

Esmolol to Treat the Hemodynamic Effects of Septic Shock

NCT02369900

September 14, 2020

****FOR CCI USE ONLY****

**Approved by the Beth Israel Deaconess Medical Center Committee on
Clinical Investigations:**

Consent Approval Date: 9/14/2020

Protocol Number: 2014P-000415

NCT02369900 / Z00.6



INFORMED CONSENT FORM TO TAKE PART IN A RESEARCH STUDY

SUBJECT'S NAME:
TITLE OF RESEARCH PROTOCOL: Esmolol to treat the hemodynamic effects of septic shock
PRINCIPAL INVESTIGATOR: Michael N Cocchi MD
PROTOCOL NUMBER: 2014P-000415

INTRODUCTION:

- This is a research study;
- Your participation is voluntary;
- A research study includes only people who choose to take part;
- You may or may not benefit from participating in the study. However, your participation may help others in the future as a result of knowledge gained from the research;
- You may leave the study at any time;
- If you choose not to take part, or if you leave the study, your decision will in no way harm your relationship with any member of the research team or any other individuals at Beth Israel Deaconess Medical Center.

Please read this consent form carefully and ask the investigators or study staff to explain any words or information that you do not clearly understand. Once you read this consent form and understand what your participation in this study will involve, you will be asked to sign this form if you wish to take part. You will be given a signed copy of the form to keep for your records.

DISCLOSURE OF SPECIAL INTERESTS OF BIDMC AND INVESTIGATORS

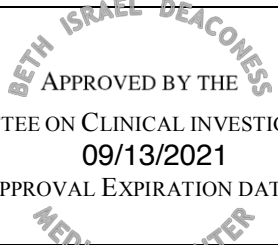
This study is being conducted by Dr. Michael N Cocchi MD and is funded by The American Heart Association. The funding agency in this study (The American Heart Association) is paying Beth Israel Deaconess Medical Center and Dr. Cocchi to perform this research. BIDMC or Dr. Cocchi have no additional interests in this research project. Dr. Michael Donnino, a co-investigator in the study, is a paid consultant to the AHA.

WHOM TO CONTACT IF YOU HAVE QUESTIONS OR PROBLEMS

If you have any questions, concerns or complaints about this research or experience any problems, you should contact Dr. Cocchi at [617] 754-2341.

PURPOSE

SUBJECT'S NAME:
TITLE OF RESEARCH PROTOCOL: ESMOLOL TO TREAT THE HEMODYNAMIC EFFECTS OF SEPTIC SHOCK
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 APPROVED BY THE COMMITTEE ON CLINICAL INVESTIGATIONS 09/13/2021 APPROVAL EXPIRATION DATE
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Septic shock is a condition where you develop low blood pressure and a fast heart rate due to a severe infection. We often treat patients in septic shock with medications to raise the low blood pressure (called vasopressors). We usually do not treat fast heart rates in patients with septic shock unless they are very fast. Esmolol is a drug called a beta-blocker that is used to treat heart rhythm disorders, including fast heart rates. The main purpose of this study is to determine the effects of treating the fast heart rate in septic shock with esmolol.

The drug involved in this study, esmolol, is FDA approved for other diseases and conditions where it is important to control heart rate, but it is currently unknown whether using esmolol in patients with septic shock will be useful, which is why we are conducting this trial. There are previous studies which have indicated benefit to treating the heart rate during septic shock, but this needs to be studied further before esmolol could be routinely used for this purpose.

As part of this study we will also obtain blood to run certain tests to compare the blood profile of patients who receive esmolol with the blood profile of patients who do not receive esmolol. These lab tests include markers of inflammation and cell function.

STUDY PARTICIPANTS

You have been asked to be in the study because you have septic shock. Approximately 110 people will take part in this study at Beth Israel Deaconess Medical Center.

DESCRIPTION OF STUDY DETAILS

If you agree to be in this study, you will be asked to read and sign this consent form. After you sign the consent form, the following things will happen:

1. **Screening Procedures:** Screening procedures are tests and procedures that will be done to determine if you are eligible to take part in the research study. For this research study, the screening procedures include: A member of the study staff will review your medical chart and speak with you and your physician to determine if you are eligible to participate in the study.
2. **Randomization Procedures:**
You will be randomly assigned (like the flip of a coin) to receive either standard care for septic shock PLUS esmolol or standard care alone (no esmolol). You have a 1 in 2 chance of receiving esmolol. You will not be able to choose the study group to which you will be assigned. Standard care for septic shock is determined by your clinical team, in accordance with national guidelines and recommendations, and usually involves antibiotics to treat the infection, as well as medications to improve blood pressure; both groups will receive this standard care.

