Official title: A prospective randomized controlled study comparing the efficacy and safety of Rezvilutamide+ADT+Docetaxel versus Rezvilutamide +ADT in the treatment of patients with metastatic hormone-sensitive prostate cancer (mHSPC)

Date: Aug 02, 2023

Primary purpose: Evaluate whether the combination of Rezvilutamide and androgen deprivation therapy (ADT) with docetaxel improves radiographic progression-free survival (rPFS) in patients with metastatic hormone-sensitive prostate cancer (mHSPC) compared to the combination of Rezvilutamide and ADT.

Secondary research objectives:

1. Observe the safety of the combination of Rezvilutamide and ADT with docetaxel compared to the combination of Rezvilutamide and ADT in mHSPC patients.
2. Evaluate the prostate-specific antigen (PSA) response rate, time to PSA progression, objective response rate (ORR), time to castration-resistant prostate cancer (CRPC), and time to next bone-related event of the combination of Rezvilutamide and ADT with docetaxel compared to the combination of Rezvilutamide and ADT in the treatment of mHSPC.

Exploratory research objective:

1. Retrospectively analyze the correlation between time to PSA progression and time to radiographic progression.

Study endpoint
Primary Endpoint: rPFS (radiographic Progression-Free Survival)
Secondary Endpoint: Safety endpoints: AE incidence rate, severity, abnormal laboratory indicators. 3) Efficacy endpoints: PSA response rate, time to PSA progression, ORR (Objective Response Rate), DoR (Duration of Response), Time to CRPC (Castration-Resistant Prostate Cancer), and time to next bone-related event.
Exploratory endpoint: 4) Correlation between time to PSA progression and time to radiographic progression.

Determination of Sample Size: The sample size for this study is not based on statistical considerations, and it is estimated to be approximately 200 cases in total.

Study subjects: Patients with mHSPC have a confirmed pathology of prostate adenocarcinoma with high tumor burden, which is defined by having at least one of the following conditions:
1) Bone scan showing ≥4 bone metastatic lesions (with at least one site outside the pelvis or spine).
2) CT/MRI revealing visceral metastatic lesions (excluding lymph nodes).

Subjects will be randomly assigned in a 1:1 ratio to two groups, including the group receiving Rezvilutamide in combination with ADT and the group receiving Docetaxel in combination with ADT. The initial plan is to include 100 subjects in each group, resulting in a total of 200 subjects.

Study Design: Subjects will be randomly assigned in a 1:1 ratio to either the group receiving Rezvilutamide in combination with ADT and Docetaxel (Group A) or the group receiving

Rezvilutamide in combination with ADT (Group B). The initial plan is to include 100 subjects in each group.

Stratification factors include: 1) ECOG score > 0; and 2) visceral metastasis.

Medication: Rezvilutamide tablets (Specification: 80 mg)

Administration: Rezvilutamide: 240 mg (3 tablets of 80 mg each) orally once daily (QD), can be taken with or without food.

Inclusion Criteria: Patients must meet all of the following inclusion criteria to be eligible for this trial:

1. Males aged ≥40 years and ≤80 years.
2. Histologically or cytologically confirmed prostate adenocarcinoma.
3. Metastatic disease.
4. Eligible for ADT and Docetaxel.
5. Started or not started first-generation androgen deprivation therapy (ADT), but not exceeding 12 weeks before randomization.
6. ECOG score of 0 or 1.
7. Laboratory tests meet the following requirements:
    - Hematology: neutrophils ≥1.5×10^9/L, platelets ≥100×10^9/L, hemoglobin ≥9g/dL.
    - Renal function: serum creatinine ≤1.5× upper limit of normal (ULN).
    - Liver function: aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤2.5× ULN, total bilirubin (TBIL) ≤1.5× ULN.
    - Coagulation function: international normalized ratio (INR) <1.5.
8. Study subjects: Patients with mHSPC have a confirmed pathology of prostate adenocarcinoma with high tumor burden, which is defined by having at least one of the following conditions:
        1) Bone scan showing ≥4 bone metastatic lesions (with at least one site outside the pelvis or spine).
        2) CT/MRI revealing visceral metastatic lesions (excluding lymph nodes).

