Introducing the Trial

ResQFoam™ is an in-situ forming polymeric foam designed to control severe, intra-cavity hemorrhage by creating conformal contact and applying pressure to an actively bleeding site. The upcoming REVIVE trial aims to demonstrate the safety, effectiveness, and benefit-risk profile of ResQFoam for the in-hospital treatment of emergent, exsanguinating, intra-abdominal hemorrhage resulting in Class III or IV hemorrhagic shock due to trauma.

This is a single-arm, multi-center clinical trial designed to demonstrate the clinical benefit and efficacy of ResQFoam by measuring improved systolic blood pressure over baseline following the intervention. Additionally, this study will evaluate the safety of ResQFoam by assessing all adverse events with discrimination against those directly attributed to the use of the device. This study will take place in Level I Trauma centers.

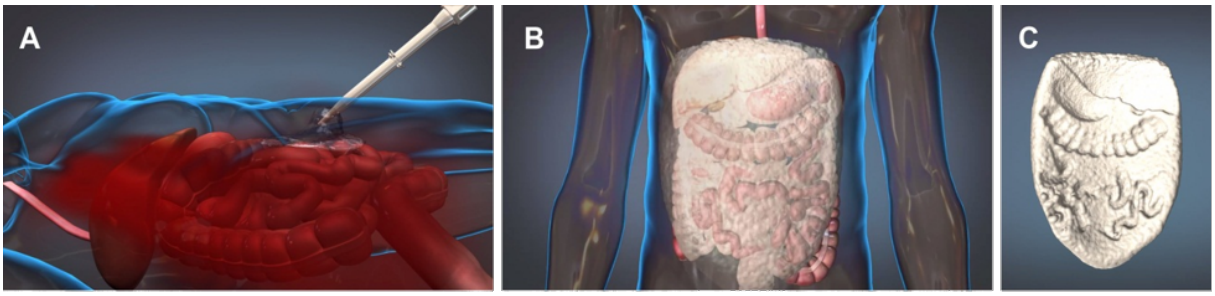
Emergency Research for Abdominal Bleeding

Patients with severe internal abdominal bleeding suffer from a high rate of death. A recent study by Harvin et al. found that over 40% of patients who lived long enough to receive emergency surgery still died at leading trauma centers. The authors concluded that the mortality rate resulting from bleeding and shock has not changed since the early 1990s, even in modern hospitals with abundant resources.

There has been very little innovation in the treatment of these patients. Pre-surgical fluids and traveling to the operating room more rapidly have not improved survival. There is a strong need to develop new therapies to reduce trauma-related death. New treatments must be studied carefully in a controlled environment by our most capable surgeons. A controlled trial is the only way to determine if new treatments help patients. Based on studies in animals, ResQFoam has significant potential benefits. This clinical study will determine if the device is safe and effective in trauma patients.

RESQFOAM BACKGROUND

Arsenal Medical has developed ResQFoam, a new device to control severe, life-threatening intraabdominal hemorrhage. ResQFoam consists of a delivery device and two liquid phase components mixed to form a foam in the abdomen. The foam surrounds abdominal organs and applies local pressure to the site of injury to control bleeding. As a result, the injured patient can be stabilized and transported to surgery. The solidified foam is removed during surgery, and bleeding is stopped surgically. An animation of the foam is shown here: (insert link)



Injury occurs and ResQFoam deployed

ResQFoam forms *in situ*

ResQFoam surgically extracted

The ResQFoam kit contains an optimized dose for use on one subject; ResQFoam is used only in adults.

Exception from Informed Consent (EFIC)

The vast majority of patients requiring an emergent intervention following trauma will be unable to provide informed consent. The Food and Drug Administration will allow for the use of Exception from Informed Consent (EFIC). https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-50/subpart-B/section-50.24

The study must involve participants suffering from a life-threatening injury

- Available treatments must be unproven or unsatisfactory
- The collection of scientific evidence is necessary to determine the safety and effectiveness of the intervention
- Obtaining informed consent must not be feasible as a result of their medical condition
- The intervention must be administered before consent can be obtained
- There is no reasonable way to identify prospectively individuals likely to become eligible for participation
- Participation in the research holds out the prospect of benefit to the subjects
- The study could not be carried out without the waiver.

Additional information regarding EFIC can be obtained here.
https://www.fda.gov/media/80554/download

Research performed with an EFIC waiver is highly regulated. The proposal is first critically appraised by another, uninvolved physician with expertise in the field of study. The proposal is also reviewed by the institutional review board (IRB) at a participating site.

The Principal Investigator must then lead a process called "community consultation." During community consultation, the study is advertised in the region where it will take place with a request for feedback and comments. The Principal Investigator also meets

with community organizations to describe the proposed study and seek in-person feedback.

Your Feedback

Greater Pittsburgh Area

If you would like to provide feedback on the EFIC process, please fill out the questionnaire found in this link. https://pitt.co1.qualtrics.com/jfe/form/SV_5bG6nZgylkxVz13

Other Geographies

If you would like to provide feedback on the EFIC process, please fill out the questionnaire found in this link. https://redcap.partners.org/redcap/surveys/?s=CWLKLFM93R

The questionnaire contains 7 brief items which will help us better understand how potential patients feel about the EFIC process.

Frequently Asked Questions

1. Who will be included in this study?

All patients presenting to a participating site with life-threatening trauma requiring immediate surgery will be screened for eligibility for the study. Patients meeting all inclusion criteria, without any exclusion criteria, will be enrolled in the study.

Inclusion Criteria:

- Estimated age of 15 years or older (or subject weight greater than 50 kg if age is unknown)
- Emergent, exsanguinating hemorrhage from abdominal source as defined by:
- Class III or IV hemorrhagic shock or
- Assessment of blood consumption (ABC) score ≥ 2
- Confirmation of abdominal hemorrhage by:
- Direct visualization or
- Positive Focused Assessment with Sonography in Trauma (FAST) or
- Diagnostic Peritoneal Aspiration (DPA)
- No other known, uncontrolled active sources of hemorrhage
- The subject is intubated and sedated per local guidelines
- The decision to administer foam is made within 30 minutes of admission to the emergency department
- Decision made to proceed to emergent laparotomy made within 30 minutes of admission to the emergency department.
- Definitive surgical care is expected to occur within three hours of foam deployment
- The subject must also be receiving a concurrent transfusion of fluids or blood

Exclusion Criteria:

- Known or suspected major diaphragm injury
- Known or suspected untreated pneumothorax
- Known or suspected untreated hemothorax
- Known or suspected blunt or penetrating cardiac or thoracic aortic trauma
- Traumatic brain injury resulting in decapitation, visible brain matter or considered non- survivable based on initial physical exam
- Received greater than five consecutive minutes of cardiopulmonary resuscitation in the pre-emergency department setting
- Patients with Pulseless Electrical Activity
- Known allergy to isocyanate
- Known or suspected pregnancy
- History of prior abdominal surgery or evidence of abdominal surgery (scars)
- A disrupted abdominal wall that, in the opinion of the investigator, would preclude ResQFoam from being adequately contained within the abdominal cavity
- Subject in whom the abdominal aortic junctional tourniquet (AAJT) or Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) techniques have been used
- Known Prisoners
- Subjects with burns > 20% of total body surface area
- Subject/legally authorized representative/subject family member purposefully opted out of participation in the study
- Known Do Not Resuscitate order (DNR) or Physician Orders for Life-Sustaining Treatment (POLST)
- Known enrollment in another randomized, interventional study

2. How many patients will be enrolled?

Up to 40 patients will be included in the study.

3. When will the study start?

The study is currently activated for enrollment.

4. Once the patient reaches the emergency department, why can't the family be contacted to provide consent?

The patient population in this study will be severely injured and suffering from severe and uncontrolled bleeding in the abdomen. Per ATLS guidelines, patients experiencing this type of bleeding are characterized by greater than 30% blood loss, reduced blood pressure, and

will have an anxious, confused, or lethargic mental status. Therefore, patients will be incapable of providing legally effective informed consent as required by 21CFR50.20. https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-50/subpart-B/section-50.20

To be effective, ResQFoam must be administered rapidly in the initial period (within 30 minutes) of patient arrival to the emergency department (ED). Due to the circumstances necessitating the medical condition, Legally Authorized Representatives (LAR), such as a spouse or family member, are often not immediately available when the patient arrives at the ED. Because of the likely unavailability of the LAR and the emergent need to treat hemorrhage due to the mortality associated with it, there may be insufficient time to obtain consent from a LAR prior to treatment with ResQFoam within this window. Because this trial involves unpredictable traumatic injury and may originate from many causes, there is no way to prospectively identify individuals who are likely to become eligible for this trial. The investigator will, at the earliest feasible opportunity, inform the subject, the subject's LAR, and/or family member (1) of the subject's inclusion in the study, the details of the investigation and other information contained in the informed consent document, and (2) that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled (21 CFR 50.24(b)). If a LAR or family member is told about the clinical investigation and the subject's condition improves, the subject must also be informed as soon as feasible.

5. Are there any risks to the patient?

There is always the potential for risks associated with both the lifesaving operation that patients will undergo due to their traumatic injuries and the use of any investigational product when enrolled in a study. In addition, there may be potential risks with the use of the foam injected prior to the surgical procedure. The potential risks of your life-saving operation have been identified and could include:

- Adverse biological reaction or toxicity
- Unnecessary surgery
- Ongoing hemorrhage or blood loss
- Compromised cardiac or respiratory function
- Death
- Inhaling fluid into the lungs or choking on vomit
- Difficulty breathing
- Infection
- Damage to organs, tissue, or vessels
- Pneumonia
- Potential loss of pregnancy
- Organ Failure

The potential risks of the use of ResQFoam have been identified and could include:

- Complications related to the abdominal incision for foam injection
- Delay in getting to surgery
- Elevated pressure in your abdomen may negatively impact your survival from your injury
- Carbon Dioxide Embolism (the accidental injection of carbon dioxide into the veins, which may result in the blockage of the cardiovascular system)
- Requiring surgery when you may not have needed a surgical procedure
- Infection
- Injury to the bowel which may require additional standard surgical intervention
- Damage to organs, tissue, or vessels
- Adverse biological reaction or toxicity

There might be additional risks that are currently unknown. There are also potential risks associated with your injury and subsequent surgical procedure(s), which would be performed whether you are in the study or not. These specific risks will be discussed with you by your trauma surgery physicians.

A committee composed of physicians and study officials will review data after every patient to assess the potential for harm. If this committee feels that the study harms patients, the study will be halted at their recommendation.

6. How can I opt-out of this trial?

If you wish to not participate in this trial, please request an "opt-out" bracelet. As many of the patients enrolled in this study will be unconscious or otherwise unable to communicate with the team of surgeons treating them, the bracelet must be worn to indicate that you do not wish to be enrolled in the study. Please see the "Opt-out of REVIVE Trial" instructions to request an opt-out bracelet.

Study Opt-Out

We will provide you with an "opt-out" bracelet at no cost for people who do not wish to participate in this study. A colored plastic bracelet with the words "RESQFOAM Ø" will indicate to ED staff that the patient should not be considered for the study. To obtain an "opt-out" bracelet, please email optout@arsenalmedical.com. Please include an address where the bracelet may be sent in the email.