CONTRACT NUMBER: W81XWH-19-F-0539

TITLE: Prehospital Analgesia Intervention Trial (PAIN)

PRINCIPAL INVESTIGATOR: Jason Sperry

CONTRACTING ORGANIZATION: University of Pittsburgh
Pittsburgh, Pennsylvania 15213

REPORT DATE: OCT 2022

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

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OCT 2022	Annual Report	20-SEP-2021 - 19-SEP-2022

4. TITLE AND SUBTITLE

Prehospital Analgesia Intervention Trial (PAIN)

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-19-F-0539

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Jason Sperry, Laura Vincent, Denise McCarthy, Meghan Buck, Laurie Silfies, Natalie Rogers

E-Mail: sperryjl@upmc.edu; vincentl3@upmc.edu; mccarthydj@upmc.edu; buckml@upmc.edu; silfiesl@edc.pitt.edu; rogersnb@upmc.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

University of Pittsburgh
Pittsburgh, Pennsylvania 15213

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

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12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT
PAIN is a proposed 4 year (3-year enrollment) multicenter, prehospital, randomized, double-blind, clinical trial comparing fentanyl versus sub-dissociative ketamine for mortality outcome differences, safety and analgesia in trauma patients with compensated shock.

Specific aims are to determine if, among prehospital trauma patients with compensated shock (Heart Rate (HR)>109 or Shock Index (SI)>0.9) and an indication for pain management, treatment with sub-dissociative IV ketamine as compared to IV fentanyl reduces mortality at 24 hours following admission, reduces the frequency of hemodynamic instability or respiratory depression associated with analgesia, decreases total prehospital exposure to opioids, 24-hour exposure to opioids, and anxiety/PTSD screen scores, improves the frequency of complications including opioid use / dependency, anxiety, and PTSD at 6 months, and improves arrival pain control as measured by numerical rating scale (NRS) and/or the critical care pain observation tool (CPOT).

15. SUBJECT TERMS
Trauma; Prehospital; Analgesia; Fentanyl; Sub-Dissociative Ketamine

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRDC
U	U	U	UU	13	19b. TELEPHONE NUMBER *(include area code)*

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

PAIN is a proposed 4 year (3-year enrollment) multicenter, prehospital, randomized, double-blind, clinical trial comparing fentanyl versus sub-dissociative ketamine for mortality outcome differences, safety and analgesia in trauma patients with compensated shock.

The primary outcome for the trial will be 24-hour mortality among trauma patients with compensated shock following administration of the prehospital analgesia. Secondary outcomes will include incidence of adverse events (hypoxia, hypotension, and need for airway management) occurring in the prehospital environment, assessed after administration of the analgesic intervention. prehospital pain assessment (NRS, CPOT) following analgesia, trauma bay arrival pain score, number of analgesic doses necessary to reduce pain level to <5 or CPOT less than 2, total 24-hour opioid use, incidence of prehospital adverse events (allergic reactions, emergence, laryngospasm, dysphoria, pruritus, and nausea), anxiety/PTSD screening, hospital length of stay, survival to hospital discharge, ventilator free days, ICU free days and long-term opioid use (6-month). Trial will utilize prehospital agencies at six LITES Network sites and will enroll a total of 1,544 subjects.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

Trauma; Prehospital; Analgesia; Fentanyl; Sub-Dissociative Ketamine

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.

What were the major goals of the project?

List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

The purpose of Task Order 0006 is to perform a prospective, interventional, randomized trial among prehospital trauma patients with compensated shock (HR>109 or SI>0.9) and an indication for pain management, comparing patient centered outcomes following prehospital administration of ketamine hydrochloride versus fentanyl citrate.

