Practical Issues Using Biologics for Psoriasis

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Conflicts/Disclosures

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Objectives

• To describe the psoriasis patient population that should be treated with biologics
  – Treatment goals (targets, comorbidities)

• Features that affect choice of a biologic
  – Efficacy
    • Durability of response
    • Psoriatic arthritis
  – Safety
    • Monitoring
  – Cost
    • Biosimilars

• Getting patients to take the drug
Disclaimer/Warning

• I have mixed feelings about almost everything
• Tendency to be cynical
When to Use Biologics

• When patients need them, not when they don’t
  – To achieve high levels of success

• Serious psoriasis, has an impact on patients’ lives
  – When the benefit warrants the risk
    • In studies, usually BSA > 10%, PASI>12
    • Approval is for moderate-to-severe, and moderate is >5%
    • Other disabling forms of the disease
  – Not for patients who respond to less risky treatment
    • Phototherapy first when reasonable
      – Office UV, home UV, tanning beds
    • For localized disease resistant to topicals?
      – It may be better to get the patient to use the topicals well first
Old Standard Model

Psoriasis

Psychosocial

Joint Symptoms

Topicals

Promote good adherence

Yes

Localized?

No

Phototherapy

Methotrexate

Biologics

Rheumatology

Psoriasis Foundation

Ibuprofen
General Recommendations from AAD Guidelines

• Topicals are reasonable for patients with localized psoriasis
• UVB is safe, effective & cost effective
  – PUVA therapy is very effective but has greater risks
• Methotrexate is effective but has many risks
• Cyclosporine is best used only intermittently
• Acitretin is not immunosuppressive but is teratogenic
• Biologics are safe & effective
THE PSORIASIS AND PSORIATIC ARTHRITIS POCKET GUIDE
TREATMENT ALGORITHMS AND MANAGEMENT OPTIONS

HEALTHY ADULT WITH CHRONIC PLAQUE PSORIASIS, W/O PsA

If UVB available, feasible, practical and suitable
- UVB phototherapy alone
- UVB phototherapy + systemic retinoids
- UVB phototherapy + adjuvant topical agents
- Goekerman

If UVB unavailable, contraindicated, ineffective or patient unable to comply

- Systemic retinoids
  - Alefacept
  - Cyclosporine
  - Etanercept
  - Adalimumab
  - Methotrexate
  - PUVA
  - Efalizumab
  - Infliximab

- Combination therapies
  - CsA + MTX
  - MTX + biologic
  - Retinoid + biologic
  - Biologic + UVB phototherapy

*NB: Narrow-band
BB: Broad-band
Treat to Target for Psoriasis

- Patients, NPF Medical Board developed treatment targets
  - 25 psoriasis experts involved
  - Published in the *Journal of the American Academy of Dermatology* (2016)
  - The first treatment targets for psoriasis in the U.S.
  - Set goals for psoriasis treatments will hopefully become a new standard for care

Armstrong AW, et al. (2016). From the Medical Board of the National Psoriasis Foundation: Treatment targets for plaque psoriasis. *Journal of the American Academy of Dermatology*. Advance online publication. doi:
What are the NPF treatment targets for psoriasis?

Preferred assessment instrument: **Body Surface Area (BSA)**

<table>
<thead>
<tr>
<th>Time Post Initiation</th>
<th>Target</th>
<th>Acceptable</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 Months</td>
<td>BSA ≤ 1%</td>
<td>BSA ≤ 3% - or − 75% Improvement</td>
</tr>
<tr>
<td>Every 6 Months</td>
<td>BSA ≤ 1%</td>
<td></td>
</tr>
</tbody>
</table>

Clearing As A Goal

- Patients do better if you get them completely clear

J Dermatolog Treat. 2016;27(3):224-7
Psoriasis is associated with many comorbidities.

