Psoriasis: Targets and Therapy

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REVIEW

Spotlight on itolizumab in the treatment of psoriasis – current perspectives from India

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Abstract: Psoriasis is a chronic, debilitating, immune-mediated, systemic inflammatory disease affecting mainly skin, nails, and joints. Several therapeutic modalities are available depending on the severity of the disease. Long-term use of these drugs results in unwanted effects and toxicities. Recently, itolizumab, a humanized monoclonal immunoglobulin G1 antibody to CD6, has shown appreciable clinical effects and safety profile in patients with moderate-to-severe chronic plaque psoriasis. A literature search was conducted using the keywords "anti-CD6", "psoriasis", "phase trials", "case series", and "case reports". The data from all studies conducted in India on efficacy of itolizumab in psoriasis and published before September 2017 were collected. This article provides an overview of the clinical data obtained in these published articles. Itolizumab has immunomodulatory and anti-inflammatory effects. It is efficacious and provides a good duration of remission, and hence represents a new biological agent that could be added to the therapeutic armamentarium of psoriasis.

Keywords: psoriasis, biologic, monoclonal antibody, anti-CD6, Humanised IgG1 monoclonal antibody, anti CD6

Introduction

Psoriasis is a chronic relapsing inflammatory disease affecting ~1%–3% of the world's population.[1,2] Recently, there has been a growing consensus that psoriasis is a systemic disorder rather than a papulosquamous disorder affecting the skin. Increased co-incidence of inflammatory arthropathy (in about 25% of the cases) and metabolic syndrome with psoriasis has supported this opinion.[3] Frequent episodes of exacerbations and remissions of the disease not only lead to physical impairment but also cause psychological, social, and even financial difficulties.[3] Several drugs are available for the management of psoriasis depending upon the severity and type of the disease. Conventional drugs including corticosteroids, retinoids, methotrexate, and anthralin are prescribed in moderate-to-severe degree of psoriasis with some success. However, these drugs on long-term use can cause toxicity. Biological agents like etanercept, adalimumab, and infliximab are considered to be superior to the conventional drugs both in terms of safety and efficacy, as they are highly specific in their action (target-specific molecules important in the pathogenesis of psoriasis).[4]

Pathogenesis of psoriasis: immunological aspects

In a genetically predisposed individual, different immune cells like dendritic cells, histiocytes, keratinocytes, monocytes, etc, under specified stimuli release several cytokines like tumor necrosis factor (TNF-α) and IL-1.[1,5] These cytokines then activate

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the antigen-presenting cells (APCs) which along with the processed antigens then activate the naïve T-cells following migration to the regional lymph nodes. Next, differentiation of naïve T-cells into different helper T-cells like Th1, Th2, Th17, and T regulatory cells occur.[2] APC-mediated activation of the T-cells requires two signals. The first one depends on the antigen (antigen-specific) and requires interaction between the T-cell receptor and the major histocompatibility complex molecules located on the membranes of the APCs, whereas the second one is not antigen specific and requires the presence of different co-stimulatory signals.[1,5] Activation of T-cells fails in the absence of co-stimulation, leading to apoptosis of T-cells.

Role of CD6 in the pathogenesis of psoriasis

CD6 has been identified as an important immune component in the pathogenesis of psoriasis. CD6 is a surface glycoprotein found on the outer surface of mature T-cells and immature B-cells; its molecular weight ranges between 105 and 130 kDa.[1,6–8] There are three scavenger receptor cysteine-rich (SRCR) domains (D) present in the extracellular region of CD6. There is a CD6 ligand, also known as CD166 or activated leukocyte-cell adhesion molecule (ALCAM), that is expressed on different cells like the T- and B-lymphocytes, APCs, and thymocytes.[1,6–8] ALCAM binds with the SRCR domain 3 (D3) of CD6 and plays an important role in interaction between T-cells and APCs.[1,6–8] Again, CD6–ALCAM interaction contributes to the formation of immunological interactions like facilitation of stable adhesion between the T-cells and the APCs and also plays important role in differentiation, proliferation, and maturation of T-cells.[1,6–8] CD6 can also activate the T-cells when there is a decrease in the levels of intracellular phosphoproteins (Figure 1).[7] It can also stimulate the proliferation of CD3 and increase the number of CD25 molecules via activating a number of co-stimulatory pathways. In addition to all these functions, CD6 can also increase the release of TNF-α, IFN-γ, and IL-6.[1] Through all these actions, CD6 can finally lead to dermal inflammation which in turn leads to activation of keratinocytes and consequent psoriatic changes like acanthosis, hyperkeratosis, and parakeratosis.[1]

