INVEST: A Single Arm, Feasibility Study of Minimally Invasive Endoscopic Surgical Treatment with Apollo / Artemis for Supratentorial Intracerebral Hemorrhage (ICH)
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TITLE OF RESEARCH STUDY:

Title: INVEST: A Single Arm, Feasibility Study of Minimally Invasive Endoscopic Surgical Treatment with Apollo / Artemis for Supratentorial Intracerebral Hemorrhage (ICH)

PRINCIPAL INVESTIGATOR (HEAD RESEARCHER) NAME AND CONTACT INFORMATION:

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WHAT IS A RESEARCH STUDY?

A research study is when scientists try to answer a question about something that we don't know enough about. Participating may not help you or others.

People volunteer to be in a research study. The decision about whether or not to take part is totally up to you. You can also agree to take part now and later change your mind. Whatever you decide is okay. It will not affect your ability to get medical care within the Mount Sinai Health System.

Someone will explain this research study to you. Feel free to ask all the questions you want before you decide. Any new information that develops during this research study that might make you change your mind about participating will be given to you promptly.

Basic information about this study will appear on the website http://www.ClinicalTrials.gov. There are a few reasons for this: the National Institutes of Health (NIH) encourages all researchers to post their research; some medical journals only accept articles if the research was posted on the website; and, for research studies the U.S. Food and Drug Administration (FDA) calls "applicable clinical trials" a description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

PURPOSE OF THIS RESEARCH STUDY:

The purpose of this study is to provide an assessment of enrollment and follow up feasibility for patients who are treated with the Apollo System or the Artemis Device. The Apollo System is a medical device which has been approved by the United States Food and Drug Administration (FDA) to gently remove fluid or soft tissue from the fluid containing ("ventricular") part or cerebrum of the

brain. This device has been effective being used in this way. However, the usage of the Apollo System in this study is experimental and investigational. The Artemis Device, also FDA approved, works in a very similar manner to its predecessor, the Apollo System. The main difference is that its energy is generated by rotational energy instead of vibrational energy. The device that you will be treated with will depend on which device is currently available at your site. You may still be treated with the Apollo or Artemis device based on your physician's best judgement if you choose not to participate in this research.

You may qualify to take part in this research study because you have had a stroke because of bleeding in your head. This particular type of bleeding is called supratentorial intracerebral hemorrhage, a type of intracranial hemorrhage (ICH).

Funds for conducting this research are provided by Penumbra, Inc, who manufactures the Apollo system and the Artemis device being tested.

LENGTH OF TIME AND NUMBER OF PEOPLE EXPECTED TO PARTICIPATE

Your participation in this research study is expected to last 12 months.

The total number of people expected to take part in this research study is 50 from 10 different sites.

DESCRIPTION OF WHAT'S INVOLVED:

If you agree to participate in this research study, the following information describes what may be involved. These research procedures will take place at Mount Sinai West.

Screening

Your medical records will be reviewed. You will be asked questions about your medical history. Results of tests you have had during this hospital stay will be collected.

Baseline evaluation

The study doctor will examine you. The study coordinator may also perform some neurological and functional assessments if they have not already been done. These will be explained to you before they are done. These involve observing and asking you, or your legally authorized representative, questions about your ability to move about and take care of yourself. During this time you may have additional testing done that is part of your routine medical care. The study team will collect the results of these tests.

If you are female and it is possible for you to become pregnant, you will have a pregnancy test done. If you are pregnant, you cannot be in this study.

Intervention Procedure

The procedure is called Apollo/Artemis Minimally Invasive Endoscopic Surgery or Apollo/Artemis MIES. It has to be done within 72 hours of your symptoms of bleeding in your head. You will be placed under general anesthesia and will be asleep during the procedure.

During the procedure you will be lying on the procedure table under a sterile drape. Under anesthesia, a very small hole, called a burr hole, will be drilled in the bone of your head. The size of the hole may vary, but it generally is about ½ of an inch across, smaller than the size of a dime. A device called an endoscope will be placed through the hole into the area of the bleed in your brain.

The endoscope is a small telescope-like device equipped with a high-resolution video camera and eyepiece on the end to allow the doctor to find and view this area. The Apollo System or Artemis Device is a device that is also placed with the endoscope. The combined instruments are used to rinse (irrigate) this area and to gently suction out the rinsing fluid and any blood or clot that are there.

During the procedure, you will have a CT scan performed which is part of normal standard of care for your condition. CT scans are done to see if enough of the blood clot has been removed and also if more bleeding or problems have happened. This may be done more than once according to your doctor's discretion.

