Informed Consent Form

Project Name: A Prospective Study of Memantine Hydrochloride for the Treatment of Prostate Cancer Patients

Department: Department of Urology

Institution Address/Postal Code: 87 Dingjiaqiao, Gulou District, Nanjing, Jiangsu Province, 210009

Principal Investigator: Bin Xu

Telephone/Email: +86 18012949196

Supervising Department: Zhongda Hospital, Southeast University

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Informed Disclosure Page

Dear Sir:

We invite you to participate in a Prospective Study of Memantine Hydrochloride for the Treatment of Prostate Cancer Patients. This study has been reviewed and approved by the Clinical Research Ethics Committee of Zhongda Hospital, Southeast University (Approval No. 2025ZDSYL1297-P01).

Before you decide whether to participate in this study, please read the following information as carefully as possible. It will help you understand the study, why it is being conducted, its procedures and duration, and the potential benefits, risks, and discomforts of participation. If you wish, you may discuss it with your relatives and friends, or ask a physician for an explanation to help you make your decision.

I. Background, Purpose, and Methods

1. Study Background

Prostate cancer (PCa) has become a major threat to the health of the male genitourinary system. The incidence of prostate cancer shows significant geographical and ethnic differences. Historically, data has shown a lower incidence in Asia compared to regions like Europe, America, Australia, and New Zealand. However, with the aging population, changes in lifestyle, and the popularization of screening methods such as Prostate-Specific Antigen (PSA) tests, the incidence of prostate cancer in our country is also showing a yearly increasing trend. It is currently known that neuroendocrine differentiation (NED) and neuroendocrine prostate cancer (NEPC) are important causes of castration resistance in prostate cancer, often occurring after long-term castration therapy for Castration-Resistant Prostate Cancer (CRPC). Its characteristic features are decreased expression of prostate-specific markers such as the Androgen Receptor (AR) and Prostate-Specific Antigen (PSA), and increased expression of neuro-related markers like Chromogranin A, Synaptophysin, and Neuron-Specific Enolase. Patients with prostate cancer featuring neuroendocrine (NE) characteristics have poor responsiveness to chemotherapy and a poor prognosis, with most having a survival period of less than one year. Considering the important role of neuroendocrine differentiation in the development and progression of prostate cancer, our team hopes that some prostate cancer patients can benefit from the long-term combined use of an NMDA receptor antagonist to reduce neuroendocrine differentiation in prostate cancer, thereby correcting castration resistance and drug resistance in advanced prostate cancer. NMDA receptor antagonists, such as the representative drug Memantine, are drugs used to treat Alzheimer's disease by regulating glutamate activity, primarily for patients with moderate to severe Alzheimer's. Therefore, exploring the use of memantine hydrochloride in prostate cancer patients to reduce neuroendocrine differentiation and correct castration resistance and drug resistance in

advanced prostate cancer has guiding significance for the clinical treatment of neuroendocrine castration-resistant prostate cancer (CRPC).

2. Study Purpose

To evaluate the prognosis of prostate cancer patients with long-term combination therapy of memantine hydrochloride in a prospective study. 3. Study Design

3.1 Study Methods

Information of patients who have undergone radical prostatectomy will be obtained from the electronic medical record systems of Zhongda Hospital and Lianyungang First People's Hospital. Patients who meet the inclusion and exclusion criteria will be screened. After signing the informed consent form, they will be administered memantine hydrochloride, and the drug's efficacy will be observed through long-term follow-up.

3.2 Participating Sites and Estimated Number of Enrolled Subjects

Participating Sites: Zhongda Hospital, Southeast University and Lianyungang First People's Hospital;

Estimated number of enrolled subjects: 15 cases. The estimated number of enrolled subjects at this center: 10 cases.

3.3 Expected Study Duration

Expected Study Duration: August 2025 to June 2028.

(The duration of study drug use is within the expected study duration).

