Efficacy and Safety of HuaShiXiaoYin Decoction Combined With Secukinumab In Moderate To Severe Plaque Psoriasis: A Study Protocol For a Randomised Controlled Trial

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Abstract

Background: Psoriasis is a chronic, relapsing inflammatory disease, with plaque psoriasis being the most common subtype and significantly impairing patients' quality of life. The advent of biologic therapies has greatly improved treatment outcomes; however, relapse after drug discontinuation remains a major challenge. Preliminary clinical observations suggest that Huashixiaoyin Decoction(HSXYD) may reduce the recurrence rate of plaque psoriasis, although its efficacy has yet to be validated in randomized controlled trials.

Objective: This study aims to evaluate the efficacy and safety of HSXYD in combination with Secukinumab for the treatment of moderate-to-severe plaque psoriasis, and to explore its potential in preventing relapse.

Methods: This prospective, multicentre, single-blind randomized controlled trial adopts a two-arm, parallel-group design. A total of 128 eligible participants will be randomly assigned to the intervention group (n=64) or control group (n=64). The intervention group will receive Secukinumab for 24 weeks combined with Huashixiaoyin Decoction for the first 8 weeks, while the control group will receive Secukinumab monotherapy for 24 weeks. The primary outcome is time to relapse during the follow-up period (weeks 24–48). Secondary outcomes include improvements in Psoriasis Area and Severity Index, Investigator's Global Assessment, Dermatology Life Quality Index, percentage of body surface area affected, and symptom scores based on traditional Chinese medicine syndrome differentiation. Safety will be closely monitored throughout the study. Patients and members of the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

Results: This study was supported financially by the China's National High Level Hospital Clinical Research Funding. The trial was registered in December 2024. At the time of submission, participant enrollment has been completed. The follow-up is still ongoing. Data analysis is anticipated to be completed by May 2026. The findings of this study will be shared at conferences both nationally and internationally and will be published in journals that are peer-reviewed.

Conclusions: This trial will evaluate the efficacy and safety of Huashixiaoyin Decoction (HSXYD) in combination with Secukinumab for the treatment of moderate-to-severe plaque psoriasis and explore its potential in preventing relapse. The findings will provide valuable clinical evidence on the role of HSXYD as an adjunct therapy, potentially offering a novel approach to sustaining long-term remission in psoriasis patients. By examining its effects, this study may contribute to the development of integrated treatment strategies for psoriasis, ultimately improving patient outcomes and reducing the recurrence of disease after discontinuation of biologic therapy. Clinical Trial: This trial was registered in the International Traditional Medicine Clinical Trial Registry(ITMCTR, https://www.chictr.org.cn/) on December 3, 2024. Clinical Trial Number: ITMCTR2025000129.

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ABSTRACT

Background Psoriasis is a chronic, relapsing inflammatory disease, with plaque psoriasis being the most common subtype and significantly impairing patients' quality of life. The advent of biologic therapies has greatly improved treatment outcomes; however, relapse after drug discontinuation remains a major challenge. Preliminary clinical observations suggest that Huashixiaoyin Decoction(HSXYD) may reduce the recurrence rate of plaque psoriasis, although its efficacy has yet to be validated in randomized controlled trials.

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Conclusions This trial will evaluate the efficacy and safety of Huashixiaoyin Decoction (HSXYD) in combination with Secukinumab for the treatment of moderate-to-severe plaque psoriasis and explore its potential in preventing relapse. The findings will provide valuable clinical evidence on the role of HSXYD as an adjunct therapy, potentially offering a novel approach to sustaining long-term remission in psoriasis patients. By examining its effects, this study may contribute to the development of integrated treatment strategies for psoriasis, ultimately improving patient outcomes and reducing the recurrence of disease after discontinuation of biologic therapy.

Trial registration: This trial was registered in the International Traditional Medicine Clinical Trial Registry(ITMCTR, https://www.chictr.org.cn/) on December 3, 2024. Clinical Trial Number: ITMCTR2025000129.

Keywords: Huashixiaoyin Decoction, Secukinumab, plaque psoriasis, Traditional Chinese Medicine, Randomized controlled trial, Protocol.

INTRODUCTION

Psoriasis is a T-cell mediated chronic inflammatory disease with multisystem involvement, resulting in aberrant keratinocyte proliferation and sustained systemic immune activation[1]. It affects approximately 2-3% of the global population[2] . In Asia, the prevalence of psoriasis varies across countries, with the incidence in China being approximately 0.47%, that in Japan being 0.34%, and that in India being 0.44%[3]. Early diagnosis and intervention are crucial for managing psoriasis, as they are associated with better clinical outcomes and improved quality of life[4].

