Protocol Title: A Phase II Study of Isatuximab (SAR650984) (NSC-795145) for Patients with Previously Treated AL Amyloidosis

Target Population: Primary Systemic Amyloidosis or Recurrent / Refractory Primary Amyloidosis

Summary: This phase II trial studies how well Isatuximab works in treating patients with Primary Amyloidosis that has come back or does not respond to treatment.

Key Eligibility Criteria:
- Patient must have Relapsed or Refractory Primary Systemic AL Amyloidosis, histologically-confirmed by + Congo Red stain with green by birefringence on polarized light microscopy, OR characteristic appearance by electron microscopy AND confirmatory AL Amyloid typing.
- Patient must have measurable disease within 28 Days prior to registration.
- Patient must demonstrate a difference in the involved serum free light chains (kappa or lambda) versus the uninvolved serum free light chain of ≥ 4.5 mg/dL within 14 Days prior to registration.
- Patient must have objective organ involvement defined by ONE (or more) of the following:
  - Kidney: Albuminuria ≥500 mg per day on a 24-Hour urine specimen within 35 Days prior to registration, OR prior kidney biopsy showing amyloid deposition
  - Heart: Mean left ventricular wall thickness on ECHO ≥ 12 mm in the absence of hypertension or valvular heart disease, OR NT-pro BNP > 332 ng/mL provided that patient does not have impaired renal function within 14 Days prior to registration, OR prior cardiac biopsy showing amyloid deposition with past documented or presently noted clinical symptoms and signs supportive of a diagnosis of heart failure in the absence of an alternative explanation for heart failure
  - Liver: Hepatomegaly demonstrated by CT or MRI within 35 Days prior to registration OR ALP > 1.5 x ULN within 14 Days prior to registration, OR prior liver biopsy showing amyloid deposition
  - Gastrointestinal Tract: Prior biopsy showing amyloid deposition AND symptoms such as GI bleeding or persistent diarrhea
  - Autonomic or Peripheral Nervous System: Orthostatic blood pressure, symptoms of nausea, early satiety, diarrhea or constipation, abnormal sensory and/or motor findings on neurologic exam, or gastric atony by gastric emptying scan
  - Soft Tissue: Macroglossia, or soft tissue deposits requiring therapy
- Patients must NOT have active symptomatic Multiple Myeloma, as defined by 2015 IMWG criteria.
- Patient must be relapsed or refractory to ≥ 1 prior line of therapy (i.e., transplant, radiation, or chemotherapy).
- Patients must not have received any or supplements which have been known to have some anti-amyloidogenic effect (i.e., Doxycycline, Curcumin, Prednisone, Dexamethasone, EGCG) within 14 Days prior to registration.
- Patients must not have any known allergies to Isatuximab or other monoclonal antibody therapies.
- Patients must not have received Daratumumab within 56 Days prior to registration nor have been refractory to Daratumumab.
- Patients must not be eligible for autologous stem cell transplantation.
- Patients must have bone marrow aspirate, including FISH and cytogenetic testing within 35 Days prior to registration.
- NT-proBNP ≤ 8500 ng/L within 14 Days prior to registration
- Patients must have a Zubrod Performance Status ≤ 2.

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For additional information: https://clinicaltrials.gov/ct2/show/NCT03499808