Management of Psoriatic Arthritis

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I am a member of the ACR/NPF treatment guidelines team – what I say today is separate from that project and doesn’t reflect that work.

Objectives

• Consider the broader context of disease in management of PsA
• Discuss treatment strategies
• Examine available therapies for PsA, their mechanisms of action, and potential benefits and risks

PsA: A heterogeneous disease

Less than 30% of patients with PsA reach remission by any definition

Ortolani et al, Ann Rheum Dis 2017
Michelson et al, J Rheumatol 2017
Treating PsA = Treating the Whole Patient

What do you need to know before choosing a therapy?

- Disease manifestations
- Concomitant Conditions
  - “Extra-articular” manifestations and comorbidities
- Prior therapies
  - Primary failure vs secondary failure
- Patient preferences
  - The target

PsA is associated with several concomitant conditions, particularly metabolic disease

Treatment Targets in PsA

- **Minimal Disease Activity (MDA)** defined as 5/7 of the following:
  - Tender joint count ≤ 1
  - Swollen joint count ≤ 1
  - PASI ≤ 1 or BSA ≤ 3
  - Patient pain VAS ≤ 15
  - Patient global activity VAS ≤ 20
  - HAQ ≤ 0.5
  - Tender enthesal points ≤ 1

- **Disease activity in PsA (DAPSA):**
  - Tender joint count +
  - Swollen joint count +
  - Patient pain (1-10) +
  - Patient global activity (1-10) +
  - CRP

Coates et al. Arthritis Rheum 2016
Smolen et al. Ann Rheum Dis 2017
Coates & Helliwell. Curr Rheum Reports 2015
Coates et al. Arthritis Rheum 2017
The Tight Control in Psoriatic Arthritis (TiCOPA) trial

However, must balance increased adverse events with better efficacy.

Therapies for PsA

Overview of disease pathophysiology

PsA: A heterogenous disease

But most clinical trial outcomes are focused on the joints . . . .

Clinical Trial Outcomes in PsA

- ACR20 – 20% improvement in tender and swollen joint counts plus 20% in at least three of the following:
  - Health Assessment Questionnaire
  - Patient pain assessment
  - Physician global assessment
  - Acute Phase Response: C-reactive protein

- PASI75 – 75% improvement in PASI (Psoriasis Area and Severity Index) score (range 0-72):
  - Head, Trunk, Arms, Legs
  - %BSA in each area, Erythema, Induration, Desquamation
  - Weighted score
Overall limited data for the **oral small molecules** ("traditional DMARDs")

- In clinical practice, they do help
- Inexpensive
- Around for a long time
- Really a lack of data; not many studies and studies use relatively low doses
- However, TiCOPA may suggest that we’re just not aggressive enough?
- Existing data does not support a “disease modifying” effect
- MTX helps psoriasis but not SSA; LEF a little but not much
- A major role may be in suppressing antibody formation and prolonging the life of the biologic

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**Methotrexate in PsA (MIPA) Trial**

<table>
<thead>
<tr>
<th>Trait</th>
<th>MTX</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>PsARC OR (95%CI)</td>
<td>1.77 (0.97-3.23)</td>
<td>0.60</td>
</tr>
<tr>
<td>ACR20 OR (95%CI)</td>
<td>2.00 (0.65-6.22)</td>
<td>0.23</td>
</tr>
<tr>
<td>DAS28 Response OR (95%CI)</td>
<td>1.70 (0.90-3.17)</td>
<td>0.10</td>
</tr>
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**Liver disease**

Liver disease risk across different conditions: RA, PsA, no DMARD, PsA, RA, no DMARD.

**TNF inhibitors**

- **Adalimumab & Golimumab**: Fully human recombinant and TNF inhibitors.
- **Etanercept**: Humanized variable region.
- **Infliximab**: Chimeric human (75%)/mouse (25%) monoclonal antibody.
- **Certolizumab pegol**: PEGylated Fab 1 fragment.

**Ustekinumab**: p40 subunit, IL12/23 inhibitor

- IL-12 receptor
- T<sub>1</sub> cell signaling
- IL-23 receptor
- T<sub>17</sub> cell signaling

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**Apremilast**, a phosphodiesterase 4 inhibitor

- **PDE4**: Degradation of cAMP
- **NF-κB**: Activation
- **CREB**: Activation
- **NF-κB**: Inhibition
- **CREB**: Inhibition

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**Differentiating Among TNFi**:

- Uveitis/Crohn’s/UC
- Severity of Psoriasis
- Mode (IV vs SQ)
- Dosing Intervals
- Insurance Coverage...

To use combination therapy or not?
IL17 inhibitors

- Secukinumab (IL17A)
- Ixekizumab (IL17A)
- Brodalumab (IL17RA)

Drugs in Development

- Brodalumab (approved for psoriasis)
- Guselkumab (approved for psoriasis)
- Tildrakizumab (approved for psoriasis)
- Rizankizumab (Phase II in PsA complete, Phase III in PsO complete)
- Upadacitinib (phase II)

Abatacept

Drugs in Development

- Guselkumab (Phase II for PsA approved in 2017)

IL23 Inhibition

- IL-23 receptor
  - T\(_{H}17\) cell signaling

Guselkumab Phase II for PsA
(approved for psoriasis in 2017)

- Deodhar et al. ACR Annual Meeting Abstract 4L
- VOGUE Trial: Blauvelt et al. JAAD 2017
Conclusions

- Key considerations in therapy selection:
  - Level of disease activity: skin and MSK severity
  - Disease manifestations
  - Comorbidities
  - Patient preference
- Treat to Target
  - Broader concept than using MDA – just use SOMETHING!
- Many new therapies in PsA and more therapies to come!
- One prescription isn’t going to solve all of the problems
  - Consider the broader context and impact of the patient’s disease in designing a management plan.

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