Adding Trauma-focused Psychotherapy To Ketamine Treatment For Chronic PTSD: A Pilot Study
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Principal Investigator: Adriana Feder, MD
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STUDY INFORMATION:

Study Title: Adding Trauma-focused Psychotherapy To Ketamine Treatment For Chronic PTSD: A Pilot Study

Study site(s): Icahn School of Medicine at Mount Sinai

Principal Investigator (Head Researcher): Adriana Feder, MD

Physical Address: 1399 Park Avenue, 2nd floor, New York, NY 10029

Mailing Address: One Gustave L Levy Place Box 1230, NY, NY 10029

Phone: 212-585-4670

SUMMARY OF THIS RESEARCH STUDY:

This document explains a research study you might be interested in joining. Participation in the study is voluntary. You can agree to join or not. Your decision will not limit your ability to receive care at Mount Sinai. You should only agree to take part if you understand the study and if all of your questions about the research study are answered. If you do join the study, the research team must share any new information with you that may change your mind about taking part.

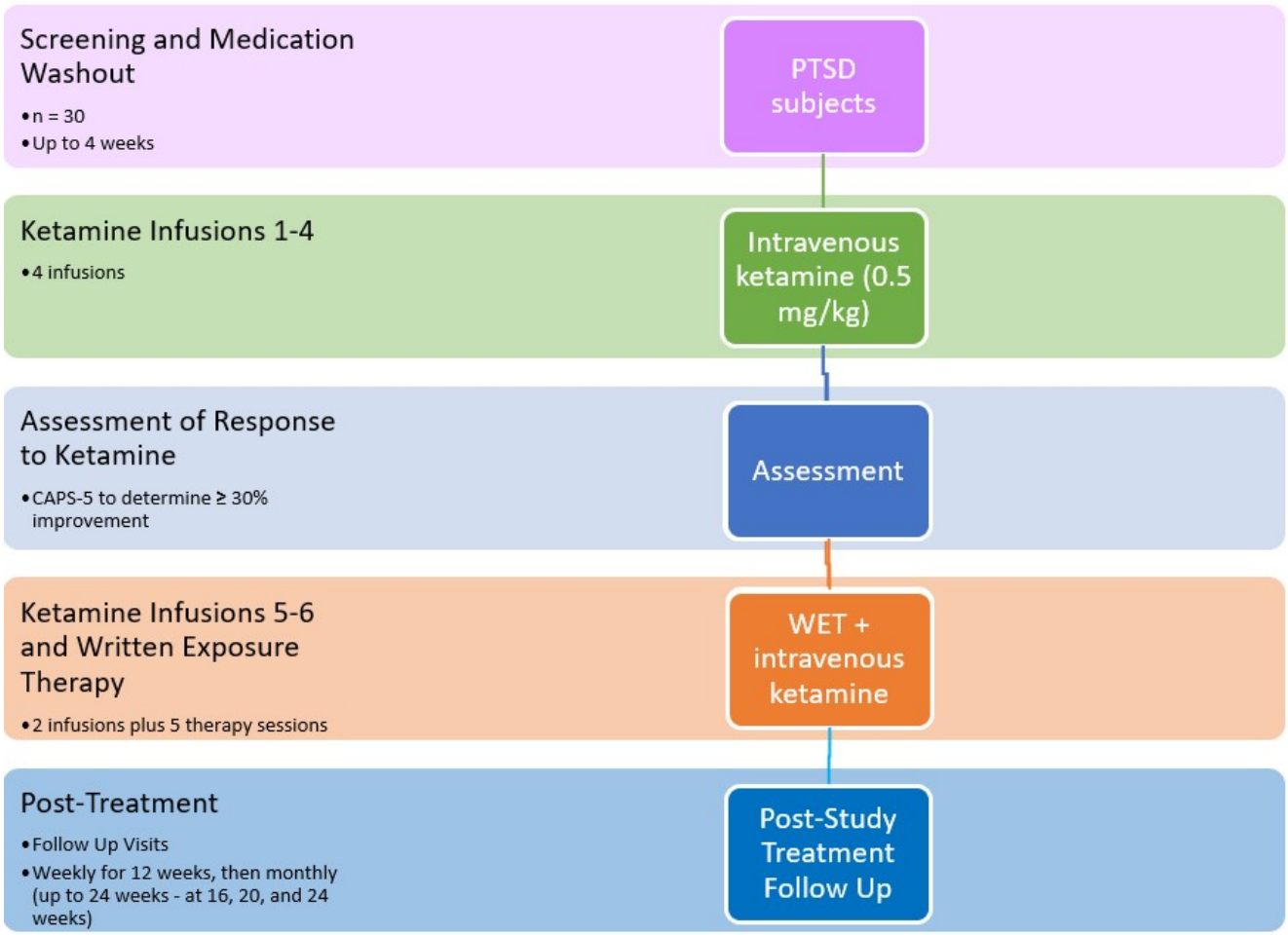
The purpose of this research study is to study new ways to treat post-traumatic stress disorder (PTSD). Treatments for PTSD do not work for everyone and it can take time to determine whether a person responds to treatment. The purpose of this study is to evaluate the preliminary efficacy of adding Written Exposure Therapy (WET) to a course of repeated IV ketamine infusions in improving PTSD symptoms and maintaining symptom improvement in patients with chronic PTSD. WET is a form of therapy that has helped alleviate symptoms of PTSD. At higher doses, ketamine has been used for many years as an anesthetic for medical procedures and at lower doses may be an effective treatment in patients with major depression and PTSD. Ketamine given for PTSD is investigational, which means that the FDA has not approved the drug for treating this condition. In this study, the effects of adding WET to ketamine treatment will be evaluated, to see their combined effect on PTSD symptoms and how long this effect lasts.

