Drug Treatments in Psoriasis

Authors: David Gravette, Pharm.D. Candidate, Harrison School of Pharmacy, Auburn University; Morgan Luger, Pharm.D. Candidate, Harrison School of Pharmacy, Auburn University; Jay Moulton, Pharm.D. Candidate, Harrison School of Pharmacy, Auburn University; Wesley T. Lindsey, Pharm.D., Associate Clinical Professor of Pharmacy Practice, Drug Information and Learning Resource Center, Harrison School of Pharmacy, Auburn University

Universal Activity #: 0178-0000-13-108-H01-P  |  1.5 contact hours (.15 CEUs)
Initial Release Date: November 29, 2013  |  Expires: April 1, 2016
EDUCATIONAL OBJECTIVES

After the completion of this activity pharmacists will be able to:

• Outline how to diagnose psoriasis.
• Describe the different types of psoriasis.
• Outline nonpharmacologic and pharmacologic treatments for psoriasis.
• Describe research on new biologic drugs to be used for the treatment of psoriasis as well as alternative FDA uses for approved drugs.

INTRODUCTION

Psoriasis is a common immune modulated inflammatory disease affecting nearly 17 million people in North America and Europe, which is approximately 2% of the population. The highest frequencies occur in Caucasians with lower frequencies in African-Americans and Asian patients. Males and females are equally affected among each race. Psoriasis tends to have onset at two peak times during life) between the ages of 20-30 or 2) between 50-60 years old, with 75% of patients having onset before 46 years of age. It typically presents as thickened erythematous skin or dermal plaques covered with a silvery scale.

Psoriasis results from a complex interplay between genetic factors and environmental influences. When patients with genetic predispositions encounter a precipitating factor, there is the potential for an outbreak of psoriasis. Some of the common precipitating and environmental factors are injury to the skin, infections, drugs (beta blockers, nonsteroidal anti-inflammatory drugs, lithium, and antimalarials), smoking, alcohol consumption, obesity, and psychological stress. There are multiple influences on the development of psoriasis, but the interactions between the innate and acquired immune systems are the true underlying problem which allows for psoriasis lesions to occur.

The interplay between the innate and acquired immune systems allows psoriasis to proliferate and spread across large areas of the body if left untreated. The first step in a psoriasis outbreak is a trigger which stresses the epithelial cells. The stress on epithelial cells causes the release of cytokines such as interferon α-2, interleukin-1β, interleukin 6 and tumor necrosis factor α, which are all part of the innate immune system. These cytokines work to activate dendritic cells and start the inflammatory process. Activated dendritic cells migrate to regional lymph nodes to activate T-cells, which are part of the acquired immune system, and continue the inflammatory process. Multiple other cytokines and growth factors are also present resulting in new blood vessel growth, and increase cell turnover. The activated T-cells along with growth factors and cytokines (specifically interleukin 22) allow the body to continue the inflammatory response and increase the thickness and area of the lesion. These immune responses allow for many drugs which act as suppressors of immune processes to be effective in the treatment of psoriasis.

Almost 50% of patients over the age of 65 with psoriasis have comorbidities that increase their rates of mortality: It is pertinent to treat and manage not only psoriasis but other underlying diseases as well. These comorbidities can also be inflammatory and autoimmune related as is the case with Crohn’s disease or multiple sclerosis. They may also have other conditions such as psoriatic arthritis, metabolic syndrome, cancer and cardiovascular disease. Patients often suffer from psychological problems such as anxiety, depression, and even alcoholism which decreases their quality of life. It is uncertain why these diseases coincide with one another, but it is hypothesized that the chronic inflammatory nature of psoriasis is the underlying problem.

With the potential comorbidities associated with this disease, it is important to treat patients appropriately. The objective of this manuscript is to assist pharmacists on how to recognize psoriasis, how to treat psoriasis, and understand the future research to improve on outcomes and decrease flare-ups.

DIAGNOSIS

There are several forms of psoriasis each of which have distinguishing characteristics that allow dermatologists to identify what type or types are present. This is done by conducting a visual inspection of the patient’s skin, nails, and scalp along with a family history. Psoriasis is diagnosed based on characteristics of the lesion and generally does not require any laboratory tests. A skin biopsy may be suggested to confirm the diagnosis in order to rule out other skin conditions such as eczema, ringworm, seborrheic dermatitis, lichen planus, and rosea.

