Supplementary files

Additional File 1

Original protocol approved by the ethics committee

Electroacupuncture combined with diclofenac emulgel for post-traumatic ankle osteoarthritis: Study Protocol for A Randomized Controlled Trial

(The translated version)

1. Purpose:

To evaluate the efficacy and safety of electroacupuncture (EA) combined with topical diclofenac emulgel in patients with post-traumatic ankle osteoarthritis (PTAOA); and to investigate whether applied locally to the ankle in PTAOA has a reparative effect on the joint cavity and periarticular soft tissues, and whether it modulates patients' serum inflammatory factors IL-6, TNF-α, and IL-1β.

2. Protocol

Participants

Refer to the diagnostic criteria for ankle osteoarthritis in the China Osteoarthritis Diagnosis and Treatment Guidelines (2024 Edition, CODTG), patients will be required to meet the following requirements:

(1) Weight-bearing pain in the ankle joint;

(2) limited joint dorsiflexion and toe flexion;

(3) Joint swelling and deformity;

(4) X-ray (standing position) within 12 months shows subchondral osteosclerosis, osteophyte formation, joint space narrowing and even deformity;

(5) Diagnosis confirmed if above criteria met, excluding other etiologies (e.g., rheumatoid OA). Diagnosis will be performed by hand and foot surgeons.

Inclusion criteria

Patients will be recruited if they:

(1) meet the diagnostic criteria of PTAOA;

(2) meet the traditional Chinese medicine (TCM) syndrome diagnosis of Gu Bi, a TCM pattern characterized by chronic joint pain, stiffness, and functional limitation, according to the relevant diagnostic standard;

(3) have a history of ankle trauma, such as ankle fracture or sports-related injury;

(4) had radiological findings within previous 12 months consistent with Takakura stage I, II, or III disease; in this study, these stages are operationally defined as early- to middle-stage PTAOA;

(5) aged 18~75, any gender;

(6) understand the content of this trial and be willing to sign the informed consent form.

Exclusion criteria

Patients will not be recruited if any of the following are met:

(1) on other pain relief treatments or have stopped the drug for less than 2 weeks;

(2) received acupuncture treatment for ankle OA in the last 6 months;

(3) ankle arthritis caused by gout, rheumatism, autoimmune diseases and other reasons;

(4) systolic blood pressure ≥ 180mmHg and/or diastolic blood pressure ≥110mmHg;

(5) have implanted medical devices such as pacemakersor metal implants in the body;

(6) severe acute or chronic organic or neuropsychiatric disorder;

(7) disorders of coagulopathy (e.g., hemophilia).

Termination criteria

Participants who develop treatment-related contraindications or treatment-related adverse reactions during the study.

Withdrawal Criteria

(1) Participants who, after enrollment, did not receive the treatment specified in this protocol, or who used other medications or therapies concurrently, making it impossible to objectively assess treatment efficacy;

(2) Participants who withdrew from the trial before its completion, or whose incomplete clinical data prevented an assessment of efficacy and safety;

(3) Participants who are discontinued from the clinical trial due to the occurrence of a serious adverse event or complication that prevents them from continuing;

(4) Keep the number of cases of detachment below 10%.

Randomization

Random sequences are generated using a random number table. The allocation scheme will controlled by personnel unrelated to this study. Based on the random number table, the corresponding group codes will be placed into envelopes and sealed (which cannot be restored after opening). When clinical physicians included subjects sequentially according to the number, the envelopes were opened. Based on the group code inside the envelope, subjects will be assigned to groups respectively. Recruitment ended after completing the total number of observed cases (78 cases).

Intervention

Topical NSAIDs are recommended as first-line treatment for osteoarthritis pain according to the Chinese guideline for diagnosis and treatment of osteoarthritis (2021 edition). Diclofenac diethylamine emulsion is an NSAID; therefore, it was selected as the base medication.

Both the EA group and SA group will be administered the Diclofenac Diethylamine Emulge (trade name Voltaren, GSK Consumer Healthcare SARL, specification: 20g/stick). Topical application twice daily, 2g per dose, for 4 weeks.

(1) Electroacupuncture group

Patients in the EA group will receive treatment 5 times a week, which has been confirmed by previous study as the better frequency for 4 weeks (a total 20 sessions).

