Sponsor: Astellas Pharma Global Development, Inc. ISN 9766-CL-0107

Patient Information Sheet

Study title: A Phase 2, Open-Label, Non-Comparative, Multicenter Study to Evaluate the Safety and Tolerability, Efficacy and Pharmacokinetics of Isavuconazonium Sulfate for the Treatment of Invasive Aspergillosis (IA) or Invasive Mucormycosis (IM) in Pediatric Subjects.

We invite you to take part in a research study

- Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve.
- Please take time to read the following information carefully. Discuss it with friends and relatives if you wish.
- You are free to decide whether or not to take part in this study. If you chose not to take part, this will not affect the care you will get.
- Please ask the study team if anything is not clear, or if you would like more information.

Important things that you need to know

- We want to know how safe and effective the study drug is for children with invasive fungal infections (IA and IM).
- The drug used in this study, Isavuconazonium Sulfate, can cause side-effects.
- You do not have to pay to take part in this study.
- You can withdraw from the study at any time.

How to contact us

If you have questions about this study, please talk to: Dr Simon Drysdale on 0208 725 2780

Contents

1. Introduction
2. What is the purpose of this study
3. How many people will take part in the study and how long will I be in the study?
4. Do I have to take part?
5. What is the drug or procedure that is being tested?
6. What will happen to me if I take part?
7. What do I have to do if I participate in the Study?
8. Who will cover the costs for my participation in the Study? Will I be compensated?
9. What are the alternatives for treatment?
10. Are there any possible side effects of the study treatment?
11. What are the possible risks of taking part?
12. What are the possible benefits of taking part?
13. What if new information becomes available?
14. What if there is a problem?
15. Will my taking part in the study be kept confidential?
16. Which Ethics Committee reviewed this study?
17. Consent Form

The study has 3 Periods:

1. **<u>Screening Period</u>**
   Once you have signed the consent form the study team will:

   - Ask you questions about yourself and your medical history
   - Conduct a physical exam, an ECG, take blood samples and a pregnancy test (if needed)

2. **<u>Treatment Period</u>** ***Day 1 and Day 2***
   The study doctor will do the following tests to make sure you qualify to be in the study:

   - Check your blood pressure, heart rate, breathing rate and temperature
   - Ask you about your medical history and any medications you are taking
   - Ask about how you are feeling and about your health since you last saw the study team
   - Do an ECG

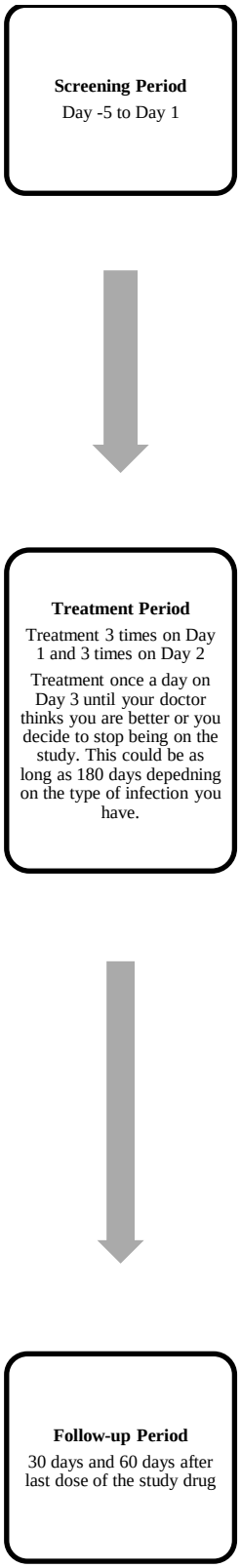
If you qualify to participate, you will be given the study medicine either intravenously or orally. On Day 1 and 2, you will receive the study drug every 8 hours for a total of 6 doses.

<u>Treatment Period</u> ***Day 3 to Last Dose***
On Day 3 to Day 84 for IA patients and Day 180 for IM patients the study team will:

- Check your blood pressure, heart rate, breathing rate and temperature
- Ask you about your medical history and any medications you are taking
- Ask about how you are feeling and about your health since you last saw the study team
- Do an ECG
- Take blood samples
- Do a pregnancy test (if applicable)
- Administer the study drug intravenously or orally, once a day.

On the day of the last dose of study medicine the study team will also do a physical exam.

3. **<u>Follow-up Period</u>**
   You may have to return to the hospital, or the study doctor might call you by phone, 30 and 60 days after your last dose of study medicine to see if there have been any changes to:
   - Your medications
   - How you are feeling



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Study title: A Phase 2, Open-Label, Non-Comparative, Multicenter Study to Evaluate the Safety and Tolerability, Efficacy and Pharmacokinetics of Isavuconazonium Sulfate for the Treatment of Invasive Aspergillosis (IA) or Invasive Mucormycosis (IM) in Pediatric Subjects.