If you choose to participate, you will be asked to:

- Complete a medical and psychiatric evaluation for the purposes of screening
- Receive six (6) repeated intravenous infusions of the study drug (ketamine)
- Receive five (5) WET sessions from a trained therapist
- Complete psychiatric tests before and after the infusions, weekly for 12 weeks after your first WET session, and then monthly up to 24 weeks after your first WET session

You will be compensated for your time, and there are no costs associated with participating in this study.

Your participation is expected to last approximately 27 weeks and involves at least 25 visits, and up to 30 visits depending on your treatment response. See below for a summary of the study flow:



The main risks to you if you choose to participate are acute ketamine side effects, discomfort from the questions asked during assessments, and loss of private information.

You may also benefit from participation in this research; it is possible that participation in this study may temporarily improve your PTSD and/or depressive symptoms. However, longer-lasting benefits after completing the study are not necessarily anticipated. It is possible that you might not respond to ketamine or WET, and thus not experience any benefit from participating in this research study. Even if you do not personally benefit, your participation in this study will help to provide more information about the treatment of PTSD.

Instead of participating in this research, your choices may include continuing the standard treatment for PTSD, which is determined by your psychiatrist based on your psychiatric symptoms and may include medication, psychotherapy, and possibly other treatments. The most common standard treatments for PTSD include talk therapy and oral medications such as selective serotonin reuptake inhibitors (SSRIs), which are antidepressant medications.

If you are interested in learning more about this study, please continue to read below.

STUDY PARTICIPATION:

You may qualify to take part in this research study because you have experienced a traumatic event and may suffer from PTSD.

Your participation in this research study is expected to last up to 27 weeks (slightly more than 6 months), depending on how you respond to the study treatments.

There are up to 20 people expected to take part in this research study at the Icahn School of Medicine at Mount Sinai (ISMMS).

Funds for conducting this research study are provided by the Icahn School of Medicine at Mount Sinai.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

DESCRIPTION OF WHAT IS INVOLVED:

If you agree to take part in this research study, here is what may be involved:

1. Medical and Psychiatric Evaluation (1 or 2 screening visits, total 5-6 hours):

Location: Depression and Anxiety Center at 1399 Park Avenue, New York, NY 10029, Clinical Research Unit at 1468 Madison Avenue, or Remotely

On the screening visit(s), you will meet with a psychiatrist and with other members of the research team at the Depression and Anxiety Center (DAC). During this part of the study, the investigator will ask detailed questions about your psychiatric and medical history. You will be given questionnaires that will involve a series of questions assessing symptoms of PTSD and depression, and a comprehensive diagnostic interview will be conducted as part of a full evaluation. In total, this first visit will take approximately 3-4 hours to complete.

Also during this screening visit, or when you return to DAC for a second screening visit if necessary (usually within a week of the first screening visit), you will complete a medical evaluation. Blood (about 4 teaspoons; 18 ml) and urine samples will be obtained for various medical tests (blood cell count, liver function, thyroid function, others). All subjects will be tested for the presence of drugs of abuse in their urine. If any of the test results are positive you will not be able to be a part of this study, but can receive other clinical care by your treating psychiatrist. In addition, your blood will be screened for Hepatitis B and C, as the presence of these viruses can also make it unsafe for you to participate in the study. An electrocardiogram (ECG), a commonly used machine that records heart electrical activity by placing sticky pads on the chest, will also be performed. This procedure takes about 5 minutes, and is administered to help identify individuals that have abnormal activity in their heart.

After you have completed the psychiatric evaluation and medical screening, the study psychiatrist will review the results of your medical tests and you will be notified if you continue to qualify for the study. Please note that if the research team finds that you not eligible after the medical tests, you will not complete the other parts of the study.

Before enrolling in the study, you will be asked to complete a Treatment Contract. In the Treatment Contract you will be asked to identify a doctor, family member or friend who is aware of your participation in this research study and who is willing to be a part of your support system. The Treatment Contract also outlines coping skills and things you can do when you are feeling depressed or anxious. The study psychiatrist may contact the person(s) who have agreed to act as your support system in the case that your symptoms worsen during the study or in case there is an emergent medical issue that requires immediate contact. You will be given a copy of this Treatment Contract for your records.