3.4 Main Inclusion Criteria for Subjects

1 Age ≥ 18 years;

2 mCRPC patients who have previously received and failed first- or second-line therapy;

3 Patients with complete clinical baseline data who agree to long-term follow-up;

4 ECOG performance status of 0-1.

II. Subject's Responsibilities

1. Before you are enrolled in the study, the investigator will inquire about and record your medical history.

Your participation is voluntary. If you are a qualified candidate, you may voluntarily participate in the study and sign this informed consent form. If you do not wish to participate, we will respect your decision.

2.If you voluntarily agree to participate in the study, you will proceed according to the following steps:

In addition to your standard conventional treatment, you will take the NMDA receptor antagonist drug, memantine hydrochloride. (The approved indications for this drug do not include the treatment of prostate cancer; the use of this drug in this clinical study has been approved by the Pharmacy Administration and Drug Therapeutics Committee) .

After starting the medication, to minimize adverse reactions, the dose should be gradually increased by 5mg weekly during the first 3 weeks to reach the maintenance dose of 20mg. Under this regimen, all patients should return to our hospital for follow-up every 3 months to re-check blood PSA, liver and kidney function, etc., and should undergo a whole-body CT scan every year. At the same time, the physician will record any

acute and subacute toxic reactions and adverse events, and document whether the drug was discontinued and if any treatment measures were taken. During the above treatment, the physician will collect and evaluate data from all subjects.

The combined use of the NMDA receptor antagonist drug, Memantine, is investigational. If you do not participate in this study, you will still receive standard treatment for your disease but will not be required to take this study drug.

3. Other matters requiring your cooperation:

You are required to come to the hospital for appointments at the follow-up times agreed upon with your doctor. Your follow-up is very important, as the doctor will evaluate the effects of the study measures based on it.

If you need to undergo any other treatments, please contact your doctor in advance.

III. Subject's Rights

Your participation in this study is voluntary, and information about your participation will be kept confidential. You can refuse to participate or withdraw from the study at any time without facing discrimination or reprisal, and your medical treatment and rights will not be affected.

You may choose not to participate in this study, or you may withdraw midway. You can ask the investigator about alternative treatment options that may be available, such as chemotherapy, immunotherapy, etc. You are not required to participate in this study to treat your disease.

Your doctor or the investigator may terminate your participation in this study at any time in your best interest if you require other treatment, if you do not comply with the study plan, or for any other reasonable cause.

If you withdraw from the study for any reason, you may be asked about your use of the trial drug. If the doctor deems it necessary, you may also be asked to undergo laboratory tests and physical examinations. This is for the benefit of protecting your health.

If any significant new information arises during the course of the study that might affect your willingness to continue participating, your doctor will promptly inform you or your legal guardian.

You may access information and progress related to this study at any time. If you have any questions related to this study, experience any discomfort or injury during the trial, or have questions concerning your rights as a study participant, you can consult the investigator at any time.

Investigator's Name: Zhu Ziqi Contact Number: 15751213558

If you have any complaints about participating in this study, please contact the Clinical Research Ethics Committee of Zhongda Hospital, Southeast University, at 025-83272015.

IV. Potential Benefits of Participation

The potential benefits include the possibility of improvement in your medical condition and a reduced risk of neuroendocrine differentiation in your prostate cancer. This study may also help in

developing a new treatment method for other patients with similar conditions. However, we cannot guarantee that you will personally receive direct benefits, and it is also possible that your condition may not improve at all.

V. Potential Adverse Reactions, Risks, Discomfort, and Inconvenience of Participation

Participation in the study may involve drug-related adverse reactions, risks, and discomfort. The overall incidence of adverse events for the study drug, memantine hydrochloride, is comparable to that of a placebo, and the adverse events that occur are generally mild to moderate in severity. Common adverse reactions to this product (incidence less than 2%) include hallucinations, confusion, dizziness, headache, and fatigue. Uncommon adverse reactions (incidence 0.1-1%) include anxiety, hypertonia (increased muscle tone), vomiting, cystitis, and increased libido. Based on spontaneous reports, there have been reports of seizures, mostly in patients with a history of convulsion

During the study period, you will need to come to the hospital for follow-up appointments on time and undergo certain examinations, which will take some of your time and may cause you trouble or inconvenience.

If you experience any discomfort, new changes in your condition, or any unexpected situations during the study, regardless of whether they are related to the research, you should notify your doctor promptly. He/she will make a judgment and provide appropriate medical treatment.

