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(54) Title: TREATMENT OF PSORIASIS USING HELMINTHIC PARASITE PREPARATIONS

(57) Abstract: Methods are provided for treating psoriasis, in particular moderate to severe chronic plaque-type psoriasis, using helminthic parasite preparations.

Dermatology Life Quality Index Form

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick one box for each question.

1.	Over the last week, how itchy, sore, painful or stinging has your skin been?	Very much ☐ A lot ☐ A little ☐ Not at all ☐	
2.	Over the last week, how embarrassed or self conscious have you been because of your skin?	Very much ☐ A lot ☐ A little ☐ Not at all ☐	
3.	Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden?	Very much ☐ A lot ☐ A little ☐ Not at all ☐	Not relevant ☐
4.	Over the last week, how much has your skin influenced the clothes you wear?	Very much ☐ A lot ☐ A little ☐ Not at all ☐	Not relevant ☐
5.	Over the last week, how much has your skin affected any social or leisure activities?	Very much ☐ A lot ☐ A little ☐ Not at all ☐	Not relevant ☐

TO FIG 1 (CONT.)

FIG. 1

WO 2014/121020 A2

TREATMENT OF PSORIASIS USING HELMINTHIC PARASITE PREPARATIONS

FIELD OF THE INVENTION

[0001] The present invention relates generally to methods of treatment of psoriasis. More particularly, the present invention relates to the use of helminthic parasite ova in pharmaceutical formulations to ameliorate symptoms of chronic psoriasis. This application claims priority to U.S. Provisional Application Serial No. 61/759,165, filed January 31, 2013, which is incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION

[0002] Psoriasis (psoriasis vulgaris) is a chronic inflammatory skin disease characterized by red, scaly, raised plaques. The disease process is driven by T-cell infiltration and associated elevation in cytokine levels leading to increased cell division and aberrant differentiation, resulting in the psoriatic phenotype. Plaque psoriasis has a worldwide prevalence of 2-3%, and is a chronic, recurrent skin condition with varying degrees of severity. Psoriasis can profoundly impact a patient's quality of life, causing disability of physical and mental functioning comparable to other major medical diseases such as type 2 diabetes, hypertension, myocardial infarction, depression, and arthritis. It is also associated with serious co-morbidities, including psoriatic arthritis, depression, malignancy, metabolic syndrome, cardiovascular morbidity and mortality and autoimmune diseases, such as inflammatory bowel disease (IBD).

[0003] While many patients with mild disease are able to control psoriasis symptoms with topical medications alone, patients with moderate to severe disease usually require treatment with systemic agents to achieve good clearance. These systemic agents are usually well tolerated, but can have potentially significant side effects including organ toxicity, infection, malignancy, and teratogenicity that limit their usefulness in the long-term management of psoriasis. Biologic agents have been a significant advancement in the treatment of moderate to severe psoriasis, but can have limited and/or diminishing efficacy and require administration by subcutaneous injection or intravenous infusion. These agents are still relatively new and long term safety issues (e.g., infection including tuberculosis, malignancies including lymphoma, and demyelinating neurologic events) are not fully understood. Despite all the available treatments, there is still a need for therapies that will

provide high continuous efficacy, improved safety, and a more convenient route of administration to maximize compliance and satisfaction with treatment, leading to decreased burden of the disease.

SUMMARY OF THE INVENTION

[0004] The present invention relates to novel therapeutic methods for the treatment of psoriasis based on an improved understanding of the autoimmune causes of psoriasis.

[0005] In particular, the present invention provides a method of treating psoriasis in a human patient comprising administering to a human patient in need thereof a therapeutically effective amount of a pharmaceutical formulation comprising a helminthic parasite or a biologically active portion thereof and a pharmaceutically acceptable carrier, wherein the helminthic parasite or portion thereof is selected from the group consisting of T. suis, S. mansoni, H. polygyrus, T. spiralis, T. trichiura and N. americanus. In some embodiments, the psoriasis may be characterized as plaque, guttate, inverse, pustular, erythrodermic, or arthritic psoriasis. In further embodiments, the psoriasis may be characterized as moderate to severe chronic plaque psoriasis. In still other embodiments, patients may present arthritic forms of psoriasis.