You will not qualify to continue in the study if the psychiatric evaluations show that you do not have the type of illness that we are studying (PTSD that is moderate or severe) or if you have other psychiatric problems that might make it dangerous for your participation. You will also not qualify to continue in the study if the medical evaluations or blood tests show that it might be dangerous for you to participate because you have medical problems. Finally, you will not qualify to continue in the study if you cannot complete the treatment contract.

Medication Taper
After the screening visit(s), if you are currently taking any medications that cannot be taken during this study (this includes for example opioid pain medications), the study psychiatrist, in consultation with your private physician, will decide if it is safe and appropriate for you to stop taking these medications. The study psychiatrist will discuss with you which medications are not allowed. If you are taking medications for your PTSD and/or depression, you will only stop taking these if they are not helping to relieve your symptoms and you want to discontinue treatment. Some medications, for example antidepressants, can be continued during the study as long as you have been taking these medications at the same dose for at least three months before starting the study. Long-acting benzodiazepines (e.g., clonazepam, diazepam) may not be taken for two weeks prior to the first infusion, and during the study treatment period. Short-acting benzodiazepines (e.g., alprazolam, lorazepam) can be continued if only taken at bedtime. If you take any type of benzodiazepine in the daytime, you may not participate in the study unless you are able to taper off the medication with your personal physician or psychiatrist.

If it is determined that it is safe and appropriate for you to stop taking any medications that are not allowed during the study, then you will begin a period during which you will be gently "tapered off," or taken off these medications. The length of this period will vary depending upon the type and dose of medications that you are taking. Your personal physician will monitor your progress throughout the medication taper, in consultation with a study psychiatrist. If your personal physician or psychiatrist feels that your condition has significantly worsened without these medications, you will be withdrawn from the study and your participation will end. You will receive recommendations about the treatment that is decided to be the most appropriate for you from your physician or psychiatrist, in consultation with a study psychiatrist.

You will not be able to begin taking a new sleep medication during the study.

Drug-Free Period
Following the medication taper, you will be required to be free of any of the medications that are not allowed in this study for a period of 2 weeks. If you were not taking medication and did not require a taper, you will proceed directly to the intravenous infusions described below.

2. Administration of study medication:

If you continue to meet study criteria the morning of the first infusion, you will receive the first intravenous infusion of ketamine. Our goal is to have first infusions take place on a Monday, second administrations on a Wednesday and the third administration on a Friday. In the event of holiday or scheduling difficulties, it is possible that you would receive 2 infusions on consecutive days (i.e., Tuesday, Thursday, Friday). You will never receive 3 infusions on 3 consecutive days. You will receive a total of 6 infusions over a period of 2 weeks, each preceded and followed by clinical assessments, and 5 sessions of WET beginning the day after the fourth infusion. The total combined treatment will be delivered over a period of approximately 3 weeks.

All infusion procedures and monitoring will take place at the Mount Sinai Clinical Research Unit (CRU) or the Psychiatry Infusion Suite. You will arrive at Mount Sinai at 7:30 am on a Monday after an overnight fast for solid food and non-clear liquids. All procedures will be performed in a private, quiet room.

You will be admitted to the CRU or the Psychiatry Infusion Suite the morning of each study treatment. On the morning of each scheduled ketamine infusion, careful monitoring will be started, including continuous monitoring of blood pressure, heart rate, and breathing rate. You will also need to provide a urine sample as all subjects will be tested for the presence of drugs of abuse in their urine. If you are a woman of child-bearing age, your urine will also be tested for pregnancy. One IV line will be placed by a registered nurse, and you may receive oxygen through your nose. At 11:00 am you will receive intravenous infusion of 0.5mg/kg of ketamine (total dose) over 40 minutes. If you are unable to tolerate the infusion, you will be withdrawn from the study and your participation will end. Immediately and at 120 minutes following the infusion, you will be repeatedly assessed by means of clinician-administered and self-report rating scales.

During the infusion procedure you will be closely monitored by a study physician. You will also be monitored for a total of 2 hours afterwards by CRU staff and/or by study staff and a study psychiatrist. At 40 minutes and 120 minutes after the start of the intravenous infusion, you will be asked questions that check for possible side effects of the drug you are receiving. Also, on the first infusion day only, a small amount of blood (1-2 tablespoons) will be collected before the infusion and at 30 minutes, 60 minutes, 90 minutes, and 120 minutes after the start of the infusion to determine how much ketamine or midazolam has entered your blood stream. No tests other than those authorized will be performed on the blood sample. After at least a 2-hour monitoring period and a check of vital signs, you will be discharged from the CRU or the Psychiatry Infusion Suite. The earliest time that you will be discharged is 130 minutes after the start of the infusion (90 minutes after end of infusion), consistent with current post-anesthesia clinical practice. You will be asked to have a family member or friend drive you home, or accompany you home by taxi or public transportation, or will be offered car service to get home. You will be instructed not to take public transportation on your own on the day of discharge from the CRU or the Psychiatry Infusion Suite. If the study psychiatrist identifies the presence of any significant and problematic side effects, you may be further monitored until 5:00 pm. If there is additional need for monitoring after 5:00 pm, you will be admitted to the Mount Sinai ED, after which you will be exited from the study.

