TITLE:	A Multi-arm, Phase 3, Randomized, Placebo Controlled, Double Blind Clinical Trial to Investigate the Efficacy and Safety of BMS-663068 in Heavily Treatment Experienced Subjects Infected with Multi-drug Resistant HIV-1
PROTOCOL NO.:	AI438047 WIRB® Protocol #20150142
SPONSOR:	Bristol-Myers Squibb
INVESTIGATOR:	Pablo Tebas, MD 502 Johnson Pavilion Philadelphia, Pennsylvania 19104 United States
STUDY-RELATED PHONE NUMBER(S):	Pablo Tebas, MD 215-349-8092 215-662-6059 Ask for the Immunodeficiency Program Doctor on call (24 hours)
STUDY COORDINATOR(S):	Aleshia Thomas, RN, BSN Joseph Quinn, RN, BSN
SITE NUMBER:	0171

1. Participation

You are being considered for participation in a research study. Your eligibility to participate in this study will be decided based on the screening procedures described below and other eligibility criteria. Before you can take part in this study, it is important that you understand what this study involves. Please read this information carefully and ask any questions that you might have. An independent Ethics Committee or Institutional Review Board has reviewed the objectives and the proposed conduct of this study and has given a favorable opinion of it.

2. Purpose of the Study

The purpose of this study is to determine if an investigational treatment regimen of BMS-663068 (BMS Attachment Inhibitor) twice a day, plus other antiretroviral medications used in combination is safe and effective for the treatment of subjects who are infected with Human Immunodeficiency Virus (HIV-1). HIV positive subjects in this research study must be “Heavily Treatment Experienced”. This means you must have taken many HIV medications during the history of your disease and must have developed resistance or become intolerant to many of these HIV medications. The other antiretroviral medications used in combination with the BMS Attachment Inhibitor are referred to in this research study as an Optimized Background Therapy (OBT).

The BMS Attachment Inhibitor is part of a new class of antiretroviral drugs being studied for the treatment of HIV. The BMS Attachment Inhibitor is NOT approved by the U.S. Food and Drug Administration (FDA) and is considered experimental. Throughout this consent form the investigational drug BMS Attachment Inhibitor and OBT medications will be referred to as the "study drugs" or "study medications".

To qualify for this research study, the HIV medication regimen you are currently taking must no longer be working effectively to control the virus. In other words, the medications must be failing.

3. Approximate Number of Participants and the Expected Duration of Your Participation in the Study

About 800 people are expected to participate in this study, with approximately 140 of them in the USA. Only 1-2 persons are expected to enroll at PENN. Even though you may meet all the criteria for participation, it is possible that you will not be enrolled in this study. If you are enrolled, the duration of your participation is expected to be at least 96 weeks.

4. Study Treatments

In this research study there will be two treatment groups. These are called cohorts. One cohort is called the "Randomized Cohort" and the other cohort is called the "Non-Randomized Cohort". Your study doctor will evaluate the history of the HIV medications you have taken and the medications you have been resistant to, or are unable to take. You will also have blood tests at the start of the study to see which HIV medications you currently have resistance to as well as medications you do not have resistance to. Your doctor will discuss with you the following issues regarding HIV medications:

- Are there any HIV medications that you cannot take because of a current or previous medical condition?
- Are there any HIV medications that you cannot take because of a side effect?
- Are there any HIV medications that you have or have not taken and which you will NOT take for any reason?
- Are there any medications that you have taken in the past that have failed to bring your HIV viral load to undetectable blood levels?

Your study doctor will use this information along with your virus resistance history to determine which treatment cohort of the study you may eligible for.

The Randomized Cohort

Once your doctor has determined that you will be eligible for this cohort, you will be randomly assigned to one of two groups in that Cohort:

- **Group 1**: There will be a 75% chance that you will be treated on Day 1 with the BMS Attachment Inhibitor + the current HIV medications you have been taking that are no longer working effectively for you. You will take this combination of medications for 8 days. On Day 9 you will switch to the BMS Attachment Inhibitor + at least two other

HIV medications (OBT) that your doctor will prescribe for you based upon which drugs your HIV does not have resistance to and what you are able to take.

- **Group 2**:There will be a 25% chance that you will be treated on Day 1 with a Placebo (a dummy treatment, one that looks like the real one but contains no active study drug) + the current HIV medications you have been taking that are no longer working effectively for you. You will take this combination of medications for 8 days. On Day 9 you will switch to the BMS Attachment Inhibitor + at least two other HIV medications (OBT) that your doctor will prescribe for you based upon which drugs you do not have resistance to and what you are able to take.

On Day 1, you will be instructed to take 1 tablet of the BMS Attachment Inhibitor (600 mg) or 1 tablet of the Placebo by mouth 2 times per day at the same time each day 12 hours apart. You will take the HIV medications that are no longer working effectively for you according to the same dosing schedule you were using before participating in the study.

