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Efficacy and Safety of Tinefcon® Tablets in Subjects with Plaque Psoriasis: An Open Label, Non-Comparative, Multicenter, Phase IV Trial

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Abstract

Importance: This post-marketing surveillance study was conducted to evaluate real-world information about the efficacy and safety of oral Tinefcon® tablets (*Sphaeranthus indicus* based) in plaque psoriasis patients. Materials and Methods: Patients aged at least 18 years and older with clinical diagnosis of plaque psoriasis, were enrolled in this open label, non-comparative, multicenter trial. All eligible subjects received four 700 mg Tinefcon® tablets/day for 12 weeks. The primary outcome measure was percent change in Psoriasis Area Severity Index (PASI) score from baseline to week 12. The secondary outcome measures were Physician Global Assessment (PGA), Nail Psoriasis Severity Index (NAPSI), Psoriatic Arthritis Evaluation and Gene Expression Profiling and Immunohistochemistry. Results: After completion of Tinefcon® treatment at 12 weeks, more than half of subjects (52%) achieved PASI 50 response; PASI 75 response was attained in 68 (23%) subjects and PASI 90 response in 22 (7%) subjects. Five subjects with severe psoriasis achieved PASI 90 without receiving any concomitant medication. Reduction in severity as assessed by PGA was observed in more than half of patients with moderate disease. Histopathological evaluation revealed that epidermal thickness was considerably reduced in 66% of subjects. The expression of inflammatory marker S100A9 protein was meaningfully reduced in 60% patients with non-significant reduction of Keratin 10 protein expression. Gene expression analysis showed increase down regulation of SERPINB4; PI3 and KRT16 genes after a 12-week treatment period in subjects with higher PASI scores. Conclusion: Oral Tinefcon® tablets showed good efficacy and had a favorable safety profile in plaque psoriasis patients.

Keywords

Psoriasis, Tinefcon® Tablet, *Sphaeranthus indicus*

1. Introduction

Psoriasis is a chronic, inflammatory, relapsing autoimmune disease of skin and joints having prevalence of 2% - 3% in the world's population [1]. The most common form of psoriasis is plaque psoriasis affecting 80% - 90% of individuals suffering from psoriasis. Plaque psoriasis or psoriasis vulgaris is predominantly characterized by red colored lesions (plaques) with silvery scale [2]. Psoriasis is also associated with other co-morbid disorders that include diabetes, dyslipidemia, obesity, hypertension and cardiovascular disease [3].

Treatment regimens available for psoriasis are topical therapy, phototherapy, systemic therapies, and biologics. Traditional topical therapy contains corticosteroids, tars, vitamin D and vitamin A analogs, and anthralin, but their use is limited to mild to moderate psoriasis [4]. Methotrexate and cyclosporine are preferred for the treatment of severe psoriasis as systemic agents but long-term treatment is associated with nephrotoxicity (cyclosporine) and hepatotoxicity (methotrexate). The long-term use of non-biologic treatment, psoralen-ultraviolet

A phototherapy (PUVA) in chronic psoriasis has been associated with skin cancer and prolonged teratogenicity with oral retinoids [5].

Newly introduced biological therapies have exhibited favorable results in treatments of moderate to severe psoriasis, but they are not free from serious and fatal adverse events (AEs). The development of anti-drug antibodies (ADAs) is reported with infliximab, ustekinumab and adalimumab in the treatment of psoriasis [6].

Currently, practice of herbal remedy in the treatment of psoriasis is getting more attention due to mild to moderate and tolerable side effects, easy mode of administration, and less expensive treatment [7]. *Sphaeranthus indicus* Linn (Family: Asteraceae) is a popular herb mentioned in the traditional (Indian) medicine system for treatment of various ailments. It is reported to have anti-inflammatory, anxiolytic, hypolipidemic, immunomodulatory, bronchodilatory, neuroleptic, antihyperglycemic and hepatoprotective activity [8].

It is also known now, from *in vitro* studies that the extract of *S. indicus* inhibits release of various cytokines involved in inflammation like TNF-α, IL-1β, IL-6, IL-8, IL-12 and IL-12/23 [9]-[11] and keratinocytes proliferation [11].

In a phase II trial of Tinefcon®, two doses (1.4 g/day and 2.8 g/day) of *S. indicus* extract tablets were tested for safety and efficacy; both the doses were well tolerated in subjects with moderate to severe plaque psoriasis. However, efficacy of higher dose (2.8 g/day) was better compared to lower dose (1.4 g/day). The percentage of patients reaching ≥75% improvement from baseline in the psoriasis area and severity index (PASI 75) at week 12 was 55%.