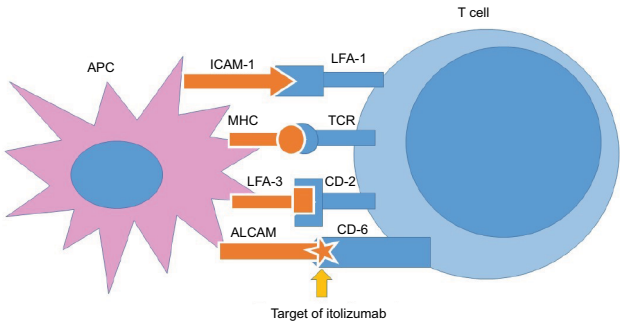

Figure 1 Itolizumab targeting CD6 (co-stimulatory signals between APCs and T-cells).
Abbreviations: ALCAM, activated leukocyte-cell adhesion molecule; APCs, antigen-presenting cells; CD, cluster of differentiation; ICAM, inter-cellular adhesion molecule; LFA, lymphocyte function associated antigen; MHC, major histocompatibility complex; TCR, T-cell receptor.

Itolizumab

Itolizumab, a humanized recombinant monoclonal antibody of immunoglobulin G1 type with a molecular weight of 148 kDa, is a selective T-cell co-stimulation modulator, targeting the SRCR-D1 of CD6 on T-cells.[1] It has two heavy chains with 449 amino acids and two light chains with 214 amino acids linked with a disulfide bond.[1]

The murinemonoclonal anti-CD6 (ior-T1) has therapeutic effects in diseases like rheumatoid arthritis and psoriasis.[9] Itolizumab, the humanized version of ior-T1, shows less immunogenicity as well as a better safety profile but exhibits the same therapeutic benefits as ior-T1.[1,8]

Mechanism of action

Several hypotheses regarding the mechanism of itolizumab have been proposed, although many of them require further evidences. The most popular theory is that itolizumab can modulate T-lymphocyte activation and proliferation through binding with CD6 (Figure 2).[1,8] However, it does not have any effect on interaction of ALCAM with CD6-expressing HEK293 cells in experimental settings and does not cause T-cell depletion in rheumatoid arthritis patients.[1,7] Also, the widespread presence of CD6 in different types of T-cells and B-cells should enable itolizumab to modulate immunological pathways in various diseases, although clinical evidence in this regard is lacking.[1,6,7]

Dosage and administration

In chronic plaque psoriasis, the recommended dosage schedule includes administration of itolizumab at 1.6 mg/kg body weight, once every 2 weeks for 12 weeks followed by once in 4 weeks for a total period of 24 weeks.[1,8] It is mixed with 250 mL of sterile normal saline at room temperature and administered as slow intravenous infusion over 2 hours, 50 mL in the first hour and the remaining 200 mL in the next hour.[1,8]

Contraindications

The drug is contraindicated in active and latent infections and in patients with hypersensitivity to any of the components of the itolizumab injection or murine proteins.[1] Hence,

