

YEAR BOOK OF DERMATOLOGY – 2018

PSORIASIS

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Foreword
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ARTICLE 1

Apremilast in Psoriasis–A Prospective Real-world Study

Vujic I, Herman R. Sanlorenzo M, et al. Apremilast in psoriasis - A prospective real-world study.
J Eur Acad Dermatol Venereol. 2018;32(2):254-9.

Abstract

Apremilast is an oral phosphodiesterase-4 inhibitor approved for the treatment of psoriasis. Various phase III trials have proved it to be safe and efficacious. This article is a prospective real-world study on the use and safety of apremilast in psoriasis and also to calculate the drug survival. About 48 patients were given apremilast and were evaluated every 4 weeks. The parameters evaluated were weight, height, age, joint involvement, PASI score, adverse effects and previous treatments. PASI 50, PASI 75 and PASI 90 were used to assess the efficacy of treatment.

COMMENT

This article is a prospective real-world study of the effect of apremilast in psoriasis patient. Apremilast is an oral phosphodiesterase-4 inhibitor used for psoriasis and psoriatic arthritis treatment.

A total of 48 patients were included in the study and the study was conducted over a period of 1 year 9 months.

The parameters studied were the drug survival (time from initiation to discontinuation of therapy) and the efficacy which was analyzed by means of PASI 50, PASI 75 and PASI 90 (Improvement in the psoriasis area severity index by 50, 75 and 90 points respectively).

The patients were followed up every 4 weeks and the parameters which were recorded in the proforma included the weight, height, age, family history, treatment history, presence of joint involvement, smoking status, PASI scores and the adverse effects if any (onset and duration).

The median drug survival was 12.5 weeks which can also be used as a measure of efficacy of the drug and compliance. PASI 50, PASI 75 and PASI 90 were achieved by eight, nine, and three patients respectively.

There was a negative impact of obesity on the PASI 50 response. Obese individuals have shown a less response to treatment in other studies as well and they also present with more severe disease.

Only 31 patients had adverse effects, the most common of which was diarrhea followed by headache and joint pain but none severe enough to stop treatment.

The trials done for apremilast in were ESTEEM and PALACE which showed significant greater results than in this real-world trial.

More long-term studies with a larger number of subjects are needed on apremilast to confirm these findings. Wide spread availability of apremilast with cost-effective rates in developing countries compared to developed countries will help in performing these studies.

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Key Messages

- ***Even with the difference in the results between trial and real-world patients, apremilast has shown to be effective in the treatment of psoriasis with up to 40% patients reaching PASI 50 or higher***
- ***Body weight affects drug response with considerably less response being seen in obese individuals.***

ARTICLE 2

Comparative Effectiveness of Abatacept, Apremilast, Secukinumab and Ustekinumab Treatment of Psoriatic Arthritis: A Systematic Review and Network Meta-analysis

Kawalec P, Holko P, Moćko P, et al. Comparative effectiveness of abatacept, apremilast, secukinumab and ustekinumab treatment of psoriatic arthritis: A systematic review and network meta-analysis.
Rheumatol Int. 2018;38(2):189-201.

Abstract

The objective of this article was to find out the comparative efficacy and safety of biologic therapies especially non-anti TNF-α agents in the treatment of psoriatic arthritis.

A systematic review and meta-analysis was done according to PRISMA requirements by two investigators of several studies including randomized control trials. The criteria taken into consideration were ACR20, ACR50, PASI, PASI 75, safety outcomes and serious adverse effects. Secukinumab gave the best ACR20 endpoint in patients who were not treated with anti-TNF- α whereas secukinumab and apremilast had the highest benefit in patients previously treated with anti-TNF-α. Secukinumab was safest in terms of overall adverse effects, whereas ustekinumab had the lowest risk of severe adverse effects.

COMMENT

This article is a review and meta-analysis to compare the efficacy and safety of non-anti-tumor necrosis factor-α (TNF-α) novel biologic therapies in the treatment of psoriatic arthritis (PsA).

Traditionally treatment for PsA starts with disease-modifying antirheumatic drugs and non-steroidal anti-inflammatory drugs. If the patient does not respond or is intolerant to this, then tumor necrosis factor-α inhibitors (TNF-α I) such as etanercept, golimumab, infliximab and adalimumab are used. In patients who show primary or secondary non-responsiveness to TNF-α I, other biologics need to be given such as abatacept, secukinumab, ustekinumab, and small molecules such as apremilast.

