

URCC 07004: Assessment of Topical Treatment Response with Amitriptyline and Ketamine: Combination Trial in Chemotherapy Peripheral Neuropathy (ATTRACT-CPN)

Fast Facts

Inclusion Criteria

1. Male or female 18 years of age or older with a history of cancer.
2. Pain, numbness or tingling in the hands or feet beginning in association with a cancer chemotherapy agent (taxane or other chemotherapeutic agent) and persisting for at least 28 days following the conclusion of the chemotherapy. Pain, numbness or tingling can be assessed 28 days or more after the conclusion of chemotherapy.
3. An average score of ≥ 4 for the 7 daily ratings of the screening (baseline) week on the 11-point rating scale of peripheral neuropathy associated with chemotherapy, with a minimum of 5 daily diary ratings completed during the baseline week.
4. Karnofsky performance status of ≥ 60 .
5. Subjects who are currently taking opioid analgesics, tricyclic or dual reuptake inhibitor antidepressants, gabapentin, or pregabalin for their CPN, or benzodiazepines for sleep, should have been maintained at a stable dosage for at least 2 weeks before the screening assessment and must be maintained at these same dosages throughout the trial. Gabapentin will be limited to 1800 mg per day, pregabalin to 300 mg per day, opioid analgesics to 60 mg of oxycodone equivalent, tricyclic antidepressants to 75mg amitriptyline equivalent, duloxetine to 60 mg daily, venlafaxine to 150 mg daily, and tramadol to 200 mg daily. Narcotic equivalents are noted in the Table on page 10 of the protocol.
6. Adjunctive analgesic therapy such as acupuncture, biofeedback, or herbal preparations should have been established at least 2 weeks before the screening visit and must remain unchanged throughout the study period.
7. Subjects must provide written informed consent.
8. Subject has adequate understanding of the English language.

Exclusion Criteria

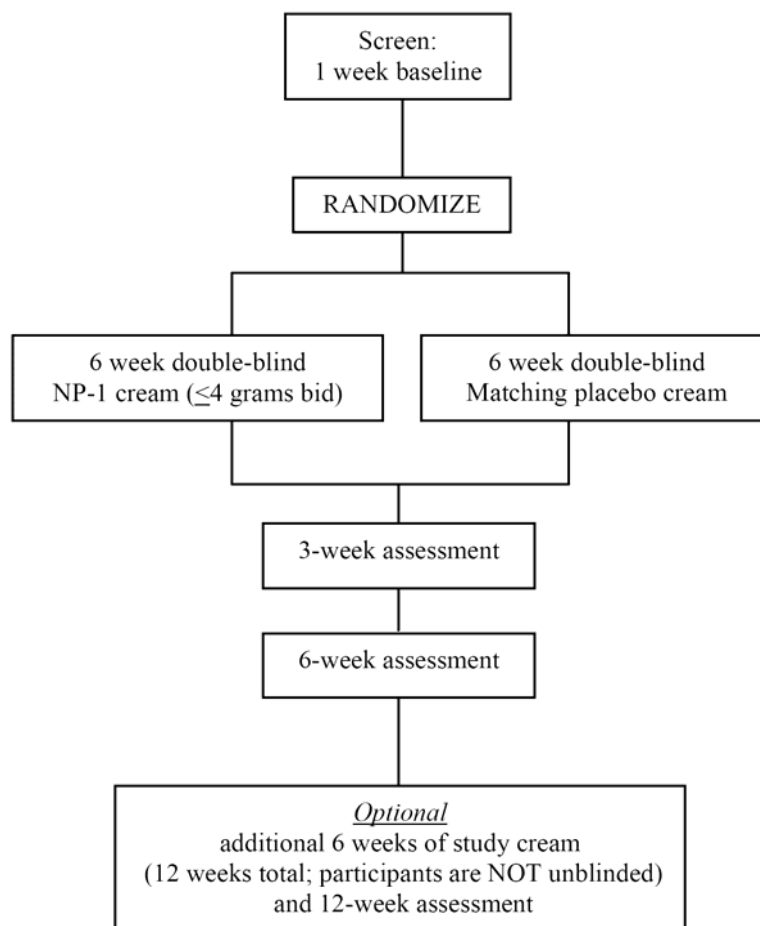
1. Allergy or hypersensitivity to ketamine or amitriptyline or any of the components of the NP-1 cream.
2. Pre-existing or history of peripheral neuropathy due to any cause other than chemotherapy, such as hereditary condition, alcohol or diabetes.
3. Clinically significant intercurrent illness (e.g., endocrine, cardiac, hepatic, renal, neurologic, hematologic, skeletal) that, in the investigator's clinical judgment, could interfere with the efficacy or safety assessments in this study.
4. Patients currently receiving active chemotherapy in the adjuvant setting or for progressive systemic disease. Subjects with stable systemic disease and/or bone involvement per investigator's assessment AND have not received chemotherapy within 3 months of the screening assessment are eligible for participation. Patients receiving ongoing treatment with non-chemotherapy agents such as monoclonal antibodies or hormonal treatment are eligible to participate in this study.
5. Use of any topical treatment, nerve blocks, implantable therapy, or peripheral nerve or spinal cord stimulation, and neurosurgical procedure for CPN.
6. Subjects suffering from glaucoma or recurrent urinary retention.
7. Subjects receiving an unapproved experimental drug or biological agent within 30 days of the screening visit.
8. Clinically significant depression or dementia that, **in the opinion of the investigator**, may interfere with a subjects' adherence to the study protocol and/or the accurate and consistent reporting of CPN.
9. Lack of adequate birth control in men or pre-menopausal women of child-bearing age and/or a positive urine pregnancy test.
10. Open skin lesions in the area where the cream is to be applied.
11. Treatment with SSRIs (e.g., fluoxetine, paroxetine, sertraline), which inhibit CP450 2D6, **unless** the patient is being treated for depression or another psychiatric disorder and in the investigator's judgment the patient's participation in the protocol can be permitted given the minimal systemic levels of amitriptyline found with NP-1 cream.

12. Treatment with monoamine oxidase inhibitors, barbiturates, anticholinergic agents, or sympathomimetic drugs, including epinephrine combined with local anesthetics. Use of oral inhalers that include any of these drugs is allowed.
13. A history of neuropathy due to a cause other than chemotherapy use (such as diabetes).
14. A creatinine >2 mg/dL obtained within 30 days prior to the screening assessment.

p. 4/28

Rev 10/08

STUDY SCHEMA



Participant completes written assessments at Screening, and 3 weeks, 6 weeks and (optional) 12 weeks on study medication. Assessments include a 7-day diary, the EORTC, BPI, HADS and Symptom Inventory.

Office visits occur prior to screening, at randomization, at 6 weeks and optional 12 weeks.

CRA contacts participant during Weeks 2, 5 and 11 to assess problems, including AEs, and remind participant to begin diary.