Protocol Number:	**9766-CL-0107**
EudraCT number:	**2018-003975-36**
Sponsor:	**Astellas Pharma Global Development, Inc.**
Research Site:	**St George's University Hospitals NHS Foundation Trust, Blackshaw Road, London, SW17 0QT**
Principal Investigator:	**Dr Simon Drysdale** **St George's University Hospitals NHS Foundation Trust,** **Blackshaw Road, London, SW17 0QT** **020 8725 0293**
IRAS Project ID. :	**263454**

1. Introduction

You are being invited to take part in this research study because you are 16 years of age or older. If you are already participating in this study, you and your parent(s)/ guardian(s) agreed to your participation before you turned 16. Now that you are turning 16 years of age, we need to ask you to read this more extensive information sheet and provide your consent.

This study is planned and paid for by Astellas Pharma Global Development. Astellas Pharma Global Development is funding St George's University Hospitals NHS Foundation Trust to conduct this research study.

The information contained within this Information Sheet is very important; it tells you what will happen in the study and what is expected from you. Please read it carefully and make sure you understand it. If you have any questions, the study doctor will answer them. Once you have read this information sheet and if you agree that you would like to take part/continue to take part, you will be asked to sign the consent form at the end of this information sheet. The consent form says that you have been informed about the study and you agree to take part/continue to take part in the study.

2. What is the purpose of this study?

You are being invited to take part in the study because you have invasive aspergillosis (IA) or invasive mucormycosis (IM), you are less than 18 years old and you may benefit/continue to benefit from treatment with an antifungal medication, isavuconazonium sulfate.

The purpose of the study is to evaluate how safe and effective isavuconazonium sulfate is for paediatric patients (also referred to as children and adolescents in this document). The study will also look at the way the body takes up, uses, breaks down and removes the study medicine. This is

important because it will help determine how the study medicine may be used safely in children and adolescents with as few side effects as possible.

Isavuconazonium sulfate has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of invasive aspergillosis (IA) and invasive mucormycosis (IM) in adult patients. IA and IM are fungal infections that can be very harmful to people who are very sick and have a weakened immune system. However, additional important safety and dosing information is needed to extend the FDA's initial approval to children and adolescents. As a result, for adolescents, the study medicine is considered "investigational". The word "investigational" means the study medicine is still being tested in research studies and is not approved by the FDA or the U.K regulatory authority the MHRA.

The information about you that is collected, as part of this study, will be kept in an unidentifiable way. Information from this study may be used to seek approval from regulatory authorities to market the medicine for IA and IM in adolescents. It may also be used in reports of the study or for scientific presentations. Astellas may also use the information from this study for future medical research.

3. How many people will take part in the study and how long will I be in the study?

This study includes boys and girls 1 year to less than 18 years old at the start of the study who have IM or IA and who meet all the other conditions necessary to take part in the study. It is expected that 30 children and adolescents will take part in this study from 30 research sites in the United States and Europe.

You will be in this study for:

- up to about 144 days if you have IA or
- up to about 240 days if you have IM.

4. Do I have to take part?

It is your choice to take part in this study. You should not feel pressured. You do not have to decide today if you will participate. You may also discuss the study and your decision with your own family doctor or family/relatives if you wish to do so. You may stop taking part at any time during the study and you do not have to give a reason why. This will not affect your regular medical treatment from your doctor. Deciding not to be in the study or leaving the study before it is done will not affect the standard of care you receive from your doctor, healthcare provider or hospital. Deciding not to take part or not to continue will also not affect any benefits to which you are otherwise entitled. You do not have to be in the research study in order to receive health care.

5. What is the drug or procedure that is being tested?

Isavuconazonium sulfate (study medicine) is a new antifungal agent that was approved for use in the treatment of invasive aspergillosis (IA) and invasive mucormycosis (IM) in adult patients. If we learn more about the safety and dosing of antifungal medicines in children and adolescents, we would have a better understanding of the medicine and be able to prevent and treat these life-threatening infections in these patients. At this time, the study medicine is not approved by regulatory agencies to treat these fungal infections in children and adolescents.

Therefore, establishing a successful and safe dosage regimen for isavuconazonium sulfate for use in paediatric patients will provide important information for doctors treating children and adolescents.