The current study was designed to evaluate efficacy, tolerability and safety of Tinefcon® tablet (containing methanolic extract of dried fruiting and flowering heads of *S. indicus* plant) in larger population of plaque psoriasis patients.

2. Materials and Methods

2.1. Patients

Patients who were at least 18 years or older with clinical diagnosis of plaque psoriasis, of both genders were considered as eligible for the study. The study was performed in a real world clinical setting involving 20 clinical sites in India.

Pregnant and lactating women, women with child bearing potential and men not agreeing to use adequate contraception during and 4 weeks after withdrawal, were excluded from the study. Subjects with solid cancer or hematologic malignancies diagnosed within last 5 years with a potential for progression were excluded from the study. Other exclusion criteria included; the presence of clinically active tuberculosis, chronic hepatitis B, HIV infection, heart failure, demyelinating disease and premalignant lesions.

This study protocol and amendments were approved by the institutional ethics committees and was registered on the clinical trial registry portal as CTRI Number CTRI/2010/091/003010 and clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT01373567).

2.2. Plant Material and Drug Preparation

Tinefcon® tablet contains a brown colored thick paste obtained from dried fruiting and flowering heads of *S. indicus*. The extract was quantified by chromatography for active constituents, and each tablet contained not less than 28 mg of 7-Hydroxy Frullanolide and 9.6 mg of Sphaeranthanolide. The extract was standardized prior to formulation for physicochemical, chromatographical parameters, microbial load as well as presence of heavy metals, residual solvents, etc.

2.3. Study Design

This study was an open label, prospective, single group, and multicenter phase IV clinical study to assess the safety, efficacy and tolerability of Tinefcon® tablets in subjects with clinical diagnosis of plaque psoriasis. The study consisted of total 5 visits; a screening visit, baseline visit, followed by three visits during the treatment period at week 4, week 8, and week 12, at which safety and efficacy assessments were performed. Screening evaluation was carried out within 7 days of signing the informed consent document. In this study, 401 subjects were enrolled at 20 clinical sites in India and were evaluated for safety and efficacy of Tinefcon® tablets. Amongst them, 299 subjects successfully completed the study. All subjects meeting the eligibility criteria received two

Tinefcon® tablets of 700 mg strength in morning and evening, preferably after food for 12 weeks. All subjects were advised not to exceed a dosage of 2.8 gm Tinefcon® in a day. The total duration of the study was approximately 14 weeks, including the screening period.

2.4. Efficacy Measures

The severity of disease was assessed by using Psoriasis Area Severity Index score (PASI) and Physician Global Assessment (PGA) score. The primary efficacy outcome measure was mean percentage change in PASI from baseline to week 12. PASI score was measured by the method described by Fredriksson and Peterson [12]. Subjects achieving PASI score of 50%, 75% and 90% improvement from baseline to week 12 were analyzed (The range of PASI score was 0 to 72). The secondary efficacy outcome measures contained Physician Global Assessment (PGA) score, Nail Psoriasis Severity Index (NAPSI) and Psoriatic Arthritis Evaluation (Physician global assessment for psoriatic arthritis).

2.5. Histopathological Evaluation

The histopathological analysis of psoriatic lesions was carried out at baseline and at week 12 (visit 3). Tissue sections were blinded and further evaluated for acanthosis, parakeratosis, papillomatosis, Munro's microabscesses, Kogoj's abscess, mitotic activity, papillae, and dermal inflammatory cells. Hematoxylin (H) and Eosin (E) (Vector Laboratories, Burlingame, CA) were used for staining tissue sections. For each morphological marker, subjects showing a lowered score post-treatment were denoted as having an "improvement" in disease severity and others were denoted as having "no improvement" in severity.

2.6. Immunohistochemistry

For immunohistochemical assessment the paraffin embedded sections were deparaffinized, rehydrated and antigen retrieval was carried out. Primary antibodies against psoriasis biomarkers, KRT10 and S100A9 (Santa Cruz Biotechnologies, Santa Cruz, CA) were applied to the slide followed by immunofluorescence method using DyLite 549 conjugated secondary antibody. Hoechst 33342 (Thermo Fisher Scientific, Waltham, USA) was used for nuclear staining. Epidermal thickness was measured and quantified using Nikon 80i microscope and Image Pro Plus software (Media Cybernetics, Silver Springs, CA).