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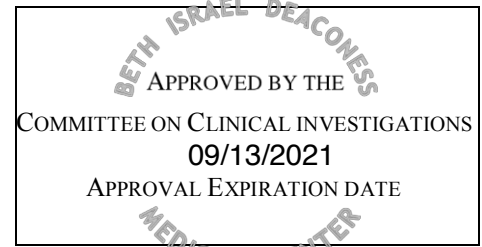


3. **Research Procedures:** If you qualify to take part in this research study, you will undergo these research procedures: Your treatment, irrespective of which group you are in, will be managed by your team of clinicians and based on BIDMC's internal guidelines for treating septic shock.

All participants in this study (those receiving the **study treatment** and those receiving **standard care**) will undergo the following procedures:

- **Study Drug:** Just after the first blood draw,
 - If you are randomized to **study drug**, you will be given an intravenous (IV) infusion of esmolol (weight-based and based on hospital guidelines). The intravenous infusion will take place over approximately 24 hours, and may be adjusted by your nurse to achieve a goal heart rate (80-94 beats per minute).
 - If you are randomized to **standard of care**, you will receive 100 mL of saline solution (lightly salted water). The saline solution is given to patients in order to keep the treatment of the two groups as similar as possible. The saline will also mark the beginning of the study in a manner similar to the patients receiving Esmolol. The initiation of the infusion will serve as the study start time for both groups. Having comparable time points in each of the groups is important in order to analyze differences in blood markers.
- **Blood Collection:** Blood will be drawn at four (4) **different times** for patients in **BOTH groups**: at the start of the study (time 0) and at 6, 12 and 24 hours after you receive the study drug (or same time points if you are in the no esmolol group). Each blood draw will be less than 3 tablespoons (approximately 40 mL). The total amount of blood for the whole study will be 12 tablespoons (160 mL).
 - The blood will be sent to the BIDMC lab to analyze for lactate. The lactate tells us about the blood supply and oxygen to your major organs- for example the heart and kidneys.
 - Remaining blood will be frozen and tested for inflammatory biomarkers- which are proteins in your blood that indicate or identify inflammation.
 - If you were not in this study, we would not be collecting your blood for this purpose.
 - The results of this testing will not be available to you, ICU staff, hospital or clinical study staff during the study and therefore will not impact your care
- **Medical record review:** We will also perform a more thorough review of your chart to see how you are doing while you are in the hospital. From your chart we will collect vital signs, laboratory results, radiological testing and other variables and record this information. We

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will collect information until you are discharged from the hospital. If you were not in this study we would not be reviewing your medical record.

- **Oxygen consumption measurements:** If you have a breathing tube in place and are on the ventilator (respirator), you will be connected to the Compact Anesthesia Monitor for continuous measurements of oxygen consumption. The Compact Anesthesia Monitor will be attached to the ventilator tubing. Your ventilator settings will not be changed by our team and a respiratory therapist will be present to connect and disconnect the monitor from the ventilator tubing.
- **Cardiac output measurements:** You will be connected to a non-invasive cardiac output monitor for continuous measurements of your cardiac index (a measure of how well your heart squeezes). Sensors will be attached to your chest wall which will provide these measurements.

RISKS AND DISCOMFORTS

As a result of your participation in this study, you are at risk for side effects listed in this section. You should discuss these with the investigator and with your regular doctor if you choose.

Esmolol risk:

More Common: Blood pressure decreased, nausea, infusion site reaction

Less Common: Peripheral ischemia, dizziness, somnolence, confusion, headache, agitation, vomiting

Rare: Abdominal discomfort, abnormal thinking, angioedema, anorexia, anxiety, bradycardia, bronchospasm, cardiac arrest, constipation, coronary arteriospasm, decompensated heart failure, depression, dyspepsia, flushing, heart block, hyperkalemia, lightheadedness, pallor, paresthesia, psoriasis, renal tubular acidosis, seizure, severe bradycardia/asystole, syncope, urinary retention, urticaria, xerostomia

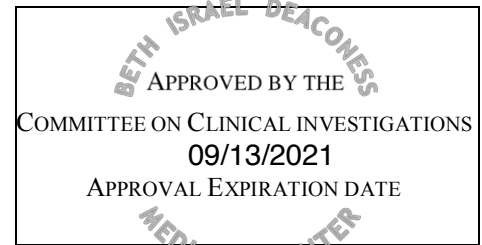
Blood Draw Risk:

Blood will be drawn from a line that you already have in place, so no additional needle sticks will be required as part of this study. Every time a central venous or arterial line is accessed there is a very small risk of infection. Standard procedures will be followed to minimize this risk.

