NIH "Dabrafenib and Trametinib in Treating Patients With Erdheim Chester Disease and BRAF Mutation"

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Basic Information about the Study

1. What is the purpose of the "Dabrafenib and Trametinib in Treating Patients With Erdheim Chester Disease and BRAF Mutation" study being conducted at the NIH?

- To test the safety and efficacy of Dabrafenib and Trametinib in treating ECD patients that have the BRAF V600E mutation.
- Determine treatment end points as well as response criteria other than just disease regression, these response criteria include, but are not limited to, quality of life improvement.

2. Why would a patient want to participate in this study?

Currently there are no approved treatments for ECD as well as no endpoints regarding response to therapy, when to stop treatment, what follow up is needed once therapy is discontinued amongst other important points. Involvement in the study will help grow experience and knowledge of Erdheim-Chester Disease that could potentially help answer these questions and help all patients in the future.

3. **How many patients are needed for the study?**

The study is currently designed for a maximum of 18 patients.

4. **Would medical records of deceased patients be of help to the study?**

No

5. **Who are the investigators involved in the study?**

The Principal Investigator is Juvianee I. Estrada-Veras, M.D (estradaverasji@mail.nih.gov). Associate Investigators are William Gahl, M.D., PhD, Clinical Director, NHGRI and Kevin O'Brien NP. The study is being conducted through the National Human Genome Research Institute with the sponsorship and guidance of the National Cancer Institute, CTEP, GSK and FDA.

Study Eligibility

6. Who is eligible to participate in the study?

To be eligible for the study, patients must:

- Have been diagnosed with Erdheim-Chester Disease based upon a pathological evaluation
- Have the BRAF V600E mutation detected in abnormal tissue. The mutation must be confirmed by the NIH if it was detected through outside testing other than NIH testing. For this, patients must submit slides or paraffin block of their biopsy used to determine their BRAF status.
- Be between 18 and 80 years of age.
- Be able to travel to the NIH hospital in Bethesda, Maryland.
- Be off any ECD therapy: interferon, anakinra, imatinib, cladribine etc for at 4 weeks before the baseline visit to the NIH.
- Patients that are using Vemurafenib, off label or through other trial, as well as any other BRAF or MEK inhibitor as automatically NOT ELIGIBLE for this study.
- Patient must be able to understand and sign the inform consent.

THERE ARE MANY OTHER CRITERIA THAT PATIENTS MIGHT NOT UNDERSTAND, IT IS ENCOURAGED THAT THEY DISCUSS THEM WITH THEIR PRIMARY PHYSICIAN.

7. Am I required to travel to Bethesda to participate in the study?

Yes, patients will need to travel to the NIH hospital in Bethesda, Maryland for 4 to 5 days in order to participate in the study. There are 8 visits to the NIH CC in a period of 12 months.

8. Are non-US citizens able to participate in the study?

Yes, non-US citizens are able to participate. As with all patients, they will need to be accepted into the study and be able to reach the NIH campus. They will be required to bring proper identification.

What Participants Should Expect

9. How long will a patient need to stay at the NIH?

Each patient will be scheduled for 4-5 days of testing at the NIH with every visit. Patients will be admitted to the hospital as an inpatient. Depending on the patient's testing schedule, it may be possible for a patient to receive a 'pass' to leave the hospital for a short time during the week.

10. Will ECD patients be evaluated at the NIH at the same time?

Maybe.

11. What tests will the patient undergo while at the NIH?

Patients will be thoroughly examined during their stay at the NIH for signs and symptoms of ECD. This examination may include, but not be limited to: (1) medical history; (2) general physical examination; (3) blood and urine samples; (4) CT, MRI, bone and/or PET scans; (5) ultrasounds; (6) skin biopsy; (7) pulmonary function test; (8) echocardiogram/

electrocardiogram/ 6-minute walk test; (9) electroencephalogram. The patient evaluation will include examinations from an ophthalmologist, cardiologist, neurologist, nutritionist, rehab specialist, and/or a pain consultant. In addition, photographs of patient's face and body, with underwear on, will be taken.

