Efficacy and Safety of Qibei Jiedu Formula Versus Placebo in Preventing and Managing Acute Radiation Dermatitis in Breast Cancer Patients: A Prospective, Double-blind, Randomized Controlled Trial
INFORMED CONSENT FORM

Plan ID: 3.0

Sponsoring Institution: National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College

Principal Investigator: Feng Li

Dear Participant:

We invite you to participate in a clinical study: Efficacy and Safety of Qibei Jiedu Formula Versus Placebo in Preventing and Managing Acute Radiation Dermatitis in Breast Cancer Patients: A Prospective, Double-blind, Randomized Controlled Trial. Before deciding whether to participate in this study, it is important to understand its significance for you. Please carefully read the following information and consult with your family and friends before making a decision. If you have thoroughly understood the study and have no further questions, and have decided to participate, you will need to sign this informed consent form.

I. Research Background

1. Nature of the study: This research was initiated and implemented by the National Cancer Center/Beijing Union Medical College Cancer Hospital, Chinese Academy of Medical Sciences (hereinafter referred to as: Chinese Academy of Medical Sciences Cancer Hospital), with Chief Physician Feng Li from the Department of Traditional Chinese Medicine serving as the principal investigator.

2. The treatment of breast cancer adopts a multidisciplinary approach combining surgery with radiotherapy, chemotherapy, endocrine therapy, and targeted therapy. Approximately 70% of patients require radiotherapy, which can increase the 5-year survival rate to over 85%, but more than 95% of patients develop radiation dermatitis. Grade 1-2 dermatitis affects quality of life, while grade 3 or higher may force 15-20% of patients to adjust their treatment plans. The pathogenesis is complex, and current treatments are primarily symptomatic. Novel therapies still need validation in terms of efficacy, cost, and safety.

Traditional Chinese Medicine (TCM) possesses unique advantages in the treatment of radiation dermatitis. The "Qibei Jiedu Formula" is a compound herbal formula developed under the theoretical guidance of Professor Feng Li, Director of the Department of Traditional Chinese Medicine at the National Cancer Center/Beijing Union Medical College Hospital, Chinese Academy of Medical Sciences, a Qihuang Scholar, and a leader of key disciplines and specialties under the National Administration of Traditional Chinese Medicine. Its main components include Astragalus membranaceus (A. membranaceus), Rehmannia glutinosa (R. glutinosa), Hedyotis diffusa (H. diffusa), Gleditsia sinensis (G. sinensis), Euphorbia hirta (E. hirta), Lithospermum erythrorhizon (L. erythrorhizon), Tribulus terrestris (T. terrestris), stir-fried Shenqu (Shenqu), and Glycyrrhiza uralensis (G. uralensis). The herbs in this formula are arranged as follows: Astragalus membranaceus serves as the sovereign herb, replenishing qi, strengthening defensive qi, and promoting tissue regeneration;

Rehmannia glutinosa cools the blood and generates body fluids; Hedyotis diffusa detoxifies and resolves abscesses; Gleditsia sinensis astringes ulcers and resolves turbidity; Euphorbia hirta dispels wind, unblocks collaterals, and stops dysentery, collectively acting as ministerial herbs; Lithospermum erythrorhizon assists Rehmannia glutinosa and Hedyotis diffusa in cooling the blood and detoxifying; Tribulus terrestris supports Gleditsia sinensis and Euphorbia hirta in soothing the liver, dispelling wind, and resolving rashes; stir-fried Shenqu aids digestion and harmonizes the stomach, while also preventing cold-induced stomach injury; Glycyrrhiza uralensis acts as the adjuvant herb, replenishing qi, detoxifying, and harmonizing the other herbs. Professor Feng Li has long been dedicated to the integrated treatment of malignant tumors and their complications with both Western and TCM approaches, accumulating extensive experience. The research team has successfully commercialized 20 million yuan in research outcomes, earning seven scientific and technological awards at various levels, including the Second Prize of Beijing Science and Technology Progress Award. In late 2023, the team

This study aims to observe and evaluate the efficacy of Qibei Jiedu Decoction in preventing and treating radiation dermatitis in breast cancer patients, employing a randomized controlled trial design, with the goal of providing novel therapeutic insights for patients with radiation dermatitis secondary to breast cancer.

