EASING THE PATIENT BURDEN OF PSORIASIS AND PSORIATIC ARTHRITIS: THE ROLE OF THE SPECIALTY PHARMACIST

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Learning Objectives

• Explain the pathophysiology, etiology, prognosis, clinical presentation, and comorbidities associated with psoriasis and psoriatic arthritis
• Identify current and emerging treatment options for psoriasis
• Examine current and emerging treatment options for psoriatic arthritis
• Determine the role of the specialty pharmacist in supporting patient education and adherence for psoriasis and psoriatic arthritis

Overview

• Psoriasis
  – Chronic inflammatory disorder of the skin
  – Affects approximately 3.2% of adults over the age of 20 in the US
  – 7.4 million adults over the age of 20 (2013)
• Psoriatic Arthritis
  – Chronic systemic inflammatory disease
  – Affects between 6 and 42% of patients with psoriasis
  – Appears before skin manifestations of psoriasis in approximately 10-15% of patients
• Both diseases affect male and female patients equally

Pathophysiology

Increased levels of pro-inflammatory mediators
Secretion of inflammatory cytokines
Long-term (ie, chronic) disruption of immune cell signaling
Lasting changes to underlying cell mechanisms in the skin and joints
Clinical presentation

Etiology

Genetic Factors
- Nine chromosomal loci have been associated with statistically significant linkage to psoriasis (PSORS1-PSORS9).
- Disease concordance studies among twins show that the risk of psoriasis is two-three times higher between monozygotic twins than it is among dizygotic twins.

Environmental Factors
- Infection (ie, streptococcal pharyngitis, HIV)
- Stress, trauma, smoking, cold weather, humidity, diet and obesity
- Drugs (ie, beta-blockers, lithium, anti-malarial, interferon)

Clinical Presentation

- **Chronic Plaque Psoriasis**
  - Most common form of psoriasis (90%).
  - Characterized by well-circumscribed, dry silvery-white scales of variable thickness
  - Lesions are typically located symmetrically and may be more apt to develop at sites of trauma or injury (i.e., Koebner’s phenomenon)
- **Other types of psoriasis:**
  - Guttate
  - Inverse (flexural)
  - Pustular
  - Erythrodermic


Clinical Presentation

- **Psoriatic Arthritis**
  - Five proposed subtypes
  - Classic presentation: distal interphalangeal joint involvement, dactylitis, and calcaneal enthesitis
  - Nail involvement is more common in patients with psoriatic arthritis than psoriasis alone
  - Development of diagnostic criteria has lagged behind that for other arthropathies (i.e., rheumatoid arthritis)


Comorbidities

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Hospitalized with Psoriasis (%)</th>
<th>Hospital-based Control (%)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Mellitus Type II</td>
<td>11.7</td>
<td>5.8</td>
<td>2.48 (1.70-3.61)</td>
</tr>
<tr>
<td>Arterial Hypertension</td>
<td>21.9</td>
<td>10.2</td>
<td>3.27 (2.41-4.49)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>5.2</td>
<td>2.8</td>
<td>2.09 (1.23-3.54)</td>
</tr>
<tr>
<td>Coronary Heart Disease</td>
<td>5.5</td>
<td>3.6</td>
<td>1.77 (1.07-2.95)</td>
</tr>
</tbody>
</table>

Comorbidities

- Patients with psoriasis are at least 1.5 times more likely to experience depression and use more anti-depressant medications than the general population.
- Psychological symptoms may not correlate with disease severity.
- Psychosocial effects:
  - Shame and embarrassment (89%)
  - Anxiety (58%)
  - Lack of confidence (42%)
  - Depression (34%)
  - Family friction (26%)
  - Reduction in participation in athletic activities (50%)
  - Major difficulties at work (44%).


Characterizing Disease Severity

- Body surface area affected:
  - < 5% → Mild Psoriasis
  - 5-10% → Moderate Psoriasis
  - > 10% → Severe Psoriasis

- Patients generally categorized as mild-to-moderate or moderate-to-severe.
- Moderate-to-severe typically defined as:
  - Involvement of more than 5% to 10% of body surface area (BSA)
  - Involvement of face, palms, or soles of feet
  - Disease that is otherwise disabling


Assessment and Prognosis

- Clinical Practice
  - Patient interview
- Assessment Tools
  - Psoriasis Area and Severity Index (PASI)
  - Physician Global Assessment (PGA)
    - Static form (standard)
    - Dynamic form
  - American College of Rheumatology (ACR) 20
- Quality of life assessment

Treatment

• Not a curable disease
• Goals of treatment:
  – Decrease lesion burden
  – Improve quality of life
• Treatments categorized:
  – Topical
  – Phototherapy
  – Systemic