The pathogenesis of psoriasis involves immune dysregulation and hyperproliferation of skin cells. Current therapies aim to reduce inflammation and normalize keratinocyte activity. Biologics such as Interleukin 17 (IL-17) and Interleukin 23 (IL-23) inhibitors block key inflammatory pathways[4], while immunosuppressants broadly regulate immune activation[5]. Topical agents like vitamin D analogues and retinoids help control epidermal turnover, while moisturizers alleviate scaling and itching[6]. Despite the availability of these treatments, up to 30% of patients fail to respond adequately or develop intolerances, and many experience relapses after treatment discontinuation[7]. Moreover, side effects such as immunosuppression and hepatotoxicity limit the long-term use of some systemic therapies[8]. Therefore, safer and more effective treatment options are urgently needed.

Given the limitations of conventional treatments, there is growing interest in complementary therapies, including Traditional Chinese Medicine (TCM). TCM has gained attention for its multi-target approach, addressing both immune dysfunction and skin cell proliferation[9]. Our team’s preliminary analysis, based on the theory of pattern differentiation, found that 58.25% of patients exhibited the 'blood-dampness' syndrome[10], which is often associated with psoriasis. To address this, HSXYD was developed as a traditional herbal for treating Spleen Deficiency and Dampness Accumulation (SDDA)-type psoriasis. It is composed of ten herbs known for their anti-inflammatory, immune-modulating, and skin-healing properties. Clinical evidence accumulated over the years has shown that HSXYD alleviates psoriasis symptoms[10], reduces side effects from biologics, and may help prevent recurrence. However, controlled data is limited, and further validation through rigorous RCTs is required.

To bridge this gap, we conducted a prospective, multicenter, single-blind randomized controlled trial to evaluate the clinical efficacy and safety of HSXYD in patients with moderate to severe psoriasis accompanied by SDDA syndrome.

METHODS

Study design and setting

This is a prospective, multicentre, single-blind randomized controlled trial. It complies with the recommendations outlined in the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guidelines. The flow diagram of the trial is shown in Figure 1. Table 2 outlines the experimental timeline.

Study Population

Patients will be enrolled from six hospitals in Beijing, China, including China-Japan Friendship Hospital, Beijing Hospital of Traditional Chinese Medicine Capital Medical University, Beijing Hepingli Hospital, Beijing Drum Tower Hospital of Traditional Chinese Medicine, Beijing Changping District Traditional Chinese Medicine Hospital, and Beijing Hospital of Integrated Traditional Chinese and Western Medicine. Each center was selected for its expertise in psoriasis treatment and TCM application, ensuring high-quality data collection and patient care, with sufficient outpatient volume to meet the target sample size.

Recruitment

A total of 128 participants will be recruited through outpatient clinics, online platforms, and community outreach programs. The China-Japan Friendship Hospital, as the main center, will recruit 53 participants, while each of the five sub-centers will recruit 15 participants.

Patient and Public Involvement

Patients and members of the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

Inclusion criteria

1. Patients aged 18-75 years;
2. Diagnosed with plaque psoriasis for ≥ 6 months with or without psoriatic arthritis;
3. Dermatology Life Quality Index (DLQI)≥ 10, Psoriasis Area and Severity Index [11](PASI) ≥ 10, Body Surface Area(BSA) ≥ 10% at baseline were included.
4. Patients who are intolerant to systemic treatment and/or phototherapy have contraindications or have poor treatment control and who are judged by the investigator to need systemic treatment;
5. Patients who meet the symptoms of psoriasis with SDDA: According to the "Guidelines for Evidence-Based Clinical Practice of Traditional Chinese Medicine for Psoriasis Vulgaris (BaiBi) (2013 Edition)"[12] and "Terms of Clinical Diagnosis and Treatment of Traditional Chinese Medicine Syndrome Part"[13].

Exclusion criteria

1. Psoriasis-related medication history: history of topical medication in the previous 2 weeks, history of traditional Chinese medicine medication in the previous month, history of non-biological systemic medication or phototherapy; history of biologic medication in the previous 3 months; history of Natalizumab, Efalizumab, or B cell or T cell regulator medication in the previous 12 months;
2. Bacillus Calmette-Guerin(BCG) vaccination within 12 months before treatment or a history of live vaccination or bacterial vaccination within 3 months;
3. History of other systemic diseases;
4. History of infection: history of infection with hepatitis B, tuberculosis, Human Immunodeficiency Virus(HIV) etc.; History of chronic opportunistic and severe infection.

