Study Title	**PROpranolol TO Survive Traumatic Brain Injury**
Funding I/C	National Institute of Neurological Disorders and Stroke (NINDS)/ NIH SIREN Neurologic Clinical Trials (UG3/UH3)
Study Description	PROpanolol TO Survive Traumatic Brain Injury (PROTOS-TBI) is a randomized, multi-center, dose-finding clinical trial aimed at identifying the optimal dose of propranolol that maximizes benefits for moderate to severe traumatic brain injury patients by reducing in-hospital and post-discharge mortality while improving neurological functional outcomes. Propranolol may reduce the incidence of agitated delirium that often occurs after brain injury, thereby improving recovery. This study will randomize patients to three propranolol dosing arms versus standard of care. The primary outcome of the study will be the win ratio for the following composite outcome (observed in-hospital mortality, withdrawal of life support, GOSE at 3 months post discharge, and agitation-free days measured via Richmond Agitation Sedation Scale).
Study Design	The **PROTOS-TBI** trial is a phase 2, multi-center, randomized, dose-finding clinical study aimed at identifying the optimal propranolol dosing for patients with moderate to severe traumatic brain injury (TBI). The primary goal is to improve survival rates, reduce post-traumatic agitated delirium, and enhance neurological outcomes. • Patients will be randomized into three propranolol dosing arms or a standard care group. • Primary outcomes include a composite win ratio measuring in-hospital mortality, withdrawal of life support (WLST), GOSE at 3 months post-discharge, and delirium-free days (CAM-ICU or RASS assessments). • Enrollment will occur within 2 to 6 hours post-injury, with data collected on agitation and restraint-free days. • Part of the SIREN network, supported by the NIH, ensuring multi-site equity and comprehensive data analysis.
IRB	Central IRB : University of Minnesota
Coordinating Center	University of Minnesota/ TIN/ Vanderbilt University
Study Length	6 years
Study Enrollment #	210 patients

Eligibility Criteria	**Inclusion Criteria**
	• Traumatic brain injury confirmed on the initial CT scan with moderate/severe TBI defined using:
	  • Marshall CT Score > 1
	• Intensive Care or Stepdown Unit Admission
	• Age >= 18 years
	• LAR provides informed consent
	  • In the event a surrogate cannot be identified by 6 hours EFIC will be used
	
	Exclusion Criteria
	• Non-survivable injuries (evidence of herniation or physician / family decision not to pursue aggressive medical and surgical intervention)
	  • Options: (Have to be GCS Motor 2+ or single pupil or at least brainstem reflex)
	• Pregnant patients
	• On pre-existing beta blockers
	• Any penetrating head injury
	• Contraindication for beta blockers
	• ED physician discretion

Total # of Sites	20-50
Site Requirements	Study sites will need to have the following at their site to be considered: • 24/7 Patient Identification and Enrollment: • High Volume of TBI Cases • Dedicated Research Staff

Site Investigator Qualifications	Site Investigators should have the following: • Specializations in trauma and/or neuro-critical care • Previous Involvement in Clinical Trials • Experience with ICU and Step-Down Units
Key Timeline Dates:	The following dates are projections and subject to change: **Site Selection Decisions**: Jan 2025 **Site Selection Notifications:** Jan-Feb 2025 **Enrollment begins: Jan 2026** **Last Patient/Last Visit: Jan 2030** **Study Closure: Jan 2031**