informed consent

Project Title : Based on the theory of ' gut-brain axis ', to explore the intervention effect and related mechanism of ganoderma lucidum spore powder on depressive symptoms in patients with thyroid cancer

Research Institution : Zhejiang Cancer Hospital

Sponsor / sponsor : Zhejiang Anticancer Association, Jinhua Shouxiangu Pharmaceutical Co., Ltd

Research project type：（☑The project has been approved ☐Project declaration）

☐Above the department level (including department-level projects), please specify_____

☐Please specify the city level_____

☐miscellaneous _____

Dear Mr / Ms :

We will invite you to participate in this clinical scientific study, which has been reviewed by the Medical Ethics Committee of the Institute.

This informed consent form provides you with detailed information to help you decide whether to participate in this project. Please read it carefully, and before you make a decision, make sure that you fully understand the contents of the document, or that your questions are answered satisfactorily. If you have any questions, please feel free to consult the competent doctor or researcher, and we will give you a comprehensive explanation. But please note that we cannot commit to the results of the study.

If you are willing to participate in this study, you will receive an informed consent form signed by both you and the researcher.

Ⅰ.Research background, purpose and research content introduction

In this study, the antidepressant mechanism of ganoderma lucidum spore powder was studied by microbial 16 s diversity analysis and metabolomics method, in order to clarify the clinical effect of ganoderma lucidum spore powder intervention on postoperative depressive symptoms of papillary thyroid carcinoma.

Ⅱ.research design

This study was only carried out in this research institution, and a total of 300 subjects were recruited to participate in this clinical study. It is expected to last from January 2022 to December 2024.

This study was divided into study group and control group, the ratio (2 : 1)

Study group : From the first day, 4g of wall-removing spore powder was taken orally every day for 90 days.

Control group : From the first day, 4g of Ganoderma lucidum spore powder simulant was taken orally every day for 90 days.

Main entry and discharge standards： 1.Patients with depressive symptoms after thyroid papillary carcinoma surgery in Zhejiang Cancer Hospital ; 2. 2.Han nationality ; 3.No previous depression and other mental system diseases ; 4.Age 18-80 years old ; 5.Gender is female ; 6.BMI : 19 ~ 24.

III.The research process (what subjects need to do) is to collect your fresh fecal samples one day before the intervention and one day after 90 days of intervention (both outpatient review time).Feces sample collection method：①Put the stool collector in the toilet, discharge the feces into the collector, and fully mix the fresh fecal samples with a small spoon with a slender handle (Note :

avoid urine contaminating feces)。②The mixed fecal samples were divided into two marked 5 ~ 10 mL sterile tubes or pre-sterilized collection tubes, and about 2 ~ 3 mL of each tube was collected.
If you volunteer to participate in this study and sign an informed consent form, the research physician will screen you before enrollment. If you meet the enrollment criteria and do not meet the exclusion criteria, you will be randomly assigned to a study group or a control group in proportion (2 : 1). Which group you will enter is systematically and randomly determined (neither you nor your research physician can choose your allocation), as if tossing a coin or drawing a lot is as unpredictable. Therefore, you can participate in this study only after you agree to receive any treatment.

1. Screening period : You will receive the following inquiries and questionnaires from the research doctor : ①One day before the intervention, one month after the intervention and 90 days after the intervention, you will come to the hospital three times a day for clinical depressive symptoms and sleep status assessment. The screening, diagnosis and evaluation of depressive symptoms follow the revised ACOS (American Society of Clinical Oncology) guidelines and the Hamilton Depression Scale-24 (HAMD-24), and the sleep status follows the Pittsburgh Sleep Quality Index Scale.

②Basic situation questionnaire survey before intervention

The research doctor will judge whether you meet the criteria for participating in this study based on the above examination results.

After the screening is qualified, you need to follow the treatment and follow-up procedures specified in the plan.

2.treatment period

Study group : If SAE occurred during the administration, the treatment was discontinued. It is necessary to come to the hospital once a day before the intervention and 90 days after the intervention (both outpatient review time), collect fresh fecal samples and detect blood immune indicators. The collection of fecal samples is recommended to come to the hospital for collection of about 2 ~ 3 mL. The blood used for immune index detection was residual blood of eight items of thyroid function, and no additional blood was taken.

