

A Real-World Study to Assess the Effectiveness of Itolizumab in Patients with Chronic Plaque Psoriasis

Abstract

Background: While clinical trial data on the efficacy of itolizumab in the management of psoriasis is relatively well documented, data on the effectiveness of this humanized IgG1 monoclonal antibody in real-world settings is sparse. **Aims:** The current study assessed the effectiveness of itolizumab in real-world settings. **Materials and Methods:** This study assessed psoriasis area severity index (PASI), dermatology quality of life index (DLQI), safety, and tolerability data from a registry of itolizumab maintained by Syngene International, Bangalore. Registry data of 155 patients who were prescribed itolizumab at a dose of 1.6 mg/kg every 2 weeks for the first 12 weeks followed by 1.6 mg/kg every 4 weeks for up to 24 weeks for chronic plaque psoriasis. **Results:** In the study, 35.48% completed itolizumab for 12 weeks and 76.59% of these patients achieved PASI 75. Furthermore, 24.51% patients completed the full Itolizumab regimen for 24 weeks, of whom 92.01% patients achieved PASI 75. The mean percent change in DLQI scores at weeks 12 and 24 were 60.19 and 82.72, respectively. Adverse events and infusion reactions noted in the study were generally of mild to moderate severity. **Conclusion:** Itolizumab is a safe and effective option in treatment-compliant patients with chronic plaque psoriasis. Effects of putative compliance-modulators such as cost, route of administration, and delayed onset of action warrant further investigation.

Keywords: Compliance, itolizumab, plaque psoriasis

Introduction

Biological therapies have emerged as important treatment options for psoriasis.^[1] While efficacy of these agents has been confirmed by a number of clinical studies, safety concerns with the use of biological therapies have been an obstinate persistence.^[2] Menon *et al.* indicate that Itolizumab, a humanized IgG1 monoclonal antibody that modulates CD6-mediated T cell co-stimulation, inhibits T-cell proliferation and inflammatory cytokine production, may have a better safety profile but comparatively less efficacy when compared to other biological agents.^[3] However, there is a paucity of head-to-head comparisons to arrive at definitive profiles of comparative effectiveness.^[4]

While randomized studies are gold-standards for assessments of efficacy under optimal circumstances, registries may be the gold-standards for real-world research.^[5] Data from registries can provide important insights into effectiveness, long-term outcomes, and rare adverse events in a more naturalistic environment.

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A key feature of long-term studies is that they can provide data on efficacy outcomes, which may crucially depend on an optimal duration of treatment.^[6] Compliance to optimal treatment duration may depend on factors such as cost, tolerance, adverse effects, and dosing schedules. Furthermore, it is also important to individualize treatment duration as patients achieving a good response before an “ideal duration of treatment” are not rare in actual clinical settings. Currently, availability of such data is relatively sparse.^[6]

Materials and Methods

Data for this analysis was obtained from a registry maintained by Syngene International, Bengaluru. This registry was started in January 2014. The study was approved by the ethics committee, and an informed consent was obtained from all the patients.

Patients with mild-to-moderate chronic plaque psoriasis who were prescribed itolizumab at a dose of 1.6 mg/kg every 2 weeks for first 12 weeks followed

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by 1.6 mg/kg every 4 weeks for up to 24 weeks were included in the study. All these patients received itolizumab intravenous (IV) infusion. Patients with other forms of psoriasis (unstable, arthritic, erythrodermic, or pustular psoriasis), serious infections, clinical suspicion of latent tuberculosis, or positive Mantoux test (>20 mm induration or ≤ 20 mm ulcerative or bullous lesion on 5 TU Mantoux test), as well as other contraindications to itolizumab were excluded from the study.

In the study, efficacy assessments included assessments of psoriasis area severity index (PASI) scores and dermatology quality of life index (DLQI) at baseline, week-12, and week-24. Furthermore, the study involved assessments of safety and tolerability (infusion reactions) at all visits. DLQI assessments were administered through standardized DLQI questionnaires administered in English or in four Indian languages (Hindi, Marathi, Telugu, and Kannada). Statistical methods involved summarization of data using descriptive statistics. Proportions of patients achieving PASI 50, PASI 75, PASI 90, and PASI 100 at week 12 and week 24 of itolizumab regimen were computed. Mean change in PASI score at week 12 and week 24 of itolizumab regimen were computed using the paired *t*-test. Furthermore, proportions of patients achieving DLQI improvements of $<50\%$, $50\text{--}75\%$ and $>75\%$ were computed. Mean change in DLQI scores at week 12 and week 24 of itolizumab regimen were computed using the paired *t*-test. Statistical tests were performed using GNU PSPP statistical analysis software, Free Software Foundation, Boston, Massachusetts". Results and insights gained from the study were used to design and develop a registry based on a case-series model.