Exclusion Criteria: Patients who meet any of the following criteria are not eligible to participate in this study:

1. Prior use of LHRH agonists/antagonists; second-generation androgen receptor (AR) inhibitors such as enzalutamide, ARN-509, darolutamide (ODM-201), or other investigational AR inhibitors; CYP17 enzyme inhibitors such as abiraterone acetate or oral ketoconazole for anti-tumor treatment of prostate cancer; chemotherapy or immunotherapy for prostate cancer prior to randomization.
2. Received radiation therapy/radiopharmaceutical treatment within 2 weeks before randomization.

3. Any of the following conditions within 6 months before randomization: stroke, myocardial infarction, severe/unstable angina pectoris, coronary artery/peripheral artery bypass surgery, congestive heart failure (New York Heart Association class III or IV).
4. Previous malignancy, except adequately treated basal cell carcinoma or squamous cell carcinoma of the skin or superficial bladder cancer not invading the deeper muscle layer (i.e., pTis, pTa, and pT1) and any other cancer in complete remission for at least 5 years before randomization.
5. Gastrointestinal diseases or procedures that are expected to significantly interfere with the absorption of study treatment.
6. Inability to take oral medication.

Criteria for discontinuing study treatment: The investigator may decide to discontinue study drug treatment for subjects in the following circumstances:

1. The subject withdraws informed consent to continue study treatment.
2. The subject meets the criteria for radiographic disease progression (as determined by RECIST 1.1 and modified PCWG3 criteria).
3. Bone-related events (such as radiation or surgery to the bone, pathologic fractures, spinal cord compression, or changes in antitumor therapy for the relief of bone pain).
4. Occurrence of any adverse events, abnormal laboratory findings, or concomitant illnesses that the investigator considers not in the best interest of the patient to continue participation in the study.
5. Other necessary situations as determined by the investigator, such as poor compliance, loss of freedom to express willingness due to incarceration or isolation, and so on.

Criteria for subject withdrawal from the trial: Discontinuation of study treatment does not automatically imply withdrawal from the trial. The investigator may decide to withdraw a subject from this study in the following circumstances:

1. The subject withdraws informed consent for further data collection.
2. The subject is lost to follow-up.

Criteria for trial termination: The trial must be terminated if any of the following occur:

1. Significant protocol violations are discovered during the trial, making it difficult to evaluate the drug effectively.
2. Sponsor requests termination while ensuring the rights and safety of the subjects.
3. The National Medical Products Administration or the Ethics Committee orders the trial to be terminated for some reason.

Safety Evaluation: Safety evaluation will be conducted using the NCI-CTC AE 5.0 criteria. From the time of subject signing the informed consent form until 30 days after the last dose of the drug, all adverse events (AEs) observed in the subjects will be observed, recorded, and assessed for their

correlation with the study drug, including clinical symptoms, vital sign abnormalities, and abnormal laboratory findings. Safety evaluations, including physical examinations, ECOG assessments, laboratory tests, and ECG examinations, will be conducted during the screening period, baseline, and after drug administration. Unscheduled visits may also be planned based on the occurrence of subjects' AEs.

Efficacy Evaluation:

1. Overall Survival (OS), radiographic Progression-Free Survival (rPFS).
2. PSA evaluation: PSA response rate, time to PSA progression.
3. CT/MRI imaging assessment: CT/MRI will be performed every 3 cycles starting from day 1 of the 4th cycle to evaluate response according to RECIST v1.1 criteria, including complete response (CR), partial response (PR), stable disease (SD), progressive disease (PD), as well as objective response rate (ORR) and duration of response (DoR).
4. Bone imaging assessment: Bone scans will be performed every 6 cycles starting from day 1 of the 6th cycle to evaluate bone-related outcomes, including progressive disease (PD) and non-PD according to the modified PCWG3 criteria.