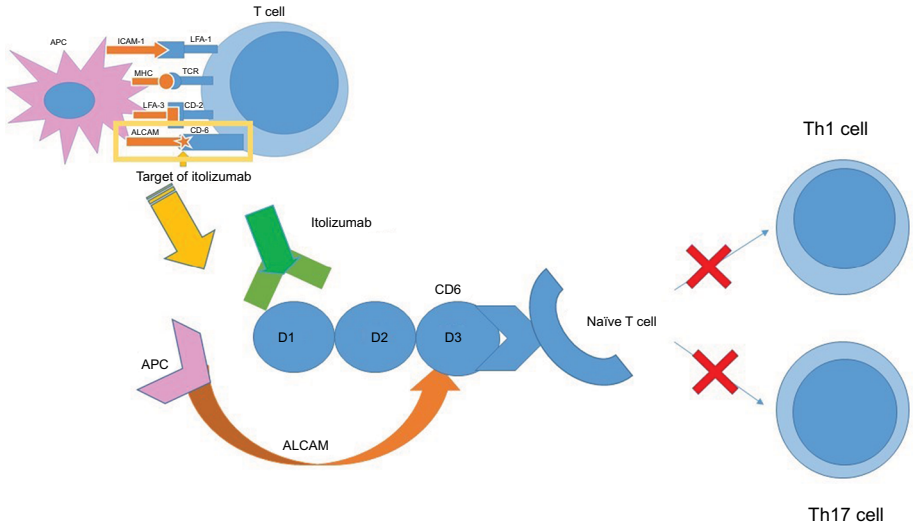

Figure 2 Site of attachment of itolizumab at extracellular domain D1 of SRCR domain of CD6 on naïve T-cell.
Abbreviations: ALCAM, activated leukocyte-cell adhesion molecule; APCs, antigen-presenting cells; D1, 2, 3, domains on SRCR of CD6; Th1, Th17, T-helper 1 and 17; CD, cluster of differentiation; MHC, major histocompatibility complex; SRCR, scavenger receptor cysteine-rich; TCR, T-cell receptor.

screening active as well as latent infections like tuberculosis is mandatory before initiating therapy. As safety of the drug is yet to be evaluated in patients with neutropenia and lymphopenia, AIDS, tuberculosis, and hepatitis B and C, itolizumab is avoided in psoriasis patients with these coexisting conditions.[1] Again, safety of itolizumab is not established in pregnant (can cross placental barrier) and lactating mothers (secreted in milk), in children <18 years, and in patients with liver and kidney dysfunctions. Hence, it is better to avoid the use of itolizumab in these people.[1]

Safety and efficacy of itolizumab for psoriasis in Indian patients

In India, the efficacy and safety of itolizumab was assessed in two different randomized, multicentric studies involving patients with stable chronic plaque psoriasis, aged ≥18 years, with Psoriasis Area and Severity Index (PASI) score ≥10 (severe disease) and in patients who showed minimal or no benefit from other systemic drugs (treatment failures or resistant).

In the study conducted by Anand et al,[10] a 32-week, randomized, single-blind, and parallel phase II study, itolizumab was administered at different doses at different intervals to 40 patients allotted to eight different groups, each group consisting of 5 patients for a total period of 8 weeks with follow-up period extended for 24 weeks.[10] The study showed statistically significant improvement in mean PASI score, Physician's Global Assessment (PGA) score, and Psoriasis Severity Scale (Table 1).[10] Quality of life of the study participants also improved with itolizumab assessed by the Dermatology Quality Life Index (DLQI) and Short Form-6.[10] At 12th week, 72.5%, 45%, 30%, and 7.5% of the patients achieved PASI scores of 50, 75, 90, and 100, respectively.[10] The study observed that 62% of patients improved or maintained their PASI improvement measured at the 8th week till the 12th week even after stoppage of the drug.[10]