3. Written Exposure Therapy Sessions:

You will also complete Written Exposure Therapy (WET), which consists of five (5) sessions completed over a span of 2 weeks. WET sessions will begin after you have completed the first four ketamine infusions. All sessions will be administered by a trained therapist remotely (via telehealth). The first session will require one hour of time, and the remaining four sessions will require approximately 40 minutes per session. During each session, you will be asked to complete a writing exercise related to your trauma, for 30 minutes, following instructions provided by the therapist. The first 2 WET sessions will be scheduled on days that alternate with your last 2 ketamine infusions, and you will complete the last 3 WET sessions over the week following your last infusion.

The written narratives that you provide as part of the WET sessions will be collected by the study team and/or study therapist. The narratives are a necessary part of treatment and are used to ensure that the instructions for each writing session are followed. We will ask you not to provide your name or identifying information on the narratives, and will collect the narratives securely (i.e., uploading a picture to the secure REDCap database, uploading a scanned copy to the secure REDCap database, or delivering the hard copy of the narratives by mail or in-person).

4.Extinction Learning Task:
This task involves an online game that measures how people learn to change their expectations. The game takes about 15 minutes total each time. The game will be played on a computer. This game will be completed at screening and again on the day after the fourth ketamine infusion.

5.Follow-Up Assessments:

In addition to the visits for intravenous ketamine infusions, following the first intravenous infusion you will be asked to connect with the study team remotely (via telehealth) 24 hours later for a follow-up assessment. We will ask you questions about the severity of your PTSD symptoms, mood and anxiety level to see if anything has changed since the infusion.

All individuals who complete the study interventions (six ketamine infusions and WET sessions) will be asked to complete weekly assessments for 12 weeks after the first WET session, and then monthly for up to 3 additional months. Each of these assessments will require no more than 2 hours of your time, and we will ask you questions about the severity of your PTSD symptoms and mood and anxiety level.

Because this research study involves the use of a study drug, a note must be included in your electronic medical record that you are taking part in the research. This way, anyone involved in your medical care will know that you are a study participant, and they can work to avoid any problems or negative outcomes that could arise if they do not know.

Pregnancy

If you can possibly get pregnant, a urine test for pregnancy will be done before you begin the study and the pregnancy test will be repeated on the morning of each infusion.

You cannot be included in the study if you are or become pregnant, as the study drug could harm your fetus. You also should not be in the study if you are producing milk to feed a child as the study drug could harm your baby.

Unless you are at least one year past menopause or have had a successful operation to make pregnancy impossible, you should use effective birth control. Unless you are sexually abstinent (not having genital sex) the recommended methods of birth control are:

- The consistent use of approved hormonal birth control (pill, patches, or rings),
- An intrauterine device (IUD),
- Contraceptive injection (Depo-Provera),
- Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam),
- Sexual abstinence (no sexual activity),
- Sterilization (a vasectomy, getting tubes tied, or a hysterectomy).

All birth control methods (other than abstinence and sterilization) are only effective if you use them properly, start them at least one month before you begin the research study, and continue using them throughout the research study and for one month after the research study ends. If you are unsure whether the method of birth control you use is approved to use while you are in this study, you should ask the Lead Researcher before you begin the study. If you are less than one-year post-menopausal, you could still become pregnant. If you or your partner becomes pregnant, or may be pregnant, at any time throughout the study you must tell a person from the research team immediately. The team may stop the study drug and refer you/your partner to an obstetrician/gynecologist for follow-up.

Should you/your partner become pregnant, whether or not you/your partner have the baby, the people funding and overseeing the research may ask for information on the pregnancy, even if you are no longer part of the study. You/your partner will be asked for additional written consent to share this information if that happens.

Semen/Sperm:

Drugs can be found in semen and alter sperm. Since you are taking part in a study using experimental drugs or treatments, it is recommended that 1) you use a condom, 2) you do not get a partner pregnant or expose them to semen, and 3) you do not donate semen. These recommendations apply both while you are taking the study drug, and for 3 months after you stop taking the study drug This is because levels of the study drug may be present in the sperm and/or semen even after you stop taking the study drug. You are encouraged to tell your female partner(s) and/or their doctor(s) that you are participating in this clinical trial.

Future Contact:

The researchers may wish to use your personal contact information to contact you in the future. Do you give the researchers permission to **contact you** in the future to request the collection of additional information about you, discuss how your private information, study data and/or samples might be used, or discuss possible participation in another research study?

Please initial your choice: Yes_____ No_____

If “Yes”, please indicate your preferred method of contact: (initial all that apply)

[ ] Email [ ] Phone [ ] Letter [ ] Text

USE OF YOUR DATA AND/OR SAMPLES:

The researchers would like your permission to keep the data collected from you during this study to use or share in future studies. You can still be part of the study if you do not allow us to use or share them. Please select Yes or No to each of the questions below. To decline all future uses/sharing please select ‘No’ each time.