On Day 9, once you have switched to the BMS Attachment Inhibitor + OBT medications, you will be instructed to take one tablet of the BMS Attachment Inhibitor (600 mg) by mouth 2 times per day at the same time each day 12 hours apart. The added HIV medications prescribed by your doctor will each have their own dosing strength and schedule which will be discussed with you. The study team will provide you with a dosing schedule for all study medications. You will remain on these study medications for the rest of the time you will be participating in the study as long as you and your study doctor feel you are benefiting from this treatment. You may be allowed to switch the OBT(s) to new ones if you are having trouble taking the medications, or if your viral load is not well controlled.

If you are treated in the Randomized Cohort, neither you nor your study doctor will know which treatment you are receiving (BMS Attachment Inhibitor or Placebo) for the first 8 days, except in case of a medical emergency.

Regardless of the treatment cohort you qualify for, it is possible that you will be required to change or stop study treatment earlier than scheduled if study treatments are not working as expected or if you have unwanted side effects from study treatment. Your doctor will talk with you about this if it occurs.

Non-Randomized Cohort

This cohort is for individuals who have had extensive prior treatment for HIV and the resistance tests in the past and now suggest that there are no “fully active” drugs to combine with the BMS attachment inhibitor. In these cases, your doctor will discuss the pros and cons of entering this study, and help you decide if this study may help you. Usually your doctor will combine antiretroviral drugs based on your history. These drugs may not be active against your HIV or be only “partially active”. As with any HIV drug combination, if you cannot control the amount of your virus in your blood, you could develop resistance to the BMS attachment inhibitor.

Once your doctor has determined that you will be eligible for this cohort, on Day 1 you will be instructed to take 1 tablet of the BMS Attachment Inhibitor (600 mg) by mouth 2 times per day at the same time each day 12 hours apart. You will also be taking other antiretroviral drugs that your doctor decides will be beneficial for you in combination with the BMS

Attachment Inhibitor. Any changes in dosing strength or dosing schedule from your current medications will be discussed with you by your doctor. The study team will provide you with a dosing schedule for all study medications. You will remain on these study medications for the rest of the time you will be participating in the study as long as your doctor feels you are benefiting from this treatment. You may be allowed to switch one or more of the OBTs for other OBTs if you are having trouble taking the medications or if your viral load is not well controlled.

As described below under "Follow-Up" in Section 5, it may be necessary to gather additional information from you after you stop taking study medications, to further evaluate the safety or efficacy of the drug.

5. Study Procedures

Screening

If you volunteer for this study, the following tests and procedures will be performed to determine if you are eligible to participate in the study:

- Medical records will be reviewed for important information related to your health and your HIV infection, including blood work, medications you have taken or are currently taking (including over-the-counter drugs and herbal supplements).
- Your study doctor will perform a screening assessment to determine if you are eligible to participate in the study. A full physical examination, including height, weight, blood pressure and heart rate will be done.
- You will have a 12-Lead electrocardiogram (ECG) to assess your heart.
- Blood will be collected for laboratory tests to see if you are eligible for this study. These blood tests will include: measuring the amount of HIV-1 RNA (HIV virus) "viral load", checking for the specific kind of HIV (known as the HIV-1 Viral Resistance), checking the CD4 count (a kind of white blood cell that helps your body fight infection), checking if you have any type of hepatitis (like hepatitis B or hepatitis C), as well as other tests of how well your liver, kidneys, blood and immune systems are working. Some of these tests require that you do not eat prior to collecting your blood (fasting). A total of approximately 4.5 tablespoons of blood may be drawn in order to complete these study assessments. State law requires that the results of positive tests for hepatitis be reported to a local health agency.

    - An additional sample of your blood (about half a tablespoon) will be collected at this visit. This sample will be stored and may be used for new tests that are being developed to help doctors in treating patients with HIV
    - The total amount of blood collected at this visit will be approximately 5 tablespoons

- A sample of your urine will be collected during this visit. One of the tests on this sample will be to see if you have been taking any drugs for recreational purposes (toxicology screening). Results of this test will be kept confidential between you, the study team, and the laboratory performing the tests. This test will be performed only at this screening visit. These results will NOT be used to determine if you are eligible for this study.

- If you are a woman capable of becoming pregnant (woman of child-bearing potential; WOCBP), you will have to take a urine pregnancy test, or serum (blood) pregnancy test as part of the screening assessment. Additionally, if you are a WOCBP or a fertile man sexually active with a WOCBP, you must agree to adhere to the contraception requirements as described within Section 8 of this document.
- If you are a woman over 45 years of age and have not had your period for 12 months for no other reasons of other than biological or physiological causes, you are considered post-menopausal. If you are a woman under the age of 55 years, you must have a serum follicle stimulating hormone (FSH) test to confirm menopause.
- You will continue to take your current HIV medications until it is determined if you are eligible for this study.

The study sponsor, Bristol-Myers Squibb (BMS) will not use any samples collected from you for any other tests without your permission. No one other than BMS (and/or people and companies BMS works with) will test any samples collected from you. BMS (and/or people and companies BMS works with) will not give or sell your blood to other people or companies.

