RePOWER TRIAL FREQUENTLY ASKED QUESTIONS: A GUIDE FOR PATIENTS AND FAMILIES

Primary Mitochondrial Disease and Primary Mitochondrial Myopathy

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1. **What are Primary Mitochondrial Disease (PMD) and Primary Mitochondrial Myopathy (PMM)?**

Primary Mitochondrial Disease (PMD) refers to a disease caused by a genetic mutation in a person's nuclear DNA (nDNA) or mitochondrial DNA (mtDNA), which results in a defect in a person's ability to adequately and appropriately produce energy for the body (also known as ATP). There are more than 200 genetic mitochondrial diseases, such as MELAS, POLG, Kearns-Sayre, etc.

Signs and symptoms of PMD are different for each person, but often affect multiple organ systems, including the eyes, central nervous system, skeletal muscle, heart and the kidneys. For a sample list of symptoms, please visit this Mayo Clinic website.

A patient with ***Primary Mitochondrial Myopathy (PMM)*** has a primary mitochondrial disease as described above, plus signs and symptoms of myopathy, which include muscle weakness (especially in the upper and lower limbs), easy fatigability, exercise intolerance and pain.

2. **What will RePOWER (SPIMM-300) study?**

Patients enrolled in the RePOWER (SPIMM-300) study will have confirmed or suspected PMD AND also have signs and symptoms of myopathy, such as easy fatigability, exercise intolerance and muscle pain.

RePOWER (SPIMM-300) is a prospective, observational only study, meaning **no treatment will be given**, and patients will be asked to complete questionnaires about their current symptoms and quality of life, and perform certain functional assessments to measure strength and endurance. The study will enroll approximately 300 patients across North America, Europe and Australia.

The study will primarily assess the relationship between a patient's diagnosis and their experience living with primary mitochondrial myopathy, as well as local and regional differences in care and diagnosis. Enrollment in RePOWER may enable the patient to participate in a potential future interventional trial in primary mitochondrial myopathy.

3. **How do patients enroll in RePOWER (SPIMM-300)?**

Patients can visit ClinicalTrials.gov to better understand whether they may be a fit for this study. Then, a patient can speak with their primary physician or contact a clinical study site for more information.

4. **How will investigators select patients to participate (inclusion criteria) in the RePOWER (SPIMM-300) study?**

The investigator will identify potential patients through existing medical records and one on-site visit, also referred to as the enrollment visit.

At the enrollment visit, a patient must meet the following criteria to be eligible for the study:

- Patient (or guardian) is willing and able to provide a signed informed consent form (ICF) prior to participation in any-trial related procedures
- Patient is between 16-65 years of age at the time of enrollment
- Patient has a clinical presentation of PMD with either signs or symptoms of myopathy, in the opinion of the investigator
- Patient is able to walk and able to attempt the 6-Minute Walk Test (6MWT)

Those who meet any of the following criteria will be deemed ineligible for the study:

- Patient who has symptoms of PMD due to secondary mitochondrial dysfunction (such as a drug toxicity)
- Patient has had prior exposure to elamipretide (prior participation in a study investigating elamipretide)
- Patient does not have the cognitive capacity to understand and complete all study assessments
- Patient has a medical history of severe renal impairment
- Patient has a history of active alcoholism or drug addiction during the year before enrollment

5. **A patient or their family member have been told that they have mitochondrial disease, but do not have a genetic diagnosis. Can they still qualify for the study?**

Yes. If a patient meets all of the other inclusion criteria and none of the exclusion criteria for the study, the investigator will consider the patient for enrollment in the study. With patient consent, Stealth will pay for genetic testing through a pre-selected genetic testing lab. A saliva sample will be collected to perform the genetic testing. If the patient has already had genetic testing, the investigator will determine if the results are acceptable. If not, the investigator may ask the patient to provide a saliva sample to complete additional genetic testing.

6. **Are children eligible to participate?**

At this time, anyone younger than age 16 is not eligible to participate in this study.

7. **How long does RePOWER (SPIMM-300) last and is hospitalization required?**

The study requires one in-person enrollment visit, at which time the patient will meet with the clinical investigator at one of the study sites. The purpose of this single visit is to collect and review existing medical information, as well as to conduct the questionnaires and functional assessments. No additional study-specific visits or hospitalization is required. Following the enrollment visit, patients will be asked to participate in telephone interviews with their clinical investigator every six months in order to discuss any change in his or her disease. Patients will continue to see their primary healthcare providers as usual during the course of the observational study and data from that visit will be recorded as part of the study.

8. **A patient doesn't live close to any of the study sites listed. Are they still eligible to participate?**

Yes, patients are still eligible to participate if they do not live close to a study site. If a patient meets the inclusion criteria as deemed by the investigators conducting the study, patients will be asked to travel one time to one of the study sites for the enrollment visit. Other than the enrollment visit, there are not any other required visits for the study.

9. **Will patients be required to discontinue their current treatment if selected to participate?**

No, patients will not be required to discontinue current treatment if selected to participate in RePOWER (SPIMM-300). Patients are allowed to continue their current treatments and therapies during the course of this observational study.

10. **If patients are enrolled in other registries are they still eligible for the RePOWER (SPIMM-300) study?**

Yes, as long as a patient meets the inclusion criteria and no exclusion criteria, prior participation in a registry does not make the patient ineligible to participate. Please note, none of the information that may have been submitted by the patient or his/her physicians to other registries may be available to the RePOWER (SPIMM-300) investigators.

11. How can patients get more information and see if they are eligible to participate?

Patients and their physicians can find information about this study and participating sites at ClinicalTrials.gov. Stealth also encourages patients and their families to learn more by visiting the websites of patient advocacy organizations in their country, such as the United Mitochondrial Diseases Foundation (UMDF), MitoAction and the Foundation for Mitochondrial Medicine, and reviewing the information available there.