QUARTERLY UPDATE

2023 QUARTER 2

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OPERATIONS MEMOS

Six new Operations Memos have been sent since the last Quarterly Update.

- **T05 # 24, distributed 12/15/22** notifying sites about adding a Notification letter for LAR refusal
- **T07 # 5, distributed 2/24/23** notifying sites about an update to the Prehospital Form (PREH), MOP Update and Patient Payment Update
- **T04 HS #5, distributed 2/24/23** notifying sites about an update to the Trauma Center Form (HSCTR)
- **T04 TBI # 6, distributed 2/24/23** notifying sites about an update to the GOSE Form instructions (TBGOS), GOAT Form (TBGOA) and CT Head Form (CTHD)
- **T05 # 25, distributed 3/3/23** notifying sites that Protocol v7.0 was available
- **T05 # 26, distributed 3/17/23** notifying sites that MOP v4.0 was available

As with all Operations Memos, please ensure that they have been read by anyone who needs the information and that copies are stored with the MOP and/or Regulatory Binder. Operations Memos can be found in the Documents Library area of the LITES website.

TASK ORDER 001 UPDATE

We truly appreciate all the time and dedication each site has exerted towards this project, and we look forward to collaborating with you on papers and presentations! Please use this link to submit your Publication Requests. **https://www.ctsiredcap.pitt.edu/redcap/surveys/?s=3LANCM7TH8**

The coordinating center continues to prioritize manuscript proposals submitted by Co-Investigators

As the DCC continues to curate and analyze the data, we ask that IRBs remain open at sites until closure memos are issued.

Vanderbilt and UT Houston have completed their Cause of Death determinations and are pending Potentially Preventable Mortality adjudications.

TASK ORDER 002 / SWAT UPDATE

The Shock, Whole Blood, and Assessment of TBI (SWAT) study is an observational, multicenter trial examining morbidity and mortality outcomes associated with whole blood resuscitation practices in trauma patients who have evidence of hemorrhagic shock. Additionally, it seeks to produce knowledge about TBI patients with evidence of hemorrhagic shock. Enrollment was completed in 2021.

We are excited to report that the manuscript was accepted for publication in the Journal of the American College of Surgeons! We will notify the study teams once it has been published.

Data analysis and manuscript preparation continues for our secondary analyses.

TASK ORDER 004 / CriSP UPDATE

Since the last quarterly update, we've enrolled over half of our target enrollment goal! All enrolling sites have completed at least one Interim Monitoring Visit and have undergone at least one quarterly consent review. The final site to start enrollment is targeting Q2 of 2023 to start. The next DSMB meeting has been delayed to coincide with interim data analysis in late July or early August. All-site meetings continue to be held on the 2nd Wednesday of every month at 12:00 EST; the CCC would appreciate that each site make an attempt to have at least one member of the team available for each meeting. The Clinical and Data Coordinating Centers want to thank the participating sites for their ongoing efforts on the study.

Cold Stored Platelet Early Intervention –Traumatic Brain Injury (TBI) (CriSP-TBI) trial, is an open label, single center, randomized trial designed to determine the feasibility, efficacy and safety of urgent release cold stored platelets in blunt injured patients with traumatic brain injury requiring platelet transfusion. Over the course of two years, 100 subjects will be enrolled by The University of Pittsburgh. Enrollment is on target with 56 subjects randomized and enrolled since study activation.

TASK ORDER 005 / PACT UPDATE

OVERALL PROGRESS

On March 15th we 'stepped' three more EMS services to the SGA-first arm! This leaves us with 6 EMS services and two steps before we end enrollments somewhere around September 2024.

Monitoring Committee/All-Site calls continue on the 2nd Friday of each month at 10am (EST). The next calls will be on April 14th, May 12th, and June 9th. This once-a-month call provides all the details of how the study is progressing and distributes the Study Monitoring Committee tables for all sites to follow on our progress.