In a study by Krupashankar et al[11] and in a letter to the editor by Dogra et al,[12] a 52-week, randomized, double-blind, placebo-controlled, parallel-arm, one-way crossover, multicentric, randomized withdrawal, phase III study of 225 patients with moderate-to-severe plaque psoriasis (PASI ≥10), the patients were randomized (2:2:1) into three groups: A, B, and C. Groups A and B were assigned different dosing schedules (week 0–12: arm A patients received a loading dose of 0.4 mg/kg/week of itolizumab for 4 weeks, followed by 1.6 mg/kg every 2 weeks as induction regimen; arm B patients received 1.6 mg/kg every 2 weeks) and group C was on placebo during week 0–12.[11]After 12 weeks, placebo crossover was conducted and group C was administered the study drug (1.6 mg/kg of itolizumab every 2 weeks till 24 weeks).[11] At 12 weeks, 27%, 36.4%, and 2.3% of patients were reported to achieve at least 75% improvement in PASI score in groups A, B, and C, respectively, thus meeting the primary end point, while 58.4%, 67.0%, and 23.3% of patients were reported to achieve PASI 50 in groups A, B, and C, respectively.[11] The reduction in PASI score was statistically significant in the treatment groups. The proportion of patients who achieved at least 75% improvement in PASI was greater for patients with baseline PASI ≥20 than

Table 1 Efficacy and adverse events of itolizumab in phase II and phase III studies in psoriasis

Study and design	Efficacy	Adverse events
1. Anand et al,[10] a 32-week, randomized, single-blind, and parallel phase II study in 40 patients to assess the safety and efficacy of itolizumab	1. Mean PASI scores at baseline: 22.32±8.84 2. PASI 75 scores at 12 weeks: 45% 3. PGA scores at 12 weeks (clear or minimal): 65% 4. Mean change from baseline PGA scores at 12 weeks: $P<0.0001$ 5. Mean change from baseline SF-6 at week 12: improved 6. DLQI scores at 12 weeks: improved 7. Reduction from baseline in mean epidermal thickness at 12 weeks: $P=0.0005$ 8. Reduction from baseline in mean rete thickness at 12 weeks: $P<0.0001$	1. Infusion-related reactions: Chills – 5.69% Pyrexia – 4.88% 2. Anti-drug antibody – one patient tested positive
2. Krupashankar et al[11] and Dogra et al,[12] a 52-week, randomized, double-blind, placebo-controlled, parallel-arm, one-way crossover study in 225 patients to assess the safety and efficacy ofitolizumab	1. Mean PASI scores at baseline: 21.3±8.46 2. PASI 75 scores at 12 weeks: arm A, 27% (A vs C, $P=0.0172$); arm B, 36.4% (B vs C, $P=0.043$); arm C (placebo), 2.3% 3. PGA scores at 12 weeks (clear or minimal): arm A: 20% (A vs C, $P=0.0001$), arm B: 16% (B vs C, $P=0.0002$), arm C: 4.9% 4. Mean change from baseline PGA scores at 12 weeks: A vs C, $P<0.0001$; B vs C, $P=0.0002$ 5. Mean change from baseline SF-6 at week 12: A: 3.5±6.5; B: 2.4±6.8; C: 1.7±6.8 6. DLQI scores at 12 weeks: A: 7.3±6.6; B: 5.8±5.8; C: 9.0±7.9 7. Reduction from baseline in mean epidermal thickness at 12 weeks: improved 8. Reduction from baseline in mean rete thickness at 12 weeks: improved 9. PASI 75 scores at 28 weeks: arm A, 46.1%; arm B, 45.5%; arm C (placebo arm crossover to itolizumab induction regimen), 41.9% 10. PASI 90 scores at 28 weeks: arm A, 19.1%; arm B, 21.6%; arm C, 27.9% 11. PGA score was similar across all arms (21%–23%) at 28 weeks 12. At 1-year follow-up, 52.5% in 1P group maintained PASI 75, 70% maintained PASI 50 13. At 1-year follow-up, 66.7% in 1M maintained PASI 75, 84.6% maintained PASI 50 14. 44.7% maintained PGA score of clear or minimal at 52 weeks of follow-up	1. Infusion-related reactions: Acute – 17% Delayed – 3.6% Pyrexia – 8.5% 2. Pyrexia due to infections – 1.3% URTI – 7.6% 3. Pruritus – 5.4% 4. Anti-drug antibody – 15.7%, with no effect on safety and efficacy of drug 5. Effect on blood cells – small and transient decrease in mean absolute lymphocyte count