Treatment Period

Day 1 Visit
If you qualify for this study, Day 1 will be your first study visit. This visit must take place within 42 days after the screening visit. The following tests and assessments will be conducted at this visit:

- You will start to receive study medications on Day 1. Your doctor will discuss with you the new medications you will take and whether or not you will continue to take any of your current HIV medications.
- Your doctor will also discuss with you any medications you have taken since the screening visit or are currently taking (including over-the-counter drugs and herbal supplements).
- A short physical exam will be done, and your weight and vital signs will be collected. You will be asked if you have had any new or changed medical issues since the screening visit.
- You will be asked some questions about your history of reliably taking your HIV medications.
- You will be asked questions about your general health, any health problems you may have had related to HIV and any healthcare you may have received related to your HIV infection.
- You will have a 12-Lead electrocardiogram (ECG) to assess your heart.
- A sample of your urine will be collected for standard urinalysis.
- If you are a woman capable of being pregnant, you will have to take a urine or serum (blood) pregnancy test to rule out pregnancy.
- The study team will provide you with an appointment date and time for your next study visit and instructions for taking your study medications.

- Blood will be collected for the following tests:
    - HIV-1 RNA levels “viral load”.
    - How well your liver, kidneys, and immune system are working. Some of these tests require that you do not eat prior to collecting blood (fasting).
    - Checking the CD4 level (a kind of white blood cell that helps your body fight infection).
    - Checking if you have hepatitis B in your blood.
    - To check for biomarkers in your blood to know how the BMS Attachment Inhibitor is distributed in your body.
    - An additional sample of blood (approximately 1 tablespoon) will be collected for back-up blood testing in the event of a lost sample or a blood test that malfunctions. If this back-up sample is not needed or used, it will be discarded by the testing laboratory.
    - The total amount of blood collected at this visit will be approximately 2.5 tablespoons.

You will receive a phone call from a member of the study team or have a brief clinic visit approximately 4 days after this visit to see if you are taking your HIV medications as you were instructed by your doctor.

Day 8 Visit
If you are assigned to the “Randomized Cohort” of this study, you will be asked to come back to the clinic for a visit on Day 8. The following tests and assessments will be conducted at this visit:

- Your study doctor will discuss with you the new medications you will take and whether or not you will continue to take any of your current HIV medications.
- Your study doctor will also discuss with you any medications you have taken since your last study visit or are currently taking (including over-the-counter drugs and herbal supplements).
- A full physical examination, including height, weight, blood pressure and heart rate will be done and you will be asked if you have had any new or changed medical issues since your last study visit.
- You will be asked some questions about your reliability in taking your HIV medications over the past 7 days.
- You will have a 12-Lead electrocardiogram (ECG) to assess your heart.
- A sample of your urine will be collected for standard urinalysis.
- If you are a woman capable of being pregnant, you will have to take a urine or serum (blood) pregnancy test to rule out pregnancy.
- The study team will provide you with an appointment date and time for your next study visit and instructions for taking your study medications.

Pharmacokinetic (PK) blood samples during the treatment period:

Three blood samples (approximately 1 tablespoon) for PK tests will be collected at Day 8. PK tests are to determine the amount of the study medication (BMS Attachment Inhibitor) in your body at different times after study medications are first taken. On this day it will be

important that you do not take your morning dose of study medications until instructed to do so by your doctor once you get to the clinic.

The first PK sample will be drawn right before you take the study drug (time 0). The second PK sample will be taken at 2-4 hours after time 0, and the last sample will be taken at 6-8 hours after time 0. After the 6-8 hour sample is collected, you will be instructed by the study team when you should take your afternoon/evening dose of study medications. You may be expected to stay at your study doctor's clinic until after all PK samples have been collected.

At the end of this visit you will be given a new supply of your study medications which are NOT to be started until the next morning and should continue to be taken until your next study visit.

In addition to the PK sample at time 0, blood will also be collected for the following tests:

- HIV-1 RNA levels "viral load".
- Testing for how well your liver, kidneys, and immune system are working. You will not be required to be fasting prior to blood collection at this visit.
- Checking the CD4 level (a kind of white blood cell that helps your body fight infection).
- Checking for the specific kind of HIV (known as the HIV-1 Viral Resistance) in your blood.
- To check for biomarkers in your blood to know how the BMS Attachment Inhibitor is distributed in your body.
- An additional sample of blood (approximately 1 tablespoon) will be collected for back-up blood testing in the event a lost sample or a blood test that malfunctions. If this back-up sample is not needed or used, it will be discarded by the testing laboratory.
- The total amount of blood collected at this visit will be approximately 4 tablespoons.

On Treatment Weeks 4, 8, 12, 16, 24, 36, 48, 60, 72, 84 and 96 visits:

The following tests and assessments will be conducted at these visits:

- You will receive a resupply of study medications to last you until the next study visit.
- Your study doctor will also discuss with you any medications you have taken since your last study visit or are currently taking (including over-the-counter drugs and herbal supplements).
- Your study doctor will discuss with you how well you are tolerating your study medications since your last study visit.
- A physical exam will be done, and your weight and vital signs will be collected and you will be asked if you've had any new or changed medical issues since your last study visit.
- You will be asked some questions about your history of reliably taking your HIV medications (Week 24 only).
- You will be asked questions about your general health and any health problems you may have had related to HIV (Weeks 12, 24, 36, 48 and each visit for every 12 weeks thereafter).

