study, if the participant regains the capacity to consent, informed consent will be obtained from the participant and the participant offered the ability to leave the study if desired.

If you are in the first part of this study, one of the study drugs that you might be assigned to is bamlanivimab or the placebo for bamlanivimab (inactive substance). If you are in the second part of this study, you might be assigned to receive one dose of 700mg of bamlanivimab. No participants will receive the placebo for bamlanivimab in the second part of the study.

Bamlanivimab is a type of drug called a monoclonal antibody. Many antibodies are naturally made by your body and help fight diseases. Bamlanivimab is made in a laboratory. “Monoclonal” means that bamlanivimab is made up of many copies of just one antibody.

If you are in the first part of this study, your assignment is random, like the flip of a coin. You will be told about all the study drugs you may be assigned to in this study. If only one study drug is available, you will have an equal chance of receiving the study drug or placebo. If two study drugs are available, you will have a two to one chance of receiving a study drug or placebo. You will not be able to choose your group, and neither you, your study doctor, nor the study staff at your site will know which group you are in. However, the study staff can find out which group you are in if there is an emergency.

[REDACTED]

The United States Food and Drug Administration (FDA) has not approved bamlanivimab for general use by the public; therefore, for this study it is considered investigational. An investigational drug is one that is not approved by the United States Food and Drug Administration (FDA). However, we have told the FDA about this study and they have given us permission to conduct this study. On November 9, 2020 the FDA issued an emergency use authorization (EUA) for bamlanivimab for the treatment of mild-to-moderate COVID-19 in patients who are 12 years of age and older and who are at high risk for progressing to severe COVID-19 and/or hospitalization. The issuance of an EUA is different from FDA approval.

The data for bamlanivimab are still limited, but in deciding whether to issue an EUA, the FDA determined that the known and potential benefits of bamlanivimab outweigh the known and potential risks for use during an emergency. As a result of the EUA it is possible that you may be able to access bamlanivimab outside of the study. The study staff can discuss this possibility with you. Even though there is now an EUA for bamlanivimab, we want to continue to study bamlanivimab so that we can collect more information about the safety of bamlanivimab and risk factors associated with COVID-19 disease progression.

ARE THERE ANY ADDITIONAL STUDY PROCEDURES IF I RECEIVE BAMLANIVIMAB OR PLACEBO?

Screening Visit

- At your screening visit, if you can become pregnant, you will be asked to give blood (1 teaspoon) or a urine sample for a pregnancy test. You cannot receive bamlanivimab or placebo if you are pregnant.

Entry Visit

- You will have blood drawn. This blood will be used for the following tests:
 - routine safety tests (liver and kidney tests and blood counts)
 - levels of antibodies to the study drug (your body's immune response to the study drug)
 - for future protocol-required testing
- You will have the infusion of bamlanivimab or placebo. The infusion will be given through a small plastic tube that will be placed into a vein in your arm. This is called an intravenous (IV) infusion. The infusion will take approximately 1 hour. You will be monitored in the clinic for 1 hour after the end of the infusion.
- You will have blood drawn to check the levels of drug in your blood. The blood sample will be collected before the study infusion and 30 minutes after the study infusion in the opposite limb as the study infusion.

Study Visits

After the Entry visit, your study visits and evaluations will be different depending on whether you are in the first part of the study or the second part of the study.

IF YOU ARE IN THE FIRST PART OF THE STUDY:

Study Visits on Days 3, 14, and 28

- You will have blood drawn. This blood will be used for the following tests:
 - routine safety tests (liver and kidney tests and blood counts)
 - on days 14 and 28, levels of the study drug and levels of antibodies to the study drug (your body's immune response to the study drug)

Study Visits on Week 12 and Week 24

- You will have blood drawn. This blood will be used for the following tests:
 - levels of the study drug
 - levels of antibodies to the study drug (your body's immune response to the study drug)
 - for future protocol-required testing
- If you can become pregnant, you will be asked to give blood (1 teaspoon) or a urine sample for a pregnancy test (week 24)

Extra Visits

If you have a bad reaction to the infusion of study drug, you may have to come back for two extra visits 4 weeks and 12 weeks after the reaction, unless there is another visit at this time.