(1) Will you allow the researchers to store your data and/or samples to use in future research studies?

Please initial your choice: Yes_____ No_____

If you select No, please stop here and move to the next section, **'Your Responsibilities If You Take Part in This Research'** section below."

If yes, please continue to the next question and tell us how your personal information, study data and/or samples may be used in future research studies.

(2) The researchers can store your data and/or samples in one of two ways:

a) Anonymously (no one will know who the data and/or samples came from). If you choose this option, you can't change your mind. So, if you wanted to have your data and/or samples destroyed in the future, the team could not do it as they would not know which data and/or samples were yours.
b) Linked to your identity (using a code that can show the information came from you personally). In this case you could ask for your data and/or samples to be destroyed in the future if you want that to happen.

How would you like your data and/or samples stored? Please initial **ONE** choice below:

I would like my data and/or samples stored anonymously _____

I would like my data and/or samples stored with a link to my identity through the use of a code_____

(3) Do you give the researchers permission to keep the data and/or samples, so they could use them in future studies that are **directly related** to the purpose of the current study?

Please initial your choice: Yes_____ No_____

(4) Do you give the researchers permission to keep the data and/or samples indefinitely, so they could use them for future studies that are **not related** to the purpose of the current study (for example a different area of research)?

Please initial your choice: Yes_____ No_____

(4.1) From time to time, researchers outside of medicine and related sciences would like to use data and/or samples. This might be in the fields such as anthropology, human origins, mapping human migration patterns. Do you give permission for researchers **outside the field of medicine** to use your data and/or samples?

Please initial your choice: Yes_____ No_____

a. If the future research in a different area can be done without having to know that the data and/or samples came from you personally, that will be done.
b. If the future research in a different area requires that it is known specifically who the data and/or samples came from, then one of the following will be done:

I. If you allowed the researchers to contact you in the future, they may be able to contact you to explain why your data and/or samples is needed and what will be done with it. Your permission will be asked to use your data and/or samples in that research project.
II. If you do not give permission to be contacted in the future, or if it is found that contacting you is not practical (for example, because you have moved), your data and/or samples may still be used. The Institutional Review Board (IRB) will be asked for permission to use the data and/or samples linked to your identity. The IRB can give permission for researchers to use and share identifiable health information without contacting you, but only if it determines that sharing the data and/or samples will not be more than minimal risk to you or your privacy. The IRB is a committee of doctors and scientists and nonscientists, including people not associated with this hospital or medical school, whose job it is to protect people who participate in research.

(5) Do you give permission to have your data and/or samples given **to other researchers,** including those at Mount Sinai, other medical or scientific institutions and for-profit companies, for use in research within the limits you have chosen above?

Please initial your choice: Yes_____ No_____

(6) Do you give permission to have portions of your data and/or samples deposited in large public databases (repositories) for use in research with the limits you may have chosen above? Please read the paragraphs below which explains repositories, then initial your choice:

To do more powerful research, it is helpful for researchers to share data and/or samples from the people they study. They do this by putting data and/or samples into a repository. A repository is where something is stored safely for a specified period of time. Data and/or samples from one study may be stored in a repository along with data and/or samples from other studies. Sample repositories are commonly called biobanks, while data repositories are commonly called databases. . Researchers can then use the data and/or samples from multiple studies to learn even more about health and disease. If you agree to take part in this study, some of your genetic and health information might be placed into one or more scientific databases, but they will not share your direct identifiers (for example, name, address, date of birth). These databases are maintained by either Icahn School of Medicine at Mount Sinai, another institution, the federal government, or private companies. Any researcher who wants to do a study using data and/or samples from the repository must apply for permission. There are different ways of reviewing such requests. Researchers with an approved study may be able to see and use your data, along with that from many other people. Researchers may use your samples for genetic sequencing and other experimental testing. Researchers will always have a duty to protect your privacy and to keep your information confidential, but there are always risks associated with data and/or sample collection and sharing. They are described in more detail in the Risks section.

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study, you will be responsible for the following things: **using birth control methods as described in the Description of What's Involved section, avoiding certain medications, and punctual attendance of study visits.**

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

If you agree to take part in this study, you will be paid up to $880 for your time and effort. *Your check will be initiated following each week of completed study visits.* Post-treatment follow-up visits are compensated $25 per visit and the total compensation due is contingent on the length of the follow-up period. **If you are unable to complete the entire study, the payment will be prorated for the part you have completed.**

Procedure	Reimbursement
Screening:	
Screening visit 1 (interview)	$50
Screening visit 2 (medical clearance)	$25
Extinction Learning Task (remote)	$10
Ketamine Infusions and Assessments:	
First ketamine infusion day	$75
24-hour follow up	$10
Second infusion day	$50
Third infusion day	$50
Fourth infusion day	$50
Ketamine responder Determination Assess.	$35
Start of Therapy Sessions (WET):	
Fifth infusion day	$50
Sixth infusion day	$50
Assessments (for 12 weeks, and after that depending on your treatment response):	
1-week Assessment	$25
2-week Assessment	$25
3-week Assessment	$25
4-week Assessment	$25
5-week Assessment	$25
6-week Assessment	$25