A standardized method for selecting acupoints will be adopted. The prescription was

formulated based on clinical experience and reviews. The standardized prescription contains: Yanglingquan (GB34), Xuanzhong (GB39), Qiuxu (GB40), Zhongfeng (LR4), Kunlun (BL60), Shenmai (BL62), Taixi (KI3), Zhaohai (KI6), Zusanli (ST36), Jiexi (ST41), Shangqiu (SP5), Sanyinjiao (SP6), and Ashi points.

Operation: Use disposable sterile acupuncture needles (produced by Beijing Tianyu Technology Co., Ltd., length: 25-40 mm, diameter: 0.25-0.30 mm). The acupuncture site and the hands of the acupuncturist should be strictly disinfected with 75% alcohol, and the acupuncturist should puncture the needle. Transparent to the skin.

The insertion depth is 5-8 mm for acupoints around the ankle and 10-20 mm for acupoints on the lower leg. After inserting the needle, perform acupuncture on all acupuncture points for about 10 seconds, depending on the degree of local soreness and swelling in the subject. After De Qi, select Taixi (KI 3, connected to negative electrode) & Zhaohai (KI 6, connected to positive electrode); Jiexi (ST 41, connected to negative electrode) & Shangqiu (SP 5, connected to positive electrode); Shenmai (BL 62, connected to negative electrode) & Kunlun (BL 60, connected to positive electrode); Qiuxu (GB 40, connected to negative electrode) & Xuanzhong (GB 39, connected to positive electrode) to connect. KWD-808I Multi-purpose Health Device (produced by Changzhou Yindi Electronic Medical Devices Co., Ltd.) is used with sparse and dense waves, frequency 20/100Hz, and the current intensity is based on patient comfort.

(2) Sham acupuncture group

In the SA group, the acupoints prescription is the same as in the EA group. After local disinfection, a circular bandage will be applied over the acupoint. The acupuncture needle will only superficially insert into the bandage (2-3 mm in depth) without piercing the skin and needle manipulation for De qi, which are considered ineffective; this is the standard practice for sham control groups in acupuncture research. The electric needle will be connected at the same position with only 0.1 mA adjusted, simulating the appearance and feel of EA treatment, but not providing actual electrical stimulation. A total of 20 times of sham acupuncture will be received.

Quality Control

(1) To avoid bias caused by variations in individual needling techniques, all treatment sessions within one cycle for the same patient were performed by a single researcher.

(2) Develop a quality control plan, documenting the specified quality control standards, resources, and related activities.

(3) All activities, procedures, and technical operations carried out during the implementation of the quality control plan shall be meticulously documented, reported, and archived to facilitate future improvements in quality control activities.

Additional File 2.

SPIRIT checklist

Section/topic	No.	SPIRIT 2025 checklist item description	Details
Administrative information			
Title and structured summary	1a	Title stating the trial design, population, and interventions, with identification as a protocol	Page 1 Electroacupuncture combined with diclofenac emulgel for post-traumatic ankle osteoarthritis: a randomized controlled trial protocol
	1b	Structured summary of trial design and methods, including items from the World Health Organization Trial Registration Data Set	Page 2 Abstracts
Protocol version	2	Version date and identifier	Additional file 1. Original protocol approved by the ethics committee.
Roles and responsibilities	3a	Names, affiliations, and roles of protocol contributors	Page 1
	3b	Name and contact information for the trial sponsor	Page 1 Fangyuan Wei, The third Hospital affiliated to Beijing University of Chinese Medicine, No. 51 Xiaoguan Street Andingmenwai Chaoyang District, 100029, Beijing, China. Email: footwfy@126.com Lina Qin, The third Hospital affiliated to Beijing University of Chinese Medicine, No. 51 Xiaoguan Street Andingmenwai Chaoyang District, 100029, Beijing, China. Email: lina1978119@sina.cn
	3c	Role of trial sponsor and funders in design, conduct, analysis, and reporting of trial; including any authority over these activities	Page 15 Author Contributions
	3d	Composition, roles, and responsibilities of the coordinating site, steering committee, end point adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable	-
Open science			
Trial registration	4	Name of trial registry, identifying number (with URL), and date of registration. If not yet registered, name of intended registry	Page 2 Trial registration Registry: International Traditional Medicine Clinical Trial Registry (ITMCTR), No. ITMCTR2025001585; registered on 24 July 2025

