

Ket-101-RSRT Ketamine Study Frequently Asked Questions for Parents and Caregivers

Why should I consider participating in the ketamine study?

- Independent labs have shown positive effects of ketamine treatment in different Rett mouse models, in both females and males, including improved brain cell function and activity, improved sensorimotor function (body movements in response to sensory input), less apnea (breath holds) and longer life-span. With the exception of gene therapy, Ketamine treatment extends life-span in animal models longer than any other drug currently in development for Rett.
- Ketamine affects many aspects of brain function, although it does not affect the mutation (change in DNA) in the MECP2 gene that causes Rett Syndrome. In animal models of Rett Syndrome, some of the positive changes in the brain after ketamine treatment seem to last for at least some time after the drug has left the body.
- One person with Rett syndrome received low-dose ketamine to treat seizures and showed improvement in other Rett symptoms as well. Participating in this study will help us answer the question if ketamine can be used to treat symptoms of Rett Syndrome generally, or if her response was unique.
- Ketamine is an FDA-approved medication for anesthesia (insensitivity to pain) and is used in surgery and other medical procedures for inducing sleep and to reduce pain. Because ketamine has been used to treat patients for over 50 years, there is a large amount of information available regarding safety and possible side effects in adults and children who have received ketamine.
- Over the past 20 years low dose ketamine has been studied in disorders affecting brain function such as depression, anxiety and Obsessive Compulsive Disorder (OCD), as well as in pain management, with positive effects.
- Participating in this study will not prevent you from participating in other studies afterward. You will need to wait about 1 week after the final phone call in this study before you can join another study. Because this study is short and lasts about 2 months, you will have plenty of time to join other studies.

Who is eligible for the ketamine study?

- Girls who are at least 6 and not older than 12, who have been diagnosed with Rett Syndrome and have a genetic report showing a mutation in MECP2.
- Individuals who are taking medications where dosing has remained unchanged and stable over the last 4 weeks, or for seizure medications stable over the last 12 weeks.
- Individuals who are not taking medications that could interfere with ketamine.

- Individuals whose current medications will not be interfered with by taking ketamine.
- The study doctor will determine if your child is eligible to participate in the study.
- Eligibility criteria help ensure your child's safety in participating in the study and make sure all participants are similar enough that conclusions about the study treatment can be made.

What will happen during the study and what do I and my child have to do?

- The study consists of 4 visits to the study doctor's clinic, a follow-up phone call, and daily phone calls during dosing days to discuss your child's side effects, if any, and confirm doses were taken.
- If you live more than 100 miles from a clinic site, the Rettland Foundation may be able to help with the cost of travel.
- No blood draws will occur in the study. The entire study will complete from the first visit to the final follow-up phone call within 8 to 10 weeks depending on how close together study visits are scheduled.
- At 2 visits, each participant will receive free of charge a bottle of medication for dosing at home. One bottle at one visit will contain 5 days of oral dosing of ketamine, and the other bottle at the other visit will contain 5 days of oral dosing of placebo. For each 5-day treatment, you will give your child 2 oral doses of study medication per day. The order in which the treatments are given is assigned by a computer and unknown by the study team. Each treatment will be evaluated by the parent and the study doctor for 2 weeks including the 5-day dosing period.
- The same parent/caregiver will accompany the child to each of the 4 in-clinic visits that occur approximately every 2 weeks. 2 visits will be about 3 hours long where your child will be observed after dosing for 2 hours to ensure her safety before continuing dosing at home. Site sites may perform an EEG (a measure of brain activity by placing a special cap on your child's head) at these 2 in-clinic dosing visits.
- The same parent/caregiver will evaluate and complete questionnaires about their child's symptoms at each visit, 2 times at home, and on the follow-up phone call.
- Your child will wear 2 wearable sensors every day during the study to collect data on how her body works including her heart and breathing, motion and sleep. One sensor, the actigraph, is worn like a waterproof watch and only removed for data transfer at the study site. The other sensor, the hexoskin shirt, is a tank top that will be worn continuously but will be removed daily for a few hours break, and to charge the device at home and upload data. 2 shirts are provided so one shirt can be worn while the other can be placed in the washing machine at home when needed.
- Dose your child twice a day on each of the 5 dosing days for each treatment, speak with the study site to discuss your child's side effects, if any, and confirm doses were taken on each dosing day and the day after dosing.
- Bring the 2 wearable sensors and used study drug bottle to each in-clinic visit.