Psoriasis is classified as mild, moderate, or severe based on common tools including the determination of the area involved in relation to the whole body surface area (BSA), or Psoriasis Area and Severity Index (PASI). The PASI defines the severity, area of coverage, and lesion characteristics over four sections of the body: the head and neck, upper extremities, trunk, and lower extremities. The lesions are characterized by erythema, scaling, and induration. The PASI is a composite score that ranges from 0 to 72 and is often used in clinical trials to assess improvement of psoriasis. A 75% decrease in the PASI score (PASI-75) identifies effective improvements in disease treatment. When only using BSA, psoriasis severity can be categorized as limited when <5% of BSA is affected, and moderate to severe when >5% of the BSA is affected or affecting areas such as the hands, feet, face, or genitals.

TYPES OF PSORIASIS

Plaque Psoriasis:

Plaque psoriasis, also called psoriasis vulgaris, affects approximately 80% to 90% of patients with psoriasis and is shown in Figure 1. Out of this population of patients with plaque psoriasis approximately 80% have mild to moderate disease with the remaining 20% having moderate to severe plaque psoriasis. A patient with plaque psoriasis typically presents with well defined, raised, and thickened patches of erythematous or salmon color plaques. These plaques are oval shape, and are covered by silvery-white scales ranging in size from 1 cm to several centimeters. Plaque psoriasis most often appears on the elbows, knees, scalp,
chest, buttokcs, limbs and lower back. The number of plaques is variable and may consist of a few lesions or numerous lesions which can nearly cover the entire body. Plaque psoriasis begins as small red bumps that gradually enlarge, and then form scales. The red bumps develop into plaques which are reddish areas of raised, thickened skin that can become dry, itchy, and can bleed or crack. This can causes discomfort especially when the lesions are over joint lines or on the palms and soles.10

Guttate Psoriasis

Guttate psoriasis, as seen in Figure 2, is the 2nd most common type of psoriasis occurring in about 10% of cases and frequently occurs in young adults less than 30 years old.6 It also can appear in children in the last 2-3 weeks of an upper respiratory infection that involves Streptococcus pyogenes.7,10 Around 10% of patients with chronic plaque psoriasis will experience flares of Guttate during the course of their disease.6 Guttate psoriasis appears quickly after infection or other triggers such as cold, tonsillitis, chicken pox, or certain medications such as antimalarias and beta blockers. It is characterized by dewdrop like red dots anywhere from 1mm to 10mm, that usually form on the trunk, arms, legs and occasionally on the scalp, face and ears with fine scales.10 Guttate may be the first type of psoriasis an individual experiences. Often times if it is a mild outbreak it will go away on its own; however, although patients may experience repeated episodes, especially during respiratory infections or during long standing plaque psoriasis.6,10

Pustular Psoriasis

Pustular psoriasis, as seen in Figure 3, occurs in less than 5% of psoriasis patients and primarily presents in adults.6 Pustular psoriasis can be triggered by infections, sunburn, pregnancy, or medications such as lithium, systemic corticosteroids, or develop from plaque psoriasis.7 Pustular psoriasis can be divided into two forms: localized and generalized.

Localized pustular psoriasis is confined to certain areas. When it is on the ends of fingernails or toes is called acropustulosis which can result after a localized trauma.7 When it is confined to the palms and soles it is called palmoplantar psoriasis.6,11 This type is characterized by swollen erythematous skin dotted with pus filled lesions. As the pus filled lesions dry they leave behind a brown dot or scale. The lesions become sore and tender making it difficult for the patient to walk or use their hands. Palmoplantar pustulosis is predominantly found in women and is associated with smoking. It is now believed that palmoplantar pustulosis may not be a form of psoriasis due to lack of genetic association and could be considered a comorbidity rather than a form of psoriasis.

Generalized psoriasis is a rare form of pustular psoriasis, also known as von Zumbusch.9 Generalized psoriasis can be life threatening and hospitalization may be required. This type of psoriasis may be triggered by infection such as strep throat, suddenly stopping steroids, pregnancy, and taking certain medications such as lithium.5,7 Lesions are widespread, swollen, erythematous, and covered with pus filled blisters. Patients will also present with fever, chills, severe itching, rapid pulse rate, loss of appetite, anemia, and muscle weakness.