VI. Regarding Costs

Your participation in this prostate cancer study will involve a series of blood tests and imaging examinations. These tests, including serum prostate-specific antigen (PSA), blood biochemistry tests, and imaging projects such as upper-middle abdomen and pelvic CT, prostate MRI, and PET-CT scans, are all necessary components of your routine diagnosis and treatment plan. Therefore, the related costs will be borne by you.

The study drug, memantine hydrochloride, used in this research will be provided free of charge by the project team.

To maximize your convenience, the data collection for this study will fully utilize your existing diagnosis and treatment follow-up schedules. Therefore, you will not be responsible for any additional transportation costs incurred as a result of participating in this study.

The costs for treating other co-existing diseases you may have, as well as costs incurred from switching to other treatments due to treatment inefficacy, are not covered.

VII. Regarding Compensation

The investigator will do their utmost to prevent and treat any harm that may result from this study. If study-related harm occurs during the research period, you will receive timely and free treatment. At the same time, the investigator will provide corresponding compensation or indemnification in accordance with laws and regulations.

VIII. Confidentiality of Personal Information

Your medical records and data will be stored securely at the hospital. The investigator, the Ethics Committee, drug regulatory authorities, and health commission administration departments will be permitted to review your medical records. Any public report of the results of this study will not disclose your personal identity. We will protect the privacy of your personal medical information to the extent permitted by law.

In accordance with the principles of medical research ethics, apart from personal privacy information, the trial data will be available for public inquiry and sharing. Such inquiry and sharing will be limited to web-based electronic databases, ensuring that no personal privacy information will be disclosed.

It is possible that your medical records may be used again in future research beyond this study. You may now declare your refusal to have your medical records used in research other than this study.

Informed Consent Form - Consent Signature Page

Consent Declaration

I have read the above information regarding this study, and I have had the opportunity to discuss and ask questions about it with the investigator. All my study-related questions have been answered, and my family and I have had sufficient time to consider this.

I understand the potential risks and benefits of participating in this study. I know that my participation is voluntary, and I understand that:

- This study has been approved by the Clinical Research Ethics Committee of Zhongda Hospital, Southeast University.
- All my information will be kept confidential.
- My rights to privacy, medical care, and compensation are protected.
- I can consult the investigator for more information at any time.
- I can choose not to participate in this study, or I can withdraw at any time without facing discrimination or reprisal, and my medical treatment and rights will not be affected.
- If I withdraw from the study midway, especially due to reasons related to the medication, I should inform the investigator of any changes in my condition and complete the corresponding physical and laboratory examinations, which will be very beneficial to the overall study.
- If I need to take any other treatment due to changes in my condition, or if I do not comply with the study plan, I will consult the investigator beforehand or truthfully inform the investigator afterward. The investigator may terminate my continued participation in this study for these or other reasonable causes.

I agree to allow representatives from the drug regulatory authorities, health commission administration departments, the Ethics Committee, or the sponsor to review my research data.

I will receive a signed and dated copy of this informed consent form.

Finally, I have decided to agree to participate in this study and promise to follow the study procedures to the best of my ability.

I agree□ refuse□ to the use of my medical records and pathological specimens in research other than this study.

Subject's Signature:_____ Date:

Contact Phone：_____

Guardian's Signature (if applicable):_____ Date: ___ Year ___ Month ___ Day ___ Hour ___ Min

Subject's Name (Printed): _____ Guardian's Relationship to Subject: _____

Guardian's Contact Phone: _____

Impartial Witness's Signature (if applicable): _____ Date: ___ Year ___ Month ___ Day ___ Hour ___ Min

Impartial Witness's Contact Phone: _____ Impartial Witness's ID Number: _____

I confirm that I have explained the details of this study to the subject, including their rights and the potential benefits and risks, and have answered their questions. The subject has voluntarily agreed to participate in this study, and I have given them a signed copy of the informed consent form.

Investigator's Signature: _____ Date: ___ Year ___ Month ___ Day ___ Hour ___ Min

Investigator's Contact Phone: _____