

INFORMATION SHEET FOR PARTICIPANTS IN THE BICAR ICU 2 STUDY

Study Title: Adjuvant Treatment of Severe Metabolic and/or Mixed Acidosis with Moderate to Severe Acute Renal Failure using Sodium Bicarbonate: A Prospective Multicenter Randomized Controlled Study
National Reference: 2019-000671-16 Project Coordinator: Dr. Boris JUNG
(University Hospital of Montpellier)

Principal Investigator at your institution:

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Dear Sir/Madam,

Your doctor has proposed your participation in a clinical research study currently taking place in our department entitled: Adjuvant Treatment of Severe Metabolic and/or Mixed Acidosis with Moderate to Severe Acute Renal Failure using Sodium Bicarbonate: A Prospective Multicenter Randomized Controlled Study, promoted by the University Hospital of Montpellier.

We kindly invite you to carefully read this information sheet, which aims to address any questions you may have before making your decision to participate. After reviewing the information sheet, you will have a period of time to consider before submitting the corresponding signed consent form.

Your participation is entirely voluntary. If you do not wish to participate in this research, you will continue to receive the best possible medical care in accordance with current knowledge.

1. Why this research? You have a disease that poses a short-term life-threatening risk. Among the consequences of your illness, there is blood acidification (known as acidemia) and sudden kidney failure (known as acute renal failure). Treatment that corrects this acidification through infusion (using sodium bicarbonate treatment) could potentially improve your health, but this remains uncertain at present. We aim to evaluate this treatment through this study conducted in multiple centers in France.
2. What is the research objective? The objective of the research is to determine if adjuvant treatment (additional treatment) using sodium bicarbonate infusion allows for a faster treatment of severe acidosis in patients with moderate to severe renal failure admitted to the intensive care unit. "Severe acidosis" is characterized by a decrease in blood pH, making it acidic. The causes of this acidity are multiple in intensive care (infections, etc.), with acidosis reflecting the severity of the disease.
3. What is the methodology? This is a therapeutic trial that will be conducted in over thirty healthcare institutions in France, where 640 patients will be recruited over a period of 5 years. As part of this project, a computerized randomization will be

performed to determine whether or not you will receive sodium bicarbonate (adjuvant) in addition to the standard treatment for your illness. Two groups of patients will be formed as a result. This procedure is commonly used in clinical research to scientifically address the study's objectives. If you receive sodium bicarbonate, it will be administered by infusion (through an existing catheter for your monitoring) at a dose of 125 ml to 250 ml of 4.2% sodium bicarbonate, with a maximum of 1000 ml to correct the pH with a target of 7.30. The quantity administered and the frequency of administrations will be adjusted according to your pH during your stay in the intensive care unit. If you do not receive sodium bicarbonate, you will be treated according to good practice recommendations. Therefore, the management of your illness will be the same regardless of whether or not you receive sodium bicarbonate."

What will be your care, treatment schedule, and medical follow-up?

If you agree to participate in the study and meet all the required conditions, after signing the informed consent, you will be monitored during your stay in the intensive care unit. You will receive either the adjuvant treatment with sodium bicarbonate or the specific therapeutic care planned by the doctor. Your health status and biological parameters will be monitored throughout your stay. After your discharge, you will be contacted by phone at 3 months and 6 months to check on your progress. The table below summarizes the care planned by the study:

Date	Day 0: Admission to the intensive care unit (ICU)	Day 0: Admission to the intensive care unit (ICU)	Day 0: Admission to the intensive care unit (ICU)
Verification of inclusion criteria for the study	X*		
Information about the study and obtaining your informed consent	X*		
Collection of your medical history	X		
Clinical examinations by the physician	X	X	

Monitoring of your biological parameters (blood tests)	X	X	
Randomization (drawing lots)	X*		
Treatment with sodium bicarbonate for the treated group	X*	X*	
Follow-up of your health condition and acidosis		X	
Quality of life questionnaires for patients followed in Montpellier and Nimes (approximately 10 minutes duration)			X*
Outcome			X*

*study-specific

What are the expected benefits?

For patients in the treated group, the potential benefit you could expect from participating in this study is a faster improvement of acidosis, meaning an increase in blood pH, which could help your organs (heart, kidneys, lungs) function better and more quickly. Conversely, if you do not receive sodium bicarbonate treatment, the correction of blood pH will be slower. However, in any case, you will receive appropriate therapeutic care tailored to the causes of your acidosis and determined by your doctor outside of the research."

What are the foreseeable risks?

