ABSTRACT
Our objective was to highlight the impact of psoriasis on patient’s quality of life, the existence of “high-need” patients and the correlation between new biological therapies and the increase of quality of life in psoriasis.

I order to do so, we presented the clinical effectiveness and side effects of Infliximab, Etanercept and Efalizumab.

It was pointed out that there is a higher percentage of patients that become clear or minimal affected in the treatment with all 3 drugs, with fewer side effects than in the traditional systemic treatment.

We conclude that these therapies, the so called biologics, aim to provide a selective, immunological directed intervention. Agents targeting TNF – alfa and agents targeting T cells seem to have a great impact on the patient’s quality of life improvement.

Key words: biological therapy, quality of life, psoriasis
OBJECTIVE

Background

Psoriasis is an incurable, chronic and commonly persistent disease that can be associated with significant morbidity. Regardless of the disease extent, psoriasis can seriously compromise patient’s quality of life. Studies examining the impact of the disease have revealed that patients experience a quality of life reduction and some patients experience psychological distress mainly related to concerns over physical appearance (1).

Of all patients with psoriasis, 20-30% present the severe form of the disease. No curative agents are available and long-term administration of the systemic agents or phototherapy is generally limited due to toxicity (3).

Biological therapies available today, may represent the beginning of a new long-term control method of psoriasis management.

QUALITY OF LIFE

Psoriasis has a significant negative impact on patients’ health-related quality of life (HRQL) and psychosocial and physical well-being. The impact of psoriasis on physical functioning and mental health is comparable to that of many chronic diseases, including cancer, diabetes mellitus and cardiac disease. Many patients with psoriasis report frustration with current therapies, and clinical efficacy of a treatment has not necessarily correlated with improvements in the psychosocial or functional aspects of living with psoriasis. Psoriasis therapies are needed that improve patients’ well-being and ability to function, as well as improving the physical symptoms of this chronic, immune-mediated disease (2, 9, 13, 14, 22).

A new outcome measure for the composite assessment of the efficacy and safety of psoriasis treatment is the so called Safe Psoriasis Control. It assesses multiple dimensions of the disease such as efficacy, quality of life, safety data and at the end it shows the proportion of patients who had treatment benefit without major side effects.

Quality of life (QOL) measures are an important adjunct to skin lesion assessments to properly assess the full effect of an illness such as psoriasis that is not life-threatening. The Dermatology Life Quality Index or SKINDEX is very useful to assess the QOL impact of psoriasis, but has a limited correlation with the severity of psoriasis (21).

Other instruments in the QOL assessment of psoriasis patients are the Salford Index and the Koo-Menter Psoriasis Instrument. They were designed to help physicians to perform a complex evaluation of patients with psoriasis including the physical severity, QOL impact and arthritis issues (21).

THERAPY

Most cases of psoriasis are treated with topical therapy (dermatocorticoids, calcipotriol, calcineurin inhibitors), but the majority of the patients (86%) report to be dissatisfied with it. Topical treatments are appropriate for patients who are candidates for localized therapy. The poor efficiency, time-consuming applicability on skin and cosmetic appeal, seem to be the major disadvantages of these treatments. Compliance is around 39% and it decreases further in younger patients (15).

Phototherapy is usually safe, effective and cost-effective. Narrowband UVB is more effective than broadband UVB and the treatment can be offered in the office or at home. Still UVB can often cause burnings, may cause concern over carcinogenicity and, in this case, it requires regular attendance at a clinic (21).

New studies show an increased efficacy of the excimer lasers which have the property that they can remove fine layers of surface material with almost no heating. PUVA therapy is considered effective in the majority of patients, with potential for long remissions, but it was associated with an increased risk of squamous cell carcinoma and possibly malignant melanoma in Caucasians. PUVA can also induce photoaging and the oral psoralen is contraindicated in pregnancy (21).

That is why, 40% of the patients with psoriasis would agree to use systemic therapy to control the disease and improve quality of life.

Systemic therapy, although it has serious side-effects, represents the traditional treatment for patients with extensive disease.

Methotrexate, Cyclosporine A and Oral Retinoids are effective agents and to be considered in case of severe, recalcitrant, disabling psoriasis that does not adequately respond to other forms of therapy, in a case of
psoriatic arthritis and in case of severe psoriasis including erythrodermic and pustular types (6).

Side effects may include:
- Hepatotoxicity – especially when use of Methotrexate
- Bone marrow depression with resultant anemia, leucopenia and/or thrombocytopenia – especially when use of Methotrexate
- Lung disease – especially when use of Methotrexate
- Skin reactions, malignant lymphomas and skin cancer – especially when use of Cyclosporine A
- Nephrotoxicity – especially when use of Cyclosporine A
- Hypertension – especially when use of Cyclosporine A
- Neurotoxicity and leukoencephalopathy
- Stomatitis, nausea, vomiting, diarrhea
- Opportunistic infections
- Gastrointestinal disorders
- Cheilitis, dryness, pruritus, skin peeling, alopecia, arthralgia, myalgia and ophthalmic effects – especially when use of Oral Retinoids.

Because of it’s teratogenic effect, Oral Retinoids should not be used in women who are pregnant or have a childbearing potential (21).

Recent clinical studies have suggested that the short – course therapy with Cyclosporine A brings significant improvement in all efficacy parameters at the end of each treatment period. This way, side effects would be less prominent and severe (5).