This is an open-label study, which means you, the Study Doctor, hospital staff, and the Sponsor, will know what treatment you receive. If you are less than 18 years old, able to swallow capsules and weigh at least 12 kg (about 26.5 pounds) you may receive oral (by mouth) study medicine. The study doctor will discuss if the oral (by mouth) medicine would be better than IV (through the vein) medicine. The oral study medicine is a capsule and you will need to swallow 2 to 5 capsules depending on your weight. The capsule is about 1.5 cm in size. The oral medicine is given 3 times a day (every 8 hours) on Days 1 and 2 (total of 6 doses). The capsules need to be swallowed within 5 minutes. This will be followed by once a day dose of the study medication. You may go home on the oral dose; you will be given one week's supply of study medication that will last until your next appointment with the study doctor; which will be once a week. You will also be given a daily dosing log to record the date and time the oral doses are taken. If the entire dose is not swallowed within 5 minutes, you should record the reason for the delay. You should also record if you vomit any of the study medicine. If this does happen, you should not repeat the dose

After you take the first dose of the oral study medication, you will be asked to complete 3 questions about the experience by pointing to a smiley face that starts with "really bad" and goes to "really good". The study team will explain this and show you the questionnaire.

If you are less than 18 years and do *not meet the criteria for oral study medicine explained above*, you will receive an IV (a drip directly into a vein) infusion of a starting dose of isavuconazonium sulfate (study medicine), 3 times a day every 8 hours, on days 1 and 2 (for a total of 6 doses). The study medicine will be given over a one-hour period. This will be followed by an IV infusion once a day.

The study medicine (oral or IV) will be given daily until you have a successful outcome as judged by the study doctor or for a maximum duration of study treatment of 84 days (IA) or 180 days (IM), whichever occurs first. You will be followed up for 60 days after your last dose of study medicine for safety. You will be asked how you feel each time the study medicine is given.

The maximum dosing regimen administered to any participant is 372 mg per dose.

Throughout the study, you need to notify the study doctor of any illnesses or ill effects you may suffer, whether or not you think they are related to the study. Also, tell the study doctor about medication you are taking, bought either by yourself or on prescription from your own family doctor.

6. What will happen to me if I take part?

If you are currently enrolled in the study and being asked to sign this consent because you are turning 16, then many or most of what is listed below may have already occurred and will not be repeated.

The study includes the following Study Periods:

- Screening Period (5 days before the start of the study up to day 1)
- Treatment Period (day 1 up to day 84 for participants with IA and day 180 for participants with IM)
- Follow-up Period (30 and 60 days from the last dose)

Screening Period

The screening period can occur up to 5 days before you begin participating in the study.

After you have signed the consent form, the following procedures will begin:

- The study team will ask for your date of birth, gender at time of birth, country of origin
- The study team will review your prior medical history (including all surgeries), prior hospitalisations and all medications you are taking
- A physical examination will be completed, including measurement of your height, weight and vital signs (blood pressure, heart rate, breathing rate and temperature)
- An ECG (electrocardiogram – which measures the electrical activity of the heart) will be done
- Blood samples for routine laboratory testing will be collected (about 1 and 1/2 teaspoons or 7.5 mL)
- Blood sample to check the fungal infection (about 1 teaspoon or 5 mL)
- The study team will examine your ability to move your arms and legs, how well you talk and the movement of your eyes
- A pregnancy test will be done if you are of child bearing potential. The test will be either a blood test or a urine test. The study doctor will tell you which one will be done.

Treatment Period

Day 1: The following tests and procedures will be performed to determine if you continue to qualify to participate in the study:

- Vital signs (blood pressure, heart rate, breathing rate and temperature) will be done before and after the study medication is given
- The study team will review all medical history and medications you are taking
- You will be asked how you are feeling and if there have been any changes in your health since the last visit.
- An ECG (electrocardiogram) will be done
- Once study eligibility requirements are confirmed, the study medication will be given IV (through a vein using a catheter which is a small hollow tube) over one hour 3 times on Day 1. If you are less than 18 years old, your study doctor and you will discuss if the oral (by mouth) capsules would be better than the IV. If everyone agrees, you will be given 2-5 capsules depending on your weight. The capsules must be swallowed within 5 minutes. The oral study medication must be taken 3 times on Day 1.

If you are given the capsules, you will be asked to complete 3 questions using a smiley face scale for the answers.

Day 2

- Vital signs (blood pressure, heart rate, breathing rate and temperature) will be done before and after the study medication is given
- The study team will review your medical and surgical history
- You will be asked how you are feeling and if there have been any changes in your medicines or in how you feel since yesterday.
- The study medication will be given IV (through a vein) over one hour 3 times on Day 2. If you are less than 18 years old, able to swallow capsules, and it was decided to give the study medication in the capsule form, you will be given 2-5 capsules depending on your weight. The

capsules must be swallowed within 5 minutes. The oral study medication must be taken 3 times on Day 2.