Topical Therapy

• Used for the majority of patients with mild-to-moderate disease (80% of patients with psoriasis)
• May be used as supportive therapy for resistant lesions in patients with more extensive disease that are receiving other therapies
• Not recommended as monotherapy for patients with extensive disease
• High efficacy and safety
• Duration of therapy dependent on clinical goals and agent potency
• Adherence is generally poor

Phototherapy

- Despite recent expansion in available biologic options, it remains an essential treatment option, Efficacious
  - Cost effective
  - No risk for systemic immunosuppressive effects


Traditional Systemic Therapy

- Used when disease is extensive, debilitating, or severely impacts quality of life
- Continue to play an important role in treatment
- Benefits include ease of administration and low cost (as compared to biologics)
- Challenges include toxicity and efficacy (as compared to biologics)


Traditional Systemic Therapy

<table>
<thead>
<tr>
<th>Common</th>
<th>Less Common (off-label)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclosporine</td>
<td>Azathioprine</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Hydroxyurea</td>
</tr>
<tr>
<td>Acitretin</td>
<td>Leflunomide</td>
</tr>
<tr>
<td></td>
<td>Mycophenolate mofetil</td>
</tr>
<tr>
<td></td>
<td>Sulfasalazine</td>
</tr>
<tr>
<td></td>
<td>Tacrolimus</td>
</tr>
<tr>
<td></td>
<td>6-thioguanine</td>
</tr>
</tbody>
</table>

Traditional Systemic Therapy

- The role of methotrexate (MTX)
  - Weekly dosages range from 7.5–25 mg
  - Titration to optimal dose is recommended
  - Consider intramuscular or subcutaneous injection for patients with adherence issues (equal efficacy)
  - Patients not benefiting from oral MTX at doses ≥ 15 mg/week may benefit from subcutaneous administration
- Combination therapy
  - For patients with psoriatic arthritis
  - Evidence indicates combination therapy with etanercept or infliximab results in better outcomes than biologic monotherapy for the treatment of psoriasis


Biologics

- TNF-α inhibitors/ blockers
  - Adalimumab
  - Etanercept
  - Golimumab
  - Infliximab
- IL-17A antagonist
  - Ixekizumab
  - Secukinumab
- IL-12/23 antagonist
  - Ustekinumab


Pathophysiology Revisited

### Biologics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Chronic Plaque Psoriasis</th>
<th>Psoriatic Arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Certolizumab pegol</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Etanercept</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Golimumab</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Infliximab</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Ixekizumab</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Secukinumab</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

*Adalimumab*

- TNF-α inhibitor
- Subcutaneous administration
- Moderate to severe chronic plaque psoriasis
  - 80 mg at day 0, followed by 40 mg at day 7 and every other week thereafter
- Psoriatic arthritis
  - 40 mg every other week
- Loss of efficacy after restart; optimal treatment strategy is continuous use

*Certolizumab Pegol*

- TNF-α blocker
- Subcutaneous administration
- Psoriatic arthritis
  - 400 mg at weeks 0, 2, and 4, followed by 200 mg every other week thereafter
  - 400 mg every 4 weeks can be considered for maintenance therapy
Etanercept

- TNF-α blocker
- Subcutaneous administration
- Plaque psoriasis
  - 50 mg twice weekly for 3 months, followed by 50 mg once weekly thereafter
- Psoriatic arthritis
  - 50 mg once weekly +/- methotrexate
- Anti-etanercept antibodies possible
  - Do not appear to reduce efficacy
- Potential for loss of efficacy over time


Golimumab

- TNF-α blocker
- Subcutaneous administration
- Psoriatic arthritis
  - 50 mg once monthly +/- methotrexate


Infliximab

- TNF-α blocker
- Intravenous infusion
- Plaque psoriasis and psoriatic arthritis
  - 5 mg/kg at weeks 0, 2, and 6, followed by every 8 weeks thereafter
- Antibodies possible and likely reduce efficacy
  - More likely to develop with intermittent therapy
  - Continuous therapy is recommended

**Ixekizumab**

- IL-17A antagonist
- Subcutaneous administration
- Moderate-to-severe plaque psoriasis
  - 160 mg at week 0, followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12, and then 80 mg every 4 weeks thereafter
- Shown to be more efficacious than etanercept in clinical trials
- High levels of response through 60 weeks of treatment
- Most common adverse events: nasopharyngitis, upper respiratory tract infection