Inverse Psoriasis

Inverse psoriasis, shown in Figure 4, is an uncommon form of psoriasis that only occurs in skin folds most often present in the overweight patients.7 It is also known as intertriginous psoriasis, or called skin fold, flexural, or genital psoriasis. This is because it only occurs in skin folds such as in the axillary region, genital area, buttocks, under breasts and also may be seen on the back of the knees or elbows. The lesions tend to be characterized by having a shiny, smooth, erythematous, and inflamed plaque where scales typically do not form.3,6 The skin is very tender, and is easily irritated by rubbing and perspiration. Inverse psoriasis usually is accompanied by another form of psoriasis elsewhere on the body.4 Inverse psoriasis may be confused with candidal, intertrigo, and dermatophyte infections.4

Erythrodermic Psoriasis

Erythrodermic psoriasis, also known as exfoliative psoriasis, is the least common form of psoriasis, occurring in 1% to 2% of psoriasis patients and is shown in Figure 5.5 It may occur suddenly in patients that have never had psoriasis or evolve from chronic plaque psoriasis.6,7,11 Erythrodermic psoriasis is characterized by having lesions where the whole body surface if affected. The lesions have severe redness, shedding of the skin,
and have the appearance of being burnt. Due to the altered thermoregulatory properties of the erythrodermic skin it may cause the patient to experience fluctuating body temperature, fluid loss which may lead to dehydration, accelerated heart rate from increased blood flow to the skin, and severe pain and itching. Triggers include infection, emotional stress, alcoholism, medications (lithium, anti-malarial drugs, strong coal tar preparation, excessive potent corticosteroid use, or stopping psoriasis medications such as cyclosporine or methotrexate). Erythrodermic psoriasis can be life threatening, and generally requires hospitalization.\(^4\,^5\)

Nail Disease (psoriatic onychodystrophy)

Nail psoriasis, shown in Figure 6, can occur with any psoriasis subtype. Approximately 50% of all patients with psoriasis have distinctive fingernails changes and 35% have toenail involvement.\(^6\) These changes can include pitting which is the most common (small pits in nail plate causing defective nail formation), oil drop sign (orange yellow sub-ungual discoloration), onycholysis (separation from the nail plate), and dystrophy (misshaped or partial destroyed nail plates).\(^6\,^10\,^11\)

**General Approach and Treatment**

Recently there has been an increased awareness of the pathogenesis of psoriasis that has led to improved management of signs and symptoms.\(^8\) In addition, there has been an increase in the research and development of biological agents that target the specific pathways of psoriasis. Currently, about 80% of patients with psoriasis are classified as mild to moderate (PASI<10) indicating the use of topical therapies alone. However, if these topical treatments are sub-therapeutic or not practical, then phototherapy with or without systemic therapy may be warranted. In general the approach to therapy is to use both nonpharmacologic and pharmacologic treatments.\(^1\)

**Goals and Strategies of Treatment**

The general goals of therapy are to decrease plaques and scales, decrease itching and tearing, reduce frequency of flares, avoid medication adverse effects, provide cost-effective therapy, provide counseling for stress-reduction, and maintain and improve quality of life.\(^1\) Treatment of psoriasis is typically a combination of nonpharmacologic and pharmacologic therapies, and this combination is necessary to reduce triggers as well as treat symptoms.

According to the guidelines produced by the American Academy of Dermatology, treatment type is determined first by whether psoriatic arthritis is present with psoriasis.\(^19\) If psoriatic arthritis is present the proper course of therapy is to use anti-tumor necrosis factor (TNF) biologics with or without methotrexate; however, if the patient is negative for psoriatic arthritis the next step is to evaluate the degree of the disease. If the patient is diagnosed with severe disease, then phototherapy, systemic, or biologic therapy is recommended. If the patient has limited disease, topical or targeted phototherapy is recommended; however, if topical or phototherapy treatment is suboptimal, it is recommended to add phototherapy, systemic, or biologic therapies.