- You will have blood drawn. This blood will be used for the following tests:
 - levels of the study drug
 - levels of antibodies to the study drug (your body's immune response to the study drug)
 - levels of inflammatory markers and cells in your blood
- You will be asked to give a urine sample to check for markers of inflammation (week 4)

IF YOU ARE IN THE SECOND PART OF THE STUDY:

Study Visit on Day 28

- You will have blood drawn. This blood will be used for the following tests:
 - routine safety tests (liver and kidney tests and blood counts)
 - levels of the study drug
 - levels of antibodies to the study drug (your body's immune response to the study drug)

Study Visits on Week 12 and Week 24

- You will have blood drawn. This blood will be used for the following tests:
 - levels of the study drug
 - levels of antibodies to the drug (your body's immune response to the study drug)

Extra Visits

If you have a bad reaction to the infusion of study drug, you may have to come back for two extra visits 4 weeks and 12 weeks after the reaction, unless there is another visit at this time.

- You will have blood drawn. This blood will be used for the following tests:
 - levels of the study drug
 - levels of antibodies to the study drug (your body's immune response to the study drug)
 - levels of inflammatory markers and cells in your blood
- You will be asked to give a urine sample to check for markers of inflammation (week 4)



WHAT ARE THE RISKS OF BAMLANIVIMAB?

There is a risk of serious and/or life-threatening side effects when non-study medications are taken with the study drugs. For your safety, you must tell the study doctor or study nurse about all medications you are taking before you start the study.

Another risk is that the study drug used in this study may have side effects, some of which are listed below. Additionally, the study drug tested in the study may have unknown side effects in persons with SARS-CoV-2 infection. In a research study, all of the risks or side effects may not be known before you start the study. You need to tell your study doctor or a member of the study team immediately if you experience any side effects.

Please note that these lists do not include all the side effects seen with this study drug.

These lists include the more serious or common side effects with a known or possible relationship to the study drug. If you have questions concerning the additional side effects, please ask the medical staff at your site.

Risks Associated with Bamlanivimab

Bamlanivimab is being administered for the first time to hospitalized and non-hospitalized persons with COVID-19 in separate studies.

There is limited safety data on bamlanivimab since it has not been given to a lot of people.

As of September 4, 2020, there have been no serious unwanted effects reported by people taking bamlanivimab or placebo to date. Most effects after taking bamlanivimab or placebo have been mild or moderate and have either all gone away or are getting better.

Of 409 non-hospitalized persons who received bamlanivimab or placebo, eight people experienced possible reactions to the infusion (“infusion reactions”) that were mild or moderate, including itching, flushing, rash, and face swelling. All eight were able to complete the infusion and all symptoms resolved with or without an antihistamine.

Among hospitalized persons, three people had difficulty breathing that was severe; all three people have either recovered or are getting better.

One subject had chills that were mild and started a few hours after bamlanivimab injection; the symptoms lasted one hour and were thought to be related to bamlanivimab.

Two people had a drop in white blood cell counts (below the normal range), which continued for a few days after bamlanivimab or placebo administration and returned to normal again soon after that.

Administration of bamlanivimab may result in allergic reactions. Signs and symptoms of these reactions include:

- Chills
- Skin rash
- Itching
- Hives
- Flushing (reddening) of the skin

- Swelling of the face or other soft tissues
- Low blood pressure
- Rapid heart rate
- Throat irritation or tightness
- Tightening of the muscles that line the airways
- Shortness of breath
- Loose stools

Administration of bamlanivimab may induce release of chemicals called cytokines in the body. These chemicals may induce allergic reactions listed above, as well as the following:

- Fever
- Muscle aches
- Nausea
- Vomiting
- Headache
- Dizziness

Some of these reactions may be serious or life-threatening including:

- Skin rash
- Swelling of the face or other soft tissues
- Low blood pressure
- Rapid heart rate
- Throat irritation or tightness
- Tightening of the muscles that line the airways
- Shortness of breath

You will be monitored closely during administration of study drug. Medical personnel, equipment, and medication will be available to manage these reactions appropriately if they occur.