- You will have a 12-Lead electrocardiogram (ECG) to assess your heart.
- A sample of your urine will be collected for standard urinalysis.
- If you are a woman of child-bearing potential, you will have to take a urine or serum (blood) pregnancy test to rule out pregnancy.
- Blood will be collected for the following tests:

    - HIV-1 RNA levels “viral load”.
    - How well your liver, kidneys, and immune system are working. Some of these tests require that you do not eat prior to collecting blood (fasting).
    - Checking the CD4 level (a kind of white blood cell that helps your body fight infection).
    - Checking if you have hepatitis B (Week 48 or end of study only).
    - Checking for the specific kind of HIV (known as the HIV-1 Viral Resistance) in your blood.
    - A single PK sample at weeks 4, 8, 12, 16 and 24. You will be instructed NOT to take your morning dose of study medications until after you arrive at the clinic and this sample has been collected.
    - To check for biomarkers in your blood to know how the BMS Attachment Inhibitor is distributed in your body.
    - An additional sample of blood (approximately 1 tablespoon) will be collected for back-up blood testing in the event a lost sample or a blood test that malfunctions. If this back-up sample is not needed or used, it will be discarded by the testing laboratory.
    - The total amount of blood collected at these visits will be approximately 4.5 tablespoons.

If you complete 96 weeks on study, you may be asked to continue participation with visits occurring every 12 weeks after Week 96. The tests and assessments conducted at these visit will be the same as for the study visits for weeks 36 and 48. Your doctor will discuss with you if you will qualify to continue your study participation after Week 96. If you continue participation in the study, the study team will provide you with an appointment for your next study visit and instructions for taking your study medications.

Weeks 20, 30, and 42:

You will receive a phone call from a member of the study team or have a brief clinic visit at Weeks 20, 30, and 42 during the study to see if you are taking your HIV medications as you were instructed by your doctor.

Follow-up

When you stop or complete study treatments you may be asked to return to the clinic for a follow-up visit. Your study doctor will continue to assess your health condition. It is important to know, for example, if you have recovered, developed an illness or suffered an important adverse event.

Your doctor will explain to you the details of the visit(s) and your responsibilities during the follow-up visit(s).

In the event it is necessary to further evaluate the safety or efficacy of the drug, it may be necessary to have access to additional information about your health status. Your study doctor may attempt to obtain study-related information about your health from you or from other sources, including your primary care physician and public sources such as national patient registries (e.g., cancer registries). This may include contacting you again by phone or letter.

If Your Study Doctor Cannot Locate You

If your study doctor needs to follow up with you but cannot find you, he/she may try to learn your new address, telephone number or current health status by calling or writing to the person(s) named as your secondary contacts. If your study doctor cannot obtain information through your secondary contacts, he or she may ask for the assistance of a third-party representative and may share with that representative limited information about you, such as your name and last known address. The representative will consult public sources, such as public health registries and databases, to obtain your current contact information. The representative will only share this information with your doctor, to help him complete the follow-up stage of the trial. Only your doctor or a member of histeam will contact you or your family members.

6. Your Responsibilities

If you qualify for this study, you will be asked to return to the office/clinic during the on-treatment phase portion of the study. The first day of “on-treatment” will be the Day 1 visit. You will also return on Weeks 4, 8, 12, 16, 24, 36, 48 and every 12 weeks from then on through 96 weeks (for as long as your study doctor feels it is safe for you and you are benefiting from being in the study). The study team will give you a schedule of study visits and a schedule for study medication dosing.

If you participate in this study in the Randomized Cohort, you will also be expected to return to the clinic for a Day 8 PK visit (described in Section 5).

You will be instructed to take the BMS Attachment Inhibitor and your OBT drugs at the same time(s) each day according to the following directions:

- **BMS Attachment Inhibitor:** You will be instructed to take one 600 mg tablet at two different times each day. The two doses should be 12 hours apart.
- **OBT Medications:** You will be taking at least 2 OBT medications each day along with the BMS Attachment Inhibitor medication. There is a possibility that your study doctor may have you take other HIV medications along with your OBT medications. Each OBT medication has its own instructions for dosing. Your study doctor will discuss the dosing instruction of each OBT medication and how you should take it at the same time you are taking your BMS Attachment Inhibitor medication.

There will be study visits when you will be expected NOT to take your study medications in the morning before the study visit. Your study team will notify you of those visit days.

At each study visit:

- You will be asked how you feel and possible side effects will be discussed.
- You must inform your study doctor of any medication (including over-the-counter drugs and herbal supplements) that you are taking while you are in this study. You will be asked to not take certain medications while participating in this study. Your study doctor will tell you if there are other medications that you should not take or should stop taking while on the study.
- You will be asked to record the date and time you take all study drugs on a dosing diary and bring the dosing diary with you to every study visit. It is very important that you accurately record the date and time you take the study drugs.
- You will be asked to take study drug as instructed and bring in all bottles of study drug, used and unused, to each study visit.
- You will be asked to report any medical visits, hospitalizations, or general changes in your health since your most recent study visit.
- Tell your study doctor or study staff if you change your address, telephone number, or other contact information.

If at any time you discontinue or complete this study, you will be expected to return to the office/clinic for a completion visit. This post-treatment study visit is very important to monitor your response to the study treatment.

You are responsible for storing your study medications in a safe and secure location.

You must always carry with you the Subject Alert Card that you have been given.

7. Risks / Possible Adverse Drug Reactions

There may be risks that are currently not known or have yet to be experienced by patients taking this drug. It is important that you report any and all symptoms or possible reactions to your study doctor and team. You will be monitored for side effects and your study doctor may decide that you should be withdrawn from the study for your safety.

Based on what the sponsor and other researchers have learned up to this point about The BMS Attachment Inhibitor (BMS-663068), the following adverse drug reactions are known:

BMS-663068: nausea, headache, vomiting, elevated level of hepatic laboratory parameters, itching, rash, abdominal pain, bloodshot eyes, dizziness, backache, tingling, swelling of the upper lip and mouth, throat tightness, lightheadedness, dry mouth, tiredness, sweating, weakness, sore throat or mouth, muscle ache or burning, bruising, sinus congestion, eye irritation, heart palpitation, ear pain, constipation, diarrhea, toothache, nervousness, cold symptoms, gas and belching, increased frequency of urination, burning with urination and changes in the electrical activity of the heart.

Four serious conditions were reported in patients who received experimental treatment with the BMS Attachment Inhibitor at any dose: viral meningitis (swelling of protective layer of brain caused by virus), Mobitz type I second degree, atrioventricular block (a type of heart rhythm defect), death due to pulmonary embolism (clot in blood vessel of lung), and anaphylaxis (an extreme allergic reaction).

The viral meningitis experienced by one participant was thought not to be due to the medication. The atrioventricular block was found on a routine ECG and found to be possibly related to study drug. The participant was comfortable and had no symptoms; and did not require treatment or medical care beyond additional heart monitoring with an ECG.

Data from other studies with BMS-663068 have not revealed clinically relevant changes in vital signs, physical examinations, ECGs or laboratory tests.

The most frequent Adverse Events in **HIV-infected subjects** treated with BMS-663068 were headache (36% (18 of 50 subjects)), rash (16% (7 subjects)), micturition urgency (a sudden compelling urge to urinate) (14% (8 subjects)), and nasopharyngitis (common cold) (12% (6 subjects)).

Most of the reported adverse symptoms were considered to be mild and did not require treatment.

ADDITIONAL RISKS OR DISCOMFORTS

Blood Draws
Blood draws may cause pain at the site of the blood draw, bruising, swelling, irritation or infection at the site of the blood draw, dizziness or faintness.

ECG
The electrocardiogram (ECG) procedure may cause minimal discomforts during the attachment and removal of the adhesive ECG leads to and from the skin.

8. Risks to Reproduction, Unborn Babies and Nursing Infants

8A. General Statement

You must not be pregnant or breastfeeding, and you should not become pregnant or breastfeed while you are taking the study treatments. You must use an acceptable method to avoid pregnancy (including at least one barrier method) for the duration of this study and for up to 60 hours (5 half-lives) after the last dose of BMS-663068. You should immediately contact your study doctor if there is a change in your method to avoid pregnancy or if you start any prescription drug or other medication (including over-the-counter drugs and herbal supplements) not prescribed by your doctor.

8B. Unforeseeable Risks

There may be unknown risks to you, your unborn baby or nursing infant if you are or become pregnant during this study or are breastfeeding during this study.

8C. Laboratory & Animal Reproductive Toxicology Findings

While laboratory and animal studies have been conducted to determine possible risks, the results do not necessarily show what will happen when the drug is used in humans.

The BMS Attachment Inhibitor was administered to pregnant rats during the period of organ development of the unborn. The BMS Attachment Inhibitor at high doses was associated with maternal rat toxicity of decreased eating and weight loss, thinning or lost hair, and red substance around the vagina. The BMS Attachment Inhibitor at high doses was associated with fetal rat toxicity and fetal malformations, including cleft palate (opening in the palate), decreased size of mouth, oral cleft (opening in the lip), testicular toxicity and decreased weight.

8D. Human Pregnancy Outcomes

BMS-663068 has not been studied in pregnant or lactating women; therefore, safe use in this study population has not been established.

8E. Findings with Similar Drugs in the Class

There are no available data on human pregnancy outcomes when exposed to similar drugs as BMS-663068.

8F. Significant Findings with Study Comparator Drugs

Many antiretroviral medications that you may use as part of this study may not have adequate or well-controlled studies on pregnancy outcomes. It is very important that you and your doctor discuss the effects of your study drugs on pregnancy, and what you should do if you become pregnant while taking them.

8G. Use of a Study-Prohibited Contraceptive Method

There are no restrictions to any contraceptive method (method to avoid pregnancy) for this study as long as it is in agreement with your study doctor. You should make sure to use the contraceptive method agreed to between you and your study doctor throughout the study and for 60 hours (5 half-lives) after the last dose of the BMS Attachment Inhibitor.

You should notify your study doctor if you do not use your contraceptive method as agreed or if you change it during the course of the study.

8H. Requirements for Pregnancy Testing

During the study you will have pregnancy tests. The number of pregnancy tests you will have will vary depending on when you discontinue the study treatment and when your participation in the study ends.

8I. Occurrence of Pregnancy or Suspected Pregnancy

If you become pregnant, suspect pregnancy or if you missed your period or it is late, or if you have a change in your usual menstrual cycle (e.g., heavier bleeding during your period or bleeding between periods), you should immediately contact your study doctor.

8J. Discontinuation from the Study

Should you become pregnant during the study, you will have the study drug discontinued if it is safe to do so and your pregnancy will be followed-up. The Sponsor has not set aside any funds to pay for any aspects of obstetric, child or related care and does not plan to pay for them.

8K. Pregnancy Reporting

In case of a pregnancy, your pregnancy and its outcome will be reported to the study Sponsor.

8L. Information for Men with Partners of Childbearing Potential

Most study drugs do not cause a risk to a woman who becomes pregnant while her male partner is a study subject. However, you are asked to inform your study doctor if your partner becomes pregnant while you are enrolled in this clinical trial, and you and your partner will be asked to provide information about the pregnancy outcome. The Sponsor has not set aside any funds to pay for any aspects of obstetric, child or related care and does not plan to pay for them. You should make sure to use the contraceptive method agreed to between you and your study doctor throughout the study and for 60 hours (5 half-lives) after the last dose of the BMS Attachment Inhibitor.

9. Benefits

The study drugs (the BMS Attachment Inhibitor combined with the OBT medications) you are being given may increase the chances of lowering the amount of HIV in your blood compared to other treatments that may be available to you. There is no guarantee that you will benefit from taking part in this study. You might not get better or the level of HIV in your blood may rise if it is not kept under control while you are in this study.

The knowledge gained from this study may also be of help to other patients in the future.

10. Alternative Treatment

You may choose not to take part in the study. There are other available treatments for HIV infection. If you decide not to participate in this study, your study doctor can discuss the risks and benefits of other drugs and prescribe one or more that may work for you.

11. Compensation for Injury

If you are injured during your participation in this study, you should contact your doctor as soon as possible in person or at the telephone number listed on page one of this consent form. Medical care may be obtained in the same way you would ordinarily obtain other medical treatment.

If you suffer a **study-related injury**, the reasonable costs of necessary medical treatment of the injury will be reimbursed to the extent these costs are not covered by your private insurance or other third party coverage.

A **study-related injury** is a physical injury that is directly caused by the study drug administered as described in the study protocol.

A **Study-related injury** does not include injuries directly caused by any of the following:

- The natural course of your underlying disease or medical condition

There are no plans to provide any other payments or other forms of compensation for a study-related injury (for example, for lost wages or discomfort). You do not give up any legal rights by signing this consent form.

Medicare, Medicaid and TRICARE Beneficiaries

If you are a Medicare, Medicaid or TRICARE beneficiary, the costs of necessary medical treatment of the **study-related injuries** described above may not be billed to Medicare, Medicaid or TRICARE. These medical bills should be submitted first to study doctor for review and payment. Contact your study doctor if you have any questions about this restriction.

12. Any Prorated Payment

As a participant in this study, you will receive $50 per visit for your participation or $75 for the Day 8 PK visit. These funds are provided to help support you with time, travel, parking, meals and other reasonable costs associated with your participation.

You will be issued a ClinCard, that will be managed by a company called Greenphire. ClinCard is a specially designed debit card for clinical research onto which your funds will be loaded as appropriate. When a visit is completed, funds will be approved and loaded onto your card. The funds will be available within 1 day and often times immediately after being loaded and can be used at your discretion. You will be issued one card for the duration of your participation. If your card is lost or stolen, please call (866) 952-3795 or ask a coordinator for a replacement ClinCard.

Additionally, you may have the option to receive updates related to appointment reminders and payment reminders and updates via text message and email message (Standard text messaging rates will apply). If available, you will have the opportunity to opt-in to receive these messages, however you are not required to provide your cell phone or email address to be enrolled in the study or use a ClinCard. If you choose to receive messages and decide at a later date that you want to stop these messages, you will have the ability to opt-out.

Greenphire will only have access to information about you that is necessary to operate and manage your ClinCard. That information is stored in a secure fashion on Greenphire's system and is deleted from Greenphire's system once the study has been completed and the funds on the card have been exhausted. Your information will not be shared with any third parties and will be kept completely confidential.

13. Voluntary Participation / Discontinuation of Treatment or Withdrawal of Consent

Your participation in this study is entirely voluntary. It is up to you to decide whether to take part or not. Even if you do decide to take part, you are free to discontinue treatment or withdraw consent from the study at any time without giving a reason. This will not affect your future medical care in any way. If you choose not to take part or to leave the study at any time, there will be no penalty or loss of benefits.

Please note that any information collected before you withdraw will be kept and used to complete the research.