It is important to note that patients with limited disease should not immediately be treated with systemic agents if topical or phototherapy did not improve symptoms.\(^18\) This is due to the risks of adverse events. Prior to initiation of a systemic agent, a comprehensive medical history, physical exam, and medication history should be completed in order to obtain baseline data. This is required since at times the addition of other systemic agents and biologics may be necessary in some patients. It is important to note that treatment of psoriasis is patient specific and there is no uniform way to treat patients.

**Treatments**

**Nonpharmacologic**

There are nonpharmacologic therapies that can be useful in reducing and improving signs and symptoms of psoriasis and are useful to reduce triggers and causes of flare-ups.

Stress reduction, such as exercise and meditation, may be used to reduce the extent and severity of psoriasis.\(^1\) Another option is nonmedicated moisturizers such as over the counter lotions or creams that do not contain corticosteroids. These products are used to maintain moisture, reduce shedding, control scaling, and reduce itching. These options are used as adjuncts to other topical agents, phototherapy, or systemic agents. They are thought to create a film over the affected area of skin allowing moisture to remain on the skin surface.\(^12\) Nonmedicated moisturizers are also safe to use in pregnancy and have no known contraindications. These products may be used up to three times daily on the affected area. Oatmeal baths may be used to reduce itching and their continued use may also reduce the need for antipruritic systemic agents.\(^1\) Sunscreen with a sun protection factor (SPF) of 30 or greater is recommended in order to avoid sunburn. Lastly, lukewarm water and lipid-free soaps should be used while skin irritants such as harsh soaps or detergents should be avoided. These nonpharmacologic treatments may be used in combination with pharmacologic agents in order to reduce or improve signs and symptoms of psoriasis.

**Topical Therapy**

As stated previously, most patients with psoriasis are considered to have mild to moderate disease that can be treated with pharmacologic topical agents.\(^12\) These topical agents can be used in adjunct with phototherapy or systemic therapy, and have been found to increase efficacy when used in combination. Topical therapy should be personalized for each patient depending...
on extent of disease, body location, type and characteristics of psoriasis, and degree of erythema and scaling. Patients need to be aware that topical therapy requires continuous application and lifetime remission may be difficult. The major limitation to using topical therapy is medication adherence. Age, cost, side effect profile, and inconvenience are the most unfavorable factors; therefore, it becomes extremely important to individualize therapy to what the patient will be comfortable with as well as stay adherent to.

Corticosteroids

Corticosteroids are widely used and considered first line medications for patients with mild to moderate psoriasis with ointments being the most effective vehicle.\(^{12,13}\) These formulations have anti-inflammatory effects, antiproliferative effects, immunosuppression, and cause vasoconstriction mediated by intracellular binding. There are a variety of strengths available for corticosteroids, and they are classified based on their ability to cause vasoconstriction.\(^{12}\) Table 1 below defines the classifications of corticosteroids.\(^{12,13}\)

Topical steroids are recommended for the use in plaque psoriasis.\(^{12}\) As monotherapy corticosteroids should be used 1-2 times per day. The highest strength corticosteroids should be used for 2-4 weeks with a gradual reduction based on clinical response.

Common adverse effects include atrophy of the skin, "spider veins", and permanent striae.\(^{12}\) These occur when used for long periods of time, if too much is administered, or if the skin is too sensitive. Systemic adverse effects, like adrenal suppression, are rare but may occur due to increased frequency or longer duration.\(^{12}\)

Corticosteroids should be attempted first due to their safety profile and efficacy for treating psoriatic skin lesions.\(^{12,13}\) They can be used as monotherapy or in combination with other topical agents, phototherapy, or systemic agents.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Strength</th>
<th>Example</th>
<th>Location for use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1</td>
<td>Superpotent</td>
<td>Clobetasone propionate 0.005% Betamethasone dipropionate 0.05%</td>
<td>Tough, thick and chronic plaques</td>
</tr>
<tr>
<td>Class 2</td>
<td>Potent</td>
<td>Amcinonide 0.1% Flucinonide 0.05%</td>
<td>Tough, thick and chronic plaques</td>
</tr>
<tr>
<td>Class 3</td>
<td>Upper Middle</td>
<td>Fluciasone propionate 0.005% Mometasone furoate 0.1%</td>
<td>Tough, thick and chronic plaques</td>
</tr>
<tr>
<td>Class 4</td>
<td>Middle</td>
<td>Betamethasone valerate 0.12%</td>
<td>Tough, thick and chronic plaques</td>
</tr>
<tr>
<td>Class 5</td>
<td>Lower Middle</td>
<td>Fluticasone propionate 0.05% Triamcinolone acetonide 0.1%</td>
<td>Face, thin skin, and skin folds</td>
</tr>
<tr>
<td>Class 6</td>
<td>Mild</td>
<td>Desonide 0.05% Fluocinonide acetonide 0.01%</td>
<td>Face, thin skin, and skin folds</td>
</tr>
<tr>
<td>Class 7</td>
<td>Least Potent</td>
<td>Hydrocortisone 0.5%, 1%, 2% or 2.5%</td>
<td>Face, thin skin, and skin folds</td>
</tr>
</tbody>
</table>