Administration of study drug may also cause the following risks and discomforts:

- Development of proteins (antibodies) against bamlanivimab. This may cause your body to get rid of bamlanivimab more quickly or change the effect of bamlanivimab on the body. Your blood will be tested to find out whether your body made antibodies to bamlanivimab. The anticipated risk of this is low because bamlanivimab is a fully human antibody. Therefore, it is less likely to be seen as “foreign” by your body’s immune system and your body is less likely to form antibodies against bamlanivimab.
- Mixture of antibody and other chemicals in the body that may be deposited in tissues such as blood vessels and kidneys.
- Unexpected increase in virus reproduction in your body. Although this has been observed with some viruses, this has not been observed with COVID-19 or with the use of serum-containing antibodies given to people with COVID-19. This risk of increased viral growth is perhaps greater when there is lower levels of antibodies in the blood in the presence of virus. To avoid this, bamlanivimab will be given at a dose that is felt to be high enough to keep this from occurring.
- There is a risk that this study drug may impact your body’s own immune response to the viral infection, like development of immunity. This might mean that you might get sick with COVID infection again in the future.

Effect on Future Vaccination

The US Centers for Disease Control and Prevention (CDC) currently recommends that people wait at least 90 days after receiving antibody treatment before receiving a COVID-19 vaccine. Bamlanivimab remains in the body for about 90 days, and there is a chance that these antibodies could interfere with how your body responds to the vaccine during those 90 days.

ARE THERE RISKS RELATED TO PREGNANCY AND BREASTFEEDING?

Pregnancy

Since there are no data regarding the use of this study drug in people who are pregnant, you are not eligible to receive this study drug if you are pregnant.

The study drug may involve risks to you (or to the embryo or fetus, if you or your partner become pregnant), which are currently unforeseen.

Females

If you are participating in sexual activity that could lead to you becoming pregnant, you must agree to use two forms of effective contraception, where at least one form is highly effective, for the entirety of the study and for 90 days after you receive the study drug.

Highly effective methods of contraception (less than 1% failure rate) include, but are not limited to:

- combination oral contraceptives
- implanted contraceptives
- intrauterine device (IUD)

Effective methods of contraception include, but are not limited to

- diaphragms with spermicide
- cervical sponges

If you think you may be pregnant, let the staff at your site know so that a pregnancy test can be done. Let your study doctor know immediately if you become pregnant. If you become pregnant while on the study, you will be asked to continue to have study visits and the study staff would like to obtain information from you about the outcome of the pregnancy (even if it is after your participation in the study ends).

Breastfeeding

It is not known if this study drug is safe to use in people who are breastfeeding. You are not eligible to receive this study drug if you are breastfeeding.

Males

If you engage in sexual activity that may lead to pregnancy in a partner, you must agree to either remain abstinent or use condoms with spermicide during the study and for at least 90 days after you last receive the study drug. Due to the potential risks of the study drug and because a male condom in combination with spermicide is not adequate contraception for this study, male subjects are strongly advised to inform all female partners of the need for them to use one of the highly effective methods of contraception approved for female subjects in this study. Female partners should be advised of the need to use highly effective contraception while the male subject is in the study and for at least 90 days after he receives his last dose of study drug.

If your partner is already pregnant you must use condoms during vaginal intercourse through 90 days after you receive the last dose of study drug.

You must not donate sperm through 90 days after you receive the last dose of study drug.

SIGNATURE PAGE

If you have read this consent form (or had it explained to you), all your questions have been answered and you agree to take part in this study, please sign your name below and provide date.

Participant's Name (print)

Participant's Signature and Date

Participant's Legally Authorized Representative
(As appropriate) Signature and Date

Legally Authorized Representative (print)

Authority of Legally Authorized Representative to consent on behalf of the Participant

Study Staff Conducting
Discussion (print)

Study Staff's Signature and Date Consent

Witness's Name (print)

Witness's Signature and Date (As appropriate)