LOSS OF CONFIDENTIALITY

There is the potential for loss of confidentiality by participating in this study. Every effort will be

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made to protect the confidentiality of your identifiable information.

However, if your participation becomes known, it could create a problem or hardship for you depending upon the type of information disclosed.

CONFIDENTIALITY

Information learned from your participation in this study and from your medical record may be reviewed and photocopied by the Food and Drug Administration (FDA) and/or other federal and state regulatory agencies, and by the drug manufacturer, accreditation agencies, the Committee on Clinical Investigations, the Human Subjects Protection Office and others involved in research administration of the Beth Israel Deaconess Medical Center with protection of confidentiality so far as permitted by applicable law. Information resulting from this study and from your medical record may be used for research purposes and may be published; however, you will not be identified by name in such publications.

MEDICAL RECORD

A copy of this consent form and information collected during this research may become part of your medical record, if the information is relevant to the care you receive at Beth Israel Deaconess Medical Center. Medical records are considered permanent records; therefore, information cannot be deleted from the record. Medical records are available to health care professionals at Beth Israel Deaconess Medical Center and may be reviewed by staff when carrying out their responsibilities, as well as by external parties such as health care insurers and others in certain circumstances. If you are not currently a patient at Beth Israel Deaconess Medical Center and do not have a medical record at Beth Israel Deaconess Medical Center, one may be created for you for your participation in this research. You may also be required to register as a patient of Beth Israel Deaconess Medical Center in order to participate in this research.

POSSIBLE BENEFITS

It is not possible to predict whether you will benefit directly from participation in this study. However, your participation may help others in the future as a result of knowledge gained from the research. The investigators believe that esmolol will lower the heart rate, allowing the heart to fill with more blood and increasing the amount of blood being pumped by the heart to the rest of the body.

OTHER AVAILABLE OPTIONS

Taking part in this study is voluntary. Instead of being in this study, you may choose not to participate.

It is important to note that it is possible to get esmolol even if you do not take part in this study. Esmolol has not been approved by the FDA specifically for treatment of your condition. However it is approved by the FDA for other conditions and is already used in certain clinical scenarios in patients

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with septic shock.

This research study is not meant to diagnose or treat medical problems. Participation in this research study does not take the place of routine physical examinations or visits to your regular doctor.

IF YOU DECIDE NOT TO TAKE PART IN THE STUDY

Participation in this study is voluntary. You have the right to decide not to take part in this study. If you choose to participate, you have the right to leave the study at any time. Your decision to not participate will not result in any penalties or loss of benefits to you. The investigators will tell you about new information that may affect your willingness to stay in this study.

If you decide not to participate in the study or decide to leave the study early, your decision will not affect your relationship with the research team or any other individual at Beth Israel Deaconess Medical Center.

INVESTIGATORS RIGHT TO STOP THE STUDY

The investigators have the right to end your participation in this study if they determine that you no longer qualify to take part, or if it would be dangerous for you to continue, or if you do not follow study procedures as directed by the investigators. Beth Israel Deaconess Medical Center or the funding source may stop the study at any time.

COSTS AND/OR PAYMENTS TO YOU

COSTS COVERED BY STUDY

You will not be charged for the research drugs or any laboratory tests that are part of this research study. However, you and your insurance company will be charged for other tests, procedures or medications of this study that are considered standard treatment for your medical condition.

CO-PAYMENT/DEDUCTIBLE STATEMENT

You will be responsible for any co-payments or deductibles that are standard for your insurance coverage.

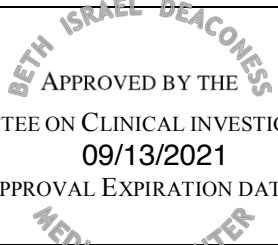
PAYMENTS TO YOU:

You will not be paid for your participation in the study.