Statistical Methods: Unless otherwise specified, data will be summarized using the following general principles for statistical analysis in this study. Categorical data will be summarized using frequency and percentage. Continuous data will be summarized using mean, standard deviation, median, maximum, and minimum values.

Safety Analysis: Descriptive statistics and listings will be used for safety set data including AE, laboratory, vital sign, and ECG data. Analyses will include but not limited to the following:

- Number and listing of dose-limiting toxicities (DLTs)
- Analysis of subject withdrawal, dose reductions, or temporary discontinuations due to AEs
- Incidence and severity of AEs
- Analysis of AE correlation with the study drug
- AE outcomes analysis
- Serious adverse events (SAE) analysis
- Descriptive statistics summary of laboratory, vital sign, and ECG data
- Incidence of abnormal laboratory findings
- Analysis of positive and negative changes in laboratory, vital sign, and ECG data compared to baseline

Efficacy Analysis: Comparison of overall survival (OS) survival functions between groups will be performed using the Log-Rank test. Kaplan-Meier estimates will be used to estimate survival rates, median OS, and its 95% confidence interval (CI) based on grouping. The Cox model will be used to estimate the between-group hazard ratio and calculate its 95% CI. Similar statistical methods will be used to analyze time to PSA progression, rPFS, and time to next bone-related event.

Objective response rate (ORR), PSA response rate, and their bilateral 95% CIs (Clopper-Pearson method) will be estimated, and the between-group difference and its bilateral 95% CI (normal approximation method) as well as the p-value for between-group comparison (Cochran-Mantel-Haenszel method) will be calculated. Descriptive statistics will be used for the duration of response (DoR).

Exploratory Analysis: This analysis will involve descriptive statistical summaries of the correlation between PSA progression and efficacy outcomes.

Study Termination: The study will end when approximately 70% of the subjects have died and 12 months have passed. After the study ends, if subjects are still receiving study drug treatment, they may continue to receive the study drug until they meet the criteria for study treatment discontinuation. SAEs occurring during the treatment period and within 30 days following the last dose of the study drug will continue to be collected and recorded in accordance with the protocol.

Informed Consent Form

We invite you to participate in a multicenter, randomized, open-label clinical study titled " A prospective randomized controlled study comparing the efficacy and safety of Rezvilutamide+ADT+Docetaxel versus Rezvilutamide +ADT in the treatment of patients with metastatic hormone-sensitive prostate cancer (mHSPC)". The study is led by Jiangsu Provincial People's Hospital and involves several renowned hospitals nationwide, including Jiangsu Cancer Hospital. Approximately 200 eligible subjects over the age of 40 who voluntarily participate will be enrolled in the study across these hospitals. The research has been reviewed and approved by the Ethics Committee of Jiangsu Provincial People's Hospital, and Dr. Huali Xin, the Director of Urology Department at our hospital, is responsible for this project. Our center plans to enroll 150 subjects. It is crucial for you to read and understand this informed consent form before agreeing to participate in this study. This document explains the research objectives, procedures, potential benefits, and risks you may face. It also outlines other treatment options available to you and your rights. You have the right to withdraw from the study at any stage. If you decide to participate, you will receive a copy of the informed consent form signed by both you and the researchers.

Why conduct this research?