Comorbidities

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Exposure</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM</td>
<td>Mild Psoriasis</td>
<td>1.47 (1.40-1.54)</td>
</tr>
<tr>
<td>DM</td>
<td>Severe Psoriasis</td>
<td>2 (1.79-2.22)</td>
</tr>
<tr>
<td>NMSC</td>
<td>Psoriasis</td>
<td>7.5 (5.07-11.10)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>Psoriasis</td>
<td>6.12 (1.53-24.47)</td>
</tr>
<tr>
<td>A fib</td>
<td>Mild Psoriasis</td>
<td>1.22 (1.14-1.30)</td>
</tr>
<tr>
<td>A fib</td>
<td>Severe Psoriasis</td>
<td>1.53 (1.23-1.91)</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>Mild Psoriasis</td>
<td>1.25 (1.17-1.34)</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>Severe Psoriasis</td>
<td>1.65 (1.33-2.05)</td>
</tr>
<tr>
<td>VTE &gt;=50 yo</td>
<td>Mild Psoriasis</td>
<td>1.26 (1.13-1.42)</td>
</tr>
<tr>
<td>VTE &gt;=50 yo</td>
<td>Severe Psoriasis</td>
<td>1.74 (1.32-2.28)</td>
</tr>
<tr>
<td>AAA</td>
<td>Mild Psoriasis</td>
<td>1.2 (1.03-1.39)</td>
</tr>
<tr>
<td>AAA</td>
<td>Severe Psoriasis</td>
<td>1.67 (1.21-2.32)</td>
</tr>
<tr>
<td>Migraine</td>
<td>Mild Psoriasis</td>
<td>1.37 (1.30-1.45)</td>
</tr>
<tr>
<td>Migraine</td>
<td>Severe Psoriasis</td>
<td>1.55 (1.29-1.86)</td>
</tr>
<tr>
<td>RVO</td>
<td>Psoriasis</td>
<td>1.46 (1.04-2.04)</td>
</tr>
<tr>
<td>MI Age 50-60</td>
<td>Mild Psoriasis</td>
<td>1.08 (1.03-1.13)</td>
</tr>
<tr>
<td>MI Age 50-60</td>
<td>Severe Psoriasis</td>
<td>1.36 (1.13-1.64)</td>
</tr>
</tbody>
</table>

Severe Psoriasis is Associated with Myocardial Infarction

- Most impactful publication in my dermatology lifetime
- “As dermatologists care for most patients with severe psoriasis, it is imperative that these patients are screened for CVD risk factors and that they are referred either to a primary care physician or to a cardiologist for management and treatment of risk factors”

Number Needed To Harm (NNTH)