COST OF RESEARCH RELATED INJURY:

If you are injured as a direct result of your participation in this study you should contact the Investigator at the number provided under the section "Whom to Call if You Have Questions" in this

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form. You will be offered the necessary care to treat your injury. You or your insurance company will be billed for medical care and/or hospitalization related to this injury. You will be responsible for all co-payments and deductibles required under your insurance. BIDMC will consider reimbursement of injury related expenses not covered by your insurance on a case-by-case basis. At this time there is no plan to reimburse you for items such as lost wages or lost time from work. By signing this consent form you have not given up any legal rights.

A description of this clinical trial will be available on 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.

AUTHORIZATION FOR USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION

As part of this study, we will be collecting, using and sharing with others information about you. Please review this section carefully as it contains information about the federal privacy rules and the use and disclosure of your information.

PROTECTED HEALTH INFORMATION [PHI]

By signing this informed consent document, you are allowing the investigators and other authorized personnel to use [internally at BIDMC] and disclose [to people and organizations outside the BIDMC workforce identified in this consent] health information about you. This may include information about you that already exists (for example: your medical records and other sources of health information, demographic information, the results of any laboratory tests, as well as any new information generated as part of this study. This is your Protected Health Information.

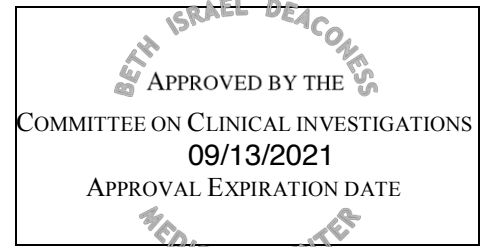
PEOPLE/GROUPS AT BIDMC WHO WILL SHARE AND USE YOUR PROTECTED HEALTH INFORMATION

Your Protected Health Information may be shared with and used by investigators listed on this consent form as well as the supporting research team [i.e. research assistants and coordinators, statisticians, data managers, laboratory personnel, pharmacy personnel, administrative assistants], and may also be shared and used by other health care providers at BIDMC who have treated you in the past and have information relevant to the research, or who provide services to you in connection with the research. Your Protected Health Information may also be shared with the members and staff of the Committee on Clinical Investigations of Beth Israel Deaconess Medical Center, which is responsible for reviewing studies for the protection of the research subjects.

PEOPLE/GROUPS OUTSIDE OF BIDMC WITH WHOM YOUR PROTECTED HEALTH INFORMATION WILL BE SHARED

We will take care to maintain confidentiality and privacy about you and your Protected Health Information. We may share your Protected Health Information with the following groups so that they

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may carry out their duties related to this study:

- Any external health care providers who provide services to you in connection with this research
- Laboratories not affiliated with BIDMC that are involved in conducting tests related to the research
- Statisticians and other data monitors not affiliated with BIDMC
- Centralized data collectors
- Your health insurance company
- The Food and Drug Administration [FDA], the Department of Health and Human Services [DHHS], the National Institute of Health [NIH], the Office for Human Research Protections [OHRP], and other federal and state agencies that may have jurisdiction over the research
- Hospital and Clinical Research Accrediting Agencies
- Data and Safety Monitoring boards that oversee this study (if applicable)

Those who receive your Protected Health Information during the course of the research may not be required by the federal privacy regulations to protect it, and they may make further disclosures to others and use your information without being subject to penalties under those laws.

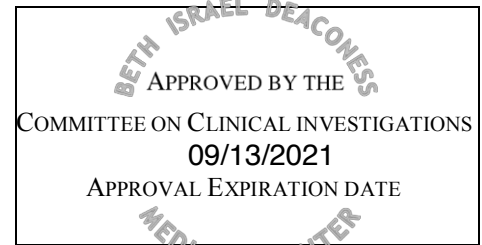
WHY WE ARE USING AND SHARING YOUR PROTECTED HEALTH INFORMATION

The main reason for using and sharing your Protected Health Information is to conduct and oversee the research as described in this Informed Consent Document. There are many other reasons beyond the research for which BIDMC may use or disclose your Protected Health Information. Not all of these reasons require your express written authorization. For example, we will use and share your Protected Health Information to ensure that the research meets legal, institutional and accreditation requirements and to conduct public health activities. The various ways in which BIDMC may use and disclose your protected health information without your authorization are explained in a document called the Notice of Privacy Practices. If you have not received a copy of BIDMC's Notice of Privacy Practices, please ask us for one and review it before signing this form. In addition to signing this document, you may also be asked to sign a BIDMC General Agreement form acknowledging that you have received the BIDMC Notice of Privacy Practices.

NO EXPIRATION DATE – RIGHT TO WITHDRAW AUTHORIZATION

Your authorization for the use and disclosure of your Protected Health Information in this Study shall never expire. However, you may withdraw your authorization for the use and disclosure of your Protected Health Information at any time provided you notify the Principal Investigator in writing. If you would like to take back your authorization so that your Protected Health Information can no longer be used in this study, please send a letter notifying the Principal Investigator of your withdrawal of your authorization to

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Dr. Michael N Cocchi
1 Deaconess Rd., W/CC2,
Boston, MA 02215

Please be aware that the investigators in this study will not be required to destroy or retrieve any of your Protected Health Information that has already been used or disclosed before the Principal Investigator receives your letter, and they are permitted to continue to use and disclose your previously collected information as necessary to complete the research.

REFUSAL TO SIGN

Your clinical treatment may not be conditioned upon whether you sign the Authorization for Research. However, if you choose not to sign this informed consent document and authorization for the use and disclosure of your Protected Health Information, you will not be allowed to take part in the research study.

RIGHT TO ACCESS AND COPY YOUR PHI

If you wish to review or copy your Protected Health Information as it is made part of your medical record, you may do so after the completion or termination of the study by sending a letter to the Principal Investigator requesting a copy of your Protected Health Information. You may not be allowed to inspect or copy your Protected Health Information until this study is completed or terminated.

ADDITIONAL CONTACT FOR QUESTIONS OR CONCERNS

You may contact the Human Subjects Protection Office at [617] 975-8500 in the event that you would like to obtain information or to offer input about the research study. This office is independent of the investigator or investigator's research staff and can also assist with questions relating to your rights as a participant in research, which may include questions, concerns or complaints about your participation in the study.

ICF REVISION DATES:

01/26/2015 first approved version


07/30/2015: addition of co-investigators, addition of normal saline to control group

09/21/2015: addition and removal of co-investigators

01/11/2016: disclosure of Dr. Donnino's (co-investigator) relationship with the funding entity.

01/15/2016: change in telephone number for PI

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THE FOLLOWING PARAGRAPHS CONTAIN SOME STANDARD INFORMATION WHICH GENERALLY APPLIES TO INDIVIDUALS PARTICIPATING IN A RESEARCH STUDY.

CONSENT FORM FOR CLINICAL RESEARCH

I have read the previous page[s] of the consent form and the investigator has explained the details of the study. I understand that I am free to ask additional questions.

If I wish additional information regarding this research and my rights as a research subject, or if I believe I have been harmed by this study, I may contact the Human Subjects Protection Office (HSPO).

I am aware that this is a research project and that unforeseen side effects may occur.

I understand that the Beth Israel Deaconess Medical Center has no formal program for compensating patients for medical injuries arising from this research. Medical treatment will be provided for injuries at the usual charge to me or to my insurer unless payment is otherwise provided for in this consent form.

I understand that participation in this study is voluntary and I may refuse to participate or may discontinue participation at any time without penalty, loss of benefits, or prejudice to the quality of care which I will receive.

I acknowledge that no guarantees have been made to me regarding the results of the treatment involved in this study, and I consent to participate in the study and have been given a copy of this form.

Signature of Subject or
Legally Authorized Representative
(Parent if the subject is a minor)

Date

Relationship of Legally Authorized Representative to Subject

The subject has been given the opportunity to read this consent form and to ask questions before signing, and has been given a copy.

SIGNATURE OF INVESTIGATOR/Co-Investigator

DATE

PRINT INVESTIGATOR'S/Co-Investigator's

NAME

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BETH ISRAEL DEACONESS
APPROVED BY THE
COMMITTEE ON CLINICAL INVESTIGATIONS
09/13/2021
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MEDICAL CENTER

THE FOLLOWING SECTIONS ARE NOT NEEDED FOR ALL STUDIES AND SHOULD BE UTILIZED AS INDICATED:

If the subject is able to speak and understand English but is not able to read or write

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

If the subject is able to understand English but is not physically able to read or write or see

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

If the subject is not English speaking and signed the translated Short Form in lieu of the English consent document.

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

Signature of Interpreter: _____

Printed name of Interpreter: _____

Date: _____