Protocol and statistical analysis plan	5	Where the trial protocol and statistical analysis plan can be accessed	Additional file 1. Original protocol approved by the ethics committee.
Data sharing	6	Where and how the individual deidentified participant data (including data dictionary), statistical code, and any other materials will be accessible	Page 15 Availability of data and materials
Funding and conflicts of interest	7a	Sources of funding and other support (eg, supply of drugs)	Page 15 Funding.
	7b	Financial and other conflicts of interest for principal investigators and steering committee members	Page 16 Disclosure
Dissemination policy	8	Plans to communicate trial results to participants, health care professionals, the public, and other relevant groups (eg, reporting in trial registry, plain-language summary, publication)	Page 12 Dissemination of results
Introduction			
Background and rationale	9a	Scientific background and rationale, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	Page 3 Introduction
	9b	Explanation for choice of comparator	Page 4 Introduction
Objectives	10	Specific objectives related to benefits and harms	Page 5 Introduction
Methods: patient and public involvement, trial design			
Patient and public involvement	11	Details of, or plans for, patient or public involvement in the design, conduct, and reporting of the trial	Page 5 Study design
Trial design	12	Description of trial design including type of trial (eg, parallel group, crossover), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	Page 7 Allocation
Methods: participants, interventions, and outcomes			
Trial setting	13	Settings (eg, community, hospital) and locations (eg, countries, sites) where the trial will be conducted	Page 6 Study site
Eligibility criteria	14a	Eligibility criteria for participants	Page 6 Participants: Inclusion criteria.

	14b	If applicable, eligibility criteria for sites and for individuals who will deliver the interventions (eg, surgeons, physiotherapists)	Page 8 Interventions
Intervention and comparator	15a	Intervention and comparator with sufficient details to allow replication including how, when, and by whom they will be administered. If relevant, where additional materials describing the intervention and comparator (eg, intervention manual) can be accessed	Page 9 Electroacupuncture Page 22 Table 2 Additional file 1. Page 9 Sham acupuncture
	15b	Criteria for discontinuing or modifying allocated intervention/comparator for a trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	Page 11 Adverse events
	15c	Strategies to improve adherence to intervention/comparator protocols, if applicable, and any procedures for monitoring adherence (eg, drug tablet return, sessions attended)	-
	15d	Concomitant care that is permitted or prohibited during the trial	Page 8 Interventions
Outcomes	16	Primary and secondary outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome	Page 10-11 Outcomes Primary outcome: American Orthopedic Foot and Ankle Society Ankle-Hindfoot Scale (AOFAS) Secondary outcomes: the Short-form of McGill pain questionnaire(SF-MPQ), Foot and Ankle Ability Measure(FAAM), the MOS item short from health survey(SF-36), Musculoskeletal Ultrasound and a biological indicator outcome.
Harms	17	How harms are defined and will be assessed (eg, systematically, nonsystematically)	Page 11 Adverse events
Participant timeline	18	Time schedule of enrollment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (seeFigure)	Table 1. SPIRIT schedule.
Sample size	19	How sample size was determined, including all assumptions supporting the sample size calculation	Page 12 Sample size

Recruitment	20	Strategies for achieving adequate participant enrollment to reach target sample size	Page 8 Recruitment
Methods: assignment of interventions			
Randomization			
Sequence generation	21a	Who will generate the random allocation sequence and the method used	Page 7 Allocation
	21b	Type of randomization (simple or restricted) and details of any factors for stratification. To reduce predictability of a random sequence, other details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enroll participants or assign interventions.	Page 7 Allocation
Allocation concealment mechanism	22	Mechanism used to implement the random allocation sequence (eg, central computer/telephone; sequentially numbered, opaque, sealed containers), describing any steps to conceal the sequence until interventions are assigned	Page 7 Allocation
Implementation	23	Whether the personnel who will enroll and those who will assign participants to the interventions will have access to the random allocation sequence	Page 7 Allocation
Blinding	24a	Who will be blinded after assignment to interventions (eg, participants, care providers, outcome assessors, data analysts)	Page 7 Blinding
	24b	If blinded, how blinding will be achieved and description of the similarity of interventions	Page 7 Blinding
	24c	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	No
Methods: data collection, management, and analysis			
Data collection methods	25a	Plans for assessment and collection of trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of trial instruments (eg, questionnaires, laboratory tests), along with their reliability and validity, if known. Reference to where data collection forms	Page 11 Data management