Ustekinumab is a human immunoglobulin G1 which binds to the common p40 subunit which is present in both IL-23 and IL-12 and is involved in PsA pathogenesis. Secukinumab is a human immunoglobin-G1 monoclonal antibody which binds selectively and neutralizes IL-17A. Abatacept is a full

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human fusion protein which binds to CD86 and CD80 and thus inhibits T cell activation and decreases serum levels of inflammatory proteins and cytokines which are involved in PsA pathogenesis. Apremilast is oral phosphodiesterase 4 inhibitor that increases expression of anti-inflammatory mediators like IL-10 and decreases the expression of inflammatory cytokines.

Ustekinumab, apremilast, secukinumab and abatacept need to be used for a period of 28, 24, 16–24 and 24–26 weeks respectively and hence follow-ups in trials with similar duration were taken for the review.

The parameters studied were ACR20 (American College of Rheumatology 20% improvement) criteria, Psoriasis Area Severity Index (PASI) score, PASI 50, PASI 75 and PASI 90.

Eligible studies were identified by searching MEDLINE via Cochrane library, Embase and PubMed and a systematic review was done using the recommendations and methods from PRISMA extension statement for reporting of systematic reviews.

In anti-TNF-α naïve population, abatacept and secukinumab were better and in patients with anti–TNF-α-failure secukinumab and apremilast were better followed by ustekinumab when ACR20 was considered. Secukinumab 150 mg and ustekinumab were safest options considering severe adverse effects and withdrawals.

Key Messages

- ***Secukinumab in a dose of 150 mg and 300 mg had the highest ACR20 endpoint in overall population and anti-TNF-α-naive subpopulation.***
- ***In the anti-TNF-α-failure population, secukinumab 300 mg and apremilast 30 mg had the highest rank***
- ***Secukinumab in a dose of 300 mg was the safest when any adverse effects were considered and ustekinumab in a dose of 90 mg was safest when risk of severe adverse effects were considered.***

ARTICLE 3

Management of Common Side Effects of Apremilast

Langley A, Beecker J. Management of common side effects of apremilast.
J Cutan Med Surg. 2018;22(4):415-21.

Abstract

Apremilast is a new small molecule which inhibits phosphodiesterase 4 and thereby inhibits the production of pro-inflammatory cytokines and increases the synthesis of anti-inflammatory cytokines. Though this is portrayed as a safer drug, it is not free from side effects. The commonly reported side effects reported are nausea, diarrhea, headache and nasopharyngitis. Though these side effects are easily manageable, adequate counseling to the patient before starting the drug is necessary, as it may lead to non-adherence and discontinuation by the patient himself/herself. This article provides the clear management of the side effects noted with the approved dose of 30 mg BD dosing of apremilast.

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COMMENT

Apremilast is indicated for the treatment of moderate-to-severe psoriasis in patients who could not tolerate other systemic agents or those in which phototherapy could not be given. This drug can also be given in psoriatic arthritis when the other classical disease-modifying antirheumatic drugs (DMARDs) fail to provide response. This drug acts by inhibiting phosphodiesterase 4, wherein the intracellular levels of cyclic adenosine monophosphate (cAMP) increase due to its decreased degradation and thereby the levels of pro-inflammatory cytokines like Tumor necrosis factor (TNF)-α, IL-17 and IL-23 are decreased. The drug is safe but has relatively mild side effects like nausea, vomiting, diarrhea and nasopharyngitis.

Various clinical trials have been conducted to determine the safety and efficacy of apremilast in the long-term treatment of psoriasis. The trials which have been conducted so far are the ESTEEM 1, ESTEEM 2, PALACE 1 and PALACE 2. These studies are the pioneers that lead the Food and Drug Administration (FDA) to approve the drug in 2014 for the said indication. Other trials for apremilast include the LIBERATE, phase 3 trial by Ohtsuki et al. and phase 2 trial by Papp et al. In this article the data from Ohtsuki et al. are presented which included the approved 30 mg twice daily dosing of apremilast. The clinical trial for psoriatic arthritis included the ACTIVE trial which presented the results of its phase 3b trial on 2016.