Prostate cancer is the second most common malignant tumor in men globally in terms of incidence and the sixth most common cause of cancer-related deaths. The incidence of prostate cancer in China is lower than in Western countries, but it has been rapidly increasing in recent years. According to the latest statistics from the National Cancer Center, in 2015, there were approximately 60,300 new cases of prostate cancer and 26,600 deaths in China, ranking it as the 7th most common and 10th most lethal cancer in males. The incidence of prostate cancer is even higher in major cities, such as Beijing, Shanghai, and Guangzhou, where the incidence rates in 2009 were 19.30/100,000, 32.23/100,000, and 17.57/100,000, respectively, ranking them as the 5th, 5th, and 7th most common cancers among urban males. With the aging population and Westernized lifestyle, it is expected that the incidence of prostate cancer in China will continue to rise rapidly. Additionally, unlike Western countries, where only 10-15% of initial cases of prostate cancer are metastatic, in China, 20-30% of initial cases are already metastatic. Androgen deprivation therapy (ADT) with or without first-generation androgen receptor (AR) antagonists (such as bicalutamide, nilutamide) is the standard first-line treatment for metastatic prostate cancer. Although most patients initially respond to treatment, the disease progresses from metastatic hormone-sensitive prostate cancer (mHSPC) to metastatic castration-resistant prostate cancer (mCRPC) after an average of 18-24 months. The main mechanisms leading to castration resistance are continued adrenal androgen secretion, intratumoral androgen synthesis, AR overexpression, and acquired AR signaling pathway reactivation due to functional mutations.

The primary objective of this study is to evaluate whether the combination of Rezvilutamide and androgen deprivation therapy (ADT) with docetaxel improves radiographic progression-free

survival (rPFS) in patients with metastatic hormone-sensitive prostate cancer (mHSPC) compared to the combination of Rezvilutamide and ADT.

What do you need to do if you participate in the study?

This study is a multicenter, randomized, positive drug-controlled, open-label clinical trial. It evaluates whether the combination of Rezvilutamide and androgen deprivation therapy (ADT) with docetaxel improves radiographic progression-free survival (rPFS) in patients with metastatic hormone-sensitive prostate cancer (mHSPC) compared to the combination of Rezvilutamide and ADT. The experimental group will receive Rezvilutamide + ADT + docetaxel (6 cycles), while the control group will receive Rezvilutamide + ADT. The entire study plans to enroll 200 patients with high tumor burden mHSPC, who will be randomly assigned in a 1:1 ratio to the experimental and control groups, with stratification factors including: 1. ECOG performance status > 0; 2. Presence of visceral metastasis. Participants are allowed to receive a maximum of 3 months of ADT treatment (with or without antiandrogen therapy) before cycle 1 day 1 (C1D1) of the study. Up to 4 weeks prior to C1D1, participants can undergo transurethral resection of the prostate or receive palliative radiotherapy or surgery for symptomatic metastatic disease (e.g., spinal cord compression or bone pain). Participants who have undergone prior ADT treatment must not have evidence of soft tissue disease progression (according to RECIST 1.1 criteria) or clinically significant prostate-specific antigen (PSA) increase (defined as ≥50% increase from the lowest level after reaching castration levels of testosterone) before C1D1. Participants who have received antiandrogen therapy prior to enrollment must discontinue it before C1D1 and beyond.

This study includes a screening period of up to 28 days to determine if subjects meet the eligibility criteria and complete the baseline assessments. During the treatment period of the study, subjects will receive investigational drug treatment according to the assigned group, until disease progression, intolerable toxicity, withdrawal of informed consent, or the investigator determines it necessary to withdraw the subject from the study.

Throughout the entire treatment period, subjects will continue to receive androgen deprivation therapy (ADT) (either through medication or surgical castration). Subjects receiving medication-based castration will follow the instructions in the drug package insert. Efficacy assessments for soft tissue and bone imaging will be conducted based on RECIST 1.1 criteria (see appendix) and the adjusted PCWG3 criteria (see section 8.1.1). An Independent Review Committee (IRC) will review the imaging evaluations from each study center.

Survival follow-up will begin after the last dose of medication on day 30 and will occur every 2 months through clinical or telephone follow-up. During these

follow-ups, information regarding survival status, bone-related events (if they did not occur prior to the survival follow-up), and subsequent anti-tumor treatments will be collected until subjects experience death, loss to follow-up, withdrawal of informed consent, or termination of the study by the sponsor.