[0006] In further embodiments, the human patient also suffers from at least one condition selected from the group consisting of pregnancy, cancer, kidney disease, liver disease, diabetes, increased blood pressure, coronary disease, immune disorders, and acute or chronic blood disorders. The human patient may, in some embodiments, be contraindicated from receiving an injection or infusion.

[0007] In still further embodiments, the biologically active portion of the helminthic parasite may be selected from the group consisting of parasite extract, parasite eggs, parasite egg extract, parasite larvae, parasite larvae extract, parasite cercariae and parasite cercariae extract. In yet further embodiments, the pharmaceutical formulation may comprise parasite eggs or parasite egg extract of *T. suis*. Additionally, in some embodiments, the pharmaceutical formulation may comprise an additional active agent such as, in further embodiments, an active agent selected from the group consisting of corticosteroids, vitamin D analogs, calcineurin inhibitors, salicylic acid, retinoids, methotrexate, cyclosporine, hydroxyurea, thioguanine, imunomodulatory drugs and antigen-specific drugs.

[0008] The therapeutically effective amount may, in some embodiments, be between about 500 and about 20,000 eggs, or, in further embodiments, between about 2,000 and about 10,000 eggs. In still further embodiments, the therapeutically effective amount may be 2,500 eggs or 7,500 eggs. The amount administered may be between about 1 and about 4 times per month for a duration of six months or greater. In further embodiments, the frequency of administration of the pharmaceutical formulation may be greater for a first period of time taking place at the outset of treatment, than the frequency of administration during a second period of time taking place after the first period of time. Alternatively or additionally, the frequency of administration of the pharmaceutical formulation may be increased for a period of time when acute symptoms of psoriasis appear or are expected to appear, followed by a return to the frequency of administration after the acute symptoms have subsided. The pharmaceutical formulation, in some embodiments, may be administered orally.

[0009] As used herein, "about" will be understood by persons of ordinary skill in the art and will vary to some extent depending upon the context in which it is used. If there are uses of the term which are not clear to persons of ordinary skill in the art given the context in which it is used, "about" will mean up to plus or minus 10% of the particular term.

[0010] As used herein, the term "active agent" is used herein to refer to a chemical material or compound that induces a desired beneficial effect when administered topically or orally, and includes agents that are therapeutically and/or prophylactically effective as pharmaceuticals ("pharmacologically active agents"). By an "effective" amount of an active agent is meant a nontoxic but sufficient amount of an active agent to provide the desired beneficial effect.

[0011] As used herein, the term "egg" refers to either embryonated or nonembryonated, viable helminth ova.

[0012] Additional features, advantages, and embodiments of the present disclosure may be set forth from consideration of the following detailed description, drawings, and claims. Moreover, it is to be understood that both the foregoing summary of the present disclosure and the following detailed description are exemplary and intended to provide further explanation without further limiting the scope of the present disclosure claimed.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] The foregoing and other objects, aspects, features, and advantages of the disclosure will become more apparent and better understood by referring to the following description taken in conjunction with the accompanying drawings, in which:

[0014] Figure 1 is a questionnaire for use in the Dermatology Life Quality Index (DLQI) test, which aids in the diagnosis of and characterization of psoriasis.

[0015] Figure 2 is a chart for use in taking the medical history of proposed study participants.

[0016] In the following detailed description, reference is made to the accompanying drawings, which form a part hereof. In the drawings, similar symbols typically identify similar components, unless context dictates otherwise. The illustrative embodiments described in the detailed description, drawings, and claims are not meant to be limiting. Other embodiments may be utilized, and other changes may be made, without departing from the spirit or scope of the subject matter presented here. It will be readily understood that the aspects of the present disclosure, as generally described herein, and illustrated in the figures, can be arranged, substituted, combined, and designed in a wide variety of different configurations, all of which are explicitly contemplated and made part of this disclosure.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0017] Psoriasis is driven by T-cell infiltration in the epidermis. The progression of psoriasis is usually clinically measured by one or more of four tests: the PASI score, sPGA, BSA, and PGA. Further, secondary objectives include assessment of the effects on quality of life and/or safety outcomes.