Sodium bicarbonate is an authorized and commercially available medication indicated for correcting metabolic acidosis. In the context of the study, possible adverse effects related to the infusion of sodium bicarbonate are mainly disturbances in certain ions or particles such as sodium, potassium, and calcium in the blood. These imbalances are common in patients in the intensive care unit regardless of their treatment, but they are exceptionally severe

because blood tests are performed several times a day as part of routine monitoring to detect and manage them. Adjustments in potassium and calcium intake, as well as a decrease in sodium intake, can easily be implemented by the medical intensive care team. In very rare cases, the pH can increase too much (over-correction of acidity), leading to a condition known as "rebound alkalosis," which can also be easily detected through the multiple blood tests performed daily on intensive care unit patients. Furthermore, the administration of sodium with sodium bicarbonate infusion may represent an excess of sodium for patients with severe heart failure. However, patients in the intensive care unit are constantly monitored by a nurse, and the medical team is trained to detect and manage the very rare decompensations of heart failure during sodium bicarbonate treatment.

The non-administration of adjuvant treatment with sodium bicarbonate also exposes patients to the risks of slower correction of blood acidity, particularly the risks of cardiac rhythm disorders, decreased cardiac pumping strength, breathing difficulties, or neurological disorders such as coma. Prolonged significant acidity in the blood poses a life-threatening risk, although it is not yet known whether this is due to the acidity itself or rather the underlying disease that makes the blood more acidic.

These described side effects are not systematic and are generally well-tolerated.

What will be the duration of your participation?

If you agree to participate in this study, your participation will last for the duration of your stay in the intensive care unit. You will then be contacted by phone at 3 months and 6 months.

What are the procedures and justification for sample collection?

Blood samples from intensive care unit patients with abnormal blood acidity are necessary to adjust the treatment and monitor patients' progress. Significant blood acidity is an important sign that the disease is severe. No additional blood samples beyond those absolutely necessary for your monitoring as part of your care will be taken.

What are the potential medical alternatives?

Blood acidity spontaneously corrects itself with specific disease-specific treatment (e.g., antibiotics for infections), and it indicates recovery. The objective of this study is to determine whether accelerating the correction of acidity improves the success of specific treatment and speeds up recovery. The alternative to the study treatment (sodium bicarbonate) in France is the absence of treatment because there are no other available medications. However, if the

acidity remains severe, it may require the temporary implementation of renal dialysis, which is a machine that replaces the natural function of toxin and acidity elimination performed by your kidneys.

What are your rights?

Your doctor must provide you with all the necessary explanations regarding this research. If you wish to withdraw from the study at any time, for any reason, you will continue to receive medical follow-up, and it will not affect your future monitoring. According to regulations, you must have social security coverage to participate in research involving human subjects.

In accordance with Article L.1111-6 of the Public Health Code, you have the right to designate a trusted person who can be a family member, a close relative, or your treating physician. This person will be consulted in case you are unable to express your will and receive the necessary information for this purpose.

"Your will is important. The testimony of your designated trusted person takes precedence over any other testimony. This designation must be made in writing and co-signed by the designated person. It can be revised or revoked at any time.

If you wish, your trusted person can accompany you in your procedures and attend medical interviews to assist you in your decisions.

In the context of the research in which the University Hospital of Montpellier proposes your participation, computer processing of your personal data will be carried out to analyze the research results in relation to the presented objective.

The controller of this processing is the University Hospital of Montpellier.

The principal investigator of the study and any other study personnel bound by professional secrecy and under the responsibility of the attending physician will collect medical data concerning you. These pieces of information, referred to as "Personal Information," will be recorded on the observation forms, called observation notebooks, provided by the sponsor. Only information strictly necessary for processing and the purpose of the research will be collected in a secure database, and will be retained by the sponsor for 25 years after the research ends.

To ensure the confidentiality of your personal information, neither your name nor any other information that would directly identify you will be entered in the observation notebook or in

any other file that the study investigator will provide to the research sponsor or to individuals or companies acting on its behalf, in France or abroad.

These data will be identified by a code (inclusion number and initials). The code will be used by the study investigator to identify you if necessary.

Under conditions ensuring their confidentiality, this data may also be transmitted to French health authorities.

In accordance with the provisions of the French Data Protection Act (Law No. 78-17 of January 6, 1978, relating to data processing, files, and individual liberties, as amended by Law No. 2018-493 of June 20, 2018, relating to personal data protection) and the General Data Protection Regulation (EU Regulation 2016/679), you have the right to access, rectify, erase, or restrict the information collected about you in the context of this processing.

In certain cases, you can also refuse the collection of your data and object to certain types of data processing. You also have the right to object to the transmission of data covered by professional secrecy that may be used in the context of this research and to be processed. You can also directly access, or through the physician of your choice, all of your medical data in accordance with the provisions of Article L1111-7 of the French Public Health Code.