Results

A total of 155 patients (113 males and 42 females) with plaque psoriasis were included in the study. The age of patients ranged from 18 to 70 years. Table 1 presents the demographic characteristics of patients included in the study. Out of the 155 patients enrolled in the study, 55 (35.48%) completed 12 weeks of itolizumab therapy (1.6 mg/kg every 2 weeks). A total of 38 (24.51%) patients completed the full itolizumab regimen (1.6 mg/kg every 2 weeks for first 12 weeks followed by 1.6 mg/kg every 4 weeks up to 24 weeks). The dropout rate (64.6%) was relatively high, and reasons for treatment discontinuation/drop out could not be elicited from patients. The mean PASI scores at baseline was 30.72 (range: 12.5–57.1) and the mean (\pm SD) DLQI scores were 16 ± 3.80 and 13.92 ± 5.70 in males and females, respectively. Table 2 presents the mean PASI and DLQI scores at baseline, week 12, and week 24 of itolizumab therapy. Compared to the baseline, the mean percent changes in PASI scores at week 12 and week 24 were 75.80% ($P < 0.001$) and 82.26% ($P < 0.001$),

respectively. As noted in Figure 1, 76.59% patients completing 12 weeks of itolizumab therapy and 92% patients completing 24 weeks of itolizumab therapy achieved \geq PASI 75 scores [Figure 2]. Among these patients, a subset achieved PASI 90 [Figure 3] and PASI 100 as compared to their baseline scores. The mean percent change in DLQI scores at week 12 and week 24 were 60.19% ($P < 0.001$) and 82.72% ($P < 0.001$), respectively. Furthermore, close to 73% patients completing 24 weeks of itolizumab therapy reported greater than 75% improvements in DLQI scores as compared to their baseline DLQI scores [Figure 4].

Adverse events noted in the study included urticaria (0.64%), nausea (1.29%), vomiting (1.93%), hypertension (0.64%), skin rashes (0.64%), chest pain (0.64%), and fever (1.29%), and were of mild to moderate severity. Itoizumab infusion reactions were rare with one patient reporting diarrhoea. Patients who completed 12 weeks and 24 weeks of treatment did not report any adverse events.

Table 1: Demographic characteristics

	Males (n=113)	Females (n=42)
Age in years (mean \pm SD)	40.41 \pm 12.72	39.90 \pm 15.67
Height in centimetres (mean \pm SD)	168.63 \pm 7.40	159.33 \pm 7.34
Weight in kilograms (mean \pm SD)	73.91 \pm 13.97	63.95 \pm 10.63
BMI (mean \pm SD)	26.24 \pm 5.20	21.16 \pm 4.49
PASI Scores (mean \pm SD)	30.72 \pm 10.62	29.47 \pm 13.00
DLQI Scores (mean \pm SD)	16 \pm 3.80	13.92 \pm 5.70

Table 2: Mean PASI and DLQI Scores at baseline, week-12 and week-24

	PASI scores (mean \pm SD)	DLQI scores (mean \pm SD)
Baseline	30.38 \pm 11.71	15.43 \pm 4.61
After 12 weeks of itolizumab therapy	7.36 \pm 5.77*	6.15 \pm 3.70 [†]
After 24 weeks of itolizumab therapy	5.39 \pm 6.06**	2.67 \pm 3.20 ^{††}

* $P < 0.001$, ** $P < 0.001$, [†] $P < 0.001$, ^{††} $P < 0.001$

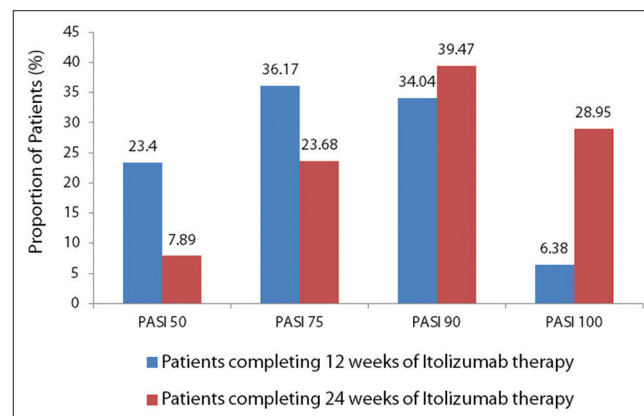


Figure 1: PASI improvement profiles in patients completing 12 and 24 weeks of itolizumab therapy