If you agree to participate in this study, please sign this informed consent form. Prior to your inclusion in the study, your doctor will inquire about and record your medical history, and you will undergo screening tests such as MRI, CT, and hematology to confirm your eligibility based on inclusion criteria.

After enrollment, you will be randomly assigned to either the experimental group or the control group in a 1:1 ratio. The experimental group will receive Rezvilutamide, ADT, and docetaxel (for 6 cycles), while the control group will receive Rezvilutamide and ADT. Throughout the treatment period, you will need to undergo regular examinations and evaluations according to the study protocol. After completion of treatment, a survival follow-up will occur every 2 months.

3. What are the criteria for participating in this study? (Inclusion criteria) In order to participate in this study, you need to meet the following criteria:

4. Age ≥ 40 years, male.

5. Physical condition with ECOG score of 0-1.

6. Histological or cytological examination confirming prostate adenocarcinoma, without evidence of neuroendocrine differentiation or small cell features.

7. High tumor burden, defined as having at least one of the following conditions: 1) Bone scan showing ≥4 bone metastases (with at least one location outside of the pelvic or spinal bones); 2) CT/MRI revealing visceral metastases (excluding lymph nodes).

8. Planned study period of receiving or maintaining ADT (Androgen Deprivation Therapy), which entails continuous LHRHa treatment or previous bilateral orchiectomy (surgical castration), along with 6 cycles of docetaxel chemotherapy.

9. Organ function levels must meet the following requirements:

- Absolute neutrophil count (ANC) ≥ 1.5 × 109/L.
- Platelets (PLT) ≥ 100 × 109/L.
- Hemoglobin (Hb) ≥ 90 g/L.
- Total bilirubin (TBIL) ≤ 1.5 ×ULN (Upper Limit of Normal).
- Alanine transaminase (ALT) ≤ 2.5 × ULN.
- Aspartate transaminase (AST) ≤ 2.5 × ULN.

- Blood urea nitrogen (BUN) (or urea) and creatinine (Cr) ≤ 1.5 × ULN.
- Left ventricular ejection fraction (LVEF) ≥ 50%.

7. Ability to adhere to the study protocol, as determined by the investigator.
8. Voluntary participation in this clinical trial, understanding the study procedures, and having signed the informed consent.

If you require more detailed inclusion criteria for participating in this study or if you have any unclear phrases or information, please consult your research doctor.

4. Who should not participate in the study? (Exclusion criteria) You should not participate in this study if you have any of the following conditions:
5. Previous treatment with ADT (Androgen Deprivation Therapy), chemotherapy, surgery, external beam radiation therapy, brachytherapy, radioactive drugs, or experimental local treatments for prostate pain, such as radiofrequency ablation, cryotherapy, high-intensity focused ultrasound, etc. However, the following conditions allow enrollment: (1) up to 3 months of ADT treatment (medical or surgical castration) with or without anti-androgen therapy before the first day of the study cycle (C1D1), with no evidence of soft tissue disease progression (according to RECIST 1.1 criteria) or clinically significant PSA elevation before C1D1 (defined as an increase of ≥50% from the lowest level after reaching castrate levels of testosterone); (2) transurethral prostatectomy or up to one course of palliative radiotherapy or surgery at least 4 weeks prior to C1D1 for the treatment of symptoms caused by metastatic disease (e.g., spinal cord compression or bone pain). All adverse events related to these treatments must have at least a grade 1 resolution before starting the study treatment (according to NCI-CTCAE v4.03).
6. Previous use or planned use of second-generation anti-androgen receptor antagonists (such as enzalutamide, apalutamide, darolutamide), abiraterone acetate, or other investigational drugs that inhibit testosterone synthesis for the treatment of prostate cancer during the study treatment period.
7. Within 4 weeks before C1D1, you have received any of the following treatments:
    - 5α-reductase inhibitors (such as finasteride, dutasteride, etc.);
    - Estrogen, progesterone-like drugs, androgen, systemic corticosteroid treatment (except for temporary use for allergy purposes);
    - Known herbal medicines with anti-prostate cancer or PSA-lowering effects (e.g., saw palmetto);
    - Treatment in other clinical trials.
8. Confirmed brain tumor lesions by imaging diagnosis;
9. Planning to receive any other anti-tumor therapy during this trial;

