INFORMED CONSENT FORM

Patients and family members:

We invite you to participate in a multi-center clinical study sponsored by us. Before deciding whether to participate in this study, please read the following carefully. If you have any questions, you can further consult with the researcher or discuss with your relatives or friends.

TITLE OF STUDY:Feasibility and safety of esketamine hydrochloride adjunct to sufentanil for non-surgical patients under mechanical ventilation in ICU (The SENSATION trial): Study protocol for a multicentre, single-blind, randomised, controlled trial.

VERSION NUMBER OF PROTOCO**L**:1.2

VERSION NUMBER OF THE Informed Consent Form: ZQ 1.2
PRINCIPAL INVESTIGATOR: Yi Long

Part 1: Notice to Participants

WHY IS THIS STUDY BEING DONE?

Pain is common in patients receiving mechanical ventilation in the intensive care unit (ICU). Intravenous opioids are recommended as the first-line therapy for pain management. However, opioids have troublesome side effects, such as unexpected sedation, delirium, respiratory depression, and ileus. Current guidelines suggest that non-opioids should be used as adjuncts in ICU analgesia to reduce opioid consumption.However, commonly used non-opioids such as acetaminophen and NSAIDs also have potential adverse effects on critically ill patients. Low-dose ketamine is recommended as an opioid adjunct to reduce opioid consumption based on low-quality evidence, and esketamine is an alternative to ketamine with greater efficacy and fewer side effects. However, evidence on the use of esketamine in patients receiving mechanical ventilation is lacking. This study investigated the feasibility and safety of esketamine as an adjunct to sufentanil for analgesic therapy in nonsurgical ICU patients under mechanical ventilation.

WHAT WILL HAPPEN IN THE STUDY?

You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. Neither you nor the study doctor will

choose what group you will be in. You will have an equal chance of being placed in either group.

Standard care group

In the standard care group, a minimal dose of sufentanil is used as the sole analgesic for pain management. Sufentanil was titrated to the minimum dose required to maintain the analgesic goal. The analgesic goal is to maintain CPOT≤ 2. CPOT will be reassessed every 2–4 hours, and the dose of sufentanil will be adjusted based on the CPOT assessment. Other analgesic measures (such as massage, music, and relaxation techniques) will follow guidelines and be determined by your treating physician.

S-ketamine group

In the S-ketamine group, esketamine hydrochloride (Hengrui Pharmaceutical Co., Ltd.) was infused at a rate of 0.2 mg/kg/h in addition to the minimal dose of sufentanil for pain management within 1 h of randomisation. After the start of ketamine infusion, the dose of sufentanil will be titrated according to the predetermined plan and the advice of your treating physician.

You will receive a maximum of 72 hours of study intervention and 28 days of follow-up. However, You can withdraw from this study at any time. If you decide to withdraw from this study, please let your doctor know.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

We are not sure if you can benefit from the research yourself. The results of this study could help future patients with your condition.

WHAT ARE THE RISKS OF THE STUDY?

Any therapeutic agents have the potential for side effects. The possible side effects of ketamine hydrochloride include hallucinations, delirium, elevated intraocular pressure, thyroid dysfunction, respiratory depression, hypertension or hypotension, drug addiction, etc.There also may be other side effects that we cannot predict. These side effects are often manageable and reversible. You will be observed for side effects, and all medically appropriate efforts will be made to prevent and/or control them. If there are side effects that cannot be controlled or reversed, they may result in serious injury or death.

The treating physician will try to prevent and treat any potential harm caused by this study. If there is any discomfort or unexpected situation during the study, please inform your study doctor immediately, who will make a judgment and provide medical treatment.

There may be situations where any treatment may be ineffective, and the condition may continue to develop due to ineffective treatment or the combination of other diseases. This is a treatment risk that every patient will face, and even if they do not participate in this clinical study, the risks caused by treatment will still exist. During the research period, if the doctor finds that the treatment measures taken in this study are ineffective, the study will be terminated and other potentially effective treatment measures will be adopted.

WHAT ARE THE COSTS AND COMPENSATION?

Taking part in this study will not lead to added costs to you or your insurance company. The trial drug and related laboratory tests are included in the routine treatment cost. The sponsor will not pay for routine costs required during hospitalization. You will receive no payment for taking part in this study.

WHAT DO YOU NEED TO COOPERATE WITH?

Cooperate with relevant examinations and treatments.

Truthfully inform your doctor about your disease condition.

If you experience any unexpected discomfort during the research period, please inform your doctor promptly.

WHAT ABOUT CONFIDENTIALITY?

Only the medical information that will be collected from you if you take part in this study.The investigator and the ethics committee may have access to your medical records. No public report on the results of this study will disclose your personal identity. We will make every effort to protect the privacy of your personal medical information as permitted by law.

WHAT ARE MY RIGHTS?

Participation in the study depends entirely on your willingness. You may refuse to participate in the study or withdraw at any time during the study, which will not affect your treatment or other benefit.

Your treating physician may suspend your participation in this study at any time during the study, in your best interest. If you withdraw from the study for any reason, you may be asked about your use of the trial drug. You may also need a laboratory and physical examination. This is very good for protecting your health.

Any new information found during the study that may affect your willingness to continue participating in the study will be provided to you and a new informed consent form and request to sign to indicate your willingness to continue participating in the study.

CONTACT INFORMATION

If you have any concerns or questions about the study, or if any emergency occurs, please contact your doctor promptly.
Doctor's name:_____, telephone number: _____
If you have any questions about your rights and interests, you may contact Tang Xiaohua, the Ethics Committee of the Affiliated Cancer Hospital of Chongqing University, telephone number:023-65075696.

Part 2: STATEMENT of CONSENT and AUTHORIZATION

I have read the above introduction to this study and have the opportunity to discuss and ask questions about this study. All the questions I have raised have been answered satisfactorily.
I am aware of the possible risks and benefits of participating in this study and volunteer to participate in this study. I confirm that I have sufficient time to consider this and understand that:

- I can always consult my doctor for more information.
- I can withdraw from this study at any time without discrimination or retaliation, and my medical treatment and interests will not be affected.

I am also aware that if I withdraw from the study, especially due to the medication, if I tell the doctor about the changes in my condition and complete the corresponding laboratory and physical examinations, it will be very beneficial to me and the whole study.
If I need to take any other medication due to the change in my condition, I will ask my doctor for his advice in advance or tell him the truth afterwards.
I agree with the relevant management, ethics committee or researchers to consult my research data.
I agree with □ or refuse□ to use my medical records, blood/urine/pathological examination specimens for studies other than this one.
I will obtain a copy of the signed and dated informed consent form.
I decided to consent to participate in this study.
Signature of the Patient/Patient's Legally Authorized Representative:_____
Date:_____
Signature of Witness to consent process:_____Date:_____

I have explained to the patient the details of the trial, including their rights and

possible benefits and risks, and gave them a copy of the signed informed consent form.

Signature of Investigator:_____ Date:_____