When the procedure is finished the Apollo System or Artemis Device and the endoscope are taken out of the small hole in your skull and the surgery site is closed.

You will be returned to the ICU or special stroke unit for at least 24 hours after the procedure.

24-hour follow-up for patients

The study doctor and/or coordinator will repeat the neurological and functional assessments that were done during your baseline evaluation to see if there have been any changes.

Your doctor will care for you according to the standard care at your hospital for people who have had similar procedures.

Discharge from the hospital or 7-day follow-up (whichever comes first)

The study doctor and/or coordinator will examine you, repeat the neurological and functional assessments again, and review your medical record to see what complications you may have had, and what medications were given to you. You will receive information on coming for your next study visit.

3-month follow-up, 6-month follow-up, and 12-month follow-up

At each of these follow-up visits you will see the study doctor and/or coordinator. You will have a physical exam and neurological and functional assessments. You will be asked about any changes in your medical condition. You will be asked about what medications you are taking.

It is very important that you come to these follow-up visits.

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study you will be responsible for the following things: following your doctor's instructions and returning for routine follow-up visits.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

You will not be paid for participating in this research study. All of your medical care while in the hospital will be charged to you or your medical insurance. The Apollo System or Artemis Device will also be charged to you or your medical insurance. There is no expectation that using this device will increase costs to you as compared to standard treatment for your condition. These costs are not covered by the study. Your follow-up visits to the study team will be at no charge to you.

POSSIBLE BENEFITS:

It is important to know that you may not get any benefit from taking part in this research. Others may not benefit either. However, possible benefits may be that you will recover better as a result of being in the study, but this is not promised and cannot be guaranteed.

REASONABLY FORESEEABLE RISKS AND DISCOMFORTS:

As with any medical intervention, there are potential risks. In this study, there are potential risks associated with usual medical management and risks associated with the use of the Apollo device or the Artemis device, which are listed below.

There is also the risk of loss of private information; this risk always exists but there are procedures in place to minimize the risk.

Some of these potential risks are:

<u>Risks of Usual Medical Management</u>

Likely risks:

- It is not uncommon for patients to bleed again into their brains. Approximately 70% of patients do. As part of your usual medical care, you will have CT scans, probably daily, to see if this rebleeding has happened.
- The radiation exposure for CT scans of the head is about 1.4 rems (14 mSv). Naturally occurring environmental radiation that happens to all people equals about 0.3 (3 mSv) per year. People who are exposed to radiation in their work often receive about 5 rems (50 mSv) per year. The amount of CT scans that you will have is up to the discretion of your doctor. They are done frequently to monitor your head to watch how the area of bleeding is doing.

CTA scans have about twice the amount of radiation exposure as CT scans. This amount of exposure is considered to be of a minimal risk to a patient.

- There are no known risks due to exposure to the magnetic field of a MRI scanner. However, some people are significantly bothered by the confinement to a small space (claustrophobia) and by the noise heard during the MRI scan. You will be given earplugs to wear while in the scanner.

  If you have a pacemaker or certain other implanted electronic or metallic devices you will not have an MRI. It is important your doctor know of all devices and other metal that you may have in your body.

Less likely risks:

- Approximately 10-20% of patients are expected to develop infections. You will be monitored closely to watch for this. You will be treated according to the usual practice of your doctors.
- Worsening of your neurological condition.
- Blood draws might cause pain and/or bruising. Some people become dizzy when they have their blood drawn and might even faint. On rare occasion someone might develop an infection where the blood is taken.
- Death.

Discomforts:

- The routine medical care while you are in the hospital, especially in the intensive care unit or special stroke unit, can result in discomforts that will vary from patient to patient. You may experience some of these.
- You might find the study follow-up visits cause you to feel tired or bored when you are being asked questions. You do not have to answer anything that you do not want to answer.

There may be additional side effects or discomforts that we do not already know about.

<u>Risks associated with the Apollo System / Artemis Device</u>

In addition to the risks with usual medical management, there are additional risks associated with the use of the Apollo System and Artemis Device.

Less likely risks:

- The rarely occurring risks of general anesthesia include temporary mental confusion, lung infections, reactions or allergies to the anesthesia medications, stroke, heart attack, and death. These are found to occur approximately 2% of the time.
- The rarely occurring risks of the procedure include bleeding, infection, or damage to surrounding bone of the skull or tissue of the brain. In previous studies about procedures similar to Apollo / Artemis MIES, these happened about 1% of the time.
- As mentioned above, in the section about the risks for people in the study who do not have the procedure, bleeding in your brain can happen again. There is a small additional risk that this may happen as a result of the procedure.

Discomforts:

- There may be some head pain following the surgery. Some people experience back pain after lying on the procedure table. If you have these they will be treated with pain medications to make you comfortable.

Pregnancy Risks

You cannot be in the study if you are pregnant. If you are a woman and could become pregnant, you will have a pregnancy test done before you are enrolled in the study.

If you become pregnant during the 1 year of follow-up, you can stay in the study. Since the follow-up only includes examining you and asking you questions, it is unlikely to cause additional risk to you or an unborn child. However, due to your serious medical condition your doctor may advise you to avoid pregnancy. Please discuss this with your healthcare provider.

In addition to these risks, this research may hurt you in ways that are not known. The unknown risks might be minor or might be major (death).

OTHER POSSIBLE OPTIONS TO CONSIDER:

You may decide not to take part in this research study without any penalty. The choice is totally up to you.

Instead of being in this research study, your choices may include:

- Usual medical management which include the following procedures:
  - Admission to an intensive care unit or special stroke unit in the hospital;
  - Making certain the patient can breathe well, which often includes using a ventilator;
  - Managing the cause of the bleeding if it has occurred as a side effect of a medication or a medical condition that reduces the ability of the body to clot;

- Controlling the blood pressure to keep it from getting too low or too high;
- Managing the pressure within the brain that will increase if a clot that is large takes up space, or more bleeding happens. This is done by placing a tube in part of the ventricle of the brain and allowing fluid to drain out. This is the area where cerebrospinal fluid, and not blood vessels, is located;
- If the pressure in the brain gets too high and cannot be lowered enough, brain surgery may be done to make more room for the brain swelling.

The important risks and possible benefits of this option can be found in the above section "Reasonably foreseeable risks and discomforts."

IN CASE OF INJURY DURING THIS RESEARCH STUDY:

If you are injured or made sick from taking part in this research study, medical care will be provided. Generally, this care will be billed to you or your insurance in the ordinary manner and you will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance. This does not prevent you from seeking payment for injury related to malpractice or negligence. Contact the investigator Dr. Christopher Kellner for more information.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this research study at any time without any penalty. This will not affect your ability to receive medical care at any of the Mount Sinai Health System hospitals or to receive any benefits to which you are otherwise entitled.

If you decide to stop being in the research study, please contact the Principal Investigator or the research staff. They will want to discuss this with you and resolve any issues that may be causing you to want to leave. They will also request that you come for a final follow-up visit so they can review your condition with you and thank you for your participation.

If you stop being in the research study, already collected information may not be removed from the research study database and will continue to be used to complete the research analysis. You may be asked whether the investigator can collect information from your routine medical care. If you agree, this data will be handled the same as research data

You may also withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use the information that was already collected if that information is necessary to complete the research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from participating in the research study.

Withdrawal without your consent: The study doctor, the sponsor or the institution may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the study team have not been followed, the investigator believes it is in your best interest, or for any other reason. If specimens or data have been stored as part of the research study, they too can be destroyed without your consent.

CONTACT PERSON(S):

If you have any questions, concerns, or complaints at any time about this research, or you think the research has hurt you, please contact the office of the research team and/or the Principal Investigator Dr. Christopher Kellner, MD at phone number 212-241-2606.

If you experience an emergency during your participation in this research, go to the nearest hospital and tell the physician on call that you are in a research study. They will call your study doctor who will make arrangements for your treatment.

This research has been reviewed and approved by an Institutional Review Board. You may reach a representative of the Program for Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai at telephone number (212) 824-8200 during standard work hours for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

DISCLOSURE OF FINANCIAL INTERESTS:

Dr. Christopher Kellner (the Principal Investigator) is a founder and equity owner of Metis Innovative, LLC (a company that coordinates investments in early stage neurotechnology companies).

Dr. Reade Delacy (a co-investigator in this study) receives financial compensation as a consultant for Penumbra (the study sponsor and manufacturer of the Apollo System being evaluated in the study).

Dr. Reade DeLeacy and Dr. J Mocco (co-investigators in this study) serve as consultants and have ownership interests (either stocks or stock options) with companies that manufacture devices for the treatment of neurovascular disorders.

If you have questions regarding paid relationships that your physician/researcher may have with industry, we encourage you to talk with him or her, or check for industry relationships posted on individual faculty pages on our website at http://icahn.mssm.edu/.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As you take part in this research project it will be necessary for the research team and others to use and share some of your private protected health information. Consistent with the federal Health Insurance Portability and Accountability Act (HIPAA), we are asking your permission to receive, use and share that information.

What protected health information is collected and used in this study, and might also be disclosed (shared) with others?

As part of this research project, the research team at the hospital(s) involved in the research will collect your name, address, telephone number, dates directly related to the individual (birth, admission, discharge, date of death, etc).

The researchers will also get information from your medical record (Mount Sinai Health System or any other hospital where you have been treated).

During the study the researchers will gather information by:

- Taking a medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- Doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- Completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.
- reviewing HIV-related information, which includes any information indicating that you have had an HIV related test, or have HIV infection, HIV related illness or AIDS, or any information which could indicate that you have been potentially exposed to HIV

Why is your protected health information being used?

Your personal contact information is important to be able to contact you during the study. Your health information and the results of any tests and procedures being collected as part of this research study will be used for the purpose of this study as explained earlier in this consent form. The results of this study could be published or presented at scientific meetings, lectures, or other events, but would not include any information that would let others know who you are, unless you give separate permission to do so.

The Principal Investigator may also use and share the results of these tests and procedures to treat you in collaboration with others in the Mount Sinai Health System.

The research team and other authorized members of The Mount Sinai Health System ("Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example, the School's Program for the Protection of Human Subjects is responsible for overseeing research on human subjects, and may need to see your information. If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes. If the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.

Who, outside Mount Sinai, might receive your protected health information?

As part of the study, the Principal Investigator, study team and others in the Mount Sinai workforce may disclose your protected health information, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Principal Investigator.)

- Other collaborating research center(s) and their associated research/clinical staff who are working with the investigators on this project:
    - Other sites available on request
- Research data coordinating office and/or their representative(s) who will be responsible for collecting results and findings from all the centers: The Mount Sinai Health System
- The commercial sponsor and/or their representative (who will use the results for submissions to the Food and Drug Administration): Penumbra, Inc.
- Academic Research Organization (whose job is to help organizations fulfill their responsibilities in the research and development process): The Mount Sinai Health System
- A Data Safety Monitoring Board or other committee that will monitor the study on an ongoing basis for safety.
- The United States Food and Drug Administration
- The United States Department of Health and Human Services and the Office of Human Research Protection.
- Core Laboratory: Oculus Imaging LLC

In all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. Some records and information disclosed may be identified with a unique code number. The Principal Investigator will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the law requires it, or rarely if the Institutional Review Board

allows it after determining that there would be minimal risk to your privacy. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, may come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, when applicable, the monitors, auditors, the IRB, the Office of Human Subjects Protection (OHRP) of the Department of Health and Human Services as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. OHRP and FDA are authorized to remove information with identifiers if necessary to complete their task. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

For how long will Mount Sinai be able to use or disclose your protected health information?

Your authorization for use of your protected health information for this specific study does not expire.

Will you be able to access your records?

During your participation in this study, you will have access to your medical record and any study information that is part of that record. The investigator is not required to release to you research information that is not part of your medical record.

Do you need to give us permission to obtain, use or share your health information?

NO! If you decide not to let us obtain, use or share your health information you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?

You may withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use your protected information that was already collected if that information is necessary to complete the study. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from being in the study. If you withdraw your permission to use your protected health information for research that means you will also be withdrawn from the research study, but standard medical care and any other benefits to which you are entitled will not be affected. You can also tell us you want to withdraw from the research study at any time without canceling the Authorization to use your data.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, even if your information will no longer be protected by federal regulations, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If as part of this research project your medical records are being reviewed, or a medical history is being taken, it is possible that HIV-related information may be revealed to the researchers. If that is the case, the following information concerns you. If this research does not involve any review of medical records or questions about your medical history or conditions, then the following section may be ignored.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 306-5070. These agencies are responsible for protecting your rights.

Signature Block for Capable Adult

Your signature below documents your permission to take part in this research and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

Signature of subject	Date
Printed name of subject	Time

Person Explaining Study and Obtaining Consent

Signature of person obtaining consent	Date
Printed name of person obtaining consent	Time

Witness Section: For use when a witness is required to observe the consent process,, document below (for example, subject is illiterate or visually impaired, or this accompanies a short form consent):

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Signature of witness to consent process	*Date*
Printed name of person witnessing consent process	Time