Withdraw criteria

If any of the following conditions occur, the medication will be adjusted or discontinued.
1. Any serious adverse events (SAEs) occurred during treatment.
2. Any significant deviations in the implementation of the protocol will make it difficult to evaluate the effectiveness of treatment if the deviation persists.
3. The principal investigator requests the trial be terminated.
4. The ethics committees request to suspend the trial.

Patients can withdraw from the trial at any time for any reason, without any consequences. Patients lost to follow-up who did not explicitly request to withdraw from the trial but no longer received the trial drug or underwent testing were also considered withdrawn.

Management of Dropout Cases

All patients who provide informed consent and meet the eligibility criteria for this randomized controlled trial will be considered dropouts if they fail to complete the study, regardless of the reason or timing of their withdrawal, except for those who discontinue due to complete symptom remission. Reasons for dropout, including adverse events, personal issues, or loss to follow-up, will be carefully recorded. Data from participants who withdraw will be retained for the intention-to-treat analysis, ensuring all patients who received the assigned treatment are included in the final analysis.

Intervention

Eligible participants will be randomized to the treatment or control group. Both groups received a standardized regimen of subcutaneous Secukinumab (300 mg), administered weekly at baseline and weeks 1–4, followed by maintenance dosing every 4 weeks until week 24. The treatment group additionally received oral HSXYD (100 mL twice daily for 8 weeks). Table 2 shows the schedule of study procedures, enrollment, interventions, and assessments.

All the botanical drugs of HSXYD are listed in Table 1. All herbal materials for HSXYD were procured and stored under standardized conditions in the TCM dispensary of the China-Japan Friendship Hospital and prepared according to standardized protocols at the hospital's dedicated

decoction facility. The raw herbal components were initially hydrated by immersion in distilled water at a 10:1 (v/w) water-to-herb ratio for 60 minutes. Following this, the mixture underwent primary aqueous extraction by boiling for 1 hour. The residual herbal material was subjected to a secondary extraction by rehydration with an equivalent volume of distilled water (10:1 ratio) and subsequent simmering for an additional hour. The resultant filtrates from both extraction cycles were pooled and concentrated under controlled conditions to yield a final HSXYD solution with a target concentration of 1.9g/mL. The concentrated preparation was then aseptically aliquoted into individual 30 mL doses for clinical administration. HSXYD extracts were vacuum packaged and stored in a cold storage dispensary of TCM of the China-Japan Friendship Hospital. The HSXYD used at each study site is prepared by the China-Japan Friendship Hospital and will be regularly shipped to the participating hospitals. It will be stored in temperature-controlled cold storage in the pharmacy.

Participants will receive detailed instructions, both verbally and in writing, regarding the dosage, administration method, and frequency of the study medication. At each visit, they will be provided with the drugs required for the next treatment period, and any unused medication from the previous cycle must be returned. Apart from the investigational product, the use of other botanical preparations, animal-derived substances, and immunosuppressive or immunomodulatory western medicines is strictly prohibited. Any non-protocol medications taken during the study must be thoroughly recorded. Participants are also required to complete a daily diary to document their drug intake and report any adverse events.

Chinese name	**Chinese pinyin**	**Scientific name**	**Family**	**Part used**	**Dosage (g)**
□□	Cang Zhu	*Atractylodes macrocephala*	Asteraceae	Rhizome	12
□□	Hou Po	*Magnolia officinalis*	Magnoliaceae	Bark	12
□□	Chen Pi	*Citrus reticulata*	Rutaceae	Dried Peel	12
□□	Ban Xia	*Pinellia ternata*	Araceae	Rhizome	12
□□□	Tu Fu Ling	*Smilax glabra*	Smilacaceae	Rhizome	15
□□□	Sheng Huai Hua	*Sophora japonica*	Fabaceae	Flower	10
□□□	Di Fu Zi	*Kochia scoparia*	Amaranthaceae	Fruit	15
□□	Mai Dong	*Ophiopogon japonicus*	Asparagaceae	Root	12
□□	Bai He	*Lilium lancifolium*	Liliaceae	Dried Bulb	12
□□	Gan Cao	*Glycyrrhiza uralensis*	Fabaceae	Root	10