		can be accessed, if not in the protocol.	
	25b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	Page 8 Interventions
Data management	26	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be accessed, if not in the protocol.	Page 11 Data management
Statistical methods	27a	Statistical methods used to compare groups for primary and secondary outcomes, including harms	Page 12 Statistical analysis
	27b	Definition of who will be included in each analysis (eg, all randomized participants), and in which group	Page 12 Statistical analysis
	27c	How missing data will be handled in the analysis	Page 12 Statistical analysis
	27d	Methods for any additional analyses (eg, subgroup and sensitivity analyses)	Page 12 Statistical analysis
Methods: monitoring			
Data monitoring committee	28a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and funder; conflicts of interest and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed.	Additional file 1. Original protocol approved by the ethics committee.
	28b	Explanation of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	Additional file 1. Original protocol approved by the ethics committee.
Trial monitoring	29	Frequency and procedures for monitoring trial conduct. If there is no monitoring, give	Page 11 Data management

		explanation	
Ethics			
Research ethics approval	30	Plans for seeking research ethics committee/institutional review board approval	Page 5 Study design The study protocol has been approved by IRB of The third Hospital Affiliated to Beijing University of Chinese Medicine (BZYSY-2025YJSKTPJ-24).
Protocol amendments	31	Plans for communicating important protocol modifications to relevant parties	Additional file 1. Original protocol approved by the ethics committee.
Consent or assent	32a	Who will obtain informed consent or assent from potential trial participants or authorized proxies, and how	Additional file 3. Model consent form.
	32b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	Additional file 3. Model consent form.
Confidentiality	33	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Page 11 Data management
Ancillary and post-trial care	34	Provisions, if any, for ancillary and posttrial care and for compensation to those who suffer harm from trial participation	No

Additional File 3

Model consent form

Informed Consent Form • Informed Notice Page (Translated Version)

Dear Madam/Sir:

You are invited to participate in a clinical study titled "Electroacupuncture combined with diclofenac emulgel for post-traumatic ankle osteoarthritis: Study Protocol for A Randomized Controlled Trial" The study aims to evaluate the effectiveness and safety of electroacupuncture (EA) therapy in treating post-traumatic ankle osteoarthritis (PTAOA).This study is planned to be conducted at one research center and aims to enroll a total of 78 subjects. The study is scheduled to commence in April 2025. The project has been reviewed and approved by the Research Ethics Committee of the Third Affiliated Hospital of Beijing University of Chinese Medicine.

Before you decide whether to participate in this study, please carefully read the following information. It will help you understand the purpose of the study, its procedures and duration, as well as the potential benefits, risks, and discomforts associated with participation. If you wish, you may discuss this with your family or friends, or seek explanations from your doctor to assist you in making your decision.

Introduction

Post-traumatic ankle osteoarthritis (PTAOA) is a form of osteoarthritis and a common chronic pain disorder. It follows a history of ankle trauma and typically presents with joint pain, swelling, and functional impairment, which in severe cases affect daily life. The EA therapy studied here uses low-frequency electrical current combined with needle insertion. Preliminary studies indicate that EA can effectively alleviate osteoarthritis symptoms and improve the inconveniences caused by osteoarthritis.

Purpose：

The aim of this study is to conduct a preliminary study of the clinical effects and safety of EA combined with topical diclofenac emulgel in treating PTAOA, to analyze its mechanisms of action in treating PTAOA, and to provide data support for subsequent investigations into the effectiveness of non-pharmacological TCM therapies for PTAOA.

Main Study Population：

(1) Weight-bearing pain in the ankle joint; (2) limited joint dorsiflexion and toe flexion; (3) Joint swelling and deformity; (4) X-ray (standing position) within 12 months shows subchondral osteosclerosis, osteophyte formation, joint space narrowing and even deformity; (5) Diagnosis confirmed if above criteria met, excluding other etiologies (e.g., rheumatoid OA). Diagnosis will be performed by hand and foot surgeons.

Who is not suitable for participating in the research?

Patients will be recruited if you:

(1) meet the diagnostic criteria for PTAOA; (2) meet the traditional Chinese medicine (TCM) syndrome diagnosis of Gu Bi, a TCM pattern characterized by chronic joint pain, stiffness, and functional limitation, according to the relevant diagnostic standard; (3) have a history of ankle trauma, such as ankle fracture or sports-related injury; (4) have radiographic findings within the previous 12 months consistent with Takakura stage I, II, or III disease; in this study, these stages are operationally defined as early- to middle-stage PTAOA; (5) aged 18-75, any gender; (6) understand the content of this trial and be willing to sign the informed consent form.