Day 3-83 for all study participants

- Vital signs (blood pressure, heart rate, breathing rate and temperature) will be done before and after the study medication is given
- The study team will review your medical and surgical history
- You will be asked how you are feeling and if there have been any changes in your medicines or in how you feel since yesterday.
- The study medication will be given IV (through a vein) over one hour every day. Depending on your age and ability to swallow capsules, you may be able to take the study medicine by mouth (2-5 capsules depending on your weight) each day. The oral study medicine capsules need to be swallowed within 5 minutes. If you are not able to tolerate the oral study medicine, the study medicine can be given IV (through a vein) instead for that dose, or any following dose.
- If you are discharged from the hospital, you will need to return every day for outpatient dosing. if the medication is given IV. If your child can swallow capsules they will need to come to hospital once per week to return any unused medications and to receive additional medications for the following week.

- An ECG (electrocardiogram) will be done on Days 7, 14, 28 and 56
- At various times during the treatment period all participants will have blood taken to check their safety. The study team will tell you when blood is being taken

Blood tests include:

- Chemistry Profile and Hepatic Panel: These tests measure materials or chemicals in your blood that show how well different organs in your body are functioning and how you are absorbing the study medicine
    - Haematology (Blood count): This test measures the amount of red and white blood cells and platelets
    - Coagulation: This test measures how well your blood is clotting
    - Pregnancy Test: This test is only for participants that are of child bearing potential. The test will be either a blood test or a urine test. The study doctor will tell you which one will be done
    - Pharmacokinetic (PK) analysis: This test shows how much study medicine is in your bloodstream

The study has additional optional PK blood samples that will be taken anytime between days 14 and 42 during the time you are receiving the study medicine. The additional samples will be taken at four different times within one day (24 hours). Each sample will be about 1 mL, so in total 4 mL (less than 1 teaspoon) of blood will be taken within this day. These optional PK samples provide more information on how the study medication is working in the body and help confirm the correct amount of medication to give to children and adolescents. These additional PK samples will not affect your study participation and are optional. You will be asked to give permission for the collection of these blood samples in the consent form at the end of this information sheet.

We will not be retaining any samples collected from you for future research. Your samples will only be used for study testing and will be destroyed once the study ends. All samples collected will be identified only by a code number, your identity will remain unknown.

Blood samples will be shipped to PPD Laboratories, Clusterpark, Kleine Kloosterstraat 19 1930 Zavenem Belgium.
Fungal culture samples will be shipped to JMI Labs, 345 Beaver Kreek Centre, Suite A North Liberty, IA USA 52317.

Day 84 (and End of Treatment for IA participants)

- Vital signs (blood pressure, heart rate, breathing rate and temperature) will be done before and after the study medication is given
- The study team will review your medical and surgical history
- A physical exam, including your weight, will be done
- You will be asked how you are feeling and if there have been any changes to your medicines or in how you feel since yesterday
- An ECG (electrocardiogram) will be done
- The study medication will be given IV (through a vein) over one hour. Depending on your age and ability to swallow capsules, you may be able to take the study medicine by mouth (2-5 capsules depending on your weight). The oral study medicine capsules need to be swallowed within 5 minutes. If you are not able to tolerate the oral study medicine, the study medicine can be given IV (through a vein) instead for that dose, or any following dose.
- Blood will be taken for a safety check. It will be the same tests as described for Day 3 – 83 (chemistry profile, hepatic panel, haematology and coagulation)
- Pharmacokinetic (PK) analysis: This test shows how much study drug is in your bloodstream
- Pregnancy Test: This test is only for participants that are of child bearing potential. The test will be either a blood test or a urine test. The study doctor will tell you which one will be done

The total amount of blood collected during this treatment period is about 7 teaspoons or 34 mL if you will not participate in the optional PK sampling.
If you participate in the optional PK sampling, the total amount of blood collected during this treatment period is about 8 teaspoons or 38 mL.

Day 85-179 for IM study participants only

- Vital signs (blood pressure, heart rate, breathing rate and temperature) will be done before and after the study medication is given
- You will be asked how you are feeling and if there have been any changes to your medicines or in how you feel since yesterday
- An ECG (electrocardiogram) will be done on Days 85, 115, and 145
- The study medication will be given IV (through a vein) over one hour every day. Depending on your age and ability to swallow capsules, you may be able to take the study medicine by mouth (2-5 capsules depending on your weight) each day. The oral study medicine capsules need to be swallowed within 5 minutes. If you are not able to tolerate the oral study medicine, the study medicine can be given IV (through a vein) instead for that dose, or any following dose.