Abbreviations: DLQI, Dermatology Quality Life Index; PASI; Psoriasis Area and Severity Index; PGA, Physician's Global Assessment; SF-6, Short Form-6; URTI, Upper Respiratory Tract Infection; 1P, Group 1 Placebo; 1M, Group 1 Maintenance Itolizumab.

for those with PASI <20. The study also observed PASI 90, reported for 11.2% and 17% of patients in groups A and B, respectively.[11] After crossover of the placebo group to receive itolizumab at week 12, the improvement in PASI scores was comparable to other treatment groups by week 20.[11] At week 28, 46.1%, 45.5%, and 41.9% of patients were reported to achieve at least 75% improvement in PASI score in groups A, B, and C, respectively, while 78.7%, 80.7%, and 79.1% of patients were reported to achieve at least 50% improvement in PASI score in groups A, B, and C, respectively.[11] At week 28, the study observed at least 90% improvement in PASI score in 19.1%, 21.6%, and 27.9% of patients in groups A, B, and C, respectively. Quality of life scores and PGA also demonstrated similar trend as PASI scores.[11] At week 12, the proportion of patients with PGA scores of "clear" or "minimal" was greater than placebo (A: 20.0%; B: 16.0%; C, 4.9%), and at week 28, it was similar across the groups (21%–23%).[11]

Furthermore, out of the 199 patients in the above-mentioned trial, at week 28, 177 patients entered randomized withdrawal phase.[12] At week 28, patients with PASI score ≥75 were re-randomized (1:1) into group 1M and group 1P to receive maintenance itolizumab therapy and placebo, respectively.[12] Patients with PASI score <50 were withdrawn, while patients with PASI score ≥50 but <75 at week 28 were reinitiated with itolizumab induction therapy. The patients of the three subgroups can be categorized as: good responders (GR), achieving long-term remission after controlled drug cessation; good responders with maintenance therapy (GM), achieving long-term remission with maintenance therapy; and late responders (LR) achieving PASI ≥75 after itolizumab reinitiation with the induction regimen.[12] At 1-year follow-up, 52.5% in group 1P maintained PASI score ≥75 (representing GR) and 70% maintained PASI score ≥50, which is a clinically meaningful response, comparable to other biologics.[12] In group 1M, significant remission was observed with 66.7% patients who maintained PASI score at 75% and 84.6% patients who maintained PASI score at 50.[12] In group 1M, 44.7% of patients maintained PGA scores of "clear" or "minimal" at week 52 vs 46.2% at week 28; in group 1P, these proportions were reported as 30% vs 50%.[12] (Table 1)

The safety of itolizumab was also established in a case series of five patients reported by Nott et al,[13] a case series of seven patients by Singh,[14] a case series of 20 patients by Parthasaradhi,[15] a case series of 155 patients by Parthasaradhi et al,[16] a case series of five patients by Pai and Pai,[17] a case report presented by Trasi et al,[18] a case report by Gupta et al,[19] and a case report by Budamakuntla et al.[20] In all the clinical studies and individual case reports or case series, itolizumab was safe and well tolerated (Tables 2 and 3).

Discussion

Itolizumab was efficacious with a significant reduction in the mean PASI, PGA, and DLQI scores in both the above-mentioned phase II and III trials. The common side effects noted were diarrhea, infusion-related reactions, and anti-drug antibodies with no effect on safety and efficacy of the drug.[11] In various case series and case reports, the results were comparable and itolizumab gave good remission. The comparative data of all the studies and case reports are summarized in Table 4.

Efficacy of itolizumab as compared to various biologics available in India for psoriasis is tabulated in Table 5.

In various randomized control trials conducted on Indian patients, PASI 75 response at week 12 was 58.5% in those who received 300 mg/kg of secukinumab,[22] 50% in those who received 150 mg/kg of secukinumab,[22] 36.4% in those who

Table 2 Case series on efficacy and adverse events of itolizumab

Author	Description of the study
1. Nott et al[13]	• A case series of five patients (four male and one female) who presented with chronic moderate-to-severe plaque psoriasis (average PASI >20). • Itolizumab was administered to the patients according to their body weight (1.6 mg/kg body weight, once every 2 week) for 8 weeks. All the patients showed significant clinical improvement by the end of 4 weeks of treatment. • The mean PGA score decreased to 1 (5.4 at baseline) and mean PASI score decreased from 34.82 to 6.18; PASI ≥75 was achieved by all patients after completion of treatment. Mean DLQI reduced to 3.6 (13.6 at baseline) after completion of treatment. Itolizumab proved efficacious for the treatment of moderate-to-severe chronic plaque psoriasis.
2. Singh[14]	• A total of seven patients (six male and one female) with moderate-to-severe psoriasis and who were intolerant/nonresponsive to conventional therapies were included. • The included patients also had psoriatic arthritis, type 2 diabetes with arterial hypertension, interstitial lung disease, alcoholic liver disease, and arterial hypertension. • Itolizumab (1.6 mg/kg) was administered to each patient fortnightly for the first 3 months and monthly for the last 3 months of the study. • The baseline mean PASI score was 22.8 which reduced to 1.53 after completion of itolizumab treatment. Similarly, mean baseline DLQI score also reduced from 10.8 to 1.57. • A total of five patients attained PASI 90 response, while two patients successfully achieved PASI 75 response after itolizumab therapy. • Patients with psoriatic arthritis found great improvement in mobility of affected joints and no significant improvement in comorbid conditions.
3. Parthasaradhi[15]	• Twenty patients from both sexes (15 male and 5 female), with a history of psoriasis for >5 years, recalcitrant to methotrexate and cyclosporine were included. • They were treated with itolizumab (1.6 mg/kg) fortnightly for first 3 months followed by once monthly for next 3 months (total ten infusions). • The mean PASI score was significantly reduced from baseline score of 26.89 to 9.35 and 3.16 at visit 7 and visit 10, respectively. • Majority of the patients had severe and moderate-to-severe disease as per PGA at baseline. After completion of treatment, the majority of patients had mild disease to almost clear skin. • There was no any severe infusion reaction or severe infection experienced in patients during treatment period. No activation of latent tuberculosis was observed during and after the treatment.

(*Continued*)

Table 2 (*Continued*)

Author	Description of the study
4. Parthasaradhi et al[16]	• A total of 155 patients (113 male and 42 female) with plaque psoriasis were 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 treatment 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. • 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. • The mean percent change in DLQI scores at week 12 and week 24 was 60.19% ($P<0.001$) and 82.72% ($P<0.001$), respectively. • Adverse events noted in the study included urticaria (0.64%), nausea (1.29%), vomiting (1.93%), arterial hypertension (0.64%), skin rashes (0.64%), chest pain (0.64%), and fever (1.29%), which were of mild to moderate severity with one patient reporting diarrhea.
5. Pai and Pai[17]	• A total of five patients, four patients with chronic plaque psoriasis and one patient with co-existent psoriatic arthropathy, were treated with itolizumab. • The drug was administered in bimonthly cycles via intravenous route in 0.9% normal saline at a dose of 1.6 mg/kg for 3 months followed by maintenance phase with monthly administration of the drug for 3 months. • PASI scores reduced from 52, 24.2, 45, 43.2, and 48.2 to 5.5, 4.2, 6.5, 5.3, and 5.5, respectively, at the end of the fourth dose in all the five patients. • All patients attained a greater than PASI 75 response on completion of the fourth dose of itolizumab with significant improvement in arthropathy.