If the research progresses smoothly and achieves the expected outcomes, it could provide a systematic treatment protocol for the integrated Chinese and Western medicine in the prevention and treatment of acute radiation dermatitis. If the efficacy of this research is confirmed, it may benefit more patients in the future. Further promotion and application could conserve medical resources, alleviate patients' psychological stress, and reduce socio-economic burdens.

3. This study has been approved by the Ethics Committee of the Cancer Hospital, Chinese Academy of Medical Sciences, which is an organization responsible for safeguarding the rights and interests of participants.

2、purpose of research

1. Primary objective/endpoint: The incidence of grade 2 radiation dermatitis was assessed using the CTCAE 5.0 grading system.

2. Secondary research objectives/endpoint indicators:

a) The median time to the first occurrence of grade 2 radiation dermatitis;

b). Skin wound healing time

c). Assessment using the Radioactive Dermatitis Symptom Rating Scale (RISRAS);

d). Quality of life: Patients' quality of life was assessed using the EORTC QLQ-BR23 and DLQI scales;

e). Skin Response Spectrophotometry (SRS) for objective evaluation of radiation dermatitis;

f). Traditional Chinese Medicine Syndrome and Pattern Scoring.

3. Exploratory study objectives/endpoint indicators:

①Serum inflammatory markers: The levels of inflammatory cytokines (TNF-α, IL-6, IL-10, IL-8, etc.) in patients' serum were measured by ELISA after treatment.

② Changes in skin microbiota;

③ Lymphocyte subset analysis: Flow cytometry was employed to determine the distribution of lymphocyte subsets in

the patients' peripheral blood.

4. Safety parameters: Complete blood count (CBC), liver function tests, renal function tests.

3、research design

This study is a randomized, double-blind, controlled clinical trial designed to evaluate whether Qibei Jiedu Formula can effectively prevent and treat skin reactions such as erythema, desquamation, and other manifestations of radiation dermatitis induced by breast cancer radiotherapy, while assessing its safety profile. The study was conducted at the National Cancer Center/Beijing Union Medical College Hospital, Chinese Academy of Medical Sciences, with a planned enrollment of approximately 60 patients. If you agree to participate, you will be assigned to one of two groups through a randomized process similar to a lottery: one group will receive Qibei Jiedu Formula, while the other will receive a placebo that visually and odorsally resembles the investigational drug. Neither you nor your research physician will be aware of your assigned group. All participants will undergo standard breast cancer radiotherapy and skin care. On this basis, you will be required to take the investigational drug (Qibei Jiedu Formula or placebo) daily starting from the first day of radiotherapy, for approximately 3 weeks. During the study, your physician will conduct regular examinations and record your skin reaction status, quality of life (assessed via questionnaires), overall health status, and any discomfort. Additionally, small blood and skin samples will be collected before and after radiotherapy for exploratory research to further investigate the drug's effects. Follow-up visits will be conducted during and approximately one month after radiotherapy to monitor your recovery progress.

IV. Research Procedures

1. Treatment Methods

If you voluntarily participate in this study, you will need to receive the corresponding treatment strictly in accordance with the study protocol under the guidance of your study physician or their team. If you have any questions regarding the treatment, please consult your study physician.

treatment group ：

Following large-field radiotherapy (40-45 Gy, 15 fractions) and the application of gel dressing, administer Qibei Jiedu decoction (a traditional Chinese herbal medicine) orally twice daily, one sachet (100 mL/sachet) per dose, for a total of 21 days (concurrently with radiotherapy).

control group ：

Following large-field radiotherapy and the application of gel dressing, the patients were administered a placebo solution (a simulated agent that visually and olfactorily matched the decoction of Qibei Jiedu Fang), with the same administration method and cycle as the treatment group.