**Secukinumab**

- IL-17A antagonist
- Subcutaneous administration
- Moderate-to-severe plaque psoriasis
  - 300 mg at weeks 0, 1, 2, 3, and 4, followed by 300 mg every 4 weeks thereafter
  - For some patients, 150 mg may be acceptable
- Psoriatic arthritis
  - When psoriasis also present, use plaque psoriasis dosing
  - Psoriatic arthritis only: 150 mg at weeks 0, 1, 2, 3, and 4, and every 4 weeks thereafter
- Shown to be more efficacious than etanercept in the treatment of moderate-to-severe plaque psoriasis


**Ustekinumab**

- IL-12 and IL-23 antagonist
- Subcutaneous administration
- Psoriasis
  - Patients weighing ≤ 100 kg (220 lbs): 45 mg at weeks 0 and 4, followed by 45 mg every 12 weeks thereafter
  - Patients weighing > 100 kg (220 lbs): 90 mg at weeks 0 and 4, followed by 90 mg every 12 weeks thereafter
- Psoriatic arthritis
  - 45 mg at weeks 0 and 4, followed by 45 mg every 12 weeks thereafter
  - 90 mg dosing regimen should be given to patients with co-existent moderate-to-severe plaque psoriasis weighing > 100 kg (220 lbs)
- Shown to be more effective than etanercept in treating moderate-to-severe psoriasis
- Biologic least likely to be discontinued

Phosphodiesterase 4 (PDE4) Inhibition


Apremilast

- PDE4 inhibitor
- Oral administration
- Moderate-to-severe psoriasis and psoriatic arthritis
  - 5 day titration, followed by 30 mg twice daily thereafter (purpose is to reduce gastrointestinal adverse effects)

<table>
<thead>
<tr>
<th>Day</th>
<th>AM Dose</th>
<th>PM Dose</th>
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<tbody>
<tr>
<td>Day 1</td>
<td>10 mg</td>
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<tr>
<td>Day 2</td>
<td>10 mg</td>
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</tr>
<tr>
<td>Day 3</td>
<td>10 mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>Day 4</td>
<td>20 mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>Day 5</td>
<td>20 mg</td>
<td>30 mg</td>
</tr>
<tr>
<td>Day 6 and thereafter</td>
<td>30 mg</td>
<td>30 mg</td>
</tr>
</tbody>
</table>


Clinical Endpoints

<table>
<thead>
<tr>
<th>Drug</th>
<th>PASI 75</th>
<th>ACR 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>77%-79%</td>
<td>50%</td>
</tr>
<tr>
<td>Certolizumab peg</td>
<td>N/A</td>
<td>54%-58%</td>
</tr>
<tr>
<td>Enbrel</td>
<td>25%-49%</td>
<td>51%</td>
</tr>
<tr>
<td>Infliximab</td>
<td>N/A</td>
<td>51%</td>
</tr>
<tr>
<td>Humira</td>
<td>70%-80%</td>
<td>50%</td>
</tr>
<tr>
<td>Infliximab</td>
<td>87%-90%</td>
<td>N/A</td>
</tr>
<tr>
<td>Ketokonazole</td>
<td>95%-98%</td>
<td>82%-85%</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>N/A</td>
<td>56%-64%</td>
</tr>
<tr>
<td>Nivolumab</td>
<td>90%-95%</td>
<td>51%-61%</td>
</tr>
<tr>
<td>Pemetrexed</td>
<td>90%-95%</td>
<td>51%-61%</td>
</tr>
<tr>
<td>Remicade</td>
<td>N/A</td>
<td>56%-64%</td>
</tr>
<tr>
<td>Secukinumab</td>
<td>65%-78%</td>
<td>42%-50%</td>
</tr>
<tr>
<td>Simponi</td>
<td>65%-78%</td>
<td>42%-50%</td>
</tr>
<tr>
<td>Taltz</td>
<td>67%-87%</td>
<td>38%-42%</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>65%-78%</td>
<td>42%-50%</td>
</tr>
<tr>
<td>Adalimumab</td>
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<td>50%</td>
</tr>
<tr>
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<td>Enbrel</td>
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</tr>
</tbody>
</table>
Emerging Therapies

• Agents targeting IL-23
  – BI-655066
  – Guselumab
  – Tildrakizumab

• Agents targeting IL-17
  – Brodalumab


BI-655066

• Targets IL-23
• Phase II trial (n=166)
  – Patients with moderate-to-severely active psoriasis randomly assigned to receive BI-655066 (180, 90/90, or 180/189 mg) or ustekinumab (45 or 90 mg, per weight), subcutaneously, at weeks 0 and 4
  – 77.1% of patients receiving BI-655066 achieved PASI 90 after 12 weeks (compared to 40% with ustekinumab)
  – Most common adverse effects: runny nose, sore throat, headache
• Trials ongoing


Guselkumab (CNTO-1959)