The end of March marks the end of Quarter 1 for the year 2023 which also marks the patient pay out period for completed data. Any subject completed and without edits on the last day of March is eligible for payout in April. As we approach the end of the original grant, we will increase payouts to sites from quarterly to monthly. So all sites will be receiving data completion reports starting April on the first of every month and sites will now bill monthly for both patient enrollments and percent effort. Please contact Rachel, the project manager if you have any questions about this process.

Sites are required to upload all consents and supporting documentation for those enrolled from Jan - March by April 30, 2023.

Please remember to constantly reach out to your participating EMS and utilize the EMS training funds to help maintain engagement from your EMS providers!

ENROLLMENT SUMMARY REPORT AS OF MARCH 28, 2023

Location	Total Registered
University of Pittsburgh	315
Allegheny-Singer	18
Oregon Health and Science University	108
Vanderbilt University	49
University of Louisville	61
East Carolina University	99
Washington University	16
Tulane University	133
Emory University	59
Chicago- Cook County (Stroger)	100
Chicago- Northwestern	59
Chicago- U of Chicago	91
Chicago- Mt. Sinai	39
Chicago Total	289
TOTAL	1147

TASK ORDER 006 / PAIN UPDATE

The Prehospital Analgesia INtervention Trial, TO-006 (PAIN) is a prospective, interventional, randomized trial in trauma patients with compensated shock (SI>0.9) who require pain management. It compares patient-centered outcomes following prehospital administration of ketamine hydrochloride versus fentanyl citrate in patients who will be brought to a LITES trauma center. The primary outcome will be 24-hour mortality among trauma patients with compensated shock following administration of the prehospital study analgesia.

The study is designed to enroll 1136 subjects with a tentative start date of June 2023. We will begin enrolling first at UPMC Presbyterian and Allegheny General, both in Pittsburgh. The enrolled subjects will be randomized to either fentanyl citrate or ketamine hydrochloride. Each blinded study kit contains two doses of the same study drug. The participating EMS agency will open a blinded study kit for patients who meet all inclusion and no exclusion criteria. Up to two doses of blinded study drug may be administered to subjects, only one study kit can be used per subject.

In the prehospital setting, the subjects will be assessed for pain, vital signs, hypoxia, airway management, allergic reactions, and adverse events. Once the subject arrives at the hospital, pain and opioid use will be followed. For a subset of subjects, who remain hospitalized at 72 hours, a survey on anxiety and PTSD will be completed, and at 6 months a survey on PTSD, pain, anxiety, and opioid use will be completed.

The Community Consultation and Public Disclosure plan has been implemented in the Pittsburgh area. Outreach has included a billboard ad, Facebook page, newspaper ads, radio ad, in person and online surveys, brochures, and a virtual meeting with the Community Research Advisory Board. The PAIN website is now active at **www.litesnetwork.org/pain** where a video can be viewed and a survey can be completed regarding the study.

The nine sites who will be participating in the study include: Allegheny Health Network in Pittsburgh, University of Cincinnati Medical Center, Cooper University Hospital, University of California San Diego, University of California San Francisco, University of Pittsburgh Medical Center, University of Utah, University of Vermont Medical Center, and Medical College of Wisconsin. Monthly all site calls began in February, and the sites continue with the sIRB reliance process and will be submitting plans for their community consultation/public disclosure plans.

Sites are also reaching out to the EMS agencies who will be collaborating on the study to inform them about the study and begin the reliance process.

We are finalizing labeling, packaging and distribution processes with Pine Pharmaceuticals.

TASK ORDER 007 / TOWAR UPDATE

Since the last quarterly update, Pittsburgh, UW, and Vanderbilt continue to enroll steadily with 52, 20, and 19 patients respectively. Houston, Mississippi and their participating EMS services received OHRO approval in December. Mississippi commenced enrollment on 3/28/2023 – congratulations on being the fourth site to initiate enrollment! Cincinnati was activated to enroll on 3/28/2023. Knoxville received full sIRB approval and is pending OHRO approval. MetroHealth finished compiling their regulatory documents and will be submitted to OHRO for initial approval. UAB and Louisville are working through their community consultation and public disclosure efforts.