Table 1 Components of Huashixiaoyin Decoction

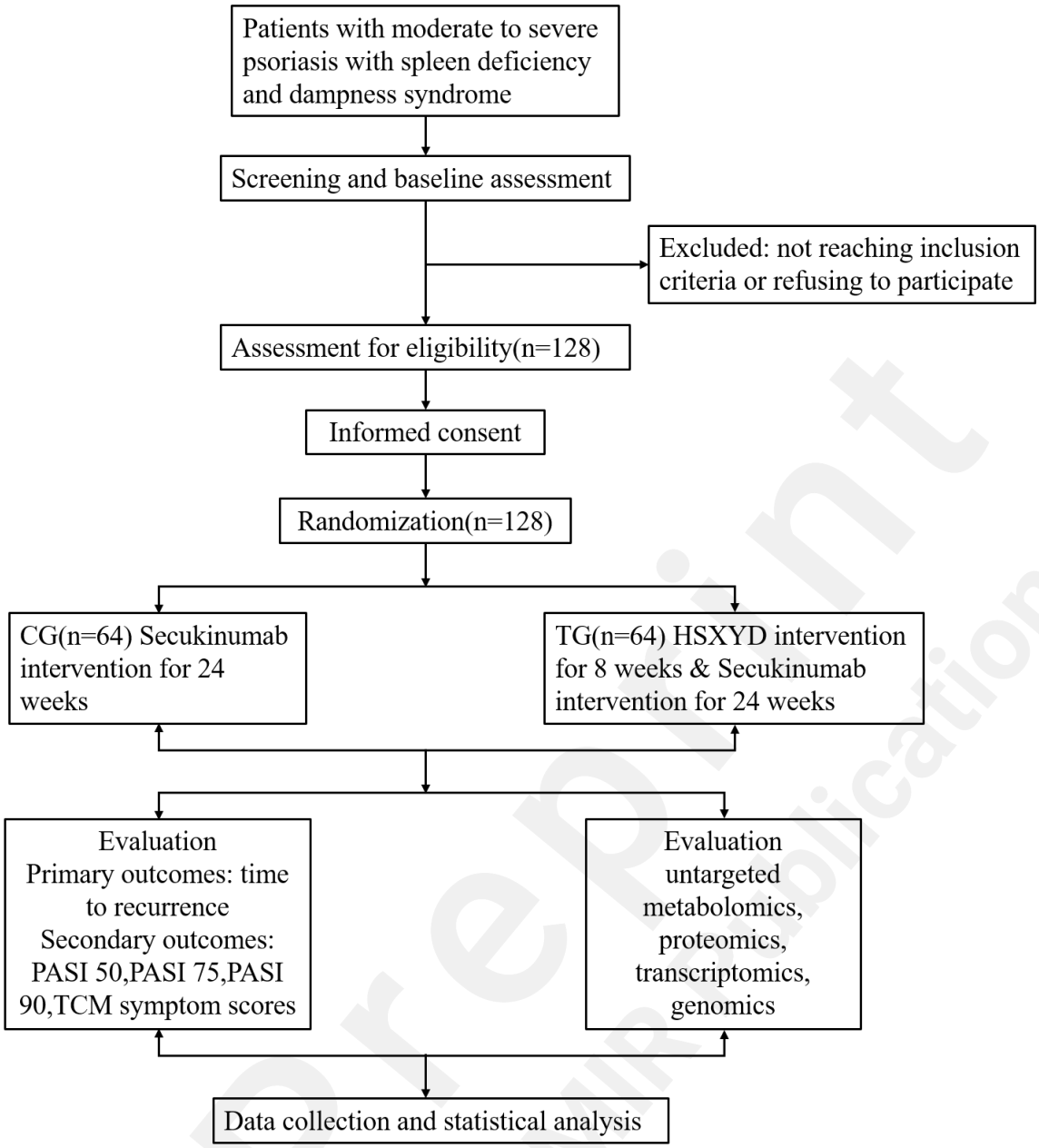

Figure 1 The flow diagram of the trial. CG, control group; TG, treatment group; HSXYD, Huashixiaoyin Decoction; PASI, Psoriasis Area and Severity Index; TCM, traditional Chinese medicine.

	Baseline	Intervention period			Follow-up period	
Visits	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**
Time point	**-1-0 days**	**Week 4**	**Week 8**	**Week 12**	**Week 24**	**Week 48**
Enrollment						
Informed consent	×					
General information	×					
Medical history	×					
Physical examination	×					
Inclusion criteria	×					
Exclusion criteria	×					
Randomization and allocation	×					
Interventions						
HSXYD and Secukinumab	♦	—	♦			
Secukinumab	♦	—	—	—	♦	
Efficacy observation						
PASI	×	×	×	×	×	×
DLQI	×	×	×	×	×	×
BSA	×	×	×	×	×	×
IGA	×	×	×	×	×	×
TCM symptom scores	×	×	×	×	×	×
Safety observation						
Blood routine test	×				×	×
Liver and kidney function tests	×				×	×
Screening for hepatitis viruses	×				×	×
Tuberculosis antibody test	×				×	×
Electrocardiogram	×				×	×
Chest X-ray	×				×	×
Adverse event record	×	×	×	×	×	×
Other						
Multi-omics testing	×				×	×
skin lesions imagine collection	×	×	×	×	×	×

HSXYD, Huashixiaoyin Decoction; PASI, Psoriasis Area and Severity Index; DLQI, Dermatology Life Quality Index; BSA, Body Surface Area; IGA, Investigator's Global Assessment; TCM, traditional Chinese medicine.