2.7. Gene Expression Studies Using RT-qPCR Assays

Extraction of RNA was carried out using RNeasy Mini Kit (Qiagen, Valencia, CA) from skin punch collected in RNAlater buffer (Qiagen Inc., Valencia, CA). Total RNA was reverse transcribed into cDNA as per protocol recommended by manufacturer (Invitrogen Inc., Carlsbad, CA) for transcript analysis. Further, it was quantified using Quantitect probe PCR master-mix (Qiagen Inc., Valencia, CA) and Eppendorf Realplex thermal cycler (Eppendorf, Hamburg, Germany). The primer and probe sequences were designed using Primer 3 v.0.4.0 (http://frodo.wi.mit.edu/primer3 web site). Primers were synthesized at BioServe Biotechnologies (Hyderabad, India). All RTq-PCR assays were performed in duplicates, and results are provided as mean +/− SD unless otherwise stated.

2.8. Safety Assessment

Incidence and severity of treatment emerged adverse events were monitored throughout study. Physical examination was conducted at screening and at weeks 4, 8, 12 of the study. Safety evaluations included vital signs, laboratory parameters, electrocardiography (ECG), medical history and concomitant medication investigations.

2.9. Sample Size and Randomization

The sample size calculation for this study was not based on power considerations. A sample size of three hundred subjects was considered to be appropriate to evaluate safety and efficacy of Tinefcon® tablets in patients with clinical diagnosis of plaque psoriasis. Randomization, stratification and blinding were not applicable for this study, since this was a single-arm open-label study.

2.10. Statistical Analysis

All proposed statistical analyses were carried out using SAS version 9.2. Baseline patient characteristics and responses have been summarized descriptively. All continuous variables were briefed by the number of subjects, mean, S.D. of mean, median, minimum and maximum, unless and otherwise stated. All categorical variables were summarized using counts and percentages.

All the statistical testing was done at 5% level of significance unless and otherwise stated. The p-values were presented up to three decimal places. Association between clinical response and histopathology markers was assessed by comparing the percent decrease in PASI scores (post-treatment)in groups showing "improvement" and "no improvement" in histopathological markers. Unpaired t-test with one-sided p-values was used in comparison. Hypothesis was mean percent decrease in PASI score which was more in the "improvement" group. Analysis of immunohistochemistry markers (S100A9 and KRT10) was carried out using single sample t-test to compare the log fold change in expression level (post-treatment/pre-treatment) to zero. Determination of relation between probability of a clinical response (PASI50 or PASI75) to the percent decrease in epidermal thickness/rete ridge length and post-treatment fold change in expression levels of S100A9 and KRT10 was done by using logistic regression models. For gene expression profiling, single sample t-test was used for evaluation of statistical significance of the molecular response while an association between clinical and molecular responses was evaluated using unpaired t-test.

3. Results

3.1. Study Population

In this study, a total of 401 subjects were enrolled. Among them, 278 subjects were male (69%) and 123 (31%) were females. The age range of subjects was 18 - 76 years and median age of subjects was 40 years (**Table 1**). All enrolled subjects (N = 401) were allocated to treatment of Tinefcon® tablet. Out of 401, total 299 subjects successfully completed 12 weeks of treatment with Tinefcon® tablet and 102 subjects were discontinued from the study. The discontinuation of subjects from the study was due to the consent withdrawal (N = 62), adverse event or serious adverse events (N = 26), investigator discretion (N = 10), lost to follow up (N = 1), and other reasons (N = 3). In this study total 35 (9%) of patients were diagnosed with nail psoriasis while six subjects had psoriatic arthritis. Study population from the study is depicted in **Figure 1**. The study was performed in a real world clinical setting involving 20 sites in India, started in December 2010 and completed in June 2012.

3.2. Efficacy Measures

The primary outcome of the study was assessed by Psoriasis Area and Severity Index (PASI) response. A total of 299 subjects completed study but PASI score of week 12 for one subject was not reported/missing; hence number of subjects evaluable for efficacy was 298. The mean baseline PASI score was measured as 12.48 ± 7.13 (N = 298). Among 298 subjects, 141 subjects (47%) had baseline PASI score of ≥12 representing that they were suffering from severe psoriasis. After completion of Tinefcon® tablet treatment, the mean percentage change of PASI score from baseline to week 12 was reported as 50.17 ± 28.77. More than half of subjects (52%) achieved

Table 1. Demographic characteristics.

Characteristic	Data
Gender	
Male	N = 278 (69%)
Female	N = 123 (31%)
Age	
Age range	18 - 76
Average age	40
Mean PASI score at baseline	12.48 ± 7.13

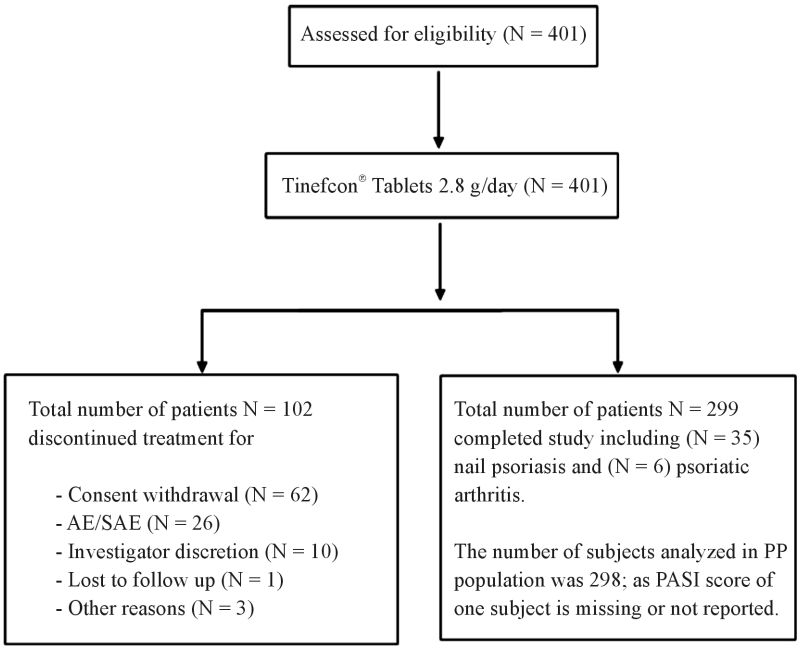

Figure 1. Subject disposition.

PASI50 response at week 12. PASI75 response was attained in 68 (23%) subjects while, PASI90 response was achieved in 22 (7%) subjects at week 12 (**Figure 2**). Remarkably, five subjects with severe psoriasis having PASI 12 - 36 at baseline achieved PASI90 response without receiving any anti-psoriasis concomitant treatment such as steroids, systemic anti-inflammatory drugs and PUVA therapy.

In nail psoriasis subjects (N = 35), nail psoriasis severity index (NAPSI) was measured. Mean NAPSI score was 5.04 ± 3.7 at visit 1 and 4.08 ± 2.99 at visit 3 respectively. The mean change from baseline to visit 3 was 0.92 ± 2.04.

For Global assessment of psoriasis, the proportion of subjects with mild and severe psoriasis disease activity were 14% and 7% respectively. At visit 3, most subjects with mild disease activity at baseline were unchanged, while more than half of the subjects with moderate disease activity at baseline showed reduction in severity. The photographic evaluation reveals that there was an improvement in erythema, plaque elevation and scaling at visit 3 as compared to baseline observations.

There was no difference observed between baseline and visit 3 score of Physician's Global assessment for Psoriatic arthritis, while in Subject's global assessment, at visit 3, there was 01 subject in the poor category.

3.3. Histopathological Analysis

The changes associated with skin lesions of psoriasis were evaluated for acanthosis, parakeratosis, papillomatosis, Munro's microabscesses, Kogoj's abscesses, mitotic activity, papillae, and the dermal infiltration of inflammatory cells. The stained skin sections of psoriatic lesions were scored for these parameters based on severity on a scale of 0-5, with 0 absence of the parameter and 5 being marked presence of the same. Maximum number of responders was observed with morphological parameter dermal inflammatory cells followed by papillae, parakeratosis, and acanthosis (**Table 2**).

Histopathological evaluation of psoriatic lesions was carried out by measuring epidermal thickening, which is a symbolic feature of psoriasis. Epidermal thickness is indicated as a sum of rete ridge length (marked elongation) and keratin thickness. It is changed by disease severity and therapy. Epidermal thickness was reduced in significant number of the subjects (66%) after 12 weeks of Tinefcon® treatment (**Table 3**).

Main histological features which were generally elevated in psoriasis like acanthosis and parakeratosis were found to be attenuated by Tinefcon® treatment (**Figure 3**). Logistic regression models showed that the probability of clinical response (PASI50 and PASI75) increases with increase in reduction of epidermal thickness/rete ridge length (**Figure 4** and **Figure 5**).