- Blood will be taken for a safety check on Days 115 and 145. It will be the same tests as described for Day 3 – 83 (chemistry profile, hepatic panel, haematology and coagulation)

Day 180 (and End of Treatment for IM participants)

- Vital signs (blood pressure, heart rate, breathing rate and temperature) will be done before and after the study medication is given
- A physical exam, including your weight will be done
- You will be asked how you are feeling and if there have been any changes to your medicines or in how you feel since yesterday.
- An ECG (electrocardiogram) will be done
- The study medication will be given IV (through a vein) over one hour. Depending on your age and ability to swallow capsules, you may be able to take the study medicine by mouth (2-5 capsules depending on your weight). The oral study medicine capsules need to be swallowed within 5 minutes. If you are not able to tolerate the oral study medicine, the study medicine can be given IV (through a vein) instead for this dose.
- Blood will be taken for a safety check. It will be the same tests as described for Day 3 – 83 (chemistry profile, hepatic panel, haematology and coagulation).
- Pregnancy Test: This test is only for participants that are of child bearing potential. The test will be either a blood test or a urine test. The study doctor will tell you which one will be done

The total amount of blood during this treatment period (i.e. Days 115, 145 and 180 or EOT) is about 3 teaspoons or 15 mL).

Follow up Period (study visits 30 and 60 days after last dose of study medication for all participants)

- These visits may be performed via telephone at the decision of the Study Doctor
- You will be asked for any changes to medications since the last dose of study medicine
- You will be asked if there have been any changes to how you have been feeling

7. What do I have to do if I participate in the Study?

In order for this study to provide good information about how this drug works in patients, you will be expected to do the following:

- Follow the instructions you are given by the Study Doctor and Staff
- Come to the study site for all scheduled study visits and procedures with the Study Staff
- Tell the Study Doctor and Staff about any changes in your health
- Tell the Study Doctor and Staff if you would like to stop being in the study at any time

Throughout the study, you are expected to notify the study doctor of any illnesses, ill effects or abnormalities you may suffer, whether or not you think they are related to the study.

8. Who will cover the costs for my participation in the Study? Will I be compensated?

There is no cost to you for the required study drug(s), procedures, tests or visits related to the study. Astellas pays the study costs including the costs of tests and procedures carried out as part of the study and the cost of the study drug.

You may be reimbursed for your travel if you agree to take part in this study.

9. What are the alternatives for treatment?

You do not have to participate in this study to receive treatment for your condition.

The study doctor will discuss the benefits and risks of other treatments with you.

10. Are there any possible side effects of the study treatment?

All medical treatments have the potential of causing undesirable effects. For this reason, the study is performed under carefully controlled conditions.

Only limited information about the side effects in children and adolescents is available at this time. In one ongoing study, 27 children and adolescents (1 to 18 years of age) received intravenous isavuconazonium sulfate. In this study, isavuconazonium sulfate was generally safe and well tolerated, with the most frequent side effects being diarrhoea/nausea, infusion-related reactions, and rash/itching.

However, isavuconazonium sulfate has been studied extensively in adults in several clinical studies and is currently available as a prescription drug in the US and Europe for adults. In adults, the most frequent side effects were nausea, vomiting, diarrhoea, headache, elevated liver chemistry tests, hypokalemia (low potassium levels in blood), constipation, shortness of breath, cough, peripheral oedema (swelling of arms and legs), and back pain.

Other important side effects were:

<u>*Infusion-Related Reactions</u>

Infusion-related reactions are side effects, which occur during, or right after intravenous dosing. These are low blood pressure, shortness of breath, chills, dizziness, and abnormal sensations.

* For participants receiving the study medicine through a vein.

<u>Allergic Reactions</u>

Severe allergic reactions have been reported with other drugs that are similar to isavuconazonium sulfate.

In addition to the risks listed above, there may be risks or side effects that are unexpected or unknown in children and adolescents at this time. You may have side effects while taking part in the research study, including the procedures being performed and taking study drug. All patients taking part in the study will be examined thoroughly and regularly for any such side effects; however, doctors do not know all the side effects that may happen. Side effects may be mild or very serious. In some cases, side effects can be long lasting, permanent or result in death.

To minimise the occurrence of undesirable effects, you are asked to report all changes in your condition to the Study Doctor as soon as possible, including any new medications. This includes medications available without a prescription (over the counter) and any alternative medicines such as vitamins, herbal remedies (e.g. St. John's Wort, valerian, etc.). Your records and the examination will allow the early detection of undesirable effects. This will lead to a prompt and an appropriate treatment, if required.

11. What are the possible risks of taking part?

<u>*Risks of Using an Intravenous (IV) Catheter:</u>

- Infection
- Pain at the site when the catheter is inserted
- Redness
- Bruising or discoloration of skin
- Vein irritation from the fluids or medication being given
- Local swelling due to IV fluid accidentally entering the tissue rather than the vein
- Blood clots, which may cause inflammation, swelling and pain

*For participants receiving the study medicine through a vein.

