Official Title Azacitidine Combined With Venetoclax and ATRA in Newly Diagnosed AML

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Informed Consent Form for Subjects
(Informed Consent Form)

Azacitidine Combined With Venetoclax and ATRA in Newly Diagnosed AML

Dear Ms./Mr.

You are being invited to participate in a clinical study. The following items describe the background of the study, the purpose of the study, the methods of the study, the benefits and possible discomfort and inconvenience of the study, and your rights and interests, and should be read carefully before you participate in the clinical study. This informed consent form provides you with information to help you decide whether to participate in this clinical study. If you have any questions, please ask the physician in charge of the study to ensure that you fully understand the content. Your participation in this study is voluntary. If you agree to participate in this clinical study, please sign the signature page of the informed consent form.

I. Background of the study

The incidence of AML is 4.3 per 100,000 people per year, the mortality rate is 2.7 per 100,000 people per year, and the 5-year overall survival rate is only 29.5%.After induction chemotherapy, the overall CR rate in young AML patients reached 60%-70%, and the survival time in chemotherapy was 8.7 months to 12.9 months. Elderly AML patients had a CR rate of only 50% and a median overall survival (mOS) of 3.4 to 9.1 months.In recent years, Venetoclax combined with demethylation therapy has been widely used in clinical treatment.A recent clinical trial of ATRA in combination with decitabine demonstrated that the addition of ATRA to demethylation therapy extended OS from 5.1 months to 8.2 months in elderly non-APL AML patients.Some research groups have also observed that ATRA and BCL-2 inhibitors significantly inhibit the proliferation of AML cells and significantly increase the apoptosis rate, which indicates that retinoic acid combined with Vinecra and azacinocytoside in the treatment of AML.To improve the prognosis and survival of patients with AML, we propose to conduct a prospective study to observe the efficacy and safety of azacitidine combined with venetoclax and ATRA in newly diagnosed AML patients ,and explore the prognosis .

II. Study name and purpose

This is a prospective clinical trial study to investigate the efficacy and safety of azacitidine combined with venetoclax and ATRA in newly diagnosed AML patients ,and explore the prognosis .

III. Study methods and content

The study is a one arm prospective study with an expected study duration of 2 years.30 subjects who meet the inclusion criteria are planned to be included in this study.All patients need to complete two cycle of induction therapy. After two cycle of induction therapy the patients who are willing to receive bone marrow transplantation can be treated with a bone marrow transplant, and

the patients who refuse the bone marrow transplantation can treated with consolidation therapy followed by connective maintenance therapy.
(1) Inductive therapy: AZA 75mg/m² per day for days 1-7 and venetoclax 100mg orally for day 2 , 200mg orally for day 3, 300mg orally for day4-6, 400mg orally for day7-10,ATRA 45mg/m² for day 12-28,every 28 days for up to 2 cycles or progression; (2)Consolidate therapy:ATRA 45mg/m2 per day for d1-21 ,AZA 70mg/m² per day for days 1-7, every 28 days for up to 4 cycles or progression; (3) Maintenance therapy:ATRA 45mg/m2 for d1-21 every 28 days,AZA 70mg/m² per day for days 1-7, every 3 month untill progression;

IV. Study procedure and time frame
The efficacy was assessed within 2 years after treatment, and the assessment indexes included bone marrow, MRD, and other peripheral blood examination.

V. Possible benefits of participating in the study
With this study, patients can receive a two-for-one offer for retinoic acid, and this study may be beneficial to improve the prognosis of patients with AML, potentially reduceing complications and financial burden.

VI. Possible risks and discomforts of participating in the study
During the treatment,we will be faced with infection,bleeding and drug related toxicity.If a very small number of patients do not recover completely from discontinuation of the drug, we can provide therapeutic support.

VII. Treatment and financial compensation for subjects with study-related injuries
In case of study-related injuries, the study sponsor will bear the relevant medical treatment costs and corresponding financial compensation according to the relevant laws and regulations of China.

VIII. Conventional treatment plan outside the study
None.

IX.Subjects rights
Subjects rights to participate in the study include voluntary participation and withdrawal at any time, informed participation, consent or non-consent, confidentiality, compensation, free treatment and compensation in case of damage, no discrimination or retaliation at any time after withdrawal, and medical treatment and rights will not be affected as a result.

X. Confidentiality of clinical research data
The information and data recorded by the subjects participating in the study will be kept strictly confidential and will not be disclosed, and if the study results are published, the subjects identity information will also be kept confidential.

XI. Collection and management of biological samples involving human subjects 3ml of peripheral blood and 3ml bone marrow will be collected from the subjects each time according to the

follow-up plan, separated from the routine examination, without additional collection times, mainly for immune cell biology analysis and translational medicine research, and the specimens will not be used for product development, sharing and secondary use, etc., and privacy protection, destruction and disposal will be strictly observed.

XII. Contact information

Contact person and contact information of the investigator (contact person: Guchengyuan, contact information: 0512-67781521), contact person and contact information of the ethics committee (contact person: Wu Shangejie, contact information: 0512-67972743), contact person and contact information in case of problems.

XIII. Declaration and signature

Subject declares that I have read this informed consent form carefully and that I have had the opportunity to ask questions and that all questions have been answered. I understand that participation in this study is voluntary and that I may choose not to participate in this study or withdraw from the study at any time with notice to the investigator without discrimination or reprisal, and that any of my medical treatment and rights will not be affected as a result. If I require other treatment, or if I fail to comply with the study plan, or for any other valid reason, the study physician may terminate my continued participation in this clinical research study.

I voluntarily agree to participate in this clinical study, and I will receive a signed copy of the "Informed Consent" form.
Subjects name (in block letters);
Subjects signature:
Date: Month and year:
Mobile phone number:
Name of legal representative (in block letters):
Signature of legal representative:
Date: Month and year.
Mobile phone number:
Relationship to subject:
Subjects reason for not being able to sign informed consent:

The investigator declares that I have accurately informed the subject of the contents of the informed consent form and have answered the subjects questions, and that the subject is voluntarily participating in this clinical study.
Investigators name (in block letters):
Investigators signature:
Date: Month and year:
Mobile phone number: