



USE OF ITOLIZUMAB IN CHRONIC PLAQUE PSORIASIS PATIENTS: CLINICAL EXPERIENCE

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Article Received on 14/01/2016

Article Revised on 04/02/2016

Article Accepted on 24/02/2016

ABSTRACT

Psoriasis is a common skin disease which carries a significant physical and psychological burden. The impact of the disease is that it not only affects the patient but, has implications on health economics. Understanding and treatment for psoriasis have moved forward greatly over the last few years. As our understanding of the immune-pathogenesis of psoriasis grows so does the opportunity for development of new therapeutic targets. We report our experience in successfully managing 5 cases of moderate to severe chronic plaque psoriasis with a novel biologic agent Itolizumab which selectively inhibits CD6 co-stimulatory pathway.

KEYWORDS: Itolizumab, Psoriasis, Psoriasis Area and Severity Index (PASI).

INTRODUCTION

Psoriasis is a chronic, complex, (auto) immune-mediated inflammatory, debilitating skin and joint disease. Psoriasis is less common in children and more common in adults. Psoriasis is characterized by exaggerated keratinocyte proliferation and influenced by both genetic and environmental factors. Assessments of a prevalence of psoriasis have varied across studies. In one interesting systematic review, Parisi *et al.* claimed that, worldwide variation in prevalence of psoriasis appeared to depend on the distance from the equator. Populations located closer to the equator being less affected by psoriasis compared with countries more distant from it (Europe and Australia).^[1] Psoriasis affects 2–3.6% of the Caucasian population.^[2,3] In India the occurrence of the disease varies from 0.44 to 2.8%.^[4] The exact etiology of the disease is unclear.

According to the National Psoriasis Foundation (US) about 65% of patients have mild (Body Surface Area > 3%) disease and about 35% (Body Surface Area < 3%) have moderate to severe disease.^[5] Significant numbers of patients are able to manage with topical therapy; up to 25% of patients need phototherapy, oral systemic medication, or biologic therapy.^[6] Dermatologists are still in search of good options which can balance efficacy and tolerability correctly especially in the management of moderate to severe Psoriasis.

During the past several years, targeted therapies have significantly improved outcomes in the treatment of

Psoriasis. Several biological agents targeting T-cells and cytokines are present for systemic treatment of Psoriasis. In a recent review Farhangian *et al.* anticipated that, Etanercept, infliximab, adalimumab, ustekinumab, and secukinumab are non-efficacious over time and subjects fail to respond to these agents. The possible attributable reason is development of antidrug antibodies (ADAs). In further discussion Farhangian *et al.* directed investigators to use of concomitant methotrexate as a tool to reduce immunogenicity.^[7] Understanding safety profile in that case may require further research. Increased susceptibility to infections due to T cell depletion is also a major concern during anti-TNF therapy.^[8,9]

Itolizumab which is currently available in India is shown to be less immunogenic (being a humanized version of IOR T1) and has a better efficacy and safety profile.^[10,11] In the current article, investigator reports his experience in successfully managing 5 cases of moderate to severe chronic plaque psoriasis with a novel biologic agent Itolizumab which selectively inhibits CD6 co-stimulatory pathway.^[10]

CASE REPORT

A total of five cases (4 males & 1 female) were reported in the clinic. All of the patients presented with chronic moderate to severe plaque psoriasis (Average PASI >20) with varying involvement of the body parts. Case no. 1, 2 and 5 were on the treatment of Anti-TNF as mentioned in Table 1. At baseline, the patient's Psoriasis Area and Severity Index (PASI), Dermatology Life Quality Index

(DLQI) and Physician's Global Assessment (PGA) were taken as mentioned in table 1.

Table 1: Demographic details and baseline PGA, PASI and DLQI score.

Case no.	Age	Gender	Year of diagnosis	Height (Cm)	Weight (Kg)	BMI	PASI	PGA	DLQI	Prior therapy
1	17	M	2002	160	70	27.3	35.3	5	6	Methotrexate, Cyclosporine, corticosteroids.
2	55	M	2001	160	83	32.4	48.8	6	16	Infliximab
3	37	M	2008	174	72	23.8	26.3	5	14	Nil
4	29	F	2008	160	53	20.7	31.5	6	17	Nil
5	66	M	2000	163	63	23.7	32.2	5	15	Etanercept

BMI= Body Mass Index, PGA=Physician's Global Assessment, PASI=Psoriasis Area and Severity Index, DLQI=Dermatology Life Quality Index

Mean PASI, DLQI and PGA scores were 34.82, 13.6 and 5.4 respectively at the baseline visit. Apart from psoriasis, all the patients were in good health and were not suffering from any other disease.

As the disease condition and assessments score were worsened, all the patients were told stop any previous treatment for a minimum period of 2 weeks after (as washout). Their diagnosis was confirmed by a skin biopsy and a histopathological test from an experienced Pathologist.

Further all the patients were investigated for Latent Tuberculosis using:

- Mantoux test
- QuantiFERON test
- Chest X-ray

Other Investigations done were

- Complete blood count
- Total Cholesterol
- Liver enzyme tests
- Hematology & LFT
- Thyroid function assessment
- Serum Creatinine

After confirming that all the investigations were within normal limits for all 5 cases, Itolizumab was prescribed after thorough clinical examination of the patient. Itolizumab dose was calculated according to body weight (1.6 mg/Kg body weight, once every 2 weeks for 12 weeks). Patients were pre-medicated with Cetirizine 10 mg per oral to prevent any possibility of cytokine reaction. Inj. Itolizumab was diluted in 250 ml of 0.9% saline solution and was administered intravenous (I.V.) over a period of not less than 120 min. The treatment was given for 8 weeks.

All the patients showed significant clinical improvement by the end of 4 weeks of treatment as shown in the photographs (Figure 1-5).



Figure 1: Case 1 Baseline and 4 week post treatment.



Figure 2: Case 2 Baseline and 4 week post treatment.



Figure 3: Case 3 Baseline and 4 week post treatment.



Figure 4: Case 4 Baseline and 4 week post treatment.



Figure 5: Case 5 Baseline and 4 week post treatment.

Itolizumab reduced the PGA, PASI and DLQI scores significantly by the end of 4 weeks in all 5 patients of Chronic Plaque Psoriasis (Table 2).

Table 2: Result after Itolizumab treatment at week 8

Caseno.	PGA			PASI			DLQI		
	Baseline	Week 4	Week 8	Baseline	Week 4	Week 8	Baseline	Week 4	Week 8
1	5	2	1	35.3	10	3	6	1	1
2	6	3	1	48.8	13	8.7	16	6	5
3	5	2	1	26.3	8	6.4	14	6	4
4	6	2	1	31.5	9	7.2	17	8	5
5	5	2	1	32.2	5	5.6	15	8	3

PGA=Physician's Global Assessment, PASI=Psoriasis Area and Severity Index, DLQI=Dermatology Life Quality Index.

The mean PGA score was 5.4 at baseline which decreased to 1 after 8 weeks of treatment. Likewise, mean PASI score was decreased from 34.82 to 6.18. PASI ≥ 75 was achieved in all the patients after completion of treatment. All patients were observed with 'Almost Clear' of their lesions based on Physician Global Assessment. Mean DLQI at baseline was 13.6 which reduced to 3.6 after completion of treatment.

No infusion reactions were observed during the treatment period. No activation of Tuberculosis or any increased incidence of intercurrent infection or MACE (major adverse cardiovascular effects) was observed during the treatment period.

DISCUSSION

Itolizumab is newly developed a humanized anti-CD6 monoclonal antibodies approved in Indian market from 2013. It acts selectively by inhibiting the CD6 molecule. CD6 itself a co-stimulatory molecule stimulates T-cell to optimal level through the antigen-presenting cells. This step plays a very decisive role in T-cell proliferation to form Th1 and Th17 cells, which plays the important role in the pathogenesis of psoriasis.^[12]

In a phase II study, 40 patients with moderate-to-severe psoriasis received Itolizumab for 8 weeks with follow-up period of 24 weeks. In this study safety and PK were the primary endpoints. Itolizumab was well tolerated and attributed to less immunogenicity.^[13] Similarly, in our

cases, no adverse event was observed during study and post-treatment follow-up visits.

Krupashankar *et al* conducted a phase III study for 52 weeks, in which they observed the 75% improvement in PASI at week 12. They employed two different arms (A = 4-week loading dose of 0.4 mg/kg/week followed by 1.6 mg/kg every 2 weeks; B = 1.6/mg every 2 weeks) in their study. Both the treatment groups displayed the significant efficacy in terms of PASI 75 at week 12 compared to placebo group.^[14] Comparing to their study, we also observed similar results but at 8 weeks.

In a long-term safety and efficacy of 50 mg etanercept, Trying *et al.* evaluated the long-term safety and efficacy of 50 mg of etanercept twice weekly in patients with psoriasis in phase 3 trial. Despite the occurrence of non-neutralizing antibodies in 18.3% of patients, they found safety or efficacy of etanercept unaffected.^[15] On a contrary, Farhangian *et al.* found that etanercept become non-efficacious if used over time due to the development of antidrug antibodies. In previously conducted studies on Itolizumab reported no correlation between ADA, safety, and efficacy.^[13,14] In the current study also, we have not observed any decrease in efficacy and safety of Itolizumab.

The incidence of infections in Itolizumab is lower as compare to Infliximab, Adalimumab and Ustekinumab. Efficacy of Itolizumab was found to be comparable with

other biologics such as infliximab, adalimumab, etanercept and ustekinumab.^[12] Further long duration studies need to be conducted to understand the side effects.

CONCLUSION

Itolizumab appears to be an efficacious and safer treatment option for moderate to severe chronic plaque psoriasis.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

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