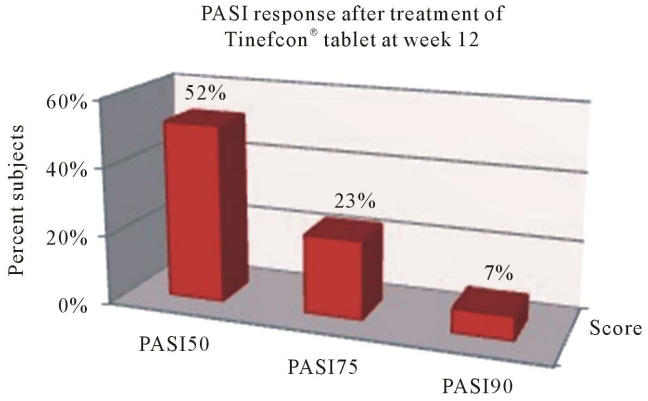

Figure 2. PASI response after treatment with Tinefcon® tablets at week 12.

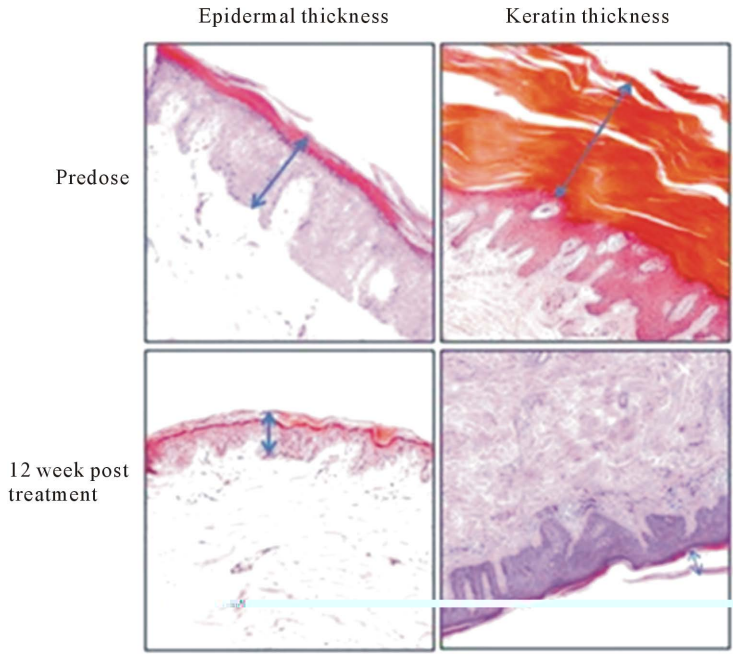

Figure 3. Effect of Tinefcon® on histopathological features of skin.

Table 2. Histopathological scoring of H & E stained skin sections.

Histopathological feature	Responders	Non-responders	No change	ND
Acanthosis	88	46	107	43
Parakeratosis	98	36	114	36
Papillomatosis	71	43	154	16
Munro's microabscess	13	8	247	16
Kogoj's abscesses	66	29	165	24
Mitotic activity	40	14	164	66
Papillae	124	57	85	18
Dermal inflammatory cells	132	36	98	18

ND: not determined.

Table 3. Effect of Tinefcon® on some histological parameters.

Sr. No.	Reduction in parameters	Percentage of patients showing reduction
1	Epidermal Thickness	66
2	Expression of S1000A9	60
3	Acanthosis	31
4	Parakeratosis	34
5	No. of inflammatory cells with lesions	46