[0018] The PASI score stands for Psoriasis Area and Severity Index. This tool allows quantification of disease severity and degree of improvement with treatment. To make up the score, the three features of a psoriatic plaque (redness) scaling and thickness are each assigned a number from 0 to 4 with 4 being worst. Then the extent of involvement of each region of the body is scored from 0 to 6. Adding up the scores give a range of 0 to 72. The improvement in the PASI score over time as a measure of a drug's effectiveness. This is generally measured as the percent change in PASI score for a given patient. If a patient has a PASI score of 20 at the start of the study and a score of 5 at the end they have had an improvement of 75% or a PASI 75 response. For many studies the proportion of patients experiencing a 75% or 50% reduction in their PASI scores over the treatment period is reported as a percentage of people achieving PASI 75 or PASI 50, respectively.

[0019] Every effort should be made to ensure that the assessor who performed the PASI evaluations for a subject at baseline should also perform all subsequent PASI assessments.

At a minimum the same assessor should perform the PASI evaluation at baseline and Week 16. The assessor should be trained to perform the assessment and documentation of this training will be maintained in the site's training files. Whenever possible, the study investigator should attempt to control lighting in the examination room where the subject is being evaluated. The PASI is calculated as follows:

[0020] The body is divided into four sections (head (H) (10% of a person's skin); arms (A) (20%); trunk (T) (30%); legs (L) (40%)). Each of these areas is scored by itself, and then the four scores are combined into the final PASI. For each section, the percent of area of skin involved, is estimated and then transformed into a grade from 0 to 6: 0% of involved area, grade: 0. < 10% of involved area, grade: 1. 10-29% of involved area, grade: 2. 30-49% of involved area, grade: 3. 50-69% of involved area, grade: 4. 70-89% of involved area, grade: 5. 90-100% of involved area, grade: 6. Within each area, the severity is estimated by three clinical signs: erythema (redness), induration (thickness) and desquamation (scaling). Severity parameters are measured on a scale of 0 to 4, from none to maximum. The sum of all three severity parameters is than calculated for each section of skin, multiplied by the area score for that area and multiplied by weight of respective section (0.1 for head, 0.2 for arms, 0.3 for body and 0.4 for legs).

[0021] Another measure of psoriasis is the static physician's global assessment (sPGA). Although different versions exist, it is generally a 6 point scale ranging from 0 (clear or almost clear) to 5 (very severe) that is a composite score based upon the evaluating clinician's assessment of plaque thickness, redness, and scale at a given point in time. While simple to perform, the sPGA does not take body surface area involvement into consideration.

[0022] The Dermatology Life Quality Index or DLQI, developed in 1990's, is a simple 10-question validated questionnaire which has been used in 33 different skin conditions in 32 countries and is available in 55 languages. Its use has been described in over 500 publications including 30 multinational studies. The DLQI is the most frequently used instrument in studies of randomized controlled trials in dermatology (see Fig. 1).

[0023] Psoriasis severity may be measured by amount of skin affected by psoriasis; this is described as the percentage of body surface area (BSA). The area beneath one hand, including fingers and thumb, is equal to 1% of your BSA. If the skin affected by psoriasis is roughly equal to the area beneath 2 hands, then about 2 percent of the body is affected. Scoring takes place as follows:

- Mild psoriasis affects less than 3% of the body.
- Moderate psoriasis affects 3 to 10% of the body.
- Severe psoriasis affects more than 10% of the body.

The physician then makes an assessment of the BSA.

[0024] Other tests may be conducted throughout the course of treatment to determine safety or efficacy of the treatment. As used herein, "clinical chemistry" comprises one or more of the tests selected from the group consisting of total protein, albumin, serum creatinine, blood urea nitrogen (BUN), uric acid, bilirubin (total & direct), alkaline phosphatase, alanine aminotransferase (ALT, SGPT), aspartate aminotransferase (AST, SGOT), creatine phosphokinase (CPK), glucose, calcium, phosphorus, sodium, potassium, chloride, and bicarbonate.

[0025] As used herein, "hematology" refers to the following tests: white blood cell (WBC) count, differential white cell count (lymphocytes, monocytes, basophils, eosinophils, neutrophils), red blood cell (RBC) count, hematocrit, hemoglobin and platelet count. As used herein, "urinalysis" refers to a group of tests comprising color, specific gravity, pH, glucose, ketones, blood, protein, nitrates, leukocyte esterase, RBC, WBC.