10. Known allergy history to the components of Rezvilutamide,, ADT, or chemotherapy drugs;
11. Presence of factors that affect swallowing, chronic diarrhea, bowel obstruction, or the intake and absorption of medication;
12. History of epilepsy or a disease that can induce seizures within 12 months before C1D1 (including transient ischemic attack history, stroke, brain trauma with consciousness disorders requiring hospitalization);
13. Active heart disease within 6 months before C1D1, including severe/unstable angina pectoris, myocardial infarction, symptomatic congestive heart failure, and ventricular arrhythmia requiring medication treatment;
14. Any other malignant tumor within 5 years before C1D1, except completely resolved in situ cancer or malignant tumors with slow progression, as determined by the investigator;
15. Active HBV or HCV infection (HBV viral load ≥104 copies/mL, HCV viral load ≥103 copies/mL);
16. History of immune deficiency diseases (including HIV positive test, other acquired or congenital immune deficiency diseases) or organ transplantation;
17. Patients who are unwilling to use effective contraception during the entire study treatment period and 30 days after the last dose;
18. Based on the investigator's judgment, the presence of comorbidities (such as poorly controlled hypertension, severe diabetes, neurological or psychiatric diseases, etc.) or any other condition that may pose a significant risk to patient safety, potentially confound study results, or affect the patient's ability to complete the study.

5. When can the study be terminated if I participate?

1. If you agree to participate in this study, you can terminate the study after completing the research tasks under the guidance of the research team.
2. During the study, you may terminate it midway under the following circumstances: a) Withdrawing informed consent (participants decide to withdraw for any reason); b) Any clinical adverse events, abnormal laboratory test results, or comorbidities identified by the researchers that are not in the best interest of the participants to continue receiving treatment and participating in the study; c) Inability to follow the study protocol.

6. What are the available treatment options? If you do not agree to participate in this study, you can choose from ADT monotherapy, ADT combined with abiraterone, or ADT combined with docetaxel. To determine which treatment option is more suitable for you, you can further consult with the specialist in the outpatient department.

7. What are the risks of participating in the study? The use of enzalutamide, ADT, and docetaxel in this study may have potential side effects, including:

- Diarrhea: Participants should be closely monitored for signs and clinical symptoms of colitis, such as diarrhea, abdominal pain, bloody or mucous stools, and fever. In symptomatic participants, infection should be ruled out, and if the symptoms persist and/or are severe, an endoscopic evaluation should be considered. It is recommended that participants with diarrhea drink plenty of water. If adequate fluid intake cannot be achieved through oral intake, fluid and electrolyte replacement should be administered intravenously.
- Anemia: Blood transfusion and hematopoietic growth factors may be used under the guidance of the researchers.
- Neutropenia: Granulocyte colony-stimulating factor (G-CSF) can be used to treat grade 3-4 febrile neutropenia.
- Bone pain: Bisphosphonates can be used to reduce the occurrence of bone disease, bone pain, and fractures under the guidance of the researchers. In addition, non-opioid analgesics can be used for symptomatic treatment.
- Anti-infective drugs: Participants with documented complications of infection can be administered oral or intravenous antibiotics or other anti-infective drugs according to standard hospital treatment protocols.
- Seizures: In the event of status epilepticus, intravenous diazepam 10 mg, rapid intravenous infusion of 20% mannitol, or intravenous dexamethasone 10-20 mg should be administered to prevent and treat brain edema. Blood glucose, electrolytes, arterial blood gas, and body temperature should be checked, and symptomatic treatment should be provided if abnormalities are detected.