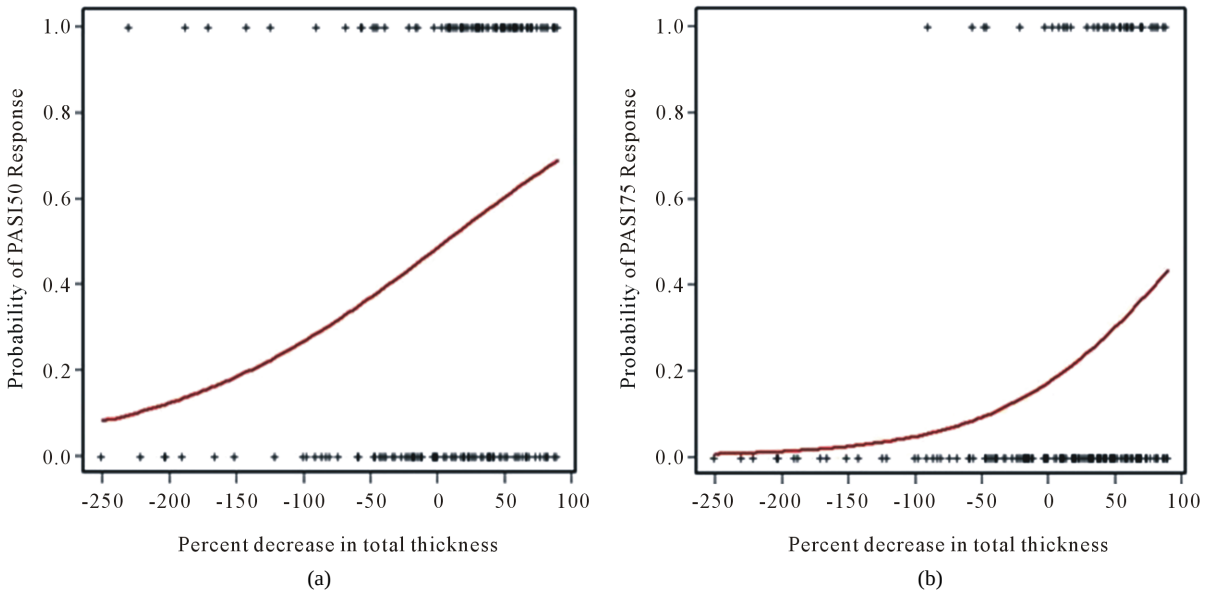

Figure 4. Logistic regression models for probability of a clinical response (a) PASI50 and (b) PASI75 as a function of percent decrease in total epidermal thickness.

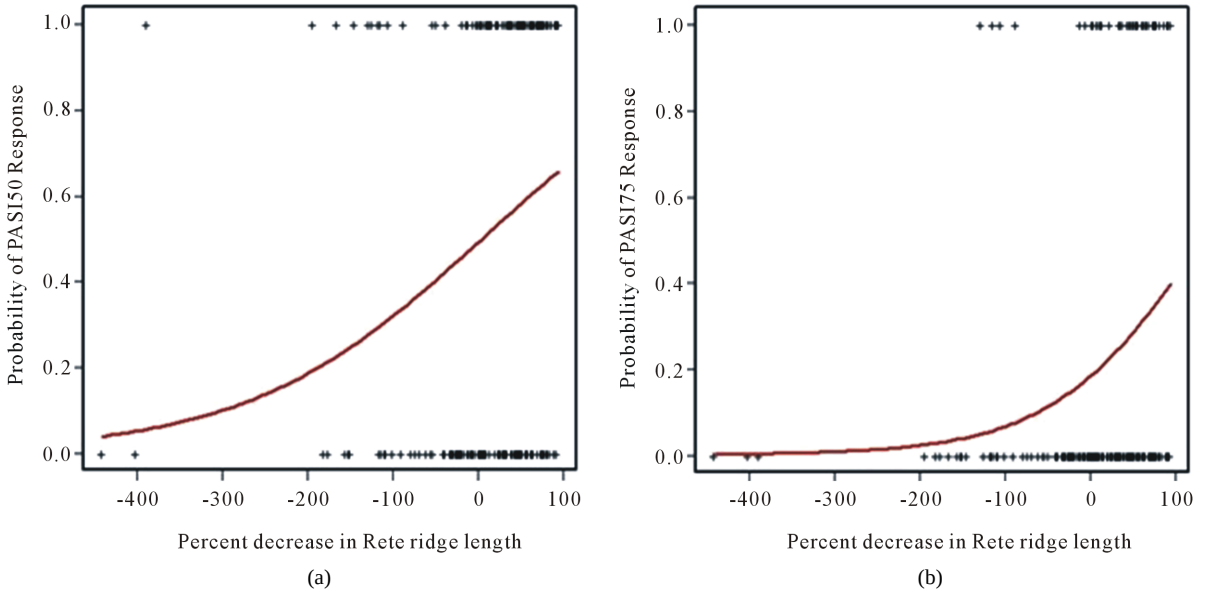

Figure 5. Logistic regression models for probability of a clinical response (a) PASI50 and (b) PASI75 as a function of percent decrease in rete ridge length.