Table 2 Schedule of study procedures

Randomization and blinding

All participants will be randomly assigned to the treatment or control group using a computer-generated block randomization scheme created by an independent statistician with SAS 9.4 PROC PLAN. A total of 128 participants will be enrolled, with 32 blocks of four participants each, ensuring a 1:1 allocation ratio between groups and minimizing bias. Trained research coordinators will enroll participants according to the allocation sequence.

This study adopts a single-blind design, as creating a visually and physiologically indistinguishable placebo for HSXYD is not feasible. To reduce bias, outcome assessors and data analysts will remain blinded. Outcome assessors responsible for clinical evaluations are independent from the intervention team and receive only anonymized subject identifiers. Statistical analyses will be performed on de-identified datasets with coded allocations, with the randomization key securely maintained by a third party until study completion. Unblinding is only permitted in emergencies, such as for clinical management of serious adverse events, and will follow a documented procedure managed by a designated unblinding officer.

Outcome

The study assesses primary and secondary outcomes at three stages: initial baseline measurements, after 24 weeks of treatment, and at the end of the 48-week follow-up period.

Primary outcome

The primary outcome of this study is recurrence time of patients during the follow-up period at week 24 and week 48, using the PASI. Recurrence was defined as a loss of ≥50% of the initial PASI improvement from baseline in patients who achieved a clinically meaningful response[15]. PASI scores were systematically recorded and compared between the treatment and control groups at both time points. Cumulative recurrence rates in the two cohorts were calculated and statistically analysed to assess intergroup differences.

Secondary outcomes

The secondary outcomes of the study encompassed multiple clinical efficacy parameters, including relapse rates observed between weeks 24 and 48 post-intervention. Therapeutic response assessments incorporated the proportions of patients achieving ≥75% improvement in PASI 75 at the 24-week endpoint, with additional evaluation of PASI 50 and PASI 90 response thresholds during this mid-term assessment phase. Furthermore, the investigation quantified longitudinal symptom amelioration through percentage improvements in Traditional Chinese Medicine (TCM)-specific clinical manifestations, measured at both the 24-week and 48-week time points to capture intermediate and extended therapeutic effects.

Safety outcomes

Safety will be assessed through monitoring adverse events (AEs), ECG, chest X-ray, and laboratory tests (blood, liver and kidney function, hepatitis, tuberculosis, and antibodies) at baseline, week 24, and week 48. All solicited and spontaneous AEs will be documented on case report forms, including severity, duration, and relatedness to the intervention. Serious adverse events (SAEs) will be evaluated per ICH E2E guidelines and reported to the sponsor and ethics committee within 24 hours, while other AEs will be reported within 48 hours. Participants with SAEs will receive appropriate care and close monitoring, and the trial may be paused or terminated if needed. Protocol deviations or operational errors will be promptly addressed, reported, and corrected to protect participants and ensure data integrity.

Sample size

This study employed a superiority design to assess the primary outcome, which is the time to recurrence of patients during the follow-up period from week 24 to week 48. The sample size was calculated via the following formula for comparing two proportions: $n=((Z_{\alpha/2}+Z_{\beta})^2\times(1-p_1)\times(1-p_2))/(p_1-p_2)^2$. Sample size estimation was performed using a priori power analysis with the following presets: $Z_{\alpha/2}=1.96$ corresponds to a two- tailed significance level of 0.05, and $Z_{\beta}=0.84$ reflects an 80% statistical power, and a 20% enrollment expansion to compensate for potential attrition. With all parameters selected based on clinical relevance and historical data, $p_1 = 0.6$ represents the relapse rate of Secukinumab monotherapy[14], derived from previous clinical trials, while $p_2 = 0.4$ represents the estimated relapse rate for the combination of Secukinumab and HSXYD. With these parameters, the required total sample size was 128 participants, with 64 individuals assigned to each group.