Helminthic Preparations

[0026] Embryonated eggs of certain helminths, such as, for example, porcine whipworm Trichuris suis (*Trichuris suis* ova, TSO), have been shown to colonize briefly the human intestine without invading or infecting. Safety of TSO has been demonstrated in Phase I clinical studies, as shown in Table 1.

Table 1: Number (%) of Patients Experiencing Treatment-Emergent Adverse Events by MedDRA Preferred Term – Sorted by Descending Incidence in the Total TSO Column (Study CNDO 201-002)

MedDRA Preferred Term	Placebo (n=9)	TSO 500 OVA (n=9)	TSO 2500 OVA (n=9)	TSO 7500 OVA (n=9)	Total TSO (n=27)
At least one TEAE	4 (44.4)	3 (33.3)	0 (0.0)	6 (66.7)	9 (33.3)
Diarrhea	0 (0.0)	2 (22.2)	0 (0.0)	0 (0.0)	2 (7.4)
Nausea	1 (11.1)	1 (11.1)	0 (0.0)	1 (11.1)	2 (7.4)
Vomiting	0 (0.0)	1 (11.1)	0 (0.0)	1 (11.1)	2 (7.4)
Abdominal pain	0 (0.0)	1 (11.1)	0 (0.0)	0 (0.0)	1 (3.7)
Flatulence	0 (0.0)	1 (11.1)	0 (0.0)	0 (0.0)	1 (3.7)
Mucous stools	0 (0.0)	1 (11.1)	0 (0.0)	0 (0.0)	1 (3.7)
Rectal hemorrhage	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.1)	1 (3.7)
Decreased appetite	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.1)	1 (3.7)
Dysgeusia	1 (11.1)	0 (0.0)	0 (0.0)	1 (11.1)	1 (3.7)
Sinus congestion	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.1)	1 (3.7)
Oropharyngeal pain	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.1)	1 (3.7)
Nasopharyngitis	1 (11.1)	0 (0.0)	0 (0.0)	1 (11.1)	1 (3.7)
Road traffic accident	1 (11.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Headache	1 (11.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Interim Study Report for Study CNDO 201-002

TEAEs were defined where dose date was on or before the onset data of the event. Events with missing onset dates are considered treatment-emergent events.

[0027] Any immunomodulatory non-infective helminth species may be used in the methods described herein, such as, for example, *T. suis,* S. *mansoni, H. polygyrus, T. spiralis, T. trichiura* and *N. americanus.* The entire adult helminth may be used, or any therapeutically effective portion thereof, such as, for example, parasite extract, parasite eggs, parasite egg extract, parasite larvae, parasite larvae extract, parasite cercariae and parasite cercariae extract. In a preferred embodiment, parasite ova are used.

[0028] Therapeutically effective amounts of the helminth or biologically active portion thereof can be empirically determined and will vary with the pathology being treated, the severity of the psoriasis, and the subject being treated. The effective amount may be determined during pre-clinical trials and clinical trials by methods familiar to physicians and

clinicians. An effective amount of a helminthic parasite preparation useful in the methods may be administered to a mammal in need thereof by any of a number of well-known methods for administering pharmaceutical compounds. The peptide may be administered systemically or locally or, in the case of a neonatal patient, may be administered to the mother. In a preferred embodiment, the administration is oral.

[0029] Oral compositions may also include an inert diluent or an edible carrier. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules, *e.g.*, gelatin capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

[0030] Additionally, the helminthic parasite preparation may also comprise a second active agent for the treatment of psoriasis. Such an active agent may be selected from the group consisting of corticosteroids, vitamin D analogs, calcineurin inhibitors, salicylic acid, retinoids, methotrexate, cyclosporine, hydroxyurea, thioguanine, imunomodulatory drugs, or any other therapeutically effective agent.

[0031] The skilled artisan will appreciate that certain factors may influence the dosage and timing required to effectively treat a subject, including but not limited to, the severity of the disease or disorder, previous treatments, the general health and/or age of the subject, and other diseases present. Moreover, treatment of a subject with a therapeutically effective amount of the therapeutic compositions described herein can include a single treatment or a series of treatments.