3.4. Immunohistochemistry

In psoriasis, elevated levels of various inflammatory markers were seen. S100A9 (S100 calcium-binding protein A9) plays an important role in keratinocyte inflammation [13] [14] expression of this protein was reduced in significant number of patients (60%) after the Tinefcon® treatment. Keratin 10 (KRT10), a marker for epidermal differentiation, is expressed in psoriatic lesions [15]. However, no statistically significant reduction was observed in KRT10 protein expression. Logistic regression model revealed that, improvement in PASI scores was associated with reduction in post-treatment levels of S100A9.

3.5. Gene Expression Study

Gene expression profiling showed statistically consequential down regulation of various inflammatory genes after Tinefcon® treatment. Significant down regulation ($p < 0.01$) was observed in KRT16, SERPINB4, PI3, S100A9, iNOS, IL-12p40/IL-23, TNFSF10 and FABP5.Whereas, IFN-γ, RAB31 and TNF-α showed statistically non-significant down-regulation (**Table 4**).

Interestingly, more than two fold down regulation was observed in transcripts of KRT16, SERPINB4, PI3, S100A9 and iNOS. Association between molecular and clinical responses (PASI50/PASI75) to Tinefcon® treatment is summarized in **Table 5**.

3.6. Safety Evaluation

The oral administration of Tinefcon® tablet was well tolerated throughout the study. At least one adverse event was experienced by each of 130 (32%) subjects in the study. As per investigator discretion, there were 98 (24%) AEs related to Tinefcon® treatment. Nausea was the most common AE observed in 47 subjects (12%) followed by vomiting in 35 subjects (9%). The reported events of nausea and vomiting were mild to moderate type (CTC Grade 1 or 2) and intermittent. These events were controllable on continuous treatment and identified to be associated with Tinefcon® treatment. No mortality and ECG abnormalities were reported during the study. Only a single serious AE (hepatitis) was reported as probably associated to Tinefcon® treatment.

Gastritis, exacerbation of psoriasis, hyperglycemia was experienced in 3%, 2% and 2% of subject respectively. Elevated levels of aspartate transaminase (AST) and alanine transaminase (ALT) in the blood of 7 subjects (2%) were reported. Other adverse events included diarrhea, dizziness, hyperchlorhydria, pain, pyrexia, vertigo, abdominal pain, gastroenteritis and hypercholesterolaemia in 1% of subjects. In this study discontinuation of subjects due to AE related to Tinefcon® was reported as 9% (38 subjects).

Table 4. Molecular response to Tinefcon® treatment.

No.	Gene	Mean log2 relative fold change in expression level	P-value
1	SERPINB4	−2.61	<0.0001
2	PI3	−2.47	<0.0001
3	KRT16	−2.15	<0.0001
4	iNOS	−1.27	<0.0001
5	S100A9	−1.05	0.0003
6	IL12B	−0.93	0.0003
7	TNFSF10	−0.73	<0.0001
8	FABP5	−0.71	0.01
9	IFN-γ	−0.57	0.02
10	RAB31	−0.45	0.05
11	TNF-α	−0.23	0.29

Table 5. Association between molecular and clinical responses (PASI50 and PASI75) to Tinefcon® treatment.

No.	Gene	PASI50			PASI75		
		Mean log2 relative fold change (Clinical responders)	Mean log2 relative fold change (Clinical non-responders)	P-value	Mean log2 relative fold change (Clinical responders)	Mean log2 relative fold change (Clinical non-responders)	P-value
1	SERPINB4	−3.41	−1.78	0.01	−4.55	−2.02	0.001
2	PI3	−3.28	−1.65	0.01	−4.02	−2.00	0.004
3	KRT16	−2.92	−1.36	0.005	−3.44	−1.76	0.008
4	iNOS	−1.59	−0.96	0.28	−2.29	−0.96	0.02
5	S100A9	−1.29	−0.78	0.37	−2.12	−0.72	0.02
6	IL12B	−1.08	−0.79	0.57	−1.51	−0.76	0.14
7	TNFSF10	−0.82	−0.65	0.64	−0.43	−0.83	0.24
8	FABP5	−0.73	−0.64	0.88	−1.13	−0.55	0.33
9	IFN-γ	−0.44	−0.69	0.61	0.09	−0.77	0.05
10	RAB31	−0.40	−0.49	0.85	0.15	−0.63	0.13
11	TNF-α	−0.13	−0.31	0.68	0.22	−0.35	0.24