Data collection methods and management

During clinic visits, all research data will first be recorded on paper case report forms and then entered independently by two staff members into the Integrated Traditional Chinese and Western Medicine Data Platform of China-Japan Friendship Hospital, with cross-verification to ensure accuracy and completeness. To support participant retention, reminders will be sent before each visit, follow-up calls will be made, and participants may receive travel reimbursement, small incentives, or motivational counselling as needed. Outcome data, including PASI, IGA, BSA, DLQI, and TCM symptom scores, will be collected even if participants discontinue or deviate from the protocol, with all adverse events and reasons for withdrawal documented. An independent Data Monitoring Committee (DMC), comprising a biostatistician, a dermatologist, and a clinical pharmacologist, will periodically review data on safety, efficacy, and trial progress, reporting directly to the Trial Steering Committee (TSC). Interim analyses at 50% and 75% of planned enrollment will assess primary endpoints, adverse events, and early efficacy signals. If safety concerns arise or efficacy is overwhelming, the trial may be stopped early based on DMC recommendations. The DMC operates independently from the sponsor and investigators, and members with conflicts of interest will be excluded.

Ethical and dissemination

This trial received ethical approval from the Clinical Research Ethics Committee of the China-Japan Friendship Hospital on July 4, 2022 (Approval No. 2022-KY-106), prior to initiation. The Research Ethics Committee (REC) will conduct regular reviews every six months, including assessments of the study protocol, informed consent forms, and recruitment materials, to ensure the rights, safety, and well-being of participants. Progress reports, including safety data and adverse events, will be submitted to the committee. Ethical approval will be renewed annually. The study adheres to the ethical principles of the Declaration of Helsinki and the International Conference on Harmonisation Good Clinical Practice (ICH-GCP) guidelines. It was registered with the International Traditional Medicine Clinical Trials Registry on December 3, 2024(Clinical Trial Number: ITMCTR2025000129). All items from the World Health Organization (WHO) Trial Registration Data Set have been completed and are publicly available on the registry website.

Protocol amendments and participant consent

Any protocol amendments (e.g., eligibility, outcomes, or analysis changes) will be reviewed and approved by the REC before implementation, then communicated to investigators, regulators, registries, and, if applicable, participants. Approved updates will be registered within seven working days. When amendments affect participant rights or safety, updated informed consent will be obtained by trained staff before study procedures, in a private setting. Participants will receive clear verbal and written information on purpose, procedures, risks, benefits, and rights, with time for questions. Consent from legally authorized representatives will be sought when participants cannot provide it.

Use of biological samples

Venous blood samples will be collected at baseline, week 24, and week 48 using EDTA tubes, kept at 2–8°C, and transported within two hours to the central laboratory. PBMCs will be isolated within four hours following standardized procedures. All staff will undergo unified training, and shipments will be tracked and quality-controlled; any samples not meeting specified conditions will be excluded. Specimens will be stored at −80°C for five years and labeled with coded identifiers to ensure confidentiality. Future use for genomic, proteomic, and metabolomic analyses, which are covered in the main consent; Provision of these samples is voluntary and does not affect eligibility for the main trial. Participants may withdraw consent at any time without affecting trial participation.

Data protection and access

Personal information will be collected by trained staff and stored securely with unique study identifiers. Only authorized personnel will access password-protected databases and locked files. De-identified data may be shared with statisticians, monitors, or regulators. Data will be retained for five years, then destroyed unless required by regulation. No third-party sharing occurs without additional

consent. The principal investigator and designated team members will access the final dataset, and external data requests will be reviewed case by case after de-identification and ethical approval.

Results dissemination and publication

Results will be disseminated through peer-reviewed journals, scientific conferences, trial registry postings, and plain-language summaries for participants upon request. Healthcare professionals and stakeholders will be informed via clinical and academic networks. As an independent investigator-initiated trial, there are no publication restrictions; manuscripts will follow ICMJE guidelines and be drafted by the research team. The protocol is publicly available on the ITMCTR website. De-identified datasets and statistical code may be shared upon reasonable request, pending ethical approval and data protection compliance.

Post-Trial care and compensation

Participants who experience trial-related adverse events will receive appropriate medical treatment at no cost. In cases of harm directly attributable to participation—including adverse reactions to study interventions—compensation will be provided according to applicable national regulations and institutional policies. Although no formal post-trial treatment is planned, participants requiring ongoing care will be referred for appropriate clinical follow-up.

Declaration of interests and authorship

All principal investigators, including those at collaborating sites, have declared no financial, personal, or professional competing interests that could influence any aspect of the study. Authorship will follow ICMJE guidelines. Eligible authors must have made substantial contributions to the study design, data acquisition, analysis, interpretation, manuscript drafting or critical revision, final approval, and accountability for the work. No professional writers will be involved; manuscripts will be prepared entirely by the study investigators.