The incidences of the common side effects are presented in terms of exposure adjusted incidence rates (EAIR). In this article, the EAIR from all the studies except for ACTIVE will be provided.

The most frequently reported side effect of apremilast is diarrhea. Diarrhea is commonly seen during the first 2 weeks of treatment with apremilast and does not last longer than 1 month. The diarrhea is usually self-limiting and severe medications can be used to control it. The drugs commonly used are loperamide and bismuth subsalicylate. Treatment for diarrhea was given in 12% of patients in ESTEEM trials and 21% of patients in PALACE trials. The diarrhea caused by apremilast is mainly secretory in nature, the mechanism is due to inhibition of phosphodiesterase 4 enzyme which causes accumulation of cAMP in the enterocytes lining the gut mucosa which in turn activate the chloride channels. The activated chloride channels promote fluid secretion into the lumen diluting the luminal contents. However, the diarrhea caused by this mechanism does not last more than 2 weeks due to upregulation of other compensatory phosphodiesterases. The initial management for diarrhea includes adequate hydration, taking split meals and avoiding foods like dairy products and caffeine. Refractory diarrhea defined by three or more loose/liquid stools per day can be treated with fiber supplementation like psyllium husk powder. The drugs which can be used are bismuth subsalicylate and loperamide. If the problem persists even after treatment, opinion from medical gastroenterologist can be obtained and later adjustment of the dose or discontinuation can be done.

The second commonly reported side effect is nausea. The mechanism for nausea in these patients are due to increased trigger of chemoreceptor trigger zone and action on central neurokinin receptors. Management for nausea includes following general measures like adequate hydration, taking split meals, avoiding exercise and avoiding excessive water during meals. Drugs like diphenhydramine, ondansetron, amitriptyline and promethazine can be given if general measures fail.

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The third common side effect in apremilast patients is headache. The mechanism of headache is not known. Initial measures like adequate sleep, adequate hydration and managing stress levels. Drugs like acetaminophen can be taken for initial management. Later non steroidal anti-inflammatory drugs (NSAIDs) can be given if the headache is severe.

The other side effect noted with apremilast is nasopharyngitis/upper respiratory tract infection. The general measures like hydration, sleep, avoiding nasal irritants and practicing hand hygiene are advised. Drugs like nasal decongestants and analgesics can be used.

Key Messages

- ***Apremilast is a safe drug approved for moderate-to-severe psoriasis***
- ***Side effects noted with this drug are nausea, diarrhea, headache and nasopharyngitis***
- ***The above-mentioned side effects can be managed with general measures and if severe, with drugs***
- ***If the side effects are very severe, discontinuation of the drug or dose alteration can be done.***

ARTICLE 4

Apremilast for the Treatment of Moderate-to-Severe Palmoplantar Psoriasis: Results from a Double-Blind, Placebo-Controlled, Randomized Study

Bissonnette R, Haydey R, Rosoph LA, et al. Apremilast for the treatment of moderate-to-severe palmoplantar psoriasis: Results from a double-blind, placebo-controlled, randomized study.
J Eur Acad Dermatol Venereol. 2018;32(3):403-10.

Abstract

Palmoplantar psoriasis has a significant effect on the quality of life of patients. Apremilast has been known to have significant benefit in palmoplantar psoriasis especially in combination with acitretin and/or phototherapy. The objective of this study was to evaluate the effect of treatment of moderate-to-severe palmoplantar psoriasis with apremilast on the work productivity and the quality of life of patients.

COMMENT

This was a randomized, double-blind, placebo-controlled study to assess the use of apremilast in the treatment of moderate-to-severe palmoplantar psoriasis. Apremilast is a phosphodiesterase 4 inhibitor used for the treatment of psoriasis and psoriatic arthritis.

In this study, 100 patients with moderate-to-severe palmoplantar psoriasis were studied. They were randomized into two groups. One group received apremilast in a dose of 30 mg twice a day and the second group received placebo. This was given for

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a period of 16 weeks. At the end of week 16, both groups received apremilast in a dose of 30 mg twice a day which was continued till week 32.

The endpoint studied was the ratio of patients achieving a PPPGA (Palmoplantar Psoriasis Physician Global Assessment) of 0 or 1 by the end of week 16.