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

Clinical Coordinating Center/Data Coordinating Center:

- Successful In Progress Review (ICP) meeting held on 17-DEC-2021
- PM, APM, and Investigators continued meeting weekly to discuss study logistics.
- CCC submitted response to FDA Full Clinical Hold in DEC-2021.
  - FDA clinical hold was lifted on 11-JAN-2022.
- Initial IRB application and Community Consultation and Public Disclosure plan submitted to sIRB 02-MAR-2022.
  - Committee review occurred 06-APR-2022; approved with minor modification on 13-APR-2022. CCC submitted response to minor modifications on 25-APR-2022.
  - sIRB approval of the study was obtained 06-MAY-2022!
- Initial OHRO Submission, 26-MAY-2022 – pending approval
  - Response to administrative review was sent on 08-JUL-2022.
  - Army Surgeon General signature of EFIC waiver – pending
- Study registered on ClinicalTrials.gov and the NCT# was released (NCT05437575) in JUL-2022.
- Study email was created (PAINStudy@edc.pitt.edu).
- CCC/DCC initiated development of data dictionary and eDCF in SEP-2022.
- Multicenter Application submitted to IND & IDE Support (IIS) on 16-AUG-2022.
  - 25-AUG, monitoring plan for the multicenter PAIN trial was reviewed and found it to be acceptable.
- University of Pittsburgh's Office of Education and Compliance pre-launch review (RISE) conducted 01-SEP-2022 – report received 06-SEP-2022.

Participating Sites

- Preliminary sites were identified in OCT-2021. Feasibility discussions with potential sites were held following FDA approval.
- Evaluated budget estimates for 6, 8, 9, 10 enrolling sites; moving forward with plans to increase to 9 sites (including Pitt) to decrease the length of enrollment period.
- CCC finalized site selection on 19-APR-2022: Pitt, Utah, Wisconsin, Cooper, UAB, San Diego, Cincinnati, Allegheny Health Network, and UCSF.
  - Arkansas and UPenn were identified as back-up sites.
- CCC met with the LITES finance team on 28-APR to finalize SOW and budget adjustments to shift to 9 enrolling sites.
- Contracts and budget templates were distributed – pending execution at all participating sites.
- CCC conducted sIRB/reliance calls with lead coordinators/study teams at participating sites.
- sIRB reliance process was initiated in SEP-2022.
- Pittsburgh Community Consultation and Public Disclosure (CC/PD) plan was finalized.
  - Assistant Project Manager prepared the CC/PD materials for use at Pitt site and distribution to enrolling sites as templates.
  - CCC worked with UPMC to finalize press release.
- Protocol modification to include Pittsburgh site CC/PD plan & materials submitted 18-JUL-2022.
  - Responses to comments were submitted and approval was granted on 28-SEP-2022.
- Site calls conducted throughout AUG-2022 to discuss logistics for narcotic distribution, storage, etc. Narcotics logistics will vary by state and agency protocols.

Pine Pharmaceuticals

- Subcontract agreement with Pine Pharmaceuticals executed on 09-DEC-2021.
- CCC, Pine Pharmaceuticals, and Pitt IDS met on 27-JAN-2022 to solidify labeling requirements and discuss packaging options.
- CCC maintaining ongoing communication with Pine Pharmaceuticals (FDA-registered 503B outsourcing facility). CCC held calls with Pine staff:
  - Regarding 120-day results & discussed reformulating fentanyl to a higher concentration (to confirm a longer stability & shelf life for the study).
  - Discuss labeling, packaging, & manufacturing processes Pine working to create the labeling and packaging of the kits
- PAIN Study Drug Validation Testing (through 120-Days): *see table below*