7-week Assessment	$25
8-week Assessment	$25
9-week Assessment	$25
10-week Assessment	$25
11-week Assessment	$25
12-week Assessment	$25
16-week Assessment	$25
20-week Assessment	$25
24-week Assessment	$25
Total – up to 12 weeks	$755
Total for participation in all parts of the study, if all follow-up visits are needed	$830

It can take up to 6 weeks to prepare and give you a check for study participation. If you do not get a check by then, you can first contact the research team. If further assistance is needed, please contact Mount Sinai's Program for the Protection of Human Subjects at (212) 824-8200.

Tax law may require the Mount Sinai Finance Department to report the amount of payment you receive from Mount Sinai to the Internal Revenue Service (IRS) or other agencies, as applicable. Generally, this happens if you receive payments that equal $600 or more from Mount Sinai in a calendar year. You would be responsible for the payment of any tax that may be due.

POSSIBLE BENEFITS:

There is a chance this study may benefit you, but this is not guaranteed. Others may benefit from what researchers learn from the study. Possible benefits to you include: temporary improvements in your PTSD and/or depressive symptoms However, longer-lasting benefits after completing the study are not necessarily anticipated. There is no firm evidence that you will respond to ketamine and/or WET and thus it is possible that you will not experience any benefit from participating in this research study. Even if you do not personally benefit, your participation in this study will help to provide more information about the treatment of PTSD.

POSSIBLE RISKS AND DISCOMFORTS:

1. Physical risks:

Risks of IV insertion and blood draw: The risks IV insertion and of blood draw include pain, bruising, and the slight possibility of infection at the place where the needle goes in. Some people feel dizzy or may faint during or after a blood draw.

Acute ketamine side effects: Ketamine has been determined to be safe for use as an anesthetic agent. Over the past several decades, ketamine has been administered as an anesthetic to several million adults and children and has a favorable safety profile overall. Ketamine may produce mild to moderate increases in blood pressure and heart rate, and performance. Additionally, some patients report dizziness or nausea. Ketamine may also cause an impairment of supply of blood to the heart in patients with underlying coronary artery disease. Five to 30% of subjects who receive ketamine may experience changes in their perceptions such as vivid dreaming, temporary visual changes, visualization of psychedelic color, feeling of suspension in space, and out-of-body experiences. Some patients report these experiences as bizarre or frightening, while others describe them as pleasurable, joyful, or fascinating. When such reactions occur, they are usually mild and brief. Studies suggest that these sensory effects of ketamine are usually short-lasting (less than 60 minutes) and rarely last longer than 2 hours. These sensory effects appear more commonly in those with preexisting psychosis (schizophrenia), which is why patients with a history of psychosis are excluded from the study.

2. Psychological risks associated with clinical interviews:

During the clinical interviews, you may become tired or upset about the questions. If this happens, you should tell the interviewer/study personnel and he/she will stop the examination. Depending upon how you feel, you may then 1) take a rest period and resume later, 2) reschedule for a later appointment or 3) decide not to finish the exam.

3. Privacy risks:

Risk of loss of private information; this risk always exists, but there are procedures in place to minimize the risk.

Your name and other information that could directly identify you (such as address, date of birth or social security number) will never be placed into a scientific database. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small, but may grow in the future. Since the database includes genetic information, a break in security may also pose a potential risk to blood relatives as well as yourself. For example, it could be used to make it harder for you (or a relative) to get or keep a job or insurance. If your private information was misused it is possible you would also experience other harms, such as stress, anxiety, stigmatization, or embarrassment from revealing information about your family relationships, ethnic heritage, or health conditions.

The Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.

• Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Group Risks - *Although your name will not be given to researchers, basic information such as your race, ethnic group, and sex may be shared. This information helps researchers learn whether the factors that lead to health problems are the same in different groups of people. It is possible that such findings could one day help people of the same race, ethnic group, or sex as you. However, they could also be used to support harmful stereotypes or discrimination.*

4. Pregnancy risks:

If you are or become pregnant, this research may hurt your baby or your pregnancy in ways that are unknown. The unknown risks might be minor or might be major (death) for the pregnancy. You should not become pregnant or impregnate a woman while on this research study. Please read the acceptable methods of birth control found under the Description of What's Involved section of this document.

5. Increased risk of suicidal thoughts and actions:

Antidepressant medicines may increase suicidal thoughts and actions in some people 24 years of age and younger, especially within the first few months of treatment or when the dose is changed. We do not expect this to occur, and in fact ketamine has been shown to reduce suicidal thinking in certain patients. However if the following should occur: suicide attempts, worsening depression, thoughts about suicide or dying, or other unusual changes in behavior or mood please contact the principal investigator immediately.