No significant difference was seen in the proportion of patients achieving a PPPGA or 0/1 in the two groups by week 16 [(p = 0.1595) <0.05]. At the end of 32 weeks of treatment a PPGA of 0/1 was achieved by 24% of the patients.

Even though there was no significant increase in proportion of patients achieving a PPGA of 0/1 in the apremilast group, there was a significant improvement in secondary end-points in the apremilast group.

There was greater proportion of achievement of PPPASI 75 (75% reduction in the palmoplantar psoriasis area severity index), in improvement of PPASI, reduction of activity impairment and improvement in Dermatology Life Quality Index (DLQI).

Further long-term studies are needed to confirm the findings in this study and to assess attainment of PPPGA of 0/1.

Key Message

- ***There is a significant improvement in the PPASI, reduction of activity impairment, improvement in quality of life and achievement of PPPASI 75 in patients with palmoplantar psoriasis as compared to placebo even though the difference proportion of patients achieving a PPGA of 0/1 was not statistically significant between the apremilast and placebo groups at week 16.***

ARTICLE 5

Long-term Safety and Tolerability of Apremilast in Patients with Psoriasis: Pooled Safety Analysis for ≥156 Weeks from 2 Phase 3, Randomized Controlled Trials (ESTEEM 1 and 2)

Crowley J, Thaçi D, Joly P, et al. Long-term safety and tolerability of apremilast in patients with psoriasis: Pooled safety analysis for ≥156 weeks from 2 phase 3, randomized, controlled trials (ESTEEM 1 and 2).
J Am Acad Dermatol. 2017;77(2):310-17.

Abstract

Various studies have been conducted regarding the safety and efficacy of apremilast but literature for long-term safety of apremilast is lacking. This randomized controlled trial was performed to analyze the long-term safety of oral apremilast, the finding reported for 0 to ≥156 weeks of exposure to the drug from the ESTEEM trial 1 and 2. The adverse events noted in the 0 to ≤52 weeks period were diarrhea, nausea, upper respiratory tract infection and headache. There was no new adverse event reported in the 0 to 156 week period. The serious adverse events like major cardiac events, malignancies and depression did not increase in comparison with the rates found during 0 to ≤52 week period. The limitations were high dropout rare. This study showed that apremilast has an acceptable safety profile and is generally well tolerated for 156 weeks.

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COMMENT

Psoriasis is a chronic systemic inflammatory disease characterized by episodes of relapses and remissions. The current systemic agents used for the treatment of psoriasis cannot be used long-term considering the safety, tolerability and inconvenience for the patients due to periodic laboratory investigations and regular monitoring.

Apremilast is a phosphodiesterase 4 inhibitor, approved in the United States and Europe for the treatment of psoriasis and psoriatic arthritis. This randomized controlled trial (RCT) was conducted in various centers in the United States and Europe to demonstrate the efficacy and safety of apremilast for moderate to severe plaque psoriasis and psoriatic arthritis.

In this RCT, patients aged more than 18 years with moderate to severe plaque psoriasis who were candidates for systemic therapy were enrolled. At the end of the week 52 visit, patients were eligible to continue apremilast for up to 4 additional years.

Exposure-adjusted incidence rates (EAIRs) were used to assess major cardiac events, malignancies, and serious infections. Safety findings are reported for 0 to 156 weeks from ESTEEM 1 and 2. The 0 to 156 week period included 1184 patients, treated with 30 mg of apremilast taken twice daily.

During the first 52 weeks of drug exposure, the common side effects encountered in >5% of patients were diarrhea, nausea, upper respiratory tract infection, nasopharyngitis and headache. From 0 to ≥156 week period, the rates of serious adverse events (AEs) did not increase from the rates found during the 0 to ≤52 week period. The serious AEs in ≥2 patients in any exposure period included coronary artery disease, acute myocardial infarction, osteoarthritis and nephrolithiasis.

Rates of serious infections remained low with long-term apremilast exposure; there were no serious opportunistic infections or reactivations of TB infection and no significant changes in laboratory test/report values. Depression was extemporarily reported by few patients at week 16, but the incidence of depression did not increase with longer apremilast use.