<table>
<tr><td colspan="2">
- Validation testing completed and 120-day report received.
- Pine will execute a test batch of the finalized reformulation of fentanyl as manufacturing date approaches to ensure the calculations meet spec (prior to manufacturing runs).
▪ CCC/DCC are having on-going discussions with Pine to solidify a process to link the kit label to the patient and pre-hospital data.
</td></tr>
<tr><td>Validation work to be completed & documentation issued to Pine for review/approval.</td><td>Week of 13-SEP-2021</td></tr>
<tr><td>Manufacture and ship stability batches to contract laboratory.</td><td>Week of 20-SEP-2021</td></tr>
<tr><td>T = 0 testing initiates at contract laboratory</td><td>Week of 27-SEP-2021</td></tr>
<tr><td>First results from T = 30 timepoint (Requested by FDA)</td><td>Week of 25-OCT-2021</td></tr>
<tr><td>Results will be available 1-2 weeks after 30-day test is completed</td><td>Week of 08-NOV-2021</td></tr>
<tr><td>Results from T = 45 timepoint
Timepoint omitted (per FDA request for 30-day)</td><td>N/A</td></tr>
<tr><td>T = 90-day results</td><td>Week of 27-DEC-2021</td></tr>
<tr><td>T = 90 report and individual lab issued COAs</td><td>25-JAN-2022</td></tr>
<tr><td rowspan="2">T = 120-day results
Both products will be evaluated for endotoxin and impurities at this timepoint</td><td>Preliminary data received 25-FEB-2022</td></tr>
<tr><td>Final report received 23-MAR-2022</td></tr>
<tr><td colspan="2">Enrollment: Not yet recruiting</td></tr>
</table>

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to report.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

- Prepare In-Progress Review (IPR) presentation for 14-NOV-2022.
- Continue ongoing communications with Pine Pharmaceuticals.
- Continue developing the eDCF.
- Initiate Pittsburgh's CC/PD activities/efforts.
- Obtain OHRO study approval.
- Obtain Army Surgeon General's signature on EFIC Waiver.
- Begin monthly Site Coordinator calls.
- Collect site budgets & executed contracts.

Travel Reporting: No travel conducted in the past quarter.

- No travel is anticipated for the next quarter.

Cumulative to Billing Period: 30-SEP-2022	**Travel Funds Budgeted**	**Cumulative Actual Spent**	**Remaining Balance**
Upcoming Travel for Quarter: **OCT-2022 to DEC-2022**	**Traveler Name**	**Destination/ Purpose**	**Estimated Date of Travel**
	N/A	N/A	N/A

4. IMPACT: Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to report.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report.

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*

- *adoption of new practices.*

Nothing to report.

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:
- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report.

5. CHANGES/PROBLEMS: The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Nothing to report.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

▪ Ongoing communication with FDA about conducting the study under EFIC (Exception from Informed Consent). ▪ Pine Pharmaceuticals implemented a new program which caused delays in finalizing Scope of Work and budget. ▪ Validation testing preliminary data showed evidence of degradation of the fentanyl product over the storage period under the assigned conditions, evidenced both by the presence of impurities and the potency of fentanyl over time at 120-day timepoint. CCC taking this into consideration in manufacture and logistical planning and continuing discussions with Pine Pharmaceuticals regarding approach to this issue. *Items noted above were resolved.*

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to report.

Significant changes in use or care of vertebrate animals

Not applicable to TO 0006

Significant changes in use of biohazards and/or select agents

Not applicable to TO 0006

6. **PRODUCTS:** List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Nothing to report.

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Nothing to report.

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to report.

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report.

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to report.

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report.

- **Other Products**
  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:
  - *data or databases;*
  - *physical collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*

- *other.*

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?
Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Example:

Name:	*Mary Smith*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	*1234567*
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support:	*The Ford Foundation (Complete only if the funding support is provided from other than this award.)*

Personnel Listing: see page 13

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to report.

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Nothing to report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

Quad Chart: see page 13

9. APPENDICES: Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

Annual and final reports are submitted to: https://ers.amedd.army.mil/

AND
One Copy: Contract Specialist, Ronnie Sanford
Email: ronald.s.sanford2.civ@health.mil

One e-Copy: Science Officer René Smith
Email: rene.k.smith.civ@health.mil

Personnel Listing (as of 30-SEP-2022)