[0032] In preferred embodiments, each dose may comprise from about 500 to about 20,000 eggs, or from about 2,000 eggs to about 10,000 eggs. In further embodiments, each dose may comprise about 1,000 eggs, about 1,500 eggs, about 2,000 eggs, about 2,500 eggs, about 3,000 eggs, about 3,500 eggs, about 4,000 eggs, about 4,500 eggs, about 5,000 eggs, about 5,500 eggs, about 6,000 eggs, about 6,500 egg, about 7,000 eggs, about 7,500 eggs, about

8,000 eggs, about 8,500 eggs, about 9,000 eggs, about 9,500 eggs, about 10,000 eggs, about 10,500 eggs, about 11,000 eggs, about 11,500 eggs, about 12,000 eggs, about 12,500 eggs, about 13,000 eggs, about 13,500 eggs, about 14,000 eggs, about 14,500 eggs, about 15,000 eggs, about 15,500 eggs, about 16,000 eggs, about 16,500 eggs, about 17,000 eggs, about 17,500 eggs, about 18,000 eggs, about 18,500 eggs, about 19,000 eggs, or about 19,500 eggs.

[0033] Administration may take place as often or as rarely as necessary to be therapeutically effective. The amount administered may be between about 1 and about 4 times per month for a duration of six months or greater, depending on the pathology of the patient and the presence of acute symptoms. In preferred embodiments, the frequency of administration of the pharmaceutical formulation may be greater for a first period of time taking place at the outset of treatment, than the frequency of administration during a second period of time taking place after the first period of time. Alternatively or additionally, the frequency of administration of the pharmaceutical formulation may be increased for a period of time when acute symptoms of psoriasis appear or are expected to appear, followed by a return to the frequency of administration after the acute symptoms have subsided.

[0034] The present invention is further illustrated by the following examples, which should not be construed as limiting in any way.

Examples

Example 1: Treatment of Moderate to Severe Plaque Psoriasis Using TSO

[0035] In order to demonstrate the efficacy of helminthic preparations in treatment of psoriasis, eight subjects suffering from moderate to severe plaque-type psoriasis (i.e., BSA $\geq$ 10%, PGA $\geq$ 3, and PASI $\geq$ 12) are recruited, having the following inclusion criteria: males or females, 18 to 75 years old, with a diagnosis of stable plaque type psoriasis for at least six months prior to baseline, good health based on medical history, physical examination, and clinical laboratories; in the investigator's opinion, must be a candidate for systemic or phototherapy of psoriasis; if a woman, postmenopausal, surgically sterile, practicing a highly effective method of birth control, or not heterosexually active; not pregnant; able to provide informed consent; agree to avoid prolonged exposure to natural sunlight, tanning beds, or phototherapy; and agree to avoid any prohibited concomitant medications as detailed below for four weeks prior to baseline and through week 16 of the study.

[0036] In addition, subjects may not have the following exclusion criteria: known history of intestinal parasitic infection, even if adequately treated, in the past 5 years; have received

antibiotic, antifungal or antiparasitic medication in the last 2 weeks prior to screening and/or would potentially require this during the study treatment period; history of drug or alcohol abuse within 6 months prior to screening; evidence of poor compliance with medical advice and instruction; unable or unwilling to swallow study medication suspension; having a significant medical condition which puts the subject at risk for study participation and/or for any reason is considered by the Investigator to be an unsuitable candidate to receive TSO or is potentially put at risk by study procedures; participation in another clinical trial within 30 days of Screening for this trial and/or any experimental treatment for this population; white blood cell count $\leq 3{,}000/mm^3$ ($\leq 3.0 \times 10^9/L$) or $\geq 14{,}000/mm^3$ ($\geq 14 \times 10^9/L$); platelet count $\leq$ 100,000/μL ($\leq 100 \times 10^9/L$); serum creatinine >2 x upper limit of normal (ULN); AST (SGOT) or ALT (SGPT) > 2 x ULN; total bilirubin >2 mg/dL (34 μmol/L); hemoglobin < 9 g/dL; subjects who are currently taking or have taken in the past 30 days, for any reason, any medication that, in the opinion of the investigator, suppressed the immune response. This may include but is not limited to systemic steroids, azathioprine, cyclosporine, FK506, mycophenolate mofetil, mycophenolic acid, etanercept, adalimumab, infliximab, ustekinumab, cimzia, or any other biologic agent targeted to any cell or cytokine in the immune system; subjects who are refractory to 2 or more biological agent plaque psoriasis therapies due to lack of efficacy; subjects currently taking or who have taken in the past 2 weeks, topical steroids; subjects on a non-stable dose of vitamin D analog in the past 30 days; subjects currently taking or who have taken in the past 30 days any medications likely to improve psoriasis and thus interfere with evaluation, including phototherapy, methotrexate, hydroxyurea, or acitretin; subjects with a diagnosis of inflammatory bowel disease (ulcerative colitis or Crohn's disease) or of irritable bowel syndrome; subjects with HIV-1/HIV-2 antibody, hepatitis B surface antigen, hepatitis C antibody; subject received non-steroidal anti-inflammatory drugs (NSAIDS) within 2 weeks before Baseline visit for more than 3 consecutive days, except acetylsalicylic acid $\leq$ 350 mg/d which is allowed; and women who are intending to become pregnant or breastfeeding or planning to breastfeed. Compliance with the inclusion and exclusion criteria is determined using the Patient Questionnaire (Fig. 2).

[0037] The active drug product, *Trichuris suis* ova 2500 or 7500 is a non-sterile, aqueous suspension of the viable, embryonated eggs of the whipworm *Trichuris suis* for oral use. Active TSO is administered in 15 mL of the suspension medium supplied in either one or two 30 mL glass containers. The suspension medium is an aqueous solution containing phosphate

buffer, pH 5 and 0.05% potassium sorbate as antimicrobial preservative. Each unit dose is supplied in a 30 mL amber glass container with black outer lacquer and is sealed with a white polypropylene screw cap and a blue tamper evident ring.

[0038] The TSO is prepared in two strengths as delineated in Table 2. Both formulations are stored at a temperature between 2°C (36 °F) and 8°C (46 °F) and are protected from any risk of freezing (i.e., not be placed directly on freezer packs or in ice that could be below 0°C or 32 °F) or temperature greater than 25° C (77 °F). TSO is agitated gently before use to disperse the ova. Following dosing, tap water is to be added to the glass container, agitated, and ingested to ensure administration of the full dose of TSO.

Table 2: TSO Product

	TSO Product	
Product Name:	TSO 2500	TSO 7500
Dosage Form:	Suspension	Suspension
Unit Dose	2500 viable, embryonated TSO/15 mL	7500 viable, embryonated TSO/15 mL
Route of Administration	Oral	Oral
Physical Description	30 mL, amber (with black lacquer), glass container with white plastic screw cap	30 mL, amber (with black lacquer), glass container with white plastic screw cap – either in one or 2 containers
Manufacturer	OvaMed GmbH	OvaMed GmbH

[0039] Following informed consent, the eight subjects are screened on the basis of clinical laboratories and psoriasis severity. PASI, PGA, BSA, vital signs, clinical laboratories, medical history and a physical examination will be conducted. Treatment then proceeds according to the Schedule of Events shown in Table 3.

Table 3: Schedule of Events

	Screening Phase	Treatment Phase			Follow-up Phase	
VISIT NUMBER	**Screening**	**Baseline**	**Weeks 2, 4, 6, 8, 10**	**Week 12**	**Phone Call (Week 16)**	**Week 38**
Informed Consent	X					
Eligibility	X	X				
Medical history	X	X				
Physical Examination (height and weight at Baseline only)	X	X		X		
Clinical Laboratories (Hematology, Chemistry)	X	X		X		
Urinalysis	X					
pregnancy test (female subjects only)	X (Serum)	X(urine)		X(urine)		
Vital Signs	X	X		X		
12 Lead ECG	X					
PASI, BSA, PGA, DLQI[1]	X	X	X	X		
Photographs of Psoriasis		X		X		
Adverse Events		X	X	X	X	X
Concomitant Medication	X	X	X	X	X	X
Dosing with Study Medication		X	X			
Stool Culture (Ova, parasites, bacterial pathogens, C. difficile toxin[2], presence of blood)	X					X

[1] The DLQI should be the first assessment performed for all visits post-screening.
[2] C-DIFFICILE TOXIN B PCR (ONLY PERFORMED ON LIQUID STOOL)

[0040] Eligible subjects are randomized to treatment with TSO 2500 or TSO 7500(in a ratio of 1:1). During the treatment phase, study drug will be provided in a liquid form and will be administered every 2 weeks, starting with the Baseline visit, through Week 144. Subjects will return to the clinic every 2 weeks through Week 16. Efficacy endpoints will be assessed at Weeks 4, 8, 12 and 16. Week 14 is the last treatment administration of the study, while Week 16 is the primary time point for assessment of efficacy. Photographs of the psoriasis pre-treatment and at Week 16 will be taken to document any changes. Efficacy and safety indices will be assessed as per the Schedule of Events.

[0041] At the screening assessments, the following evaluations are performed: informed consent, inclusion and exclusion criteria, medical history, physical examination, clinical

laboratories (including hematology, serum chemistry), urinalysis, pregnancy laboratory (serum test for female subjects only), vital signs, 12-Lead ECG, PASI, BSA, PGA, DLQI, prior and on-going medications, and stool culture.

[0042] Subjects who satisfy eligibility requirements from screening will return to the clinic for their baseline (pre-treatment) assessments. If subjects are still deemed to be eligible, the subject will be randomized and treated with their first dose of study medication. Baseline assessments will include: DLQI (performed before other assessment tools), inclusion and exclusion criteria to ensure subject still meets requirements, medical history to assess any changes since screening, physical examination to assess any changes since screening, clinical laboratories including hematology and serum chemistry, urine pregnancy laboratory (female subjects only), vital signs, PASI, BSA, PGA, photographs of the psoriasis, prior medications and on-going medications. For patients who still meet eligibility criteria, the subject will be randomized and receive their first dose of medication.

[0043] At weeks 2, 4, 6, 8, 10, 12 and 14, Subjects return to the clinic for the following assessments: DLQI (perform before other assessment tools), PASI, BSA, PGA, adverse events, concomitant medications, and dosing with study medication.

[0044] At week 16, the end of the treatment phase, subjects return to the clinic for the following end-of-treatment phase assessments: DLQI (perform before other assessment tools), PASI, BSA, PGA, photographs of the psoriasis, physical examination, vital signs, clinical laboratories (including hematology, serum chemistry), urine pregnancy laboratory (female subjects only), adverse events, and concomitant medications.

[0045] At week 20, the site will call the subject to assess adverse events and concomitant medications. Finally, at week 42, the subject returns to the clinic. A stool culture will be obtained along with an assessment of adverse events and concomitant medications.

[0046] Data analysis will be primarily descriptive. Outcomes will be tabulated by treatment group. Inferential statistics may be provided for within-group changes from pre-treatment and between-group differences for the primary endpoint if outcomes warrant. Efficacy outcomes will be evaluated using the Intent to Treat population (all subjects randomized and treated with at least 1 dose of study medication). A Completer's analysis (in which subjects who both complete the full 16-week treatment period and have a PASI score at Week 16) will also be performed.

[0047] Changes and percent changes from pre-treatment to on-treatment time points will be calculated for continuous efficacy endpoints. Graphical displays of changes over time are presented for key outcomes. All data captured on the case report form (and in the clinical laboratory and other electronic databases) will be presented in by-domain data listings.

[0048] The foregoing description of illustrative embodiments has been presented for purposes of illustration and of description. It is not intended to be exhaustive or limiting with respect to the precise form disclosed, and modifications and variations are possible in light of the above teachings or may be acquired from practice of the disclosed embodiments. It is intended that the scope of the invention be defined by the claims appended hereto and their equivalents.

WHAT IS CLAIMED IS:

1. A method of treating psoriasis in a human patient comprising administering to a human patient in need thereof a therapeutically effective amount of a pharmaceutical formulation comprising a helminthic parasite or a biologically active portion thereof and a pharmaceutically acceptable carrier, wherein the helminthic parasite or portion thereof is selected from the group consisting of *T. suis,* S. *mansoni, H. polygyrus, T. spiralis, T. trichiura* and *N. americanus.*

2. The method of claim 1, wherein the psoriasis is characterized as plaque, guttate, inverse, pustular, or erythrodermic psoriasis.

3. The method of claim 1, wherein the psoriasis is characterized as moderate to severe chronic plaque psoriasis or an arthritic form of psoriasis.

4. The method of claim 1, wherein the human patient also suffers from at least one condition selected from the group consisting of depression, pregnancy, cancer, kidney disease, liver disease, diabetes, increased blood pressure, coronary disease, immune disorders, and acute or chronic blood disorders.

5. The method of claim 1, wherein the human patient is contraindicated from receiving an injection or infusion.

6. The method of claim 1, wherein the biologically active portion of the helminthic parasite is selected from the group consisting of parasite extract, parasite eggs, parasite egg extract, parasite larvae, parasite larvae extract, parasite cercariae and parasite cercariae extract.

7. The method of claim 1, wherein the pharmaceutical formulation comprises embryonated parasite eggs or embyronated parasite egg extract of *T. suis.*

8. The method of claim 7, wherein the therapeutically effective amount is between about 500 and about 20,000 eggs, and wherein the amount is administered between about 1 and about 4 times per month for a duration of six months or greater.

9. The method of claim 8, wherein the therapeutically effective amount is between about 2,000 and about 10,000 eggs.

10. The method of claim 8, wherein the therapeutically effective amount is about 2,500 eggs.

11. The method of claim 8, wherein the therapeutically effective amount is about 7,500 eggs.

12. The method of claim 8, wherein the frequency of administration of the pharmaceutical formulation is greater for a first period of time taking place at the outset of treatment, than the frequency of administration during a second period of time taking place after the first period of time.

13. The method of claim 8, wherein the frequency of administration of the pharmaceutical formulation is increased for a period of time when acute symptoms of psoriasis appear or are expected to appear, followed by a return to the frequency of administration after the acute symptoms have subsided.

14. The method of claim 1, wherein the pharmaceutical formulation is administered orally.

Dermatology Life Quality Index Form

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick one box for each question.

1.	Over the last week, how itchy, sore, painful or stinging has your skin been?	Very much ☐ A lot ☐ A little ☐ Not at all ☐	
2.	Over the last week, how embarrassed or self conscious have you been because of your skin?	Very much ☐ A lot ☐ A little ☐ Not at all ☐	
3.	Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden?	Very much ☐ A lot ☐ A little ☐ Not at all ☐	Not relevant ☐
4.	Over the last week, how much has your skin influenced the clothes you wear?	Very much ☐ A lot ☐ A little ☐ Not at all ☐	Not relevant ☐
5.	Over the last week, how much has your skin affected any social or leisure activities?	Very much ☐ A lot ☐ A little ☐ Not at all ☐	Not relevant ☐

TO FIG.1 (CONT.)

FIG. 1

FROM FIG.1

6.	Over the last week, how much has your skin made it difficult for you to do any sport?	Very much ☐ A lot ☐ A little ☐ Not at all ☐	Not relevant ☐
7.	Over the last week, has your skin prevented you from working or studying?	Yes ☐ No ☐	Not relevant ☐
	If "No", over the last week how much has your skin been a problem at work or studying?	A lot ☐ A little ☐ Not at all ☐	
8.	Over the last week, how much has your skin created problems with your partner or any of your close friends or relatives?	Very much ☐ A lot ☐ A little ☐ Not at all ☐	Not relevant ☐
9.	Over the last week, how much has your skin caused any sexual difficulties?	Very much ☐ A lot ☐ A little ☐ Not at all ☐	Not relevant ☐
10.	Over the last week, how much of a problem has the treatment for your skin been, for example by making your home messy, or by taking up time?	Very much ☐ A lot ☐ A little ☐ Not at all ☐	Not relevant ☐

Please check you have answered EVERY question. Thank you.

FIG. 1 (CONT.)

Site #	Patient #	Medical History, Condition / Diagnosis (one per line)	Start Date (mm/yyyy)	End Date (mm/yyyy)	Continuing y/n	Comment
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FIG. 2