The lack of impact of apremilast on blood cell counts, serious opportunistic infections, serious infections, and malignancies suggested that apremilast does not appear to have immunosuppressive effects such as those associated with cyclosporine or tofacitinib. The dropout rate in this study was high, but not because of safety concerns.

Apremilast is a safe and well tolerated drug which can be given long-term even in patients with comorbidities. The ease of administration, lack of laboratory monitoring and no specific organ toxicities makes it an enticing option for psoriasis patients.

Key Messages

- ***Apremilast is a safe and well tolerated drug which can be given long term even in patients with comorbidities***
- ***The ease of administration, lack of laboratory monitoring and no specific organ toxicities makes it an enticing option for psoriasis patients.***

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ARTICLE 6

Secukinumab and Apremilast Combination Therapy for Recalcitrant Psoriasis

Hadi A, Lebwohl M. Secukinumab and apremilast combination therapy for recalcitrant psoriasis.
Journal of Psoriasis and Psoriatic Arthritis. 2017;2(2):59-60.

Abstract

Psoriasis is a chronic inflammatory disorder and affects the joints and the skin. It is associated with aberrant activity of Th1 and Th17 cells and is also associated with systemic inflammation. Many treatment options are available for psoriasis and combination treatment is also used. However a few cases are refractory to all modalities of treatment which indicates the need for newer innovative combination treatment for the management of refractory psoriasis and psoriatic arthritis. In this case report, a case of resistant plaque psoriasis was treated successfully with a combination of secukinumab and apremilast. This is the second reported case treated successfully with this combination.

COMMENT

This article is a case report of refractory psoriasis with psoriatic arthritis in a 61-year-old woman who treated with secukinumab and apremilast with significant improvement.

The patient has a 1-year history of psoriatic arthritis. She was initially started on adalimumab in a dose of 40 mg subcutaneously fortnightly. Subsequent to this she developed plaque psoriasis. This may be because of the development of paradoxical inflammatory disorders in patients treated with Tumor necrosis factor-α (TNF-α) inhibitors.

Subsequently the patient was treated with ustekinumab with no improvement which was followed by treatment with a combination of methotrexate and infliximab for a period of 10 months with not much improvement.

Secukinumab has already been proven to be effective in resistant cases of psoriasis in various studies. In this case, secukinumab produced a significant improvement in the psoriatic arthritis but only a modest improvement of the skin lesions. On introduction of apremilast, there was a significant improvement in both psoriasis and psoriatic arthritis. The patient was subsequently maintained on 300 mg of secukinumab monthly and 30 mg twice daily dose of apremilast with no adverse effects.

This is the second report of psoriasis patient resistant to other modalities of treatment being successfully treated with a combination of apremilast and secukinumab, the first being reported by Rothstein et al.

Apremilast is a phosphodiesterase4 inhibitor and has been shown to be effective in moderate-to-severe psoriasis. It has the benefits of being an oral therapy, not having the same risk of immunosuppression seen in biologics and not requiring any investigations for inception or monitoring of therapy. Apremilast has shown to be effective in combination

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with methotrexate, acitretin, cyclosporin, infliximab, adalimumab, ustekinumab and narrow-band ultraviolet B (NB-UVB).

Various combination therapies have been used in psoriasis which has proven to be effective in psoriasis refractory to monotherapy.

More case reports and studies are necessary to confirm the usefulness of secukinumab, apremilast combination in refractory psoriasis.

This combination may also prove to be expensive to the patient to continue on a long-term basis.

Key Messages

- ***Combination therapy of secukinumab and apremilast can be a promising treatment for the management of refractory psoriasis.***

ARTICLE 7

Apremilast: A Review in Psoriasis and Psoriatic Arthritis

Deeks ED. Apremilast: A review in psoriasis and psoriatic arthritis.
Drugs. 2015;75(12):1393-403.

Abstract

Apremilast is an oral phosphodiesterase 4 inhibitor used for the treatment of adult psoriasis and psoriatic arthritis. Sustainable improvements up to 52 weeks in case of psoriasis and up to 104 weeks in case of psoriatic arthritis have been seen in ESTEEM and PALACE trials respectively. Both of these are phase III clinical trials. Improvement was seen within 16 weeks in both the trials.