Auditing of trial conduct

The trial will undergo regular audits every six months to ensure compliance with the protocol, regulatory requirements, and good clinical practice (GCP). Audits will assess the accuracy and completeness of case report forms (CRFs), informed consent procedures, data integrity, and adverse event reporting. In addition, study documentation, including informed consent forms and regulatory submissions, will be reviewed. The auditing process will be carried out by an independent third-party audit firm, which will operate independently from both the investigators and the sponsor to ensure the impartiality and transparency of the audit process.

Practitioner training and quality control

Evaluators will be trained and certified, with two independent investigators assessing participants at each follow-up. Ratings will be averaged, with discrepancies resolved by a third investigator. Paper records will be retained for verification. The principal investigator and supervisors will oversee accuracy and completeness, supported by regular onsite audits. Trial oversight is ensured by the Clinical Research Ethics Committee and independent external audits to monitor compliance, detect deviations, and resolve data issues.

Statistical analysis

All data analysis and visualization will be performed by statisticians who are blinded to group allocation, using IBM SPSS (V.25.0) and R (V.4.1.1). For continuous variables following a normal distribution, the t-test will be performed with the null hypothesis that there is no difference between groups, and a p-value <0.05 will be considered statistically significant. For continuous variables that do not follow a normal distribution, the data will be presented as median (interquartile range) [M (P25, P75)], and comparisons will be made using the non-parametric rank sum test. Categorical variables will be reported as frequencies and percentages (%), and intergroup differences will be assessed using the χ^2 test or Fisher's exact test. Both primary and secondary outcomes will be analysed using intention-to-treat methodology. Survival analysis will be conducted using the Kaplan-Meier method, with comparisons between groups performed using the Log-rank test. The Cox proportional hazards regression model will be used to assess the effects and influencing factors of the

different treatment approaches. A two-sided test will be applied, with a P-value < 0.05 considered statistically significant.

The analysis population will include all participants who were randomized into the study (intent-to-treat analysis). Participants who deviate from the intervention protocol (e.g., missed doses, early withdrawal) will be included in the analysis according to their randomized group, regardless of adherence to the study treatment. Sensitivity analyses may be conducted to assess the impact of protocol non-adherence on the study outcomes. Missing data will be handled using multiple imputation methods, where missing values will be imputed based on the observed values of other variables. We will assume that data are missing at random (MAR). The number of imputations will be determined based on the extent of missing data. Sensitivity analyses will be performed to examine the impact of different missing data handling methods on the results.

Results

This study was supported financially by the China's National High Level Hospital Clinical Research Funding. The trial was registered in December 2024. At the time of submission, participant enrollment has been completed. The follow-up is still ongoing, with the expected date of the last patient's last visit scheduled for April 2026. Data analysis is anticipated to be completed by May 2026. Participant enrollment for the trial began in August 2022. The findings of this study will be shared at conferences both nationally and internationally and will be published in journals that are peer-reviewed.

DISCUSSION

Expected Findings

This study introduces several significant innovations in the treatment and clinical characterisation of moderate-to-severe plaque psoriasis with Spleen Deficiency and Dampness Accumulation syndrome (SDDA), a subtype commonly recognised in psoriasis but often underexplored in clinical research. First, this is the first prospective, multicenter, single-blind randomized controlled trial (RCT) to evaluate the combination of Huashixiaoyin Decoction (HSXYD) and Secukinumab compared to Secukinumab monotherapy in patients with SDDA-type moderate-to-severe psoriasis. This novel approach allows for a controlled assessment of how combining TCM with biologic therapy may improve patient outcomes, specifically in reducing relapse rates and prolonging remission. The design provides rigorous clinical evidence for integrating TCM and modern biologics in treating chronic inflammatory diseases like psoriasis. Second, the study adopts an integrated multi-omics approach, combining transcriptomic, proteomic, metabolomics, and microbiome analyses. To our knowledge, this is the first time that this comprehensive approach has been applied in the context of SDDA psoriasis. This method offers a systematic understanding of how the immune and metabolic systems are modulated by TCM and biologics, shedding light on the underlying mechanisms of treatment efficacy and recurrence prevention. This innovative approach contributes to advancing the molecular understanding of TCM interventions in dermatology. Third, the study will develop a syndrome diagnosis prediction model that integrates clinical symptoms and multi-omics data. This model enables quantitative and accurate syndrome diagnosis, facilitating precision medicine by predicting disease progression and response to therapy. This represents a breakthrough in bridging the gap between TCM syndrome differentiation and modern biomedical research, providing a more personalized and effective approach to managing psoriasis. Finally, the combination of HSXYD with Secukinumab offers a unique treatment paradigm for SDDA-type psoriasis. While biologics such as Secukinumab are effective in controlling inflammation, the integration of TCM provides a holistic approach aimed at addressing the underlying constitutional imbalances, particularly in cases where the disease is prone to relapse. This innovative combination therapy has the potential to improve long-term outcomes and reduce recurrence, advancing the management of psoriasis and chronic inflammatory diseases.