12. Will patients be required to use their home medications while in the NIH hospital, or will the hospital pharmacy be providing their medications, including their ECD treatments?

The study drugs will be provided at no cost by the NIH through the NIH pharmacy. Patients should bring their home medications with them. Patients will be asked to send a list of their medications to the NIH in advance of their travel. The NIH will check to determine what medications can be provided by the NIH pharmacy. Patients taking medications not kept in the NIH pharmacy will be required to use their home medications while an inpatient. Refrigeration for medication will be available.

13. Will follow up visits to the NIH be required?

There are 8 visits needed during a 12 month period.

14. Will patients be required to stop taking medications or supplements while a participant in the study?

YES, ALL medications need to be reviewed before enrollment and the specific drug to treat ECD must be stopped 4 weeks in advance minimum.

15. Will a patient receive the results of their tests?

All clinical data will be given directly to the patient at a debriefing session just prior to discharge. Study participants will be encouraged to stay in contact with the principal investigator who will be able to communicate advances made. Study participants may also be invited to enroll in pertinent future studies.

Registering for the Study

16. How do patients enter the study?

Patients can contact the study investigators or ask their doctors to do so. Patients must provide their medical summary, not as extensive as with the natural history protocol, to be accepted into the study. Scans, biopsy results, a medical summary provided by a treating or diagnosing doctor, a current medication list, and a completed medical history questionnaire are the minimum amount of records needed, although all pertinent records will be helpful.

17. How is patient participation scheduled?

Patients can contact the principal investigator, Dr. Juvianee Estrada-Veras (estradaverasji@mail.nih.gov) or Kevin O'Brien NP, or Kathy Brewer (support@erdheim-

chester.org) to begin the process. Once the patient provides the needed medical records, s/he will work with personnel at the NIH to schedule their travel and their stay at the NIH.

Costs Related to the Study

18. Will patients be charged any medical costs for participating in the study?

No, the NIH will cover all medical costs. This includes the cost of the patient's hospital stay, tests performed and evaluations by consulting physicians.

19. Who pays for travel costs incurred by the patient?

The NIH hopes to pay travel costs for all patients who need assistance. However, the budget of the NIH may be affected by federal budget cuts that are often discussed. If this should happen, the NIH will be required to re-evaluate their ability to cover travel costs. The patient and only ONE family member will be covered if funding permits. For international patients, we can discuss cases individually, but at this point the NIH will consider to sponsor travel from the point of entry to the USA to the NIH campus in Bethesda, MD.

20. Will reimbursement of travel costs for non-US citizens be considered?

Currently the NIH will pay for travel costs incurred within the USA. This means a patient would need to cover their transportation costs from their home to US soil. Once on US soil, the NIH could then pick up the cost of travel. However, the budget of the NIH may be affected by federal budget cuts that are often discussed. If this should happen, the NIH will be required to re-evaluate their ability to cover travel costs.

21. Will travel costs be paid for a family member/caregiver traveling with a patient?

The NIH hopes to pay travel costs for ONE family member or caregiver traveling with the patient. However, the budget of the NIH may be affected by federal budget cuts that are often discussed. If this should happen, the NIH will be required to re-evaluate their ability to cover travel costs of family members.

22. Can the NIH cover the travel costs of multiple family members traveling with a patient?

No, the NIH is able to cover the travel costs of only a single person traveling with the patient.

Rights of the Study Participants

23. Will participating patients have the right to refuse a single test in the evaluation if they choose to do so?

Yes, patients can refuse a test if they so desire. However, the goal of the study is to have a complete suite of tests on all patients for the best data and analysis. If patients refuse a procedure, it is acceptable. The goal of the study to determine how these drugs can be used in treating ECD and having all tests done on all patients is key for the success of the study.

24. Can a patient bring a family member/care giver?

Yes.

25. How will patient privacy be protected?

Patient samples, cell lines and data files will be coded with numbers, not names. The code to patient identities, as well as other patient data, will be kept in a password protected database. Access to the code will be restricted to the principal investigator and an associate investigator, Dr. William Gahl. Paper records will be kept in a locked file cabinet.