• Targets IL-23
• Phase II trial (n = 293)
  – Double-blind, randomized, placebo-controlled, dose-ranging, active-comparator study
  – Results
  – Proportion of patients achieving PGA score of 0 or 1 was significantly higher in the 50, 100, and 200 mg guselkumab groups than in the adalimumab group
• Phase III trials ongoing

<table>
<thead>
<tr>
<th>Treatment</th>
<th>PGA Score of 0 (clear) or 1 (almost clear) in 16 Weeks</th>
<th>PASI 75 at 16 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guselkumab 5 mg</td>
<td>39%</td>
<td>64%</td>
</tr>
<tr>
<td>Guselkumab 10 mg</td>
<td>67%</td>
<td>73%</td>
</tr>
<tr>
<td>Guselkumab 100 mg</td>
<td>78%</td>
<td>91%</td>
</tr>
<tr>
<td>Guselkumab 200 mg</td>
<td>89%</td>
<td>97%</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>69%</td>
<td>81%</td>
</tr>
</tbody>
</table>

Placebo     7%  5%

† 80 mg at week 0, 40 mg at week 1 and every other week thereafter.

Tildrakizumab (MK-3222)

- Targets IL-23
- Phase IIb trial (n = 355)
  - Patients randomized to receive tildrakizumab at a dose of 5, 25, 100, or 200 mg or placebo, subcutaneously at weeks 0, 4, and every 12 weeks thereafter
  - After 16 weeks, the proportion of patients achieving PASI 75 was significantly higher, when compared to placebo, for all doses
  - Low relapse rate after cessation of therapy
- Phase III trials are ongoing

<table>
<thead>
<tr>
<th>Treatments</th>
<th>PASI 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tildrakizumab 5 mg</td>
<td>33.3%</td>
</tr>
<tr>
<td>Tildrakizumab 25 mg</td>
<td>64.4%</td>
</tr>
<tr>
<td>Tildrakizumab 100 mg</td>
<td>66.3%</td>
</tr>
<tr>
<td>Tildrakizumab 200 mg</td>
<td>74.4%</td>
</tr>
<tr>
<td>Placebo</td>
<td>4.4%</td>
</tr>
</tbody>
</table>


Brodalumab

- Targets IL-17
- Initially showed very promising results for moderate-to-severe plaque psoriasis in phase III trials
  - PASI 75 in 83-86% of patients after 12 weeks (210 mg dose)
- Phase III trials were halted in May 2015 due to "events of suicidal ideation and behavior in the brodalumab program, which…likely would necessitate restrictive labeling"
  - Importance of context
- Further development to be determined


Role of the Specialty Pharmacist

- Promote adherence
  - Extent to which patients take medications as prescribed by their health care providers
  - Types of adherence
    - Intentional (i.e., skipping doses, changing the dose, self-discontinuation)
    - Unintentional (i.e., forgetfulness, running out, carelessness)

Role of the Specialty Pharmacist

• Poor adherence rates
  – Up to half of patients do not adhere to treatment
  – Most commonly reported reasons:
    • Lack of efficacy/frustration
    • Forgetting
    • Too busy
    • Regimen too time consuming or inconvenient


Role of the Specialty Pharmacist

• Memory aids
  – Pill boxes/dose packaging
  • Studies demonstrating impact also utilized educational interventions

• Motivational interviewing
  – Studies in psoriasis significantly demonstrate:
    • Reductions in disease severity
    • Improvements in psoriasis self-management levels


Role of the Specialty Pharmacist

• Technology
  – Text message interventions in psoriasis
    • Included reminders (3x/week) and educational tools (4x/week)
    • Significant improvements seen in adherence and disease severity

• Patient access support
  – Higher costs are correlated with lower adherence
  – Copay assistance helps lower patient cost-share
    • Copay cards
    • Foundational assistance

Role of the Specialty Pharmacist

- Injection technique
  - Patients may be new to injectable medications
  - Coach on:
    - Storage
    - Proper injection sites and rotation
    - Injection preparation
    - Injection technique
    - Proper disposal


Role of the Specialty Pharmacist

- Adverse event counseling
  - Expectation setting
  - Adverse event mitigation strategies
- Pharmacists often get questions related to injection site reactions and pain
  - Symptoms should go away within a few days
  - Follow up with provider if persistent
  - Review injection technique
- Infections
  - Follow up with provider; patient may need to interrupt therapy


Role of the Specialty Pharmacist

- Lifestyle modification
  - Up-to-date vaccinations
  - Healthy diet
  - Avoid smoking, minimize alcohol
  - Patient must know how to care for their skin
    - Hygiene
    - Clothing types
    - Sun exposure
    - Moisturizing