Limitations

This study is limited by the absence of a placebo-controlled, double-blind design; instead, a single-blind randomized controlled trial was conducted. The objective was to assess whether adding Huashixiaoyin Decoction (HSXYD) to Secukinumab improves efficacy, quality of life, and relapse prevention. A concentrated decoction was chosen for patients with SDDA to optimize extraction of active compounds such as Atractylodes macrocephala and Magnolia officinalis. However, its distinctive taste and aroma made an indistinguishable placebo unfeasible, raising the risk of expectation bias, especially among participants familiar with traditional medicine. To mitigate this, blinded outcome assessments and analyses were conducted independently, with randomization keys secured by a third party. While decoctions are difficult to standardize, they may provide superior bioavailability and therapeutic benefit. Nevertheless, the lack of double-blinding and intervention complexity limit internal validity and generalizability. Future larger multicenter trials with standardized forms are warranted.

TRIAL STATUS

This study is currently in the recruitment phase. The first patient was randomized on August 17, 2022, and the last patient's last visit is expected to occur on June 30, 2026.

DECLARATIONS

Ethics approval and consent to participate

This trial received ethical approval from the Clinical Research Ethics Committee of the China-Japan Friendship Hospital on July 4, 2022 (Approval No. 2022-KY-106), prior to initiation.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated or analysed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors have no conflicts of interest to disclose.

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This study was supported financially by the China's National High Level Hospital Clinical Research Funding. The sponsor and funders had no role in the study design; collection, management, analysis, and interpretation of data; writing of the report; or the decision to submit the report for publication. The investigators have full autonomy over all aspects of the study.

Author contributions

Qiuchen Huang: Writing – original draft.
Lei Wang: Conceptualization, Methodology.
Jingkai Xu: Formal analysis.
Hongda Yu and Yuemin Zou: Writing – review & editing.
Qianwei Liu and Haoyu Yang: Project administration.
Yanping Bai: Supervision, Writing – review & editing.

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Not applicable.

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Protocol version

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Trial sponsor information

The trial sponsor is China's National High Level Hospital Clinical Research Funding. Contact: Mrs. Lin Li, Science and Technology Department, zryykyc@126.com, +86-010-84205698. The

study sponsor and funders have no role in the design of the study; collection, management, analysis, or interpretation of the data; writing of the report; or the decision to submit the manuscript for publication. The investigators have full autonomy over all aspects of the study.

Coordinating centre

This study is a prospective, multicentre, single-blind randomized controlled trial. To ensure the scientific rigor and quality of the trial, several oversight and operational groups have been established.

The coordinating centre is led by the Science and Technology Department of China-Japan Friendship Hospital, responsible for the overall implementation, organization, and coordination of the trial. The steering committee is composed of senior experts from the academic team of Academician Xiaolin Tong, Chinese Academy of Sciences. This committee provides high-level strategic and methodological guidance throughout the study. The data management team is led by Professor Xianbo Zuo from the Center for Data Science. This team is responsible for developing the data management plan, supervising data entry, and ensuring data quality and integrity. The endpoint adjudication committee and statistical analysis team are coordinated by Professor Yanfen Chen from the Department of Clinical Research. This team is responsible for developing and executing the statistical analysis plan, as well as adjudicating clinical endpoints. Ethical and regulatory oversight is provided by Professor Xiuyun Jin and her team from the Ethics Office of China-Japan Friendship Hospital, who are in charge of ethics submission, approval coordination, and ongoing compliance monitoring.

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Abbreviations

HSXYD	Huashixiaoyin Decoction
RCT	randomized controlled trial
SDDA	Spleen Deficiency and Dampness Accumulation
ICMGE	
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
PASI	Psoriasis Area and Severity Index
IGA	Investigator's Global Assessment
DLQI	Dermatology Life Quality Index
BSA	Body Surface Area
TCM	Traditional Chinese Medicine
BCG	Bacillus Calmette-Guerin

HIV	Human Immunodeficiency Virus
SAEs	serious adverse events
CG	control group
TG	treatment group
PROC PLAN	Procedure for Experimental Design Planning
IL	Interleukin

Supplementary Files

CONSORT (or other) checklists

URL: http://asset.jmir.pub/assets/7d03374e6510b7626efe08bcfd3c9b83.pdf