Vitamin D Analogues

Two topical vitamin D3 products currently available include calcipotriene (Dovonex) and calcitriol (Vectical).\(^{13}\) These two agents are roughly equivalent to a medium-potent corticosteroid and are used for mild to moderate plaque psoriasis. It is hypothesized that these agents act by binding vitamin D receptors and lead to inhibition of cell proliferation and differentiation. These agents are effective alone, but can provide additional benefits when combined with corticosteroids. Vitamin D analogues should be applied twice a day. Vitamin D analogues can be considered a second line therapy after corticosteroids. Typically these products are used in combination with corticosteroids or phototherapy, and a combination of calcipotriene and betamethasone propionate. There are no contraindications with vitamin D analogues and ultraviolet B (UVB) wave therapy; however, ultraviolet A (UVA) waves inactivate vitamin D analogues and therefore should be applied after UVA therapy.

Common adverse effects include itching, burning, skin discomfort, peeling, and erythema, but as treatment continues the side effects should diminish.\(^{12,13}\) Systemic side effects, like hypercalcemia and parathyroid hormone suppression, can occur but are rare.

Tazarotene

Tazarotene (Tazorac) is categorized as a topical acetylenic retinoid, and acts to normalize skin cell differentiation, decrease hyperproliferation, and reduce the expression of inflammatory markers.\(^{12,13}\) It has been effective in treating plaque psoriasis, and in some individuals the effects of therapy are seen even after therapy has stopped.

Tazarotene should be applied once a day and is most effective when used in combination with topical corticosteroids.\(^{12}\) There is a potential for tazarotene to be photosensitizing and therefore caution needs to be taken when combining with phototherapy (Menter, section 3). As a retinoid, tazarotene is teratogenic and is a pregnancy category X, even though systemic absorption is minimal.\(^{12,13}\) Common adverse effects with the gel formulation are erythema, burning, itching, and peeling; therefore, the cream is better tolerated with peeling being the most frequent side effect.\(^{13}\)

Tacrolimus and Pimecrolimus

Categorized as topical calcineurin inhibitors, tacrolimus and pimecrolimus act to inhibit synthesis of inflammatory cytokines.\(^{12}\) These agents cannot penetrate through thick plaques, but are beneficial for thinner areas of the skin, such as face and skin folds and should be applied twice a day. The most common adverse effects of burning and itching are reduced as therapy continues. Calcineurin inhibitors should not be applied immediately after bathing. In addition, caution should be taken in patients that are receiving phototherapy in order to reduce the risk of malignancies. Calcineurin inhibitors should only be considered for thinner areas of the skin, and should only be attempted after other agents have failed.
Phototherapy

Phototherapy is considered to be efficacious, cost-effective, and in general lacks systemic immunosuppression. Phototherapy acts locally to suppress the skin cells and indirectly effects cytokines and other immune system functions.

UVB phototherapy can be used in monotherapy or in combination with topical agents or systemic agents. UVB is used when psoriasis is extensive or unresponsive to topical therapies. Narrow-band UVB lamps have improved the use of UVB and have also been more effective than the traditional broad-band UVB therapy. Emollients enhance the transmission of UV waves and improve the efficacy of the phototherapy. In particular topical tazarotene, when used in combination with UVB, may improve the efficacy of the UVB wave. UVB phototherapy can also be combined with systemic and biologic agents, and it has been determined that methotrexate and retinoids improve phototherapy. On the contrary, cyclosporine and biologics have not been as extensively studied and should be used with caution. Common adverse effects of both types include burning, itching, and stinging while some more serious side effects include lesional blistering.