2. Follow-up visits

You are required to attend follow-up visits at the hospital as per the study protocol requirements until the conclusion of the study. The purpose of these follow-ups is to assess the efficacy of your treatment, monitor for any adverse reactions, and

implement appropriate interventions.

Primary follow-up is conducted in the hospital, supplemented by telephone or WeChat follow-ups.

Your physician may also recommend additional tests based on the needs of your condition.

3. Biomarker/Hematology-related indicators/dermal microbiota testing

This study will collect venous blood samples and skin surface samples (skin swabs) from the irradiated area before the initiation of radiotherapy and after the completion of the entire treatment course, respectively. These samples will be used for exploratory biomarker analysis, including serum inflammatory factors (e.g., TNF-α, IL-6), skin microbiota, and lymphocyte subsets. The aforementioned test results will facilitate a more comprehensive evaluation of the clinical efficacy and safety of Qibei Jiedu Fang in the prevention and treatment of radiation dermatitis. We appreciate your contribution to the advancement of medical research in China!

V. Alternative Therapies

Participation in this study is entirely voluntary. The intervention in this study constitutes an additional loading beyond standard radiotherapy and skin care. Therefore, if you decide not to participate in this study or opt out at any stage of the study, you will continue to receive the same standardized postoperative radiotherapy for breast cancer and standard skin care. You will not be subjected to any unfair treatment or have your routine medical care affected.

VI. Potential Risks

The Qibei Jiedu Formula applied in this study has been clinically used for many years, and preliminary observations have demonstrated its good safety profile. However, all medications carry the potential risk of adverse reactions. As a traditional Chinese herbal decoction, its distinctive odor may induce nausea, gastric discomfort, and decreased appetite. Although no severe adverse reactions were observed in the preliminary studies, we will continue to monitor closely. Adjuvant radiotherapy itself may lead to fatigue and physical exhaustion, which are well-documented in conventional disease management. We will closely monitor and standardize the management of any discomfort you experience. If you experience any discomfort, please inform your study physician immediately.

VII. Possible Benefits

By participating in this clinical study, if you are assigned to the group receiving the "Qibei Jiedu Formula" and the drug is proven effective, you may benefit from it, such as reduced risk of severe radiation dermatitis, alleviation of skin discomfort symptoms, or accelerated skin healing. Additionally, you will receive closer monitoring and care of your skin condition. Regardless of which group you are assigned to, the information you provide through this study will serve as a critical basis for the scientific evaluation of the efficacy and safety of the "Qibei Jiedu Formula." Your contribution will help future physicians develop better skin management strategies for more breast cancer radiotherapy patients. We sincerely appreciate your efforts and contributions to medical progress!

VIII. Research Expenses

This study provides trial medications (Qibei Jiedu Formula or placebo) free of charge. You are responsible for the associated diagnostic and treatment costs of breast cancer radiotherapy and radiation dermatitis, as well as any non-study protocol medical expenses incurred for any reason.

IX. Handling of Damages

If you experience severe adverse reactions during the study, your physician will conduct an examination and provide symptomatic treatment (discontinuation of the medication and symptomatic management for specific adverse drug reactions). If you cannot tolerate the adverse drug reactions or fail to comply with the physician's instructions, the physician will recommend your withdrawal from the study.

X. Principle of Voluntariness

Participation in this study is entirely voluntary, and you may withdraw at any time without justification. Your decision to participate or withdraw from the study will not affect your relationship with healthcare providers or the diagnosis and treatment of your condition. If you choose to participate in this study, your physician will inform you of any information that may impact your physical condition or influence your decision to continue participating during the study.