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

Table 3 Case reports on efficacy of itolizumab in psoriasis

Author	Description of the study
1. Trasi et al[18]	• A case report of a patient with moderate chronic plaque psoriasis who received itolizumab as the first line of therapy. • The patient achieved maximum clearance of his psoriatic lesions and reduction in PASI score from baseline score of 40.1 to 3.7 after treatment. • Itolizumab treatment led to complete clearance of the lesions with a continued remission for >4 months with adjunctive cyclosporine therapy.
2. Gupta et al[19]	• In a letter to editor reporting the effect of itolizumab in a patient with severe recalcitrant psoriasis who received the drug fortnightly, PASI score dropped to 12.1 from baseline score of 33.5 after 6 weeks and 1.4 at the end of induction phase after 12 weeks. His PASI score was 1.8 after three 4-weekly infusions during the maintenance phase. • PGA score, nail psoriasis severity score, and DLQI score were parallel to this improvement. The patient was advised regular follow-up and biweekly narrow band ultraviolet B therapy which was replaced with topical corticosteroids. • Remission at 15 months was reported in a patient. At 15-month follow-up, the PASI score was reported as 4 with some fresh papules and plaques along with persistent lesions around the ankles. • The patient was counseled regarding the possibility of continuing itolizumab infusions to avoid severe relapse.
3. Budamakuntla et al[20]	• A case report of a female patient with moderate chronic plaque psoriasis for ~11 years without periods of remission who consented to participate in the trial entitled "A phase II Study to Evaluate the Safety and Efficacy of Anti-CD6 Monoclonal Antibody (T1 h mAb) in Patients with Active Psoriasis". • She received itolizumab at the dose of 0.4 mg/kg weekly for 8 weeks, followed by 28 weeks of treatment-free follow-up as per protocol. • The PASI score reduced to 0.40 (12.2 at baseline) at week 8. • PGA, PSS, and DLQI reduced to 1 (clear), 1 (clear), and 0 (no effect on patient's life), respectively (3, 6.2, and 2, respectively, at baseline), at week 8. • Patient was in remission for 4 years and 5 months.

Abbreviations: DLQI, Dermatology Quality Life Index; PASI; Psoriasis Area and Severity Index; PGA, Physician's Global Assessment; PSS, Psoriasis Severity Score.

Table 4 Summarized data of the studies on itolizumab

Parameters	Anand et al[10]	Krupashankar et al[11,12]	Nott et al[13]	Singh[14]	Parthasaradhi[15]	Parthasaradhi et al[16]	Pai and Pai [17]	Trasi et al[18]	Gupta et al[19]	Budamakuntla et al[20]
No of cases	40	225	5	7	20	155	5	1	1	1
Dose (mg/kg) and duration	As described in the text	As described in the text	1.6 two weekly for 8 weeks	1.6 once in two weeks for 3 months and monthly for 3 months	1.6 two weekly for 3 months and monthly for 3 months	1.6 two weekly for 12 weeks and four weekly till 24 weeks	1.6 two weekly for 3 months and monthsonthly for 3 months	Mentioned as standard dosing regimen	1.6 two weekly for 3 months and monthly for 3 months	0.4 weekly for 8 weeks
Reduction in PASI mean PASI score	PASI 75 in 45% at 12 weeks	PASI 75 in 27%, 36.4%, and 2.3% at 12 weeks	PASI 75 in 100% at 8 weeks	PASI 90 in 5 and PASI 75 in 2	PASI 95, 90, and 75 in 4, 10, and 4, respectively	Mean PASI of 30.38 at baseline to 5.39	PASI 75 in 100% by fourth dose	40.1 at baseline to 3.7	33.5 at baseline to 1.8	12.2 at baseline to 0.4
Mean reduction in PGA	$P<0.0001$	A vs C, $P<0.0001$; B vs C, $P=0.0002$	Reduced from 5.4 to 1	No data	Majority mild/ clear at the end	No data	No data	No data	5 to improved (score not mentioned)	3 at baseline to 1
DLQI	Improved	Improved	13.6–3.6	10.8–1.57	No data	15.43–2.67	No data	12–4	18 to improved	2–0
M/C adverse events	Chills, pyrexia,	Pyrexia reaction and infection	None	None	None	Vomiting, nausea, fever	None	No data	None	None
Duration of remission	Remission maintained in 62% until 12 weeks	52.5% maintained PASI 75 at 1 year[6]	No data	No data	No data	29% maintained remission for 6 months	No data	For 6 months with concomitant cyclosporine	After 15 months PASI increased to 4	Remission maintained for 4 years and 5 months

Abbreviations: A, B, C, arms of the study; DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment.