You may withdraw your consent to the collection of your data at any time in the context of this processing. In this case, in accordance with Article L.1122-1-1 of the French Public Health Code, the data concerning you that have been collected prior to your withdrawal of consent may not be deleted and may continue to be processed in accordance with the research provisions.

Finally, you can request that the personal information collected be provided to you or to a third party in a digital format (right to data portability).

The aforementioned rights can be exercised with the physician who is following you in the context of the research and who knows your identity.

If you have any other questions regarding the collection, use of your personal information, or the associated rights, you can contact the Data Protection Officer of the University Hospital of Montpellier (email: dpo@chu-montpellier.fr) or the principal investigator of the study.

If, despite the measures put in place by the sponsor, you believe that your rights are not being respected, you can file a complaint with the competent data protection supervisory authority in France, the National Commission for Data Protection and Liberties (CNIL).

If the data controller wishes to carry out further processing of personal data concerning you for a purpose other than that for which your personal data were collected, you will be informed in advance of this other purpose, the duration of the retention of your data, and any other relevant information to ensure fair and transparent processing.

In accordance with Law No. 2012-300 of March 5, 2012, regarding research involving human subjects:

This research has obtained a favorable opinion from the Committee for the Protection of Persons of Nord Ouest 1 and the authorization of the National Agency for the Safety of Medicines and Health Products (ANSM).

The sponsor of this research has taken out civil liability insurance (contract number 166244) with the Société Hospitalière d'Assurances Mutuelles located at 18 rue Edouard Rochet, 69372 LYON CEDEX 08, France - 04 72 75 50 25).

Individuals who have suffered harm following participation in research involving human subjects may assert their rights with the regional commissions for conciliation and compensation for medical accidents.

When this research is completed, you will be personally informed of the overall results by your physician as soon as they become available, if you so desire.

After reading this information sheet, do not hesitate to ask your physician any questions you may have. After a period of reflection, if you agree to participate in this research, you must complete and sign the consent form. A copy of the complete document will be provided to you."

**CONSENT FORM FOR PATIENTS PARTICIPATING IN RESEARCH
BICAR ICU 2**

**Study Title: Adjuvant Treatment of Severe Metabolic and/or Mixed Acidosis with
Moderate to Severe Acute Renal Failure using Sodium Bicarbonate: A Prospective
Multicenter Randomized Controlled Study**

National Reference: 2019-000671-16

Project Coordinator: Dr. Boris JUNG (University Hospital of Montpellier)

Investigating Physician at your institution:

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I, the undersigned (full name), certify that I have read and understood the information provided to me.

I had the opportunity to ask any questions I wanted to Dr./Prof. (name) who explained to me the nature, objectives, potential risks, and constraints associated with my participation in this research.

I am aware that I have the option to withdraw from this research at any time without having to justify my decision, and I will make every effort to inform the physician overseeing my participation. This will not affect the quality of subsequent care.

I have been assured that decisions regarding my health will be made at any time in accordance with the current state of medical knowledge.

I understand that this research has received favorable opinion from the Ethics Committee (Comité de Protection des Personnes) Nord Ouest 1, authorization from the ANSM (Agence Nationale de Sécurité du Médicament et des Produits de Santé), and compliance with the General Data Protection Regulation.

The research sponsor (University Hospital of Montpellier - 191, avenue du G GIRAUD 34295 Montpellier Cedex 5) has obtained liability insurance coverage for potential harm from the Société Hospitalière d'Assurances Mutuelles (contract number 166244), located at 18 rue Edouard Rochet, 69372 LYON CEDEX 08, France – 04 72 75 50 25).

I accept that individuals collaborating on this research or appointed by the sponsor, as well as potentially the representative of Health Authorities, may have access to information with the utmost respect for confidentiality.

I agree that the data collected during this research may be subject to computer processing under the responsibility of the sponsor.

I have taken note that, in accordance with the provisions of the law relating to information technology, files, and freedoms, I have the right to access, rectify, limit the processing of my data, and lodge a complaint with the National Commission on Informatics and Liberties (CNIL): <https://www.cnil.fr/>. I also have the right to object to the transmission of data covered by professional secrecy that may be used in the context of this research and processed. Lastly, I have the right to withdraw my consent at any time. These rights can be exercised with the physician overseeing my participation in this research, who is aware of my identity. My consent in no way relieves the investigator and the research sponsor of their responsibilities towards me. I retain all rights guaranteed by law.

The overall results of the research will be directly communicated to me if I wish, in accordance with the law of March 4, 2002, concerning patients' rights and the quality of the healthcare system.

Having had sufficient time for reflection before making my decision, I freely and voluntarily agree to participate in the BICAR ICU 2 research.

At any time, I may request additional information from the physician who invited me to participate in this research.

Date:

Date:

Patient's Signature: Physician's Signature: