An Open Label, Multi Center Clinical Study to Evaluate the Efficacy and Safety of a New Topical Cosmeceutical in Relieving the Redness, Scaling and Flaking Associated with Severe Skin Conditions

A Pilot Study

Sponsor:	Astrel Genome Ltd
Name of investigational product:	D-Psoria®
Indication studied:	To assess the dermatological and ophthalmologic safety of using D-Psoria for scalp and body psoriasis and to study D-Psoria efficacy using PASI scores.
Study Type:	Open
Protocol Identifier:	CRS-0001/2008.
Consent:	Prior to the beginning of the study, the participating subjects signed an informed consent and an agreement of voluntary participation.
Study initiation date:	3/26/08
Study completion date:	11/2/08
Principle Investigator:	Dr. Sai Krishna
Contract Research Organization:	Biotrail Pharma Services Ltd
Date of the report	2/9/09

I. Introduction

1. Disease Background

Chronic plaque psoriasis is the most common form of psoriasis, is a papulosquamous disease defined by erythematous plaques with a silvery scale. The diagnosis is usually clinical, biopsy is done for confirmation. Psoriasis affects 1 to 3 percent of the U.S. population, and about 30% of affected patients have first-degree relative with the disease. Psoriasis is a T-cell-mediated autoimmune disease, but certain medications and infections are well known risk factors. The process begins with an environment factor, perhaps a viral antigen, which induces T-cells to produce cytokines. The cytokines stimulate keratinocyte proliferation and production of antigenic adhesion molecules in the dermal blood vessels. These adhesion molecules further stimulate T-cells to produce cytokines, thus perpetuating the response. Immunomodulatory drugs offer novel treatment options for psoriasis. Management of psoriasis includes education about chronic, realistic expectations, and use of medications. Steroids and vitamin D derivatives (calcipotriene) are the mainstays of topical therapy.

It is worthwhile to note that psoriasis is a chronic disease without cure. Hence, any new treatment should not only focus on improvement but also disappearance of lesions.

2. Objective

Primary Objective: To study the dermatological safety and efficacy of D-Psoria™ in the treatment of psoriasis involving arms and/or trunk and/or legs and/or scalp.

Secondary Objectives:

1. To evaluate the ophthalmological safety of D-Psoria®.
2. To evaluate the effect of D-Psoria treatment on quality of life.

3. Drug Background

D-Psoria is formulated as shampoo and as a cream. The key ingredients of the formulation are as follows:

- Kadali (Banana Plant) Extract: This has all the nutrients to help the skin to repair on its own, besides having curative properties of minerals and phytochemicals present in the natural extract.
- Lavendula (Lavender) Extract: This is known for its anti-inflammatory properties. This reduces the inflammation (redness and swelling) of the psoriasis-affected skin.
- Navasara (Ammonium Compound): Besides increasing speed of repair process of the skin, it also reduces the perforin content at psoriasis-affected area of the skin.

4. Scientific Rationale

Treatment of psoriasis depends on 2 phases, one is removing the scales to improve the general appearance of the patient and second to control and reduce the psoriasis so that future scales formation will be reduced or almost stopped.

It is known that psoriasis patients skin cannot perform one basic function i.e. prevention of water and heat loss from the skin. Total water loss (TWL) of psoriatic skin is about 6-8 times higher than normal healthy skin. Only way to protect the water and heat loss is by causing vasoconstriction to the skin or giving a protective layer, which controls water and heat loss and helps in self-repair of the skin.

D-Psoria Shampoo is a special formulation directed towards removal of scales on the scalp and body with minimum effort while having shower with lukewarm water.

D-Psoria Cream is formulated to give a protective layer to the psoriasis affected and exposed (by removing scales) skin. By applying D-Psoria cream immediately after the shower will form a protective layer on the skin, which protects the skin from water and heat loss and pathogens from entering into exposed skin.

STUDY PROCEDURES

1. Study Duration:

Duration of the study: the total duration of the study for each individual patient was 12 weeks.

After screening, a one week wash out period was given during which patient was not allowed to apply any topical steroids. All the selected patients had to visit the test site on screening (1st week), 2nd week, 4th week, 6th week, 8th week, 10th week and 12th week i.e., total of 8 visits.

During these 8 visits patient was provided with the study agent and was given instructions on method of application. Subject compliance with protocol was asserted by collecting the empty tubes and containers. Subjects were provided with sheets to document their usages daily. The study procedures and study agent usage by subjects are enclosed as annexure.

2. Number of subjects studied:

The total numbers of 42 subjects were enrolled in the study based on the inclusion and exclusion criteria.

2.1 Inclusion Criteria

- Male and female patients age between 18 years and 65 years

- A clinical diagnosis of psoriasis vulgaris involving arms and/or trunk and or legs. Subsequent histopathological confirmation of psoriasis will be made.
- The minimum PASI score should be ≥ 2 in at least one body region (i.e. 10% or greater surface area involvement)
- After providing study information (both verbally and in Writing) in detail, subject should be willing and able to provide written informed consent
- Women of childbearing ability will have to undergo urine pregnancy testing.
- Subjects who satisfactorily complete their medical screening
- Should be available for all study related visits
- Patients with extensive hyperkeratosis; scales can be removed with salicylic acid (5%) in petrolatum, within 1 day prior to start of the study.
- Subjects who clears the general health check-up and clinical examination.

2.2 Exclusion Criteria

- Patients with acute guttate, generalized pustular or erythrodermic exfoliative Psoriasis, atopic dermatitis, seborrhoeic dermatitis or other inflammatory skin diseases
- Systemic antipsoriatic treatment or phototherapy within the last 6 weeks
- Patients who had used any topical antipsoriatic treatment on the body within the previous 2 weeks, except emollients.
- Usage of corticosteroids for any reason within the last 6 weeks of the start of the study
- Patients using concomitant medications (e.g. beta blockers, lithium etc.) that affect their psoriasis during the study period
- Women who are nursing, pregnant or wish to become pregnant during study duration
- Known or suspected hypercalceamia.
- Subjects with eye infections.
- Known history of hypersensitivity to the study compound.
- Participation within last 3 months in any of the clinical trial.
- Any disease or condition of the skin that the Principal Investigator deems inappropriate for participation.

- Subjects with uncontrolled metabolic diseases such as diabetes/hypertension, hyper- or hypothyroidism.

Of these 42 subjects 2 subjects were drop out in the 2nd visit due to lack of study compliance.

3 Method of application:

D-Psoria Shampoo: Wash the psoriasis affected area of skin/scalp once a day while having shower, preferably in the morning.

D-Psoria Cream: Apply 2-3times a day on psoriasis affected area of the skin/scalp after washing it with D-Psoria Shampoo once a day and with normal water in other times, and after pat drying the skin/scalp with dry cotton towel.

4 Evaluation of efficacy:

At each of these 8 medical evaluations, each of the subjects was evaluated using 2 criteria.

4.1 PASI(Psoriasis Area and Severity Index)
4.2 Dermatological quality of life index.

5 PASI(Psoriasis Area and Severity Index)

The following features were evaluated

- Erythema(Redness)
- Induration
- Scaling
- Percentage of area involved in each individual site namely head trunk, upper limb and lower limb.

The method of calculation is as follows.

5.1 Steps in generating PASI score

Step 1: Divide body into four areas: head, arms, trunk to groin, and legs to top of buttocks. (Patients with scalp psoriasis will be rated based on Modified Finlay – Khan Questionnaire)

Step 2: Generate an average score for the erythema, thickness, and scale for each of the 4 areas (0 = clear; 1–4 = increasing severity)

Step 3: Sum scores of erythema, thickness, and scale for each area.
Step 4: Generate a percentage for skin covered with psoriasis for each area and convert that to a 0–6 scale (0 = 0%; 1 = <10%; 2 = 10–<30%; 3 = 30–<50%; 4 = 50–<70%; 5 = 70–<90%; 6 = 90–100%)
Step 5: Multiply score of item (Step 3) above times item (Step 4) above for each area and multiply that by 0.1, 0.2, 0.3, and 0.4 for head, arms, trunk, and legs, respectively
Step 6: Add these scores to get the PASI score.

Erythema, induration and scale is measured on a 0–4 scale (none, slight, mild, moderate, severe)

5.2 Area Scoring Criteria

- 0: 0 (clear)
- 1: <10%
- 2: 10–<30%
- 3: 30–<50%
- 4: 50–<70%
- 5: 70–<90%
- 6: 90–<100%

5.3 PASI = $0.1(R_h + T_h + S_h)A_h + 0.2(R_u + T_u + S_u)A_u + 0.3(R_t + T_t + S_t)A_t + 0.4(R_l + T_l + S_l)A_l$

- Where R_h, R_u, R_t, R_l = redness score of plaques on the head, upper extremities, trunk, and lower extremities, respectively (0-4) T_h, T_u, T_t, T_l = thickness score of plaques on the head, upper extremities, trunk, and lower extremities, respectively (0-4);
- S_h, S_u, S_t, S_l = scaliness score of plaques on the head, upper extremities, trunk, and lower extremities, respectively (0-4); and
- A_h, A_u, A_t, A_l = area of psoriatic involvement score for the head, upper extremities, trunk, and lower extremities, respectively (0-6).