Psoralen plus ultraviolet A (PUVA) therapy is a technique that uses a photosensitizing agent, 8-methoxypsoralen, to improve cell sensitivity to UVA light. This type of phototherapy is an effective treatment based on its ability to penetrate the skin and effect dendritic cells, fibroblasts, and inflammatory cells. However, there is an increased risk of skin cancer and therefore caution should be taken.

In general, phototherapy is an effective option for patients with unresponsive psoriasis or extensive disease (PASI >10). Prior to therapy, a complete patient and family history as well as physical exam should be acquired in order to determine if a patient is a candidate. Although phototherapy is an effective option, it can be time consuming and requires multiple courses of treatments at the doctor’s office or at home using a recommended phototherapy lamp. As with all therapies for psoriasis, treatment is patient dependent and treatments need to be tailored to each individual.

SYSTEMIC THERAPY

In general, systemic agents have been reserved for extensive psoriasis in which topical therapy or phototherapy were ineffective, or patients with a PASI >10. More recently systemic therapy has been used in patients with severe psoriasis of the palms and soles or severe scalp psoriasis. Traditional systemic agents are still used for psoriasis based on their oral administration and low cost verses the newer biologic agents.

Methotrexate

Methotrexate is the most common systemic therapy for psoriasis. It competitively inhibits dihydrofolate reductase and therefore inhibits proliferation of immune tissue. Methotrexate is indicated to control severe psoriasis that is unresponsive to topical treatment and phototherapy.

Methotrexate should be given in low doses of 7.5mg to 25mg once a week and doses should be tailored to the lowest effective dose in order to control disease signs and symptoms as well as side effects. Patients need to be aware that following dosage adjustments, clinical effects may take up to four weeks. In addition, patients may taper off methotrexate and reintroduce when psoriasis reoccurs. Common adverse effects include nausea, abdominal discomfort, and fatigue. Serious side effects include hepatotoxicity and hematologic toxicity indicating the importance of gradually and slowing adjusting doses as well as patient history and closely monitoring lab results. Due to methotrexate’s immunosuppressive characteristics, it should not be used in those with active infections, such as hepatitis B or C and tuberculosis. Methotrexate is teratogenic and therefore contraindicated in pregnancy.

Cyclosporine

Classified as a calcineurin inhibitor, cyclosporine is as effective for psoriasis as methotrexate. Cyclosporine acts by inhibiting T-cell activation and therefore produces an immunosuppressive response.

Cyclosporine should be administered consistently at the same time of day. The solution can be mixed with milk or orange juice, but not grapefruit juice due to cytochrome reactions. An initial dose of 2.5 to 3mg/kg in two divided doses is recommended. This stable dose should be maintained for four weeks before dosing adjustments are made. Dose increases should be made in increments of 0.5 mg/kg/day until control of disease signs and symptoms is met. A maximum dose of 5 mg/kg/day is appropriate for psoriasis patients. The most common and serious adverse effects include hypertension and nephrotoxicity. Therefore, renal function and blood pressure should be monitored regularly. It is also important to accurately obtain information about the patient’s current medications due to the risk of drug interactions. Antifungals, diuretics, and calcium channel antagonists are a few medication classes that may interfere with cyclosporine.

Retinoids

Oral retinoids are known to alter skin cells proliferation and differentiation as well as anti-inflammatory activity. Acitretin replaced etretinate, and is considered a practical alternative to methotrexate and cyclosporine. Acitretin is predominantly efficacious for erythrodermic and pustular psoriasis. Retinoids are not immunosuppressive and may be more effective in those with chronic infections or malignancies. In addition, acitretin is more effective when used with phototherapy.

Acitretin 10-50 mg/day in a single dose is recommended in order to reduce the area and severity of psoriasis. There have been reports of synergy with UVB or UVA therapy indicating that the dose of phototherapy should be reduced. Common adverse effects include skin and mucous membrane dryness, dyslipidemia, altered liver function tests, myalgia, reversible alopecia, and sweating. Based on these side effects it is important to monitor liver function tests, lipid profiles, and gather patient history. Acitretin is teratogenic and therefore is contraindicated in pregnancy.
BIOLOGIC THERAPY

Biologic agents are divided into three separate groups: TNF inhibitors, IL-12/23 antibodies, and immune suppressants. These agents are more expensive than the traditional systemic agents available, but may not be any more effective. When compared to methotrexate, adalimumab (Humira) did show greater efficacy; however, long-term safety is still a concern for the biologic agents. Biologics target the immune system and therefore it is necessary to monitor for infection. Prior to biologic treatment, a complete patient medical history, family history, and current medication list should be obtained as well as baseline lab data. Once patient background information is obtained, a proper course of treatment may be initiated.

TNF Inhibitors

Tumor necrosis factor (TNF) is an important inflammatory cytokine involved in the pathogenesis of psoriasis. Inhibition of this process leads to a decrease in inflammation and clinical improvement of symptoms. Currently there are four TNF-inhibitors indicated for psoriasis: adalimumab (Humira), etanercept (Enbrel), golimumab (Simponi), and infliximab (Remicade). In general TNF-inhibitors are contraindicated in patients with active and serious infections, which may cause demyelinating diseases (ie, multiple sclerosis), and may cause worsening congestive heart failure. Common adverse effects for all four TNF-inhibitors include injection site reactions, drug-induced lupus, and abnormal liver function tests.

All four medications play a role in treating psoriasis. Adalimumab and etanercept are indicated for moderate to severe psoriasis and psoriatic arthritis. Infliximab is indicated for severe psoriasis as well as moderate to severe psoriatic arthritis. Adalimumab is recommended as a subcutaneous injection of 80 mg the first week, 40 mg the second week, then 40 mg every other week; etanercept subcutaneous injection of 50 mg twice per week for 3 months followed by 50 mg once per week; and infliximab infusion of 5 mg/kg at weeks 0, 2, and 6, then every 6-8 weeks, the and dose and interval may be adjusted as needed. Golimumab is indicated only for psoriatic arthritis and is dosed as 50 mg subcutaneous injection once a month.

IL-12/23 Antibodies

Ustekinumab (Stelara) is a monoclonal antibody that is targeted against interleukin (IL) 12 and 23. It is the only interleukin antibody that is approved for the treatment of moderate to severe psoriasis with an approved dosing of 45 mg subcutaneous injection initially and 4 weeks later followed by 45 mg every 12 weeks for patients 100 kg or less. For patients greater than 100 kg, use 90 mg subcutaneous injection initially and 4 weeks later, followed by 90 mg every 12 weeks. Clinical improvement may be seen 24 weeks following initial therapy. Common adverse effects include injection site reactions, headache, and arthralgia. As with other biologics, caution should be taken in patients with chronic infections. When compared to the TNF-inhibitors, ustekinumab does not induce demyelinating diseases and therefore may be a preferred treatment in patients at risk.

Immune Suppressor

Alefacet (Amevive) acts binding CD2 on T lymphocytes and which inhibits the activation and reduces the number of T cells. This agent is approved for adults with moderate to severe chronic plaque psoriasis. Alefacept may be used if the patient is a candidate for systemic therapy or phototherapy. Prior to therapy and throughout therapy, a CD4 T-lymphocyte count must be measured. Patients cannot receive alefacept if CD4 is below normal due to chronic infection or if patients are infected with HIV due to the risk of CD4 depletion. Dosing is 15 mg every week as an intramuscular injection for 12 weeks, then a 12-week follow-up nontreatment period. Common adverse effects include injection site reaction and chills.

FUTURE PROGRESS

The current treatment of psoriasis has led to the incorporation of biologic agents and small molecules. These agents have multiple mechanisms of action to try to treat this multi-faceted disease. Also in the same light many companies are now making free apps for patients and health care providers to allow for the best treatment and management of symptoms. The use of technology is truly changing psoriasis treatment.

The American Academy of Dermatology has released a free app for healthcare providers to help with the management of psoriasis and psoriatic arthritis. This app takes the current guidelines published in the Journal of the American Academy of Dermatology and puts them into easy to read formats with categories that allow providers to assess evidence based treatment options in a timely manner. Many other apps are currently available for patients and health care providers which help to quickly and efficiently answer questions, determine PASI scores, track adverse drug reactions, and monitor psoriasis symptoms. Other changes that are occurring in psoriasis treatment is the development of new biologic drugs such as CEP-37247, SCH900222, CNTO1959, secukinumab, and ixekizumab as well as finding alternate FDA uses for approved drugs such as abatacept, and certolizumab-pegol.