We will monitor your hematological and non-hematological toxicities through regular examinations, observe the efficacy of the drug, and take appropriate measures for symptomatic treatment of adverse events. If you experience any discomfort or adverse reactions, please contact the research doctor promptly. Since enzalutamide, ADT, and docetaxel are conventional treatments for prostate cancer in clinical practice, there is a possibility of experiencing these side effects/adverse reactions even if you do not participate in this clinical study. In addition, any treatment may be ineffective, and the disease may continue to progress due to treatment failure or the presence of other comorbidities.

8. What are the potential benefits of participating in the research? By participating in this study, there is a possibility that your condition may improve (or it may not). This research also helps determine which treatment methods can effectively and safely treat other patients with similar conditions to yours.

9. Are there any costs associated with participating in the research? The cost of medications and related examinations used in the study, as well as

outpatient fees, transportation costs, medication costs, and examination fees, are the responsibility of the patient. There are no other subsidies. If any harm occurs as a result of the trial, appropriate treatment and compensation will be provided according to relevant national regulations.

10. Compensation: a) Compensation for participating in the study There will be no financial compensation for participating in this study or reimbursement of treatment-related costs.

11. Is personal information kept confidential? The results of this research project may be published in medical journals with the understanding and assistance of you and other participants. However, we will keep your research records confidential as required by law. The personal information of research participants will be strictly protected, and your personal information will not be disclosed unless required by relevant laws. When necessary, government authorities, hospital ethics committees, and other relevant researchers may have access to your data according to regulations.

12. Am I required to participate in the research? Participating in this study is completely voluntary. You have the right to refuse participation or withdraw from the study at any stage without discrimination or retaliation, and your medical treatment and rights will not be affected. If you decide to withdraw from this study, please contact your doctor for appropriate diagnosis and treatment of your condition.

13. What other treatment options are available if I don't participate in this research? If you do not agree to participate in this study, you can choose between ADT monotherapy, ADT combined with abiraterone, or ADT combined with docetaxel. To determine which treatment option is more suitable for you, you can further consult with the attending expert in the outpatient clinic.

14. Who can I consult if I have questions? If you have any questions regarding research information and participant rights or if any research-related harm occurs, you can contact the researchers and the ethics committee along with their contact details. Researchers: Lixin Hua; Shangqian Wang, phone: 13770561625; Medical Ethics Committee of Jiangsu People's Hospital, phone: 025-68306360.

Informed Consent Form
Signature page

Subject's Declaration: I have read the introduction to this study and my research personnel have fully explained and clarified the purpose, procedures, potential risks, and potential benefits of participating in this study, and have answered all my relevant questions. I voluntarily agree to participate in this study.

I agree □ or refuse □ to allow my research data and biological samples to be used for other studies besides this research.

Subject's Printed Name: Subject's Signature: Date: _____ Year _____ Month _____ Day Subject's Contact Phone Number: Mobile Number: _____

Legal Guardian's Printed Name: (if applicable) Relationship with the subject: Legal Guardian's Signature: Date: _____ Year _____ Month _____ Day Reason for the legal guardian's signature:

Witness's Printed Name: (if applicable) Witness's Signature: Date: _____ Year _____ Month _____ Day Reason for witness's signature:

Doctor's Statement: I have explained the relevant details of this study to the volunteer participating in this study and provided them with an original signed informed consent form. I confirm that I have provided a detailed explanation of the study, particularly regarding the ethical principles and requirements of risks and benefits, free participation, compensation, harm and compensation, voluntary participation, and confidentiality.

Doctor's Signature: Date: _____ Year _____ Month _____ Day Doctor's Contact Phone Number:
Medical Ethics Committee, Jiangsu Provincial People's Hospital, Contact Phone Number: 025-68306360