Control group : if SAE occurred during the administration, the treatment was discontinued. It is necessary to come to the hospital once a day before the intervention and 90 days after the intervention (both outpatient review time), collect fresh fecal samples and detect blood immune indicators. The collection of fecal samples is recommended to come to the hospital for collection of about 2 ~ 3 mL. The blood used for immune index detection was residual blood of eight items of thyroid function, and no additional blood was taken.

If at any time you decide to withdraw from the study, please inform the research physician.

During the study, you must inform the research doctor of any medications you use during this period. During the study period, unless the researcher determines that it is necessary to use, you may not use the following drugs : chemotherapy, radiotherapy, biological therapy, Chinese herbal medicine, antibiotics, microecological modulators, antidepressants, other health products with immunomodulatory functions, psychotropic drugs, etc.

Please inform the research doctor about any changes in your health status, including any favorable or unfavorable changes. If you experience any discomfort during your study, you should contact your research physician in a timely manner.

All samples collected in this study are only used for this study, and will be destroyed according to the regulations of the research center.

Ⅳ.Risks and discomfort：

In this study, there may be a risk of the following adverse reactions, and there may also be unpredictable situations or adverse reactions that have not been found in previous clinical studies. You should be fully aware of it before deciding whether to participate in this study.

1.The Ganoderma lucidum powder and simulant involved in the study were customized for Jinhua Shouxiangu Pharmaceutical Co., Ltd. (listed company), purchased by the research group, with quality inspection report, no side effects, and will not increase your costs and risks.

If you have any questions, you should contact the research doctor at any time.

2.Risks and discomforts related to inspection, operation and other aspects during the test

① In all clinical studies, the treatment and research process may involve unknown risks. They may lead to unforeseen adverse reactions. Once any discomfort occurs, please contact the doctor in time, and the doctor will treat you reasonably.

②During the duration of this study, you need to go to and from the hospital three times to cooperate with the doctor to complete the collection of relevant data, which may bring inconvenience to your life.

Any treatment may be ineffective, and the disease continues to develop due to ineffective treatment or combined with other diseases. Similarly, the treatment regimen included in this study may not necessarily improve your depressive symptoms and tumor conditions. Therefore, during your participation in this clinical study, your condition may remain unchanged or may progress.

Ⅴ.Research related damage：

During the study, in order to ensure your safety, doctors will pay close attention to your physical changes. If you experience damage during the course of a study, please notify your research physician immediately, regardless of whether the damage is related to the study.

If research-related damage occurs as a result of your participation in this clinical study, the research team will bear the related treatment costs if you act in accordance with the research doctor 's instructions. And in accordance with laws and regulations and the two sides agreed to give compensation.

If you have other diseases at the same time, the required treatment and examination, as well as the cost of switching to other treatments due to ineffective treatment, will not be within the scope of free.

Ⅵ.Possible benefits

By participating in this study, you may benefit from an improvement in your condition, but there is no guarantee that you will benefit, but your participation will help us determine which treatment options are safer and more effective for other patients with similar conditions. Let life continue, let love pass.

Cost : The costs of Ganoderma lucidum powder, simulant, stool test, blood immune index test and psychological consultation and treatment involved in the study were paid by the research group.

VII.privacy problem

If you decide to participate in this study, your participation in the trial and your personal data during the trial are confidential. Information about your identity will not be disclosed to members outside the research team unless you have obtained your permission. All research members and research sponsors are required to keep your identity confidential. Your files will be stored in a locked filing cabinet for researchers to access only.

In order to ensure that the research is conducted in accordance with the regulations, the members of the Ethics Committee, the management of research institutions, national regulators and sponsors may, if necessary, have access to the original medical records containing your personal information and your signed informed consent for research or regulatory purposes. These inspectors have assumed the responsibility of subject information confidentiality.

If the study is published in a research journal, your name and other information that identifies you will be deleted and replaced with a subject number. The subject number is linked to your identification information, but only the persons mentioned above have direct access to your original medical records. Your identity will not be disclosed, and it is theoretically impossible for unauthorized individuals to identify your identity. We will make every effort to protect the privacy of your personal medical data within the scope of the law.

VIII**.Voluntary choice to participate in research and drop out of treatment or research**

Whether or not to participate in the study depends entirely on your willingness, and you can discuss it with your family or friends before making a decision. Before you make a decision to participate in the study, please ask your doctor about the problem as much as possible until you fully understand the content of this informed consent.