Certolizumab-pegol, an anti-TNFα drug currently used for Crohn’s disease and rheumatoid arthritis (RA), has completed a 12 week phase II, double blind, placebo controlled clinical trial and is showing promise. The drug showed a statistically significant decrease in signs and symptoms of psoriasis based on a greater than 75% improvement in baseline PASI. This was seen in 75% of the patients taking certolizumab-pegol 200mg SC and 83% of patients who were taking the 400mg dose. Another anti-TNFα drug in the pipeline for treatment of psoriasis is the investigational drug CEP-37247. This drug is a low molecular weight functional antibody fragment that is predicted to have improved immunogenicity and tissue distribution. This drug is currently in phase II clinical trials.

Secukinumab, ixekizumab, and brodalumab are interleukin-17 (IL-17) pathway modulators. The cytokine IL-17 has been associated with skin inflammation thus potential exists to reduce the chronic inflammation associated with psoriasis. These drugs have all undergone phase II clinical trials and have achieved
at least 75% improvements in PASI scores in the majority of patients treated. These drugs are currently undergoing phase III clinical trials, and more information about their effects on psoriasis will be seen in the near future.20

Efforts are also being made to find drugs which specifically target interleukin-23 (IL-23) and stop differentiation of T-helper 17 cells.1 IL-23 was shown effective in a previous investigational drug briakinumab, whose application for approval was withdrawn due to increase in cardiovascular events. Briakinumab targeted both IL-12 and IL-23 causing differentiation of T-helper 1 and T-helper-17 cells to be decreased. Two investigational drugs, SCH900222 and CNT01959, are currently being researched for potential use in blockade of IL-23 action to stop T-helper 17 differentiation without significant effects on T-helper 1.15 By focusing only on T-helper 17 this should minimize adverse drug reactions.

Abatacept has completed phase II clinical trials and has shown to be an effective treatment in patients with psoriasis and psoriatic arthritis.21 More studies are needed before this drugs gets an FDA labeled indication but this T-cell modulator is showing promise. Another T-cell modulator, siplizumab, has undergone phase II clinical trials and has been shown to have an acceptable safety profile. More studies will be done to decide on the efficacy of this drug.22

Another new line of drug treatment has shown effective outcomes in psoriasis as well. The use of small molecule drugs (<800Daltons) to manipulate immune function by acting on intracellular signaling are currently undergoing clinical trials.8,23 One such drug is voclosporin which inhibits calcineurin and decreases activation of lymphocytes. This drug has completed phase III clinical trials and at a dose of 0.4mg/kg, 47% of patients achieved greater than 75% PASI response rates.23 Many other drugs, such as tofacitinib which acts on janus kinase to disrupt the amplification and transduction of cytokine signaling, are currently undergoing clinical trials. A phase IIb 12 week trial showed PASI 75 response rate which were statistically higher in groups taking tofacitinib twice daily as compared to placebo.

Other small molecule treatments which are in the pipeline for drug approval include apremilast, a phosphodiesterase 4 inhibitor (PDE-4), currently in phase III clinical trials and ACT-12880, a sphingosine 1-phosphate receptor agonists, which is currently in phase II clinical trials.14,20 These drugs will hopefully lead to a better understanding of psoriasis and help to identify potential areas of drug development.

CONCLUSION

Psoriasis affects millions of patients in America every year. The large range of symptoms and comorbidities associated with psoriasis make it imperative to treat this disease, along with other underlying diseases. A proper evaluation of psoriasis types should be done at initiation in order to form a tailored medication regimen. The treatment options chosen for patients should always be individualized due to the potential consequences of these medications. With the emergence of biologics and the development of new drugs psoriasis treatment is rapidly changing. Increasing awareness to the public and health care professional will allow for more informed decisions about treatment options. Further research in psoriasis is needed to define exact causes of the disease in order to manufacture drugs better tailored for medication regimens.

REFERENCES