All remaining sites are targeting Q2 of 2023 for activation. The Clinical and Data Coordinating Centers want to thank the participating sites for their ongoing efforts on the study.

TASK ORDER 008 / DEEP UPDATE

The DSUVIA Early Evaluation of Pain (DEEP) study is an open-label, three-year prospective, randomized, interventional trial comparing the standard pain medication used in an emergency department (ED) for moderate to severe pain with DSUVIA (Sublingual Sufentanil) for trauma patients in a hospital setting.

The DEEP study aims to examine the effectiveness, safety, and acceptability of DSUVIA following traumatic injury with moderate to severe pain. DSUVIA is an opioid agonist, is FDA approved, and indicated to treat adults in severe acute pain in a certified medically supervised health care setting (REMS certified) where alternative treatments are inadequate. The primary outcome for the trial will be the Verbally administered Numeric Rating Scale (VNRS) for clinical pain measurement at 30 minutes following randomized medication administration. Secondary outcomes include adverse events, cognitive and sedation assessments, and feedback from health care providers about study medication.

Enrollment commenced in August 2022, and 50% of enrollment (75 subjects) was achieved on March 6th, 2023. Currently there are 83 subjects enrolled at UPMC.

The study is funded by the U.S. Department of Defense. Clinical and data coordination is being handled by the University of Pittsburgh. We thank everyone involved for their ongoing efforts in this trial.

TASK ORDER 010 / CAVALIER UPDATE

The CAlcium and VAsopressin following Injury Early Resuscitation trial (CAVALIER), or Task Order 10, is a double blind, multicenter prehospital and in-hospital randomized trial designed to determine if prehospital calcium, early in-hospital vasopressin, or both improve outcomes in injured patients at risk of hemorrhagic shock.

The Clinical Coordinating Center would like to thank everyone for their participation in the CAVALIER feasibility and site selection process throughout 2023 Q1. Site Selection was based upon a number of factors given the complexity of this trial design and extensive discussion both internally and with potential sites. We are thrilled to announce the sites who will be participating in CAVALIER alongside the University of Pittsburgh: University of Arizona, University of Colorado Denver, Hennepin County Medical Center, University of Miami, University of Mississippi, University of New Mexico, Ohio State University, Texas Tech University Health Sciences Center, Tulane University, and University of California San Francisco.

Logistical and reliance planning meetings with CAVALIER sites are already underway and will continue throughout 2023 Q2. Additionally, the CCC continues to work through the Investigational New Drug (IND) application with the FDA to conduct this trial under Exception from Informed Consent (EFIC).

IMPORTANT DATES

April 5, 2023	12:00 pm ET	TOWAR monthly call
April 12, 2023	12:00 pm ET	CriSP monthly call
April 12, 2023	2:30 pm ET	PAIN Monthly call
April 14, 2023	10:00am ET	Study Monitoring Committee T05 and Conference call with T05/PACT sites
May 3, 2023	12:00 pm ET	TOWAR monthly call
May 10, 2023	12:00 pm ET	CriSP monthly call
May 12, 2023	10:00am ET	Study Monitoring Committee T05 and Conference call with T05/PACT sites
June 7, 2023	12:00 pm ET	TOWAR monthly call
June 9, 2023	10:00am ET	Study Monitoring Committee T05 and Conference call with T05/PACT sites
June 14, 2023	12:00 pm ET	CriSP monthly call
July 5, 2023	12:00 pm ET	TOWAR monthly call
July 12, 2023	12:00 pm ET	CriSP monthly call
July 14, 2023	10:00am ET	Study Monitoring Committee T05 and Conference call with T05/PACT sites

Any opinions, findings and conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the DoD.

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