Trial Innovation Network Expression of Interest:
Post-CA Neuroprotection with Magnesium

Study Title	Neuroprotection following Cardiac Arrest: A randomized Control Trial of Magnesium
Funding I/C	R34, NIH, NHLBI
Study Description	We are proposing a double-blinded, multi-site feasibility studying the administration of magnesium (Mg), in addition to standard of care for cardiac arrest (CA), to adult patients who achieved return of spontaneous circulation (ROSC) following CA. We propose to use Mg therapy to target several key steps in the post-resuscitation period to help minimize excitotoxicity, mitochondrial dysfunction, oxidative damage, and neuronal cell death. By doing so, we hope to improve overall cardiac arrest survival but most importantly, to minimize functional and neurological disability due to cerebral ischemia. In this initial study, our primary objective is to evaluate the ***feasibility*** of implementing this approach in a real world setting. In addition, we further hypothesize that by using Mg therapy as neuroprotection in the post-resuscitation period, patients will have lower serum markers of neuronal injury, inflammation and oxidative damage, which would ultimately lead to improved long term survivorship and functional status.
Study Design	This is a double-blinded, multi-site, Phase 1 feasibility study to assess the ***feasibility and safety*** of administering magnesium as a neuroprotective medication in the post-cardiac arrest period. Eligible patients will be randomized into one of two groups: Treatment Group (4g IV bolus of Mg, followed by 16g drip IV Mg OR 4 more 4g IV boluses over 24 hrs) or Control Group (equivalent saline). We aim to identify at least 10-20 sites who can enroll apprixmately 4-8 patients each. Research staff will attend each CA as notified through their respective hospital paging system. Research staff will evaluate each CA patient for eligibility for enrollment into the study. If the patient meets the inclusion/exclusion criteria, the patient will be determined to be eligible for this study. This study has been approved for an exception from informed consent per 21CFR 50.24.
IRB	NYU Langone IRB will serve as the central IRB for all sites
Coordinating Center	NYU Langone Tisch Hospital
Study Length	3 years (90 days for participants), recruitment to end around March 2026
Study Enrollment #	Plan to enroll approximately 40 patients across all NYU Langone sites (NYU Langone Tisch, NYU Langone Brooklyn, NYU Langone Long Island, and Bellevue Hospital), and 4-8 patients at external sites
Eligibility Criteria	<u>Inclusion Criteria</u> 1) Age ≥18 ≤85 years 2) IHCA and OHCA 3) Non traumatic CA 4) Documented post-cardiac arrest patient with sustained ROSC (≥ 20 minutes) achieved <2 hours prior to recruitment 5) Patient who is unresponsive/unable to follow motor commands after ROSC 6) No plan for withdraw of life support within 72 hours of ROSC <u>Exclusion Criteria</u> 1) Patients < 18 years or 85 years of age 2) Traumatic CA 3) Unsustained ROSC 4) Patient who is responsive/able to follow motor commands after achieving ROSC 5) Plan for withdrawal of life support within 72 hours of ROSC after discussion with family and/or physicians 6) Known pregnant women at the time of the cardiac arrest 7) Known prisoners at the time of the cardiac arrest.
Total # of Sites	At *least* 10-20 sites
Site Requirements	<u>Study sites will need to have the following at their site to be considered:</u> • Research team capable of working with pharmacy and clinical team to administer the first dose of magnesium/placebo within 2 hours of ROSC • Site will permit conducting research under EFIC (Exception from Informed Consent) circumstances – please note that the coordinating site will assist external sites with EFIC requirements, such as community consultation and public disclosure

Site Invesitgator Qualifications	Site Invesitigators should have the following: • Must be able to be notified of cardiac arrests in real-time at their institution (i.e. paging system) • Should have a research team capable of assisting with checking patient eligiblty, randomization, coordination with pharmacy, data entry, and safety monitoring
Key Timeline Dates:	The following dates are projections and subject to change: **Site Selection Decisions**: 12/15/2024 **Site Selection Notifications:** 12/20/2024 **Enrollment begins:** 05/01/2025 **Last Patient/Last Visit:** 03/01/2026 **Study Closure:** 06/01/2026