COMMENT

This study is a review article on the use of apremilast in psoriasis and psoriatic arthritis (PsA). Apremilast is a small molecule administered orally and inhibits phosphodiesterase 4 (PDE-4). It acts intracellularly to modulate pro and anti-inflammatory mediators. PDE-4 inhibition increases cyclic adenosine monophosphate (cAMP) levels which down regulates inflammatory mediators such as Tumor necrosis factor-α (TNF-α), IL-23 and increases anti-inflammatory cytokines like Interleukin 10 (IL-10).

This article takes into consideration the two major clinical trial programs done for apremilast in psoriasis namely ESTEEM 1 and 2 (Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis) and PALACE 1–3 (Efficacy and Safety Study of Apremilast to Treat Active Psoriatic Arthritis).

Apremilast showed significant improvement in the extent and severity of plaque psoriasis with improvement in the scalp, nail and palmoplantar lesions at 16 weeks with sustained benefits till 52 weeks as compared with placebo. Apremilast also showed significant improvement of PsA in patients even when treated with Disease-modifying antirheumatic drugs (DMARDs) in 16 weeks of

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treatment which was sustained till 104 weeks of treatment.

The most common early side effects were nausea and diarrhea which started in the first two weeks and resolved by 4 weeks of treatment. Upper respiratory tract infection and nasopharyngitis were seen in the later stages of treatment.

The review is based on only a few trials which were mainly conducted in western patients. A mention of a trial on Indian patients would also be helpful in guiding usage of this medication in the Indian subcontinent. Moreover, the ESTEEM trial had a high dropout rate of around 21% the reasons of which were not safety related. The cost of the medication may also prove to be a limiting factor in the usage of medication in India though the rates are less compared to biological agents.

Long-term tolerability and efficacy data would be useful especially since psoriasis is a chronic condition and medication is needed for a long period of time.

Key Messages

- ***The most common side effects in the initial stages of treatment with apremilast were nausea and diarrhoea and with continued treatment were upper respiratory tract infection and nasopharyngitis***
- ***Apremilast is a well-tolerated and effective drug in the treatment of psoriasis and psoriatic arthritis in adults with improvement in PsA being sustained for up to 104 weeks of treatment and improvement in skin lesions being sustained for up to 52 weeks of treatment.***

ARTICLE 8

Serum Squamous Cell Carcinoma Antigen in Psoriasis: A Potential Quantitative Biomarker for Disease Severity

Sun Z, Shi X, Wang Y, et al. Serum squamous cell carcinoma antigen in psoriasis: A potential quantitative biomarker for disease severity.
Dermatology. 2018;234(3-4):120-26.

Abstract

Serum squamous cell carcinoma antigen (SCCA) can be utilized to determine the association with disease severity and treatment in psoriasis patients. In this pilot study, 15 patients of psoriasis were treated with adalimumab after assessing psoriasis area and severity index (PASI) before and after treatment. The SCCA was detected using microparticle enzyme immunoassay. The SCCA levels were increased in patients with psoriasis and decreased levels were observed after treatment. Therefore, SCCA can serve as a useful quantitative biomarker for psoriasis disease activity.

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COMMENT

Squamous cell carcinoma antigen (SCCA) is a member of serpin family, used in the diagnosis of squamous cell carcinoma. Localization of SCCA in psoriatic epidermis varies depending on its concentration in the patient's sera.

With low levels of the SCCA, weak and scattered staining could be noted in the granular layer. When the concentration is more, there is strong staining from the suprabasal to the granular layer and condensed staining around the plasma membranes and intercellular region was noted in the affected epidermis.

This study was done with the objective of using biomarkers like SCCA in association with disease severity and treatment response in psoriasis patients. In this study, 15 patients chosen were treated with adalimumab after calculating PASI score and body surface area (qBSA) before and after treatment.

SCCA was detected using microparticle enzyme immunoassay for both cases and controls. The serum SCCA level in psoriasis group was significantly higher than the control group. The levels of SCCA decreased after treatment and correlated well with PASI and qBSA.

SCCA contains two homologs, SCCA1 and SCCA2, which belong to the high molecular mass serine proteinase inhibitor superfamily, serpin. SCCA1 is very different from other serpins and inhibits papain-like cysteine proteinases, cathepsins K, L, and S. SCCA2 shows ordinary serpin-like properties and inhibits chymotrypsin-like serine proteinases, cathepsin G and mast cell chymase. SCCAs play a protective role against various proteinases in pathophysiologic events of psoriasis.