Table 5 Comparison of efficacy of various biologics available in India for psoriasis

Investigators, trial and year	Biologic	Study group details	Dose	Efficacy
Sridhar et al,[21] 2006	Infliximab	Open-label pilot study (N=3)	5 mg/kg dose induction at 0, 2, and 6 weeks, followed up to 10 weeks	PASI 75 at week 10: 100%
Sub-analysis from FIXTURE, Bhat et al,[22] 2017	Etanercept	Randomized, double-blind, placebo-controlled, 52-week, phase III trial (N=149)	Induction with 50 mg twice weekly for 12 weeks, then weekly once	PASI 75 at week 12: 19.4%; 7% (placebo)
Sub-analysis from FIXTURE, Bhat et al,[22] 2017	Secukinumab	Randomized, double-blind, placebo-controlled, 52-week, phase III trial (N=149)	Induction with 300 mg and 150 mg once weekly for 5 weeks, then every 4 weeks	PASI 75 at week 12: 58.5% (300 mg/kg); 50% (150 mg/kg); 7% (placebo)
Kripashankar et al,[11] 2014	Itolizumab	Randomized, double-blind, placebo-controlled, phase III trial (N=225)	Two groups (A and B) with different dosing schedules: A, 0.4 mg/kg/week for 4 weeks, then 1.6 mg/kg every 2 weeks; B, 1.6 mg/kg every 2 weeks	PASI 75 at 12 weeks: 27% (A); 36.4% (B); 2.3% (placebo)

Abbreviation: PASI; Psoriasis Area and Severity Index.

received 1.6 mg/kg two weekly who received 1.6mg/kg of Itolizumab once in 2 weeks,[11] 27% in those who received 0.4 mg/kg/week for 4 weeks and then 1.6 mg/kg every 2 weeks of itolizumab,[11] and 19.4% in those who received etanercept.[22]

Conclusion

Psoriasis is a chronic inflammatory disease that can result in significant physical, psychological, and social morbidity with severe impairment of quality of life. Being a T-helper cell-mediated, type 1 immunological disease, it does not just affect the skin but goes more than "skin deep" and evokes a state of systemic inflammation.

Most of the conventional treatment modalities for psoriasis provide only temporary relief and are riddled with potential toxicities which result in high rates of treatment failures and dissatisfaction among these patients. Introduction of "biological" agent as a therapeutic option has revolutionized the treatment of psoriasis. The threshold for treatment success has now changed and achieving clear or almost clear skin with 90%–100% improvement in baseline PASI scores is most desirable and relevant. Until recently, biological treatment was limited to TNF-α inhibitors (infliximab, etanercept, and adalimumab), IL-12/IL-23 antagonist (ustekinumab), and IL-17 antagonist (secukinumab).

Itolizumab is a novel biological agent that targets CD6 receptors on T-cells. It has better side effect profile but lower efficacy than other biologicals. The clinical trials on its use in moderate-to-severe plaque psoriasis have shown that itolizumab has favorable clinical effects and a safety profile as monotherapy in patients who fail to respond to conventional systemic therapies. Few studies have also shown that itolizumab provides a longer remission even after treatment withdrawal. The drug was first approved in Cuba. Based on the multicentric clinical phase II and III trial results, the Drugs Controller General of India approved this drug in India in January 2013 for the management of plaque psoriasis.

Disclosure

The authors report no conflicts of interest in this work.

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