W81XWH-16-D-0024 / W81XWH-19-F-0539			
Department	**Personnel Name**	**UPitt Role**	**T0 % Effort**
Surgery	Brown, Joshua B	Co-PI	3%
Surgery	Gimbel, Elizabeth	Assistant Project Manager	5%
Emergency Medicine	Guyette, Francis X III	Co-PI	15%
Surgery	Hayes, Hannah E	Clinical Researcher II	10%
Epidemiology (GSPH)	Kania, Michael A	Systems Developer III	30%
Epidemiology (GSPH)	Macey-Kalcevic, Melody	Research Specialist IV	50%
Surgery	McCarthy, Denise Jean	Health Prof II	50%
Emergency Medicine	Pacella, Maria Lynn	Co-Investigator	5%
Epidemiology (GSPH)	Pattison, Angela Dawn	Research Specialist IV	50%
Surgery	Peet, Chelsea Ann	Asst Project Mgr.	44%
Surgery	Rogers, Natalie	Research Coordinator (CRC)	28%
Epidemiology (GSPH)	Silfies, Laurie N	Systems Engineer IV	17%
Surgery	Sperry, Jason L	Co-Investigator	25%
Surgery	Vincent, Laura Everett	Program Director	17%
Emergency Medicine	Warchol, Joel	Assistant Professor	12%
Epidemiology (GSPH)	Wisniewski, Stephen R	Co-PI	5%

YEAR 3 QUAD CHART

Linking Investigations in Trauma and Emergency Services – TO6

17052001-TO6/W81XWH-16-D-0024, W81XWH19F0539

Prehospital Analgesia Interventional (PAIN) Trial - LITES Task Order 0006

PI: Jason Sperry MD MPH **Org:** University of Pittsburgh **Award Amount: $8,798,845**

STUDY AIMS

Determine if prehospital management of moderate to severe pain with sub-dissociative IV ketamine as compared to IV fentanyl in patients at risk of hemorrhage or compensated shock:

I. Reduces 24-hour mortality
II. Improves the incidence of hemodynamic instability or respiratory depression (hypotension, hypoxia or need for airway management) following analgesia for traumatic injury
III. Decreases total prehospital exposure to opioids, 24-hour exposure to opioids, and Anxiety/PTSD screen scores
IV. Improves the frequency complications including opioid use/ dependency, anxiety, and PTSD at 6 months
V. Improves pain control as measured by NRS or CPOT scores in patients at risk of hemorrhage or compensated shock

Multicenter, prehospital, randomized, double-blind, clinical trial

ACCOMPLISHMENTS

- ✓ PAIN study was registered on Clinicaltrials.gov (NCT05437575)
- ✓ Site participation was finalized: Pitt, Utah, Wisconsin, Cooper, UAB, San Diego, Cincinnati, Allegheny Health Network, and UCSF
- ✓ Initial sIRB approval of the study was granted in MAY-2022!
  - Pittsburgh sites CC/PD plan & materials were sIRB approved in SEP-2022

Timeline and Cost

Activities CY	SEP-19	20	21	22	23
Startup, Hiring, IRB approval, Contracts, Single IRB organization, Database creation, site selection					
4-year (3-year enrollment), 1544 patients (772 per group)					
1/3 enrollment; interim analysis					
2/3 enrollment; interim analysis					
Estimated Budget	252K	252K	252K	4M	4M

Updated: (University of Pittsburgh 14-OCT-2022)

Goals/Milestones

CY19 | CY20 | CY21 Goal – Study Development & Staffing
- ✓ Base Hiring & Budget negotiation

CY22 Goal – Study Startup, Site Selection
- ✓ FDA approval
- ✓ IND, single IRB approval
- ❑ Community Consultation/Public Disclosure
- ❑ Army Surgeon General EFIC waiver approval; HRPO approval

CY23 Goal – Patient Enrollment
- ❑ Data base creation and CRF completion, data dictionary
- ❑ Site Initiation Visits
- ❑ Begin Patient enrollment
- ❑ Reach accrual goal for 1/3 interim analysis
- ❑ Request No Cost Extension (NCE)
- ❑ Reach accrual goal for 2/3 interim analysis
- ❑ Finish enrollment
- ❑ Data analysis and publication

Budget Expenditure compared to Actual thru 30-SEP-2022
- Actual Expenditures: $1,524,154.49
- Scheduled Expenditures: $5,368,786.78