4. Discussion

In this phase IV study we found that Tinefcon® tablet (2.8 g/day) was effective in reducing the severity of plaque in patients suffering from psoriasis after a 12-week treatment regimen. Remarkable PASI score improvement was observed in Tinefcon® treated psoriasis patients; PASI50 was attained in 52% of patients, PASI75 attained in 23% patients while PASI90 attained in 7% of patients after completion of the treatment. Near to similar types of results were reported in a study of a novel biological etanercept (25 mg subcutaneously twice a week) for the treatment of psoriasis, where PASI75 was achieved in 30% patients at week-12 [16]. In another clinical trial, Kim *et al.* mentioned that weighted average PASI75 scores at 12 week for infliximab, ustekinumab, adalimumab, etanercept were 78.6%, 72.1%, 70.5%, 48.1%, and alefacept 21% respectively [17]. The PASI75 response exhibited by Tinefcon® was higher as compared to alefacept while it was lower as compared to infliximab, ustekinumab, adalimumab and etanercept.

PGA assessment score was unchanged at visit 3 for most of the subjects with mild disease activity at baseline but more than half of patients with moderate disease activity showed reduction in severity. Thus reduction in psoriasis severity was seen with both PGA and PASI assessments. PGA assessment at visit 3 revealed that Tinefcon® treatment reduced disease progression and severity of psoriasis in most of the subjects.

Histopathological assessment of psoriasis showed that morphological changes such as acanthosis, dermal inflammation, papillomatosis and parakeratosis were enhanced and this improvement is significantly associated with changes in the PASI scores ($p < 0.01$). The improvement in PASI score was supported by reduction in acanthosis and parakeratosis. Patients (46%) showed drastic reduction in the number of inflammatory cells in the lesions; these cells play an important role in severity of disease hence suggesting the anti-inflammatory activity of Tinefcon®. The improvement in PASI score was also related to reduction in epidermal thickness and Rete ridge length.

As per logistic regression models, it was observed that a reduction in post-treatment levels of S100A9 is associated with the clinical response as measured by PASI scores. S100A9 has been shown to be an inflammatory protein in rheumatoid arthritis and inflammatory bowel disease [18]. Hence reduced staining of S100A9 in skin lesions demonstrates anti-inflammatory potential of Tinefcon®.

Increase in KRT16 expression is a marker of keratinocyte hyperplasia [19]. Serine protease plays an important role in immune response [20]. Elevated expressions of serine protease inhibitors SERPINB3 and SERPINB4 are an indicator of early inflammation and barrier dysfunction leading to skin disorders [21]. Peptidase inhibitor

3 or elafinare proteins encoded by the PI3 gene. Over expression of PI3 has been implicated in pathogenesis of psoriasis [22]-[24]. Gene expression analysis in the present study reveals down-regulation for SERPINB4, PI3 and KRT16 after Tinefcon® treatment. It was also associated with the clinical response as measured by PASI. Increased down regulation of SERPINB4, PI3 and KRT16 were observed in subjects with higher PASI scores (PASI75 responders) as compared to subjects with lowering PASI score (PASI50 responders). These findings are similar to those reported by Hendricks *et al.* and confirmed that down regulation of KRT16 and PI3 are strongly correlated with improvement in PASI score [25].

Safety data of Tinefcon® indicates a good tolerability profile, and no deaths were reported. The observed adverse events were mild to moderate in nature. Only one serious adverse event of hepatitis was reported. Nausea and vomiting were the common AEs related to Tinefcon®. Other AEs are consistent with those mentioned in Investigator's Brochure. No new adverse event was reported in this study.

The improvement in PASI score indicates a reduction in psoriasis severity in subjects after Tinefcon® treatment. Histopathological evaluation revealed that higher reduction in acanthosis and parakeratosis parameter as improvement in the PASI score. Further, gene expression study demonstrated that down regulation of SERPINB4, PI3 and KRT16 genes increased in subjects with greater PASI scores. Thus, this study provides evidence that skin histopathology and molecular response markers have good correlation of the PASI score. In this study, an important achievement of Tinefcon® formulation was that; 05 subjects with severe psoriasis achieved PASI90 without receiving any significant concomitant medication. Tinefcon® can be safely prescribed with topical steroids and systemic anti-inflammatory drugs during the treatment of psoriasis. Tinefcon® showed good efficacy in plaque psoriasis patients, further long duration study is required to confirm the long-term safety of Tinefcon®.

5. Conclusion

Oral Tinefcon® tablets showed good efficacy and had a favorable safety profile in a larger number of plaque psoriasis patients.

Conflicting Interest

We have no conflict of interest.

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