What will be required if you participate in the study?

1. Before you are enrolled in the study, you will undergo the following examinations to determine whether you can participate:

You will be questioned by a physician to record your medical history, and you will undergo relevant examinations such as ankle joint function assessment, ankle function scale evaluation, pain scale assessment, laboratory tests, and ultrasound examinations to determine whether you can participate in the study.

2. If you pass the above screening, the study will proceed according to the following steps:

Random grouping will be performed. This study is divided into topical diclofenac diethylamine emulgel (Voltaren Emulgel) treatment and combined EA treatment. You will draw an envelope to determine which group you will enter and receive treatment; group assignment is equally probable and randomized. Once enrolled, you will receive one month of treatment, five sessions per week. The investigator will assess you before treatment, after 2 weeks of treatment, and after 4 weeks of treatment using the SF-MPQ, AOFAS Ankle–Hindfoot score, FAAM scale, and SF-36 quality of life questionnaire. Venous blood draws and musculoskeletal ultrasound of the ankle will be performed before treatment and after 4 weeks of treatment. Your condition changes will be queried and recorded, and you will be followed up one month after the end of treatment.

3. Important Reminders for Participants

You and society may benefit from this study. Such benefits include improvement in your condition, as well as the potential development of better treatments that could help other patients with the same disease. You will receive quality medical care throughout the study.

By participating in this study, you are expected to adhere to the research protocol, including undergoing scheduled examinations and cooperating with follow-up visits by the research team.

Possible risks and discomforts of participating in the research

The potential risks of participating in this study primarily involve adverse events that may occur during acupuncture treatment:

(1) Needle fainting: Stop acupuncture immediately, remove all needles, and have the patient lie flat while keeping them warm. For mild cases, provide warm water or sugar water; for severe cases, stimulate points such as Renzhong (GV26), Suliao (GV25), Neiguan (PC6), and Zusanli (ST36), or apply moxibustion to points like Baihui (GV20), Guanyuan (CV4), and Qihai (CV6).

(2) Stuck needle: If caused by local muscle over-contraction due to patient nervousness, the needle retention time can be slightly extended, or the area around the stuck needle can be massaged or the needle handle tapped. If caused by improper manipulation, rotate the needle in the opposite direction and use handle-scraping or handle-tapping techniques to release the entangled muscle fibers.

(3) Bent needle: Cease all manipulations and slowly remove the needle following the direction of the bend; do not force the needle out.

(4) Broken Needle: Do not change the patient's original position. If the broken end is exposed, use tweezers to remove it. If the broken end is recessed below the skin, use two fingers to press vertically downward on both sides of the needle hole, then use tweezers to remove it.

(5) Subcutaneous Hematoma: Mild cases require no treatment. For severe cases, apply a cold compress within 24 hours and a hot compress after 24 hours.

If you experience any discomfort, new changes in your condition, or any unexpected circumstances during the study - regardless of whether they are related to the medication - please inform your doctor promptly. He/she will make a timely judgment and provide medical treatment. There is a possibility that the study intervention may be ineffective, and your condition may continue to progress due to treatment failure or complications from other diseases. If the investigator obtains information that may affect your continued participation in the trial, you will be notified in a timely manner.

Alternative treatments outside of this study

You may choose not to participate in this study or withdraw at any time. Alternative rehabilitation and physiotherapy treatments remain available. Your physician will

provide helpful guidance, any necessary and beneficial treatment, or refer you to other departments as appropriate. This will not adversely affect your access to routine care.

Potential Benefits of Participating in the Study

By participating in this study, you may receive free treatment with diclofenac diethylamine emulgel combined with EA, which may to some extent improve your condition; during the study you will receive good medical care.

We cannot guarantee improvement in your health. We hope that the information obtained from your participation in this study can be used in the future for other patients with similar conditions.

Signing this informed consent form will not cause you to lose any lawful rights. Whether to participate in this study is your own decision, and you may withdraw from the study at any time without affecting your medical treatment or legal rights.

Related Costs

Our research team will cover the costs of study-related examinations you undergo for participating in this study (such as inflammatory marker tests), and will provide study medications, treatments, and ultrasound examinations free of charge.

If you have other concurrent conditions requiring treatment and examinations, these will not be covered by this study.

The physicians and researchers involved in this study will make every effort to prevent and treat any harm that may arise from the study. In the event of study-related injury, our research team will cover your medical expenses and provide appropriate financial compensation, as stipulated in China's "*Good Clinical Practice for Drug Clinical Trials*."

Confidentiality of the research

All information concerning you, including your identity, medical history, condition, physical examinations, and laboratory test results, will be kept strictly confidential within the limits permitted by law. Researchers, the principal investigator, the ethics

committee, and drug regulatory authorities will be permitted to access your medical records related to this study to verify the authenticity and accuracy of the data collected, but this will not involve your personal details. Any public information or reports regarding the results of this study will not disclose your personal identity.

Complaints from participants

If you have any medical questions related to this study, please contact the principal investigator (Phone number: xxxxxxxxx).

Should any important new information arise during the course of the study that may affect your willingness to continue participating, your physician will promptly inform you.

If you wish to report any concerns or dissatisfaction regarding your participation in this study, or if you believe your personal rights have been compromised, please contact the Research Ethics Committee of the Third Affiliated Hospital of Beijing University of Chinese Medicine (Phone number: xxxxxxxx).

Your Rights and Interests

Participation in this study is entirely voluntary. You may refuse to participate or withdraw from the study at any time during the research process. This will not affect your relationship with your doctor, nor will it impact your medical care or result in the loss of any other benefits.

If circumstances arise during the study that make it unsuitable for you to continue, your doctor or the investigator may suggest that you withdraw or terminate your participation at any time, keeping your best interests in mind.

If you choose not to participate in this study or withdraw midway, there are many alternative treatment options available, such as rehabilitation therapy or surgical treatment. You are not required to participate in this study to receive treatment for your condition.

If you withdraw from the study for any reason, you may be asked about your use of the study medication. If the doctor deems it necessary, you may also be requested to

undergo laboratory tests and physical examinations. This is highly beneficial for protecting your health.

The following is the signature section of the informed consent form.

Informed Consent Form • Consent Signature Page

Participant

I have carefully read the "Subject Information for the Clinical Study of Electroacupuncture combined with diclofenac emulgel for post-traumatic ankle osteoarthritis" and fully understand the purpose, content, and methods of this clinical study, as well as the potential benefits and risks of participation. The doctor has clearly explained the relevant medical terms, and all my questions have been answered in an easy-to-understand manner. I understand that I may refuse to join the study or discontinue and withdraw from the study at any time and under any circumstances without facing discrimination or retaliation, and my medical treatment and rights will not be affected.

My participation in this study is entirely voluntary. I have had sufficient time for full consideration and understand the therapeutic effects and potential risks that the study medication may bring to my condition. I have received complete and truthful information regarding this study, and I fully understand and support this clinical research. I ensure that I have truthfully provided the investigator with my past medical history, medication history, and participation in other clinical trials. Without any pressure and with the freedom to choose, I have decided to participate in this clinical study voluntarily and will endeavor to comply with the protocol requirements and the investigator's recommendations.

I agree to allow the drug regulatory authorities, clinical study auditors and monitors, the Ethics Committee, or representatives of the sponsor to review my study records.I will receive a signed and dated copy of this Informed Consent Form.

(Please sign in block letters using a black ink pen; stamps cannot be used as a substitute for a signature)

Patient (Signature): _____ Date: ____ Year ____ Month ____ Day___

(Or Legal Guardian (Signature):_____) Relationship with Patient: _____

Phone Number: _____

Reason why the subject is unable to sign:

In cases where neither the subject nor their guardian possesses the ability to read, a witness must be present during the informed consent process. After the informed consent has been explained in detail, the witness shall confirm that the content of the written informed consent form is consistent with the oral explanation. Upon the oral consent of the subject or their guardian, the witness shall sign and date the informed consent form.

I confirm that the information in the informed consent form has been accurately explained and that the subject and/or the subject's legally authorized representative have understood this information. The subject has voluntarily agreed to participate in this study.

Fairness witness(Signature): _____ Date: ____ Year ____ Month ____ Day___

Phone Number: _____

Researcher

I confirm that I have provided detailed explanations of the content, procedures, potential risks, and benefits of this study to the participant mentioned above. I have answered any questions raised by the patient satisfactorily, and the patient has expressed understanding and satisfaction with the responses provided.

Researcher (Signature): _____ Date: ____ Year ____ Month ____ Day___

Phone Number: _____