- The highest potential PASI score is 72; the lowest is 0. PASI scores are nearly continuous, with 0.1 increments within these values.

6 Dermatology Quality of life index.

The subject is evaluated on the scale of personal satisfaction as excellent, good, bad, after using the medication.

The health related quality of life will be assessed using "Dermatology Quality of Life". The DOQL has been used in a number of studies of dermatological diseases including eczema, chronic idiopathic urticaria and psoriasis to evaluate the impact of treatment in these patients. It has been developed as a brief questionnaire for routine clinical use to assess the limitations related to the impact of skin disease and has been shown to be responsive to clinical changes in a study of dermatology

7 Side effects:

Recoding of side effects began on 3rd visit on the characters of side effects noted and summary evaluation of side effects was done at the completion of the study. Both cutaneous and ophthalmologic side effects were particularly noted.

8 Evaluation of the results:

Efficacy was mentioned by 2 end points.

8.1 The PASI scores.

Where evaluation of improvements was done as follows.

Worsened	PASI score higher than baseline
Not improved	PASI decrease 0-25%
Moderate improvement	PASI decrease 26-50%
Good improvement	PASI decrease 51-75%
Outstanding improvement	PASI decrease 76-100%

8.2 Dermatological quality of life index.

Where evaluation of improvements was done as follows.

- Very much
- A lot
- A little
- Not at all

9 Results:

9.1 Study Data:

Study Start date: 03/26/08
Study end date: 11/2/08
Total number of patients included in the study: 42
Patients dropped: 2
Total number of patients completed the study: 40

9.2 Demographics of the subjects:

9.2.1 Age of subject
Mean age: the youngest patient's age is 21 yrs and the oldest age is 63
Mean age of the study was 42

9.2.2 Gender Distribution:

Total number of males is 30. (71.4%)
Total number of females is 12. (28.6)

S. No.	Patients	Total	Percentage
1.	Male	30	71.4
2.	Female	12	28.6

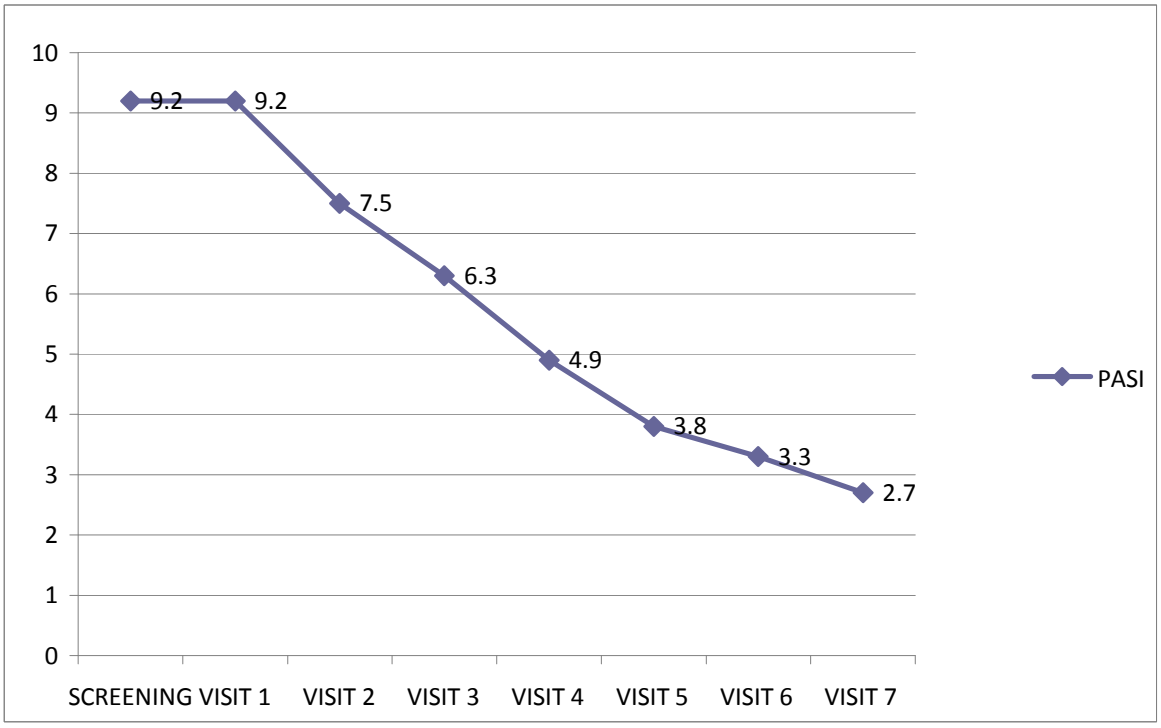
9.2.3 Characteristics of the psoriasis in the subjects selected:

The mean disease duration of psoriasis was 10.5 years.