Remember that Section 5 describes follow-up activities that may begin after you decide to stop study treatments. If you decide to stop study treatments, your study doctor will not presume that you have withdrawn from the study, but will assume that you will continue to participate in any follow-up activities described in Section 5. If you do not want to participate in any or all follow-up activities, you must inform your study doctor in writing and clearly identify the activities you do not want. Please note that even if you withdraw consent for further follow-up or contacts, if the investigator becomes aware of additional safety information this will be reported to the sponsor in order to comply with legal or regulatory requirements.

Your study doctor, the Sponsor of the study or designee may discontinue your participation in this study at any time without your consent if continuation in this study is not in your best interest, if you develop specific laboratory abnormalities, if your HIV is not responding to the study drug, or if you fail to follow directions for participating in the study.

Your study doctor may decide to discontinue your study assigned treatment if the treatment offers you little or no future benefits, if you develop severe or life-threatening side effects, if you develop another illness or condition in which your study doctor may feel continued treatment with study therapy is not in your best interest.

If you become pregnant during the course of the study, you will be discontinued from the study and you will be referred for obstetrical care.

The Sponsor of the study may terminate the study at any time.

14. Sponsoring Company

The pharmaceutical company sponsoring this study is Bristol-Myers Squibb. Your study doctor or hospital will be paid for including you in this study.

15. Confidentiality, Collection and Use of Study Data

15A. Collection of Study Data

Your study doctor and study staff will collect information about you which is relevant to this study; specifically, information about your name, address, contact details, date of birth, medical history, your race, ethnic origin and your life habits and sexual life. This collected information about you is called “data” or “study data” in this document.

15B. Confidentiality of Study Data and Key-coded Data

For the purposes of your participation in this study and the protection of your identity, your study doctor will assign you a unique code, such as a series of numbers and/or letters. Your doctor will record the study data collected from you in a report form that uses your assigned code, not your name. This is to protect your study data by making it anonymous for most study purposes.

The data that is recorded with your assigned code rather than your name is called "**key-coded data**". The key-coded data will be entered into the study's computer database. Your study doctor will keep a confidential list linking your name to your code and only authorized persons will have access to this list. The ways in which key-coded data may be used and shared is described below in Section 15C.

Some study data will identify you (such as medical records), and the ways in which this data may be used and shared is described below in Section 15D.

15C. Use and Sharing of Key-Coded Data

Your key-coded data may be shared with and used by the following:

- Your doctor and study staff;
- The study sponsor, its current or future research partners, collaborators, assignees, licensees or designees and their affiliates, agents, and employees;
- Other individuals and organizations that analyze or use your information in connection with these research activities, including laboratories and study sites (in the event you transfer to another study site);
- Domestic or foreign health authorities e.g., the Food and Drug Administration (FDA);
- Institutional Review Boards (IRBs); and
- Other persons required by law.

Your key-coded data will be used in connection with this study and may also be:

- used for other current or future research involving the same drug(s), the same or related health conditions, or for other relevant health research;
- transferred to individuals or companies located outside of the country or region in which you reside. However, all access to the key coded data will be controlled in accordance with applicable laws and regulations. This may include written agreements that require that the data be kept confidential and secure and be used only for the purposes permitted by this consent form or applicable laws and regulations;
- used in publications about this study but it will remain coded. Your identity will not be revealed in any compilation, study report or publication at any time.

15D. Use and Sharing of Study Data that Identifies You

Records identifying you will be kept confidential and, to the extent permitted by applicable laws and/or regulations, will not be made publicly available. All of your study

data will be kept in a secure location. Your personal information may be given out if required by law. If you test positive for HIV, Hepatitis B or Hepatitis C, by law we have to report the infection to the City of Philadelphia Health Department/PA Department of Health. We would report your name, gender, racial/ethnic background, and the month and year you were born. This is to keep track of how many people in the U.S. have HIV infection. It is also to make sure that states get enough money from the federal government to support the medical care of people living with HIV. The Health Department does not share the names of HIV infected people with anyone else. It removes all personal identifiers, such as your name, before giving information on the number of HIV infections to the federal government. Please note that it is likely that this information has been already reported to the PA Health Department as the HIV test being done for this study is not the first test for you. In the event of any publication regarding this study, your identity will remain confidential.

The authorization part of the consent gives more detailed information about how your personal health information may be used and disclosed by the University of Pennsylvania Health System (UPHS), the School of Medicine and the individual Principal Investigator, subject to University of Pennsylvania procedures.

What personal health information is collected and used in this study and might also be disclosed?
The following personal health information will be collected, used for research, and may be disclosed during your involvement with this research study:

- Name, address, telephone number, date of birth
- Social Security Number (if you receive more than $600 for participating in studies at PENN, we will need your SSN for the W-9)
- Personal and family medical history
- Current and past medications or therapies
- Results of physical exams, laboratory tests and procedures you will undergo during this research study

Why is your personal contact and health information being used?
Your personal contact information is important for the research team to contact you during the study. Your personal health information and results of tests and procedures are being collected as part of this research study. In some situations, your personal health information might be used to help guide your medical treatment.