OTHER OPTIONS TO CONSIDER:

You may decide not to take part in this research study. If you decide not to take part, this will not affect the clinical care you receive at Mount Sinai. The choice is totally up to you. Instead of being in this research study, your choices may include continuing the standard treatment for PTSD, which is determined by your psychiatrist based on your psychiatric symptoms and may include medication, psychotherapy and possibly other treatments. The most common standard treatments for PTSD include talk therapy and oral medications such as SSRIs like sertraline. The benefits of these treatments are that talk therapy has few side effects and therefore limited risk. Also, the benefits of SSRIs like sertraline, is that they have been shown to be useful in a wide variety of patients with PTSD, and have been used widely, so the side effects are well understood. These options are also available outside of a research context. However, **the important risk of these alternatives is the possibly limited and slower effect of these standard treatments on the symptoms you are suffering from. In addition, no matter what treatment you receive, you will be exposed to the specific side effects of that treatment.**

IN CASE OF INJURY DURING THIS RESEARCH STUDY

If you are injured or made sick from taking part in this research study, you will get medical care. Generally, it will be billed to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, copayments, and coinsurance. This does not prevent you from seeking payment for injury related to malpractice or negligence. You can contact the Lead Researcher for more information.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this study at any time. No matter what you choose, your care and benefits through Mount Sinai will not be negatively impacted.

If you decide to stop being in the study, please contact the Lead Researcher or the research staff.

You may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page. Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected if that information is necessary to complete the research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.
If you decide you don't want your samples and/or data to be used for research anymore, you can contact the researcher and ask to have your samples and/or data removed from future use. If any samples or data have already been shared without your identity, it won't be possible to retrieve them because no one will know who you are. Samples and data that have already been used will not be affected by your decision. Any samples and/or data that are still linked to your identity by a code the researcher has will be withdrawn so that no future sharing of your samples and/or data will take place. If your samples have already been deposited in an external repository, the study team will request that your samples be removed.

Withdrawal without your consent: The Lead Researcher, the funder or Mount Sinai may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the research team have not been followed, the Lead Researcher believes it is in your best interest, or for any other reason. If data and/or samples have been stored as part of the research study, they too can be destroyed without your consent.

CONTACT INFORMATION:

If you have any questions, concerns or complaints at any time about this research, or you think the research has harmed you, please contact the office of the research team and/or the Lead Researcher at phone number 212-585-4670.

If there is an emergency, please call 911 or go to the emergency room. Let the emergency room staff know you are in a research study so they can contact the Lead Researcher if needed.

DISCLOSURE OF FINANCIAL INTERESTS:

Researchers sometimes get paid for consulting or doing work for companies that produce drugs, biologics or medical devices. If you have questions regarding industry relationships, you are encouraged to talk to the Lead Researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

Dr. Dennis Charney (Dean of Icahn School of Medicine at Mount Sinai) and Dr. Adriana Feder (the Principal Investigator on this study) are named co-inventors on a patent application filed by Mount Sinai for the use of ketamine as a therapy for post-traumatic stress disorder (PTSD, a type of anxiety disorder). At the current time, the medical school is seeking a licensing agreement with a pharmaceutical company in order to develop ketamine as a therapy for PTSD.

In addition, Dr. Charney is a named co-inventor on several issued U.S. patents, and several pending U.S. patent applications filed by the Icahn School of Medicine at Mount Sinai (ISMMS) related to pharmacologic therapy for treatment-resistant depression, suicidal ideation and other disorders. ISMMS has entered into a licensing agreement with Janssen Pharmaceuticals, Inc. and it has and will receive payments from Janssen under the license agreement related to these patents. As a coinventor, Dr. Charney is entitled to a portion of the payments received by the ISMMS. Since SPRAVATO (esketamine) has received regulatory approval for treatment-resistant depression, ISMMS and Dr. Charney as its employee and a co-inventor, will be entitled to additional payments, under the license agreement.

One or more researchers has a financial interest that could be affected by the outcome of this research study.

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MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As part of this study, some of your private and/or protected health information will be obtained, used, and shared with your permission. There is a Federal Health Insurance Portability and Accountability Act (HIPAA) that makes sure this is done correctly and safely.

<u>What is protected health information (PHI)?</u>
PHI is the combination of two things:

1. PHI contains information that identifies you. It will be used to contact you and link you to your health information, like name, date of birth, medical record number, and address.
2. PHI also contains health information, including information about your mental and physical health from your visits to doctors or hospitals, or from study visits.

Every time you visit a hospital or your doctor, PHI is created and recorded in your medical record by your healthcare providers. In the same way, the PHI created as part of this study will be linked to who you are and your medical information.

<u>What PHI is collected and used in this research study, and might also be shared with others?</u>

As part of this study, the research team at the hospital(s) involved in the research will collect your name, address, telephone/fax numbers, dates directly related to you as an individual (birth, admission, discharge, date of death, etc.), e-mail addresses, social security number, medical records number.