At each visits the PASI scores were calculated. And the evaluation of the improvement and hence the efficacy were evaluated at the end of the study.

The mean PASI scores after each visit were as follows. (Table 2. Fig.1).

Change in PASI score in absolute values



Mean PASI Score

No. of visit	% decrease in PASI	Mean % cured	PASI score
Screening	100%	0%	9.2
Visit 1	100%	0%	9.2
Visit 2	81.5%	19%	7.5
Visit 3	68.4%	31.6%	6.3
Visit 4	53.2%	46.8%	4.9
Visit 5	41.3	58.7%	3.8
Visit 6	35.8	64.2%	3.3
Visit 7	29.3	70.7%	2.7

Side effects:

- Recoding of side effects began on 3rd visit on the characters of side effects noted and summary evaluation of side effects was done at the completion of the study. Both cutaneous and ophthalmologic side effects were particularly noted.
- No side effects in terms of skin and eye were noted by the subjects and by the physician during entire course of the study.

10. Evaluation of the results:

Efficacy was mentioned by 2 end points.

1). The PASI scores.

Where evaluation of improvements was done as follows:

Worsened	PASI score higher than baseline
Not improved	PASI decrease 0-25%
Moderate improvement	PASI decrease 26-50%
Good improvement	PASI decrease 51-75%
Outstanding improvement	PASI decrease 76-100%

2). Dermatological quality of life index.

Where evaluation of improvements was done as follows:

Very much
A lot
A little
Not at all

11. Changes noted in the subjects as per PASI scores.

Worsened ---------- 0
Not improved---------- 1 (2.5%)
Moderate improved ---------- 5 (12.5%)
Good improvement ---------- 7 (17.5%)
Out standing improvement---------- 27 (67.5%)

12. Subjective evaluation by the subjects in efficacy.

Very much ---------- 6
A lot ---------- 21
A little ---------- 12
Not at all ---------- 1

13. Discussion.

The study was completed in 40 of 42 subjects originally included. Two (2) subjects dropped out due to lack of compliance. The study was performed on patients who fulfilled the inclusion and exclusion criteria. Care was taken not to include patient with extreme unstable or erythrodermic psoriasis.

Minimum PASI score was equal to or more than 2 in at least one region at the time of screening. Psoriasis was confirmed using histopathological examination of skin biopsy specimen were ever required after taking informed consent form. In other subjects the diagnosis was made on clinical grounds. The mean duration of psoriasis was 10.2 years. Response was graded at each visit using PASI score and the patient self assessment.

Side effects were specifically asked and noted by the physician. In this study no side effects or adverse events were noted during entire course the study.

Improvement was noted on basis of PASI scores at each visit and 19% improvement in mean PASI score were noted at 2^{nd} visit, 31.6% at 3^{rd} visit, 46.8% at 4^{th} visit, 58.7% in 5^{th} visit, 64.2% in 6^{th} visit, 70.7% in 7^{th} visit that mean as at the end of the study the mean PASI scores were in the range of good improvement.

Based on PASI score only one patient did not improve though was symptomatically better at the end of the study. Patient had few lichenfied plaques and this being the reason for not so significant improvement.

Five (5) patients (12.5%) had moderate improvement 1 patient (17.5%) good improvement and 27 patients (67.5%) had out standing improvement. In entire study 9 patients had more than 90% improvement. 3 patients with low PASI score in range of 2-5 at screening had localized plaque psoriasis and had 100% response at completion of trail.

Subject improvement was marked as very much in 6 patients, a lot of improvement in 21 patients, that implies that these patients improvement correlated with moderate to good improvement seen by PASI scores. 12 patients had little improvement. 1 patient as mentioned above had not improved at all.

14. Conclusion

The product provided significant clinical improvement as a single agent. No side affects were noted during the entire study. Hence, the product is a safe and effective method of relieving the redness, scaling and flaking in severe skin conditions. Though the author feels that being not a controlled study this study has its own limitation and had to be followed up by more controlled studies to help understanding better.