Which of our personnel may use or disclose your personal health information?
- The following individuals may use or disclose your personal health information for this research study:
    - The Principal Investigator and the Investigator's study team
    - Authorized members of the workforce of the UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need to access your information in the performance of their duties (for example: for research oversight and monitoring, to provide treatment, to manage accounting or billing matters, etc.).

Who, outside of UPHS and the School of Medicine, might receive your personal health information?
As part of the study, the Principal Investigator, the study team and others listed above, may disclose your personal health information, including the results of the research study tests and procedures. This information may be disclosed to those listed below:

- Individuals or organizations responsible for administering the study:
- Pharmaceutical sponsor (Bristol-Myers Squibb): This is the company that supplies drugs for the study. Information regarding safety and adverse effects needs to be collected and monitored.
- Contract Research Organization: Monitors will visit the site on a regular basis to review data and assure accuracy and completeness of information before the data are analyzed.
- Regulatory and safety oversight organizations
- The Food and Drug Administration and regulatory agencies in other countries
- The Office of Human Research Protections
- The Study Monitoring Committee

Once your personal health information is disclosed to others outside of UPHS or the School of Medicine, it may no longer be covered by federal privacy protection regulations. Data are reported to the sponsor on Case Report Forms that identify you by your unique study number and not your name or medical record number. Information regarding your health, such as side effects of the study medications you experience will be reported only by code number. All samples collected for analysis will be labeled with your study number, visit number and date of your visit.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may UPHS and the School of Medicine be able to use or disclose your personal health information?
Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research repository (database). However, UPHS and the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization to do so
- The University of Pennsylvania's Institutional Review Board grants permission after ensuring that appropriate privacy safeguards are in place
- As permitted by law

Will you be able to access your records?
You will be able to access some or all of your medical records after the study is over. The Principal Investigator is not required to release research information to you that is not part of your medical record.

Can you change your mind?
Yes, at any time you may withdraw your approval to allow the use and disclosure of your personal health information as described here. You must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission to use your personal health information, you will also be withdrawn from the research study.

If you withdraw your permission to use any blood or tissue obtained for the study, the Sponsor may need to retain and use any samples that have already been collected to comply with its legal obligations and to maintain the scientific integrity of the study.

You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study. You will also be given the UPHS and School of Medicine's Notice of Privacy Practices that contains more information about the privacy of your personal health information.

WHAT IS AN ELECTRONIC MEDICAL RECORD?
An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any results of procedures performed as part of this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Results of research procedures performed as part of your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

15E. Your Access to and Correction of Study Data that Identifies You

You have the right to obtain any initial and updated information about the study data that identifies you, as well as the right according to local law and procedures to require the correction of any errors.

This information, as well as the fact of your participation in this study, can also be provided or made known to your primary physician if you wish.

You can discuss this further with your study doctor, who will be your primary contact person for your access rights.

15F. Use of Your Tissue or Blood Samples in this Study

Like key-coded data, these samples will be labeled with a unique code instead of your name. These samples and any information created from using these samples will be treated as key-coded data as described above in this consent.

16. Questions/Information

- If you or your representative(s) have any questions, concerns, or complaints regarding this study or in case of study-related injuries, you should contact your study doctor at the telephone number given on page one of this form.
- If you or your representative(s) have any questions regarding your patient rights as they relate to this study or if you have questions, concerns, or complaints about the research, you should contact Western Institutional Review Board® (WIRB®), 1019 39th Avenue SE Suite 120, Puyallup, Washington 98374-2115 by phone at 1-800-562-4789 or 360-252-2500, or by e-mail at Help@wirb.com.

  WIRB is a group of people who perform independent review of research.

  WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

- If you seek emergency care, or if hospitalization is required, please inform the treating doctor that you are participating in a clinical trial.
- If any new information becomes available during the course of this study that may affect your willingness to participate, you will be informed.
- 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.

17. SIGNATURE

- I have read and understand the information presented in this Informed Consent Form. I have been given the opportunity to ask questions and all my questions have been answered.

- I confirm that I have received a Subject Alert Card providing the contact details of the study doctor. I agree to carry this card with me at all times.
- I shall receive a signed and dated copy of this Informed Consent Form.

Check One:

☐ I agree that my study doctor may tell my personal doctor that I am taking part in this study.

☐ I do not want my study doctor to tell my personal doctor that I am taking part in this study.

I FREELY ACCEPT TO PARTICIPATE IN THIS STUDY

To be signed simultaneously, (i.e. on same date), by all parties:

Distribution: original for study doctor, signed copy to Subject / Patient

Print Name (Last Name, First Name) of Subject / Patient	Date (to be entered by Subject)	Signature

Print Name of person obtaining the consent	Date	Signature

The information in this informed consent document was read to the study participant. I believe he/she understands what was read and explained and is freely agreeing to participate in the study. The subject has signed or made his/her mark on the signature line above.

Name of Impartial Witness	Date (to be entered by witness)	Signature

At any given time an incapacitated individual may explicitly refuse to participate in or request to be withdrawn from the clinical trial. The study doctor must respect the request.