Blood Sample Collection

The general risks associated with taking blood samples, necessary for blood tests, are discomfort (stinging) or slight bruising where the needle is inserted into your vein. The bruise should go away within a few days.

During the collection of blood samples, you may experience pain and/or bruising at the needle injection site. Although rare, localised clot formation and infections may occur. Lightheadedness and/or fainting may also occur during or shortly after the blood sample is taken or catheter insertion.

Electrocardiogram (ECG)

The ECG test is a recording of the electrical activity of your heart. The sticky pads used may be cold when applied and sometimes cause some discomfort or temporary skin reaction such as redness or itching. If the hair under the patches needs to be shaved, irritation from shaving also could occur. In addition, these pads may cause some discomfort when they are removed, similar to the pulling sensation associated with removal of a plaster.

Pregnancy

Participants who are pregnant, breastfeeding or plan on becoming pregnant during the study must not take part. A test will be requested to make sure you are not pregnant.

Participants who are of child bearing potential and could become pregnant must use highly effective contraceptive methods during the course of this study.

If you are female, you must either:

Be unable to have children:

- Clearly premenarchal (have not started your period) in the judgment of the study doctor
- Documented to be surgically sterile

Or, if able to have children:

- Agree to use highly effective contraceptive methods* (listed below) at the time of your signing of the consent form and throughout the treatment period and for at least 30 days after the final study drug administration
- And have a negative urine or serum (blood) pregnancy test at screening
- must agree not to breastfeed starting at screening and throughout the study and for 30 days after the final study drug administration

- must not donate ova (eggs) starting at screening and throughout the study and for 30 days after the final study drug administration

The study doctor will require participants who take part in the study to have pregnancy tests during the study treatment. A pregnancy test does not keep you from becoming pregnant. If participants become pregnant while taking part in the study, they should immediately tell the study doctor. In the event the female participant becomes pregnant, they will be asked to provide information regarding the outcome of the pregnancy, if known.

Male participants:

Any male participant whose partner becomes pregnant while taking part in the study should immediately tell his study doctor. In the event the female partner of a male participant becomes pregnant the male participant's pregnant partner will be asked to sign a consent form agreeing to the study team and study sponsors collection of information about the pregnancy. The pregnant partner's decision to allow collection and use of information about the pregnancy and the birth and heath of the baby is voluntary.

A male participant and his female spouse/partner who is able to have children must be using highly effective contraception consisting of 2 forms of contraception* (at least one of which must be a barrier method) starting at screening and continuing throughout the study, and for 30 days after the final study drug administration.

A male participant must not donate sperm starting at screening and throughout the study and, for 30 days after the final study drug administration.

** Highly effective forms of contraception include:*

- *consistent and correct usage of established oral hormonal contraception,*
- *established intrauterine device (IUD) or intrauterine system (IUS) and*
- *barrier methods of contraception: condom or occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/suppository.*

12. What are the possible benefits of taking part?

You may or may not receive any direct medical benefit from being in the study. Your condition may improve, worsen, or stay the same. However, a possible advantage of you participating in this study is that the study medication may be more effective in its ability to fight off fungal infections and/or have fewer side effects compared to other drugs treating fungal infections. However, it cannot be guaranteed and no assurance can be made that you will benefit from this treatment. In addition, you will be closely monitored throughout the study. Your participation in this study will allow further evidence to be obtained on the effectiveness and safety of this medication.

13. What if new information becomes available?

During the course of the study, significant new findings may become available about the treatment/drug that is being studied, which may influence your willingness to continue to take part in the study. If this happens, the study doctor will tell you about it and discuss if you wish to continue in the study. You may withdraw from the study at any time. If you decide to withdraw, the study doctor will discuss your treatment options with you and your future medical care will not be affected. If you decide to continue in the study, you may be asked to read an updated information sheet and sign an updated consent form.

Also, on receiving significant new findings, the study doctor might consider it to be in your best interest to withdraw you from the study. He/she will explain the reasons and arrange for your care to continue.

In addition, the entire study or your participation in the study could be stopped at any time as a result of the discovery of significant new findings or for other reasons by the following entities: study doctors, Astellas, the regulatory health agencies, and the Ethics Committee if the safety of research patients is found to be at too much risk. Additionally, Astellas may decide, at any time and without your permission, to stop the study. If the study is stopped for any reason, you may be asked to go through a final examination (the End of Study Visit). The study doctor will discuss making arrangements for your care to continue.