You can withdraw from research and / or treatment at any time without giving any reason. This will not affect your relationship with your doctor, nor will it cause any loss of your medical or other benefits. We will retain and use the research data collected up to your exit.

If the study is no longer in your best interests or for other scientific or safety reasons, the research physician or the research initiator also has the right to decide that you withdraw from the study.

In the following cases, the researcher will notify you to stop participating in the study：

1.You have disease progression, unless you meet the criteria for continued treatment after progression ;

2.Any clinical adverse events, laboratory abnormalities or concurrent diseases, researchers believe that continuing to participate in the study is not in your best interests ;

3, you are pregnant during treatment ;

4, the researchers believe that it is necessary to withdraw from the study of other cases (such as you need other treatment, or you did not comply with the study plan) ;

5. This study was suspended or terminated by the State Food and Drug Administration.

6. The research initiator / researcher or the ethics committee terminated the study for any safety or other special reasons ;

if your research doctor terminates your participation in this study, he / she will discuss the main reasons with you.

IX**.How to get more information ?**

You can ask any questions about this study at any time. Your research doctor will leave you his / her phone number so that you can contact him / her.

If there is any important new information in the course of the study, including but not limited to adverse events and major findings that may affect your willingness to continue to participate in the study, your doctor will notify you in time. You will be asked to re-sign an informed consent form to record the updates you have received and your willingness to continue participating in the study.

X**.If you have questions, who to contact ?**

If you have questions about any aspect of this study 's research steps, clinical efficacy, adverse drug events, or rights in the study, or if you think you have been harmed by the study, please contact your research doctor. You may be asked to perform a relevant examination, which is beneficial to protect your health.

fellow_____contact phone_____；

If you need to see another doctor during the study, please inform him / her that you are participating in the clinical study. For questions about the rights and interests of participants in this study, please contact the Medical Ethics Committee (Tel : 0571-88122564, Address : 316, Administrative Research Building, Zhejiang Cancer Hospital, E-mail address ec @ zjcc.org.cn).

As a subject, you need to : provide a true picture of your medical history and current physical condition, and tell the investigator of any discomfort that occurred during the study ; tell the researchers whether they have been involved in other studies recently, or are currently involved in other studies.

Thank you for reading the above materials. If you decide to participate in this study, please tell your doctor that he / she will arrange everything for you to participate in this study.

Consent statement by the patient (subject) and / or guardian

I have obtained a copy of the informed consent (signed name and date). He has read and fully understood the above introduction to this study, and has the opportunity to discuss and ask questions about this study with researchers. All the questions I asked were answered satisfactorily, and I fully understood the risks and benefits that may arise from participating in this study. I volunteered to participate in this study.

Patients (subjects) (regular script)： _____

Patient (subject) signature_____ contact phone：_____ Signature date：____

Guardian (when applicable)

［The consent of the legal representative of the subject shall be obtained from (or concurrently with) his / her guardian when the subject has no capacity for informed consent, or is unable to give full informed consent (e.g. minors, or patients with severe dementia), and in case of emergency. When minors can make a decision to participate in the study, they must also obtain their own consent.］

Patient (subject) guardian (regular script)：_____Relationship with subjects：

Patient (subject) guardian signature_____contact phone：_____Signature date：_____

Witness (when applicable)

［When the subject or his guardian is illiterate, he or she must give informed consent to the subject or his or her guardian in detail, and be signed by the witness who witnessed the process. If the subject or his or her guardian can sign, he or she also needs to sign at the same time.］

I certify that the researcher has accurately explained the information in this informed consent form to the subject or his guardian, and that the subject or his guardian has fully understood the information. I also certify that, as a witness, I hereby sign and certify that the patient or his guardian, in my presence, fully and voluntarily consented to participate in the study.

Witness signature： Signature date： contact phone：

Name of witness (in regular script)： Witness ID number (or provide a copy of the ID card)：

A statement by researchers

I confirm that the details of this study have been explained to the subjects and / or guardians, including their powers and possible benefits and risks, and give the subjects the opportunity to ask and answer questions about the nature, risks and benefits of participating in this study. I will provide a signed and dated copy of this consent to the patient and / or certifying person, legal representative.Name of researcher (written in regular script)：

Researchers signature_____ Signature date_____year_____month____day