A wide research program in establishing the role of the immune system in the pathogenesis of psoriasis has led to the development of targeted therapies directed against key steps in the immunological cascade that produces psoriasis, the so called biological therapies or biologics.

**ELIGIBILITY CRITERIA**

Patients must have moderate-severe disease to be eligible for biological therapy. The PASI score (Psoriasis Area and Severity Index, range 0-72) must be 10 or more and the Dermatology Life Quality Index (DLQI) greater than 10 (range 0-30). Where PASI is not applicable, BSA (Body surface area) can be used and it must be at least 10 % (The Rule of 10) (8).

The disease should have been severe for 6 months, resistant to treatment and the patient should be a candidate for systemic therapy. Patients have to fulfill at least one of the following clinical categories (7,18):
- Are at risk or have developed clinically important drug-related toxicity
- Are intolerant to standard systemic therapy
- Are unresponsive to standard systemic therapy
- Have disease that can only be controlled by repeated in patient management
- Have coexisting, unrelated comorbidity
- Have pustular or erythrodermic psoriasis
- Have psoriatic arthritis

In clinical trials, until recently there has been mostly one eligibility criteria, the extent and character of the skin lesion. Nowadays, a key role is played by the impact of the skin lesions on patient’s lives which has to be corroborated with the severity of the skin lesion (21).

**THE DRUGS**

There are two main groups of biological therapist agents:
- Agents targeting TNF – alfa: Infliximab, Adalimumab, Etanercept
- Agents targeting T cells: Alefacept, Efalizumab and a new group of agents targeting the P40 protein family (IL-12/23): Ustekinumab

**CLINICAL EFFECTIVENESS/SIDE EFFECTS**

Infliximab is effective in the treatment of chronic plaque psoriasis. 82 % of patients become clear or minimal affected at 10 weeks after following 5mg/kg at weeks 0,2 and 6 and 91 % of patients after therapy with 10mg/kg. Therapy may be initiated at a dose of 5 mg/kg at weeks 0,2 and 6 and subsequent maintenance infusions given at 8-week interval. The drug may also be of value in generalized pustular psoriasis and for concomitant systemic therapies (4).

Side effects may include hypersensitivity reactions, hypotension, formation of autoantibodies and lupus-like syndrome, heart failure, sepsis, histoplasmosis, coccidiodomycosis, listeriosis, pneumocystosis, tuberculosis, other bacterial, mycobacterial and fungal...
infections, optic neuritis, seizures, malignancy (17).

**Etanercept** is also effective in the treatment of chronic plaque psoriasis. Treatment should be initiated at 25 mg twice weekly, but based on the individual patient basis it can be upgraded at 50 mg twice weekly, no more than 24 weeks. Results show that 56% of patients with a 25 mg X 2/week treatment for 24 weeks and 60% of patients with a 50 mg X 2/week treatment for 24 weeks become clear or minimal affected (12).

Side effects may include serious infections and sepsis, hypersensitivity reactions and rarely tuberculosis, pancytopenia, anemia, optic neuritis, formation of autoantibodies, and lupus-like syndrome, malignancy.

**Efalizumab** is effective in the treatment of moderate to severe chronic plaque psoriasis. The weekly dose of 1 mg/kg should be used and treatment should be discontinued after 12 weeks in those who do not respond.

Results show that one third of patients become clear or almost clear after 12 weeks. Administrated longer than 3 months it produces a constant growth of the PASI score (10, 11), (Figure 1).

Side effects may include infections, thrombocytopenia, malignancy, worsening of the disease during or after discontinuation.

**CHOICE OF DRUG TO USE**

In choosing the adequate biological therapy, the most important issue is the clinical pattern of psoriasis. The pre-existing comorbidity, local facilities, patient preference and prescriber preference should also be taken into consideration.

Etanercept should be used where there is a stale psoriasis and should be considered first choice for patients with uncontrolled psoriatic arthritis.

**FIGURES 1,2,3,4.** Clinical effectiveness of treatment with Efalizumab after 3 months (anterior and posterior view)
Infliximab is of value in erythrodermic or psoriatic arthritis and all other uncontrolled forms that require a rapid disease control.

Efalizumab should be considered first choice for patients with a risk of latent tuberculosis or demyelinating disease, but not in psoriatic arthritis. (16, 19).

CONCLUSION

In order to consider a treatment successful there must be a beneficial effect on HRQOL. There is no doubt that the impact of the new biological therapies on HRQOL is of great importance for patients and physicians.

A significant reduction in the impact of psoriasis on all aspects of HRQOL including daily activities, work, study, social functioning, personal relationships, can be reported already after a short period of treatment. With Infliximab, result can be seen as soon as after 3 weeks and after the 10-th week of treatment patients can report that psoriasis no longer has any effect on their HRQOL (20).

The characteristics of the chosen therapy may directly impact patients’ quality of life, requiring treatment to be adapted to the patient’s specific situation. In the case of patients with psoriasis of the palms and soles, the disease tends to have more impact than extensive involvement of the trunk. These patients should be considered candidates for systemic and biological therapies (21).

A full evaluation of the risk–benefit profile and cost-effectiveness of new biological treatments in patients with psoriasis is to be conducted.

REFERENCES