The Study Doctor or Sponsor can remove you from the study at any time, even if you want to stay in the study. This could happen if:

- The Study Doctor believes it is best for you to stop being in the study
- You do not follow directions about the study
- The Sponsor stops the study for any reason
- You experience an infusion-related reaction
- You become pregnant

If you want to stop participating in the study, tell the Study Doctor and/or Staff. Upon permanently discontinuing study drug treatment, you may be asked to continue with the protocol-defined study visit schedule as outlined above for the collection of safety information.

If you decline to be followed up upon permanently discontinuing study drug treatment, the Study Doctor will ask if you are willing to take part in an end of treatment visit. This visit will include vital signs check (body temperature, blood pressure and heart rate), an electrocardiogram, pregnancy test (for applicable girls), and a blood sample (haematology, chemistry including hepatic [liver] panel, and study drug levels). You will be asked to report any new medications you have taken and side effects that may have occurred since the last visit.

14. What if there is a problem?

Complaints

If you have a concern about any aspect of this study, you should speak to the researchers who will do their best to answer your questions 020 8725 2780. If you remain unhappy and wish to complain formally, you can do this by contacting St George's NHS Patient Advice and Liaison Service (PALS) on 020 8725 2453. Details can be obtained from your study team.

What happens if I am injured during the study?

Astellas will provide compensation for any injury caused by taking part in this study in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI). Astellas will pay compensation where the injury probably resulted from a drug being tested or administered as part of the study protocol or any test or procedure you received as part of the study.

Any payment will be without legal commitment (please ask if you wish for more information on this).

Astellas would not be bound by these guidelines to pay compensation where the injury resulted from a drug or procedure outside the study protocol or the protocol was not followed.

No other financial compensation is available.

15. Will my taking part in the study be kept confidential?

Astellas Pharma Global Development, Inc. is the sponsor for this study taking place in the United Kingdom and elsewhere. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. St George's University Hospitals NHS Foundation Trust will keep identifiable information about you for 25 years after the study has finished as required by law. The information may be stored for longer, for example, when used in applications for approval to market a medicine.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information by contacting the Astellas Data Protection Officer at: privacy@astellas.com.

We use personally-identifiable information to conduct research to improve health and care. As a pharmaceutical company we have a legitimate interest in using information relating to your health and care for research studies, when you agree to take part in a research study. This means that we will use your data, collected in the course of a research study, in the ways needed to conduct and analyse the research study. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO). Our Data Protection Officer can be contacted at privacy@astellas.com.

The study site will keep your name, NHS number and contact details confidential and will not pass this information to Astellas. The study site will use this information as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Certain individuals from Astellas and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Astellas will only receive information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details. Astellas may forward information about you(again, without any identifying information) to its service providers, for activities related to the study, such as laboratory analysis.

The study site will keep identifiable information about you from this study for 25 years after the study has finished.

Astellas will collect information about you for this research study from your medical records. Your medical records will not provide any identifying information about you to Astellas. We will use this information for the purpose of the research study.

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

By signing this participant information sheet and informed consent form, you consent to the study doctor and his or her staff collecting and using personal data about you for the study. This includes your year of birth, your sex, your ethnic origin and personal data on your physical or mental health or condition. Your consent to this does not have a specific expiration date, but you may withdraw your consent at any time by notifying the study doctor.

Information that contains your identity may also be disclosed in certain circumstances. For example, at any time during or after the study, information may be shared with representatives of medicines regulatory authorities based in countries outside the European Economic Area, including for example Japan, the United States, Canada, EU, Latin America and Asia. Other countries may not have the same legal levels of protection for personal data as apply within the United Kingdom.

If the sponsor transfers your coded data outside the EU to the entities of their group, to service providers or to investigators that collaborate with them, the data will be protected with safeguards such as contractual clauses, known as Standard Contractual Clauses, issued by the European Commission. Some of those entities may be in countries, which may not have the same legal levels of protection for personal data as apply within the European Economic Area. If you want to know more about this, you can contact the Sponsor Data Protection Officer at privacy@astellas.com.

By signing this Participant Information Sheet and Informed Consent Form, you are authorising such access to information about you.

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 trial may also be registered on national registries and a summary of the results may be posted on publically accessible databases (such as https://www.clinicaltrialsregister.eu, www.astellasclinicalstudyresults.com or other national databases), if required by local laws or regulations. The summary of results will not include information that can identify you.

You have the right to see and copy your health and treatment information related to the study for as long as the information is held by the study doctor. However, to ensure scientific integrity of the study, you have to agree that you may not be able to review some of your records related to the study until after the study has been completed.

16. Which Ethics Committee reviewed this study?

International guidelines exist to ensure that clinical studies are performed safely and ethically. These are called "Good Clinical Practice" and the "Declaration of Helsinki". All Astellas studies are performed in accordance with these standards. This study has also been approved by the East of England- Cambridge South Research Ethics Committee.