During the study, the researchers will gather information by:

- Reviewing and/or taking your medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- Doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate, and temperature.
- Completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.
- Reviewing narratives and therapist notes from the Written Exposure Therapy sessions conducted as part of this study

Why is your PHI being used?
Researchers need the information that identifies you so they can contact you during the study. They need your health information and the results of any tests and procedures being collected as part of this study to answer the questions posed in the study. The purpose of the study is discussed earlier in this consent form. Before researchers analyze the data, they remove any information that would let others know who you are or that you took part in the study. If researchers publish or present study results at scientific meetings, lectures, or other events, their presentations would not include any information that would let others know who you are, unless you give separate permission to do so.

The Lead Researcher may also use and share the results of these tests and procedures with other healthcare providers at Mount Sinai who are involved in your care or treatment. The research team and other authorized members of The Mount Sinai Health System ("Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example:

- The Mount Sinai Program for the Protection of Human Subjects is responsible for overseeing research on human participants and may need to see your information.
- If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.
- I*f the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.*

Who, outside Mount Sinai, might receive your PHI?
As part of the study, the Lead Researcher, research team and others in the Mount Sinai workforce may disclose your PHI, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Lead Researcher.)

- The United States Department of Health and Human Services (DHHS) and the Office of Human Research Protection (OHRP) (the government organization that is responsible for protecting human research participants).
- Outside laboratory who will be performing laboratory analysis for all the research centers involved in this project: LabCorps
- A Data Safety Monitoring Board or other committee that will monitor the study on an ongoing basis for safety.
- The United States Food and Drug Administration.

In almost all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier. Some records and information disclosed may be identified with a unique code number. The Lead Researcher will ensure that the key to the code will be kept in a locked file or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the Institutional Review Board (IRB) allows it after determining that there would be minimal risk to your privacy. The Certificate of Confidentiality obtained from the Department of Health and Human Services will not be used to prevent disclosure to local authorities of child abuse and neglect, or harm to self or others. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, may come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, *OHRP, as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. OHRP and FDA are authorized to remove information with identifiers if necessary to complete their task. By signing this document, you are authorizing this access.* The results of this research may be published. However, your name and other identifying information will be kept confidential.

For how long will Mount Sinai be able to use or disclose your PHI?
Your authorization for use of your PHI for this specific study does not expire.

Will you be able to access your records?
During your participation in this study, you will have access to your medical record and any study information that is part of that record. The research team is not required to release research information to you that is not part of your medical record.

Do you need to give the researchers permission to obtain, use or share your PHI?
NO! If you decide not to let the research team obtain, use or share your PHI, you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment, or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?
If you decide to stop being in the study, please contact the Lead Researcher or the research staff.
The research team may ask you whether they can continue to collect information from your medical record. You will also have to decide if you wish to limit the continued use of the information collected

during the study. Under US privacy laws you may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page.

Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected, but only to complete this research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.

If you have not already received it, you will also be given The Hospital's Notice of Privacy Practices that contains more information about how The Hospital uses and discloses your PHI.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If researchers are reviewing your medical records or asking questions about your medical history or conditions, it is possible that they may learn information related to your HIV status. If that is the case, the following information concerns you. If researchers are not reviewing your medical records or asking questions about your medical history or conditions, then you may ignore the following section.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 306-5070. These agencies are responsible for protecting your rights.

Certificate of Confidentiality: To further protect your privacy, the researchers have obtained a Certificate of Confidentiality from the Department of Health and Human Services. This is intended to ensure that your identity as a participant in this research study will not have to be disclosed as a result from a subpoena, for the purpose of identifying you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings other than to the FDA or OHRP as identified above.

The research staff will not share any of your personal information, study data and/or samples with anyone who is not a member of the research team, including any family members or friends, other than those identified above. However, you should know that if it is learned that you or someone else is threatened with serious harm, such as a child or an elderly person being abused, the research team may notify the appropriate authorities if necessary to protect you or others. A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information

about yourself or your involvement in this research. This means that you and your family must also actively protect your own privacy. If an insurer or employer learns about your research participation, and you agree that they can have your research information, then the researchers may not use the Certificate of Confidentiality to keep this information from them.

How the Institutional Review Board (IRB) can help you:

This research has been reviewed and approved by an Institutional Review Board (IRB). You may reach a representative of the Mount Sinai Program for Protection of Human Subjects at telephone number (212) 824-8200 during regular work hours (Monday-Friday, 9am-5pm, excluding holidays) for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

ADULT PARTICIPANT:
Your signature below documents your permission to take part in this research study and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

_____	_____	_____	_____
Signature of Participant	Printed Name of Participant	Date	Time

PERSON EXPLAINING STUDY AND OBTAINING CONSENT:

_____	_____	_____	_____
Signature of Consent Delegate	Printed Name of Consent Delegate	Date	Time

WITNESS SECTION:
My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant, and that consent was freely given by the participant.

_____	_____	_____	_____
Signature of Witness	Printed Name of Witness	Date	Time