XI. Privacy and Confidentiality Principle

In this study, your information and medical data will be kept confidential within the scope required by law. We will use personally identifiable information for identification and processing to protect your privacy: after enrollment, you will be assigned a unique project number, and your personal information and medical data will be collected by your physician or their research team. The data will be coded, stored, and protected, with users only seeing the individual number and no access to your name or other personal information. The refrigerator storing your biological samples is a dedicated biological sample storage refrigerator, and the key is kept by a designated person responsible for sample management. You have the right to inquire about the recorded information at any time and request corrections if errors are found.

Your research physician will analyze your data and may further collect additional data required for this study from your medical records. During or at any time after the study, within the limits permitted by law, members of the ethics committee or government regulatory authorities may access your personal data as appropriate to verify the authenticity, accuracy, and reliability of the study data. The study results will be published in the form of statistically analyzed data, which does not contain any identifiable patient information.

XII. Study Termination

During the study, you may withdraw from the study at any time without justification, and your decision will not affect your continued medical treatment. Your physician may also discontinue your study medication for the following reasons:

- You did not take the medication as instructed by your study physician.

- If the disease progresses or intolerable adverse reactions occur, and the study physician determines that continuing to participate in the study would pose a risk to you.
- You have received treatment that is not permitted in this study.
- The study was stopped by the physician, the ethics committee, or the government regulatory authorities.

When you withdraw from the study or the study is terminated, the study physician will discuss subsequent treatment measures with you.

XIII. Consultation on Research

If you have any questions regarding this study, please contact Dr. Feng Li at the Cancer Hospital of the Chinese Academy of Medical Sciences directly at (010) 87788030. For inquiries related to the rights of participants, or to report difficulties, dissatisfaction, or concerns encountered during the study, or to provide feedback and suggestions regarding this research, please contact the Ethics Committee of the Cancer Hospital of the Chinese Academy of Medical Sciences at 010-87788495 or via email at cancergcp@163.com.

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Informed Consent Form Signature Page

Subject Statement

The research physician has provided me with a detailed explanation of the purpose, procedure, and potential risks and benefits associated with participating in this study. I have carefully reviewed the informed consent form, and all questions have been satisfactorily addressed, with full comprehension achieved.

I hereby consent to my research physician collecting and utilizing my medical records. I agree that the Cancer Hospital of the Chinese Academy of Medical Sciences may review my medical data and research findings for scientific purposes. I consent to the ethics committee members and representatives of government regulatory authorities accessing my medical records under the principle of confidentiality and within their respective authorized scope. I acknowledge that these records are being reviewed to ensure the authenticity, completeness, and reliability of the data collected from this study.

I hereby declare: I am voluntarily participating in this study, and I may withdraw from the study at any time without affecting my subsequent medical treatment or legitimate rights and interests.

I have obtained a signed copy of the informed consent form. By signing this consent form, I have not waived any of my legitimate rights and interests.

I agree to participate in the biomarker testing (tumor tissue/blood, etc.) for this study (without affecting my participation in the study):

Yes (check the box) □

No (check the box) □

Patient signature--

Legal Representative's Signature* -

- -

Unless the subject is unable to read (e.g., illiterate or blind) or cannot sign for other reasons, the signature of a legal representative is not required.

Statement of the Investigator

I hereby commit to strictly adhering to Good Clinical Practice (GCP) principles and relevant regulations of the National Medical Products Administration (NMPA) and the Cancer Hospital of the Chinese Academy of Medical Sciences in clinical research, safeguarding the rights and interests of participants, and ensuring the authenticity, completeness, and reliability of research timelines and data. I consent to the Cancer Hospital of the Chinese Academy of Medical Sciences reviewing the medical records and research findings of this study for scientific research purposes. I also agree to return any remaining biological specimens to the Cancer Hospital of the Chinese Academy of Medical Sciences for preservation.

I have fully explained to the patient the purpose, procedure, and potential risks and benefits of this study. The patient has been provided with sufficient information to make an informed decision to participate in this study. I will provide the patient or their legal representative with a signed and dated copy of the informed consent form.

Researcher's signature_____Date----------

Contact information for researchers: 010-87788030