Upregulation of SCCA1 mRNA can be detected in the psoriatic skin when compared to the normal skin, whereas SCCA2 is not expressed in normal skin. SCCA2 is exclusively expressed in psoriatic skin. This suggests that SCCA1 is overexpressed in the psoriatic skin and SCCA2 is newly transcribed in psoriatic skin and is absent in normal skin.

Key Message

- ***Serum squamous cell carcinoma antigen might be a useful biomarker for detecting/testing psoriasis disease severity.***

ARTICLE 9

Long-term Real-life Safety Profile and Effectiveness of Fumaric Acid Esters in Psoriasis Patients: A Single-Centre, Retrospective, Observational Study

Dickel H, Bruckner T, Altmeyer P. Long-term real-life safety profile and effectiveness of fumaric acid esters in psoriasis patients: A single-centre, retrospective, observational study.
J Eur Acad Dermatol Venereol. 2018. doi:10.1111/jdv.15019.

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Abstract

Fumaric acid esters (FAEs) are used in the treatment of moderate to severe psoriasis. The long-term safety and effectiveness of FAE either as a monotherapy or combination treatment is not known. Therefore, this monocentric retrospective, observational study was performed to assess the long-term safety and efficacy of FAE monotherapy or combination with other therapies. The most common side effect observed was in the gastrointestinal tract. Adverse events leading to treatment discontinuation were observed in 12.9% of patients. A median duration of 1 year was observed in all three treatment subcohorts (p = 0.70) from initiation of FAE treatment to a 50% response rate, where response was defined as achieving a cumulative static Physician's global assessment (PGA) score of 'light' and at least a 2-point reduction in baseline PGA. Therefore, this study reveals that FAE either as monotherapy or combination are safe and beneficial for long-term use.

COMMENT

Psoriasis is a chronic inflammatory autoimmune disease affecting the skin and the joints mediated by Th1, Th2 and Th22 cells. It is the most frequent immune mediated disease in humans. Patients with moderate to severe psoriasis generally require long-term or even lifelong systemic therapies.

Fumaric acid esters (FAEs) are recommended in European guidelines for the induction and long-term treatment of adults with moderate to severe psoriasis. Schweckendiek was the first to describe the use of fumaric acid for the treatment of psoriasis. Commercially available fumaric acid esters are a mixture of dimethyl fumarate and calcium and magnesium salts of monoethyl fumarate.

The current evidence suggests that monomethyl fumarate is the pharmacologically active compound with immunomodulatory properties particularly inhibiting Th17 and Th1 responses in psoriasis.

The objective of the study was to examine the long-term safety and effectiveness of FAEs as monotherapy and in combination with phototherapy or methotrexate in patients with psoriasis treated at a single center in Germany.

This was a monocentric, retrospective observational study with a follow-up period of 32.5 years. The study included 859 patients of which 626 received FAE monotherapy, 123 received FAEs with concomitant phototherapy and 110 received FAEs with methotrexate. All the patients additionally received other topical treatments for psoriasis.

The mean patient age group was 46.3 years. Approximately one-third of patients had family history of psoriasis and two-thirds were smokers. Approximately half of patients (49.0%) reported adverse events (566 total events), most of which involved the gastrointestinal tract. Usually, the gastrointestinal symptoms are mild to moderate and resolve with continued treatment.

In this study, the symptoms were rarely severe, requiring discontinuation of the treatment. The other common side effect was flushing of the skin, which is not serious and resolves with the administration of acetylsalicylic acid. Hematological disorders like lymphopenia and eosinophilia were the third most reported adverse effect. Although opportunistic infections are rare, 19 cases of progressive multifocal leukoencephalopathy

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Year Book of Dermatology – 2018
PSORIASIS

Key Features

- The Year Book of Dermatology – 2018 *Psoriasis* brings to you a collection of meticulously chosen articles focusing on the latest advances in management of Psoriasis from various peer reviewed journals that were published in the previous year
- Each article has been reviewed by subject reviewers who have written comments on value of the article, previous knowledge on the subject, what the article adds to the prevailing knowledge and practices, strong points and weaknesses of the article, and other similar observations that have come in the last 12-month period
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