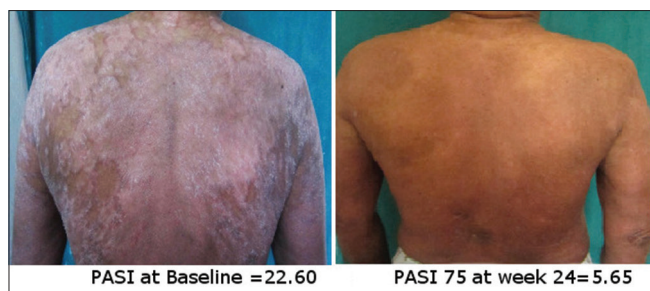


Figure 2: Clinical images of PASI 75 response at week 24



Figure 3: Clinical images of PASI 90 response at week 24

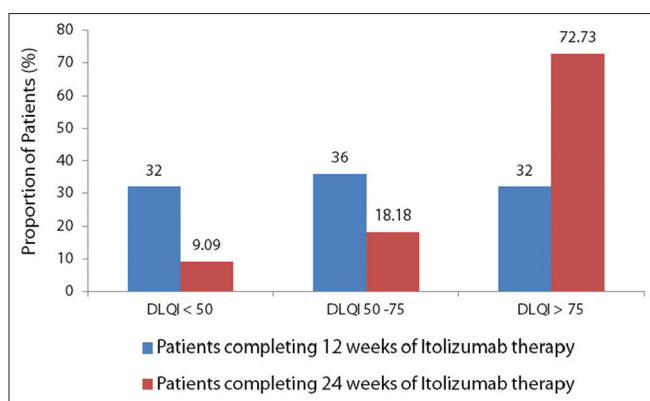


Figure 4: DLQI improvement profiles in patients completing 12 and 24 weeks of itolizumab therapy

Discussion

A study by Krupashankar *et al.* indicates that itolizumab has a good safety profile as compared to other biologics.^[7] According to the study, itolizumab therapy was associated with pyrexia (1.3%) and skin rashes (5.4%) along with infusion site reactions (acute: 17%, and delayed: 3.6%). Results of the current study are in agreement with the published data on the safety of itolizumab.^[7,8] Only 9 out of 155 patients experienced mild-to-moderate adverse events. Furthermore, no adverse events and infusion reactions were noted in patients who received itolizumab for the first 12 weeks and among those who completed the full regimen. Thus, our data indicate that safety issues are not a limiting factor for treatment adherence to itolizumab regimen.

With respect to efficacy, 11 out of 38 patients who received the full itolizumab regimen achieved PASI 100. This observation possibly indicates that itolizumab efficacy

is associated with compliance to itolizumab therapy for optimal treatment duration of at least 12 weeks. Furthermore, Itolizumab efficacy for providing long-lasting remission has been previously reported in literature.^[9] Elyoussfi *et al.* in a recent article emphasized that a number of treatment options that are not part of current guidelines can be effectively used in individualized patient settings based on the disease phenotype and clinician experience.^[10] Results of the current study indicates that itolizumab is a safe option with significant improvements in PASI and DLQI scores. As per our data, 76.59% patients completing 12 weeks of itolizumab therapy and 92.10% patients completing 24 weeks of itolizumab therapy achieved PASI 75. Furthermore, close to 29% patients completing 24 weeks of itolizumab therapy achieved complete remission for about 6 months. Thus, adherence to full treatment regimen appears to be important for optimizing outcomes.

In the study, approximately 24.51% patients received the full itolizumab regimen. Only 9 out of 155 patients experienced mild-to-moderate adverse events. Thus, safety issues may not be the contributing factor for this low compliance to full treatment regimen. However, a number of other factors such as delayed onset of action, costs, and route of administration could be putative contributors to low compliance. A key limitation of this study was that reasons for treatment discontinuation/drop out could not be elicited from patients. Though there is a chance for attrition bias, we could not employ logistic regression analysis. However, efficacy seems to depend on compliance to full treatment regimen and adverse events were generally mild-to-moderate in patients that received itolizumab for the duration they did.

Currently another registry has been instituted with the name PSOCARE that can be accessed at www.psocare.in. The objective of this registry is to identify the optimal duration of itolizumab treatment along with an assessment of the association of itolizumab safety and efficacy with the duration of treatment. Furthermore, the Psocare registry will evaluate factors that influence compliance to optimal duration of itolizumab therapies.

Conclusion

In conclusion, Itolizumab appears to be a safe and effective option for patients with psoriasis. However, compliance to optimal treatment regimen seems important to optimize outcomes. Thus, factors affecting compliance need to be addressed in clinical settings and future studies.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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