Contact for further information

Thank you for reading this information sheet. Remember, you do not have to take part in this research if you do not want to and you can stop taking part at any time.

If there is anything you do not understand or if you have other questions, please ask the study doctor or nurse at the next available opportunity.

You can ask questions about the study at any time. You can call the Study Doctor at any time if you have any concerns or complaints. You should call the Study Doctor if you have questions about the study procedures, or if you get hurt or sick during the study. In the event that you sustains any injury during the course of the research, please contact the study team. If such problems occur, the study doctor and research team will help you to get the appropriate medical treatment. Treatment will be available including first aid, emergency treatment, and follow-up care as needed.

Contact details:

Study Doctor:	Dr Simon Drysdale St George's University Hospitals NHS Foundation Trust, Blackshaw Road, London, SW17 0QT 020 8725 0293
Lead Research Nurse:	Nicole Branch Room 2.216F, 2nd Floor Jenner Wing, St George's, University of London, Cranmer Terrace, London, SW17 0RE 020 8725 2780
Contact for Research Patient Rights	Joint Research and Enterprise Services (JRES) Corridor 10, Ground Floor Jenner Wing, St George's, University of London Cranmer Terrace London, SW17 0RE 020 8725 4986
Contact in case of Research-Related Injury	St George's NHS Patient Advice and Liaison Service (PALS) PALS Office St George's Hospital

Blackshaw Road
London
SW17 0QT
020 8725 2453

Sponsor: Astellas Pharma Global Development, Inc. ISN 9766-CL-0107

Patient Consent Form

Study Title:	A Phase 2, Open-Label, Non-Comparative, Multicenter Study to Evaluate the Safety and Tolerability, Efficacy and Pharmacokinetics of Isavuconazonium Sulfate for the Treatment of Invasive Aspergillosis (IA) or Invasive Mucormycosis (IM) in Pediatric Subjects
Protocol Number:	9766-CL-0107
Patient No.:	
IRAS Project ID:	263454

The patient should complete the following:

		Please Initial
1.	I confirm that I have read and understand the information sheet (V4.0, 14 April 2020) for the above study.	
2.	I confirm that the study has been explained to me and that I have had the opportunity to ask questions and ample time to decide whether I would like to participate.	
3.	I consent to take part in the study.	
4.	I agree that my health information may be added to research databases and used in the future by Astellas and its affiliated companies to study treatments for patients or to develop a better understanding of diseases.	
5.	I understand that my medical records can be released to assist with the study, including for review for research or legal purposes to the Astellas group, the Contract Research Organisation involved in the study, study doctors, and auditors from governmental agencies such as, the FDA, PMDA, EMA, Department of Health and Human Services agencies, Competent Authorities. I give permission for these individuals to have access to my medical records.	
6.	I agree that biological samples (blood/urine) collected from me can be used for the purposes of this study as explained in this information sheet.	
7.	I agree that my personal data, including data related to my physical or mental health or condition, and race or ethnic origin, may be used as described in this consent form, including transfer to countries outside the European Union.	

8.	While taking part in this study (meaning from the time I sign this Consent Form until completion of the last study visit), I agree that I will not join another investigational drug study (except for an oncology) study and I am not already a participant in another investigational drug study (except for an oncology) study. If I participate in more than one investigational drug study (except for an oncology) study including this study at a different site, I will be withdrawn from the study.	
9.	I agree to my GP being informed of my participation in this study.	

Optional 24-hour PK samples

☐ Yes, I agree to participate

☐ No, I do not agree to participate

The patient should complete the following:

If I withdraw from the study before all visits are completed, the study doctor may need to follow up with my doctor (such as medical records or labs results) for safety reporting. The information may be useful scientifically and may be helpful to others requiring the same treatment. For any samples of blood or urine that were collected before I withdrew consent, the tests specified in the study protocol will be completed. I have been asked to allow the study doctor to continue to follow-up and collect data after my withdrawal from the study.

☐ Yes, I agree

☐ No, I do not agree

Signature Page

I have read the information above and have discussed any questions I had with the study doctor. My signature below means I have read this information sheet and consent form, understand its contents, and all my questions about the study and my participation in it have been answered by the study doctor and his/her staff.

I will receive a signed copy of this Information Sheet and consent form. I will not lose any of my legal rights by signing this consent form. The original signed consent form will be filed with the study doctor.

Printed Name of Participant

_____

Signature of Participant

_____

Date (dd/MMM/yyyy)

By signing below, I attest that I have fully informed the participant about the study.

_____

Printed Name of Person Obtaining Consent

_____

Signature of Person Obtaining Consent

_____

Date (dd/MMM/yyyy)

When completed: 1 for participant; 1 for researcher site file; 1 (original) to be kept in medical notes