- You would need to see a very large number of patients with psoriasis before, on average, you’d see one more case of comorbidity due to psoriasis.

```
<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Exposure</th>
<th>NNTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM</td>
<td>Mild Psoriasis</td>
<td>580</td>
</tr>
<tr>
<td>DM</td>
<td>Severe Psoriasis</td>
<td>272</td>
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<tr>
<td>NMSC</td>
<td>Psoriasis</td>
<td>1551</td>
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<tr>
<td>Melanoma</td>
<td>Psoriasis</td>
<td>20135</td>
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<tr>
<td>A fib</td>
<td>Mild Psoriasis</td>
<td>1500</td>
</tr>
<tr>
<td>A fib</td>
<td>Severe Psoriasis</td>
<td>623</td>
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<tr>
<td>Ischemic stroke</td>
<td>Mild Psoriasis</td>
<td>1320</td>
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<tr>
<td>Ischemic stroke</td>
<td>Severe Psoriasis</td>
<td>508</td>
</tr>
<tr>
<td>VTE &gt;=50 yo</td>
<td>Mild Psoriasis</td>
<td>1895</td>
</tr>
<tr>
<td>VTE &gt;=50 yo</td>
<td>Severe Psoriasis</td>
<td>666</td>
</tr>
<tr>
<td>AAA</td>
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<tr>
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<td>Mild Psoriasis</td>
<td>700</td>
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<td>Severe Psoriasis</td>
<td>471</td>
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<tr>
<td>RVO</td>
<td>Psoriasis</td>
<td>8801</td>
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<td>MI Age 50-60</td>
<td>Mild Psoriasis</td>
<td>2146</td>
</tr>
<tr>
<td>MI Age 50-60</td>
<td>Severe Psoriasis</td>
<td>430</td>
</tr>
</tbody>
</table>
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*J Am Acad Dermatol. 2017 Mar;76(3):531-537*
Biologics Improve Coronary Arteries

- Biologic therapy was associated with a 6% reduction in non-calcified plaque burden ($P = 0.005$)
- Decrease in non-calcified plaque burden in the biologic treated group was significant compared with slow plaque progression in non-biologic treated
Change in Plaque Burden

B

Change in Non-Calcified Plaque Burden over One-Year

\[ P = 0.17 \]

\[ P = 0.005 \]

Non-calcified plaque burden, mm²

No biologic

Biologic

Treatment

Baseline

One-year

Cardiovasc Res. 2019 Feb 5
Comorbidities in Children!

- Crohn’s was 20 times as prevalent in children with psoriasis!
- The incidence was 3 times as high!

<table>
<thead>
<tr>
<th></th>
<th>Psoriasis (N=7,686)</th>
<th>Nonpsoriasis (N=30,744)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crohn’s prevalence</td>
<td>N=86</td>
<td>11</td>
</tr>
<tr>
<td>Crohn’s incidence</td>
<td>N=14</td>
<td>0.97</td>
</tr>
</tbody>
</table>

- 1 in 1,000 children per year with psoriasis developed Crohn’s

Pediatr Dermatol. 2019 Feb 21
Clearing As A Goal

• How much better do patients do if you get them completely clear?

• Symptoms, activities, leisure & relations domains combine 2 questions

• Each on a 0-3 scale

• 1 is “a little”
Good Drugs With Lousy Data

- High levels of clearance give statistically better quality of life if you have sufficient sample size to detect the difference.
- But even low levels of high improvement are associated with good improvements in patients’ quality of life.
We Have To Address Arthritis?

- Baseline Sharp score: ~35
- Change at 24 weeks: ~2 with placebo & 0.4 with golimumab
Most Don’t Progress Without Drug, Some Do Progress With Drug

Figure 2. Changes in PsA-modified SvdH at Week 24: proportions of patients receiving IV treatment with no new erosions or JSN in joints with score = 0 at baseline (full analysis set for structural damage endpoints). IV: intravenous; JSN: joint space narrowing; PsA: psoriatic arthritis; SvdH: Sharp/van der Heijde score.
Which one is best? There may not be one best biologic

• Characteristics vary and are weigh differently in unpredictable ways
  – What may be best for me may not be what a patient would choose
  – How we perceive things is not fixed, either

• My approach: educate patients about options, involve them (as much as they want) in the choice, & guide them to a good decision
Characteristics of Biologics

• Most effective: not etanercept or ustekinumab
• Most convenient: ustekinumab, tildrakizumab
• Most effective for joints: maybe not ustekinumab
• Most cost effective
  – I’ve written several papers on this (and have no idea which is the most effective)
• Safest: Very hard to say
  – Anti-IL12 and/or 23 (possibly anti-IL17 drugs)
Dimensions to Consider

- Mechanism
- Efficacy
  - Durability
  - Psoriatic arthritis
- Safety
  - Monitoring
- Cost
  - Biosimilars
- Adherence
Immunopathology of Psoriasis

CCL: chemokine (C-C motif) ligand; CXCL: chemokine (C-X-C motif) ligand; IFN: interferon; IL: interleukin; NKT: natural killer T cell; Th: T helper; TNF: tumor necrosis factor.

Efficacy of Systemic Treatments for Psoriasis
Biologic vs Methotrexate

- 40mg every other week of adalimumab
- Methotrexate

<table>
<thead>
<tr>
<th>Week</th>
<th>0-1</th>
<th>2-3</th>
<th>4-7</th>
<th>8-11</th>
<th>12-15+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max dose mg/wk</td>
<td>7.5</td>
<td>10</td>
<td>15</td>
<td>20</td>
<td>25</td>
</tr>
</tbody>
</table>

Secukinumab vs Ustekinumab

J Am Acad Dermatol. 2015 Sep;73(3):400-9
Secukinumab vs Ustekinumab

PASI 90 Response

Secukinumab 300 mg (n=334)
- Week 8: 79.0%
- Week 12: 57.6%

Ustekinumab (n=335)
- Week 8: 57.6%
- Week 12: 44.3%
- Week 16: 28.4%

PASI 100 Response

Secukinumab 300 mg (n=334)
- Week 12: *
- Week 16: *

Ustekinumab (n=335)
- Week 12: †
- Week 16: *

J Am Acad Dermatol. 2015 Sep;73(3):400-9
Efficacy of Gusekumab vs Adalimumab

Guselkumab vs Adalimumab

https://www.nice.org.uk/guidance/ta521/documents/committee-papers
Guselkumab vs Secukinumab

Week

Percentage of Patients

Week

Guselkumab 100 mg (N=534) Secukinumab 300 mg (N=514)
TNF-Inhibitor Treatment Retention

Dupan SM, Arthritis & Rheumatism (Arthritis Care & Research) 2009; 61: 560–568
DERMBIO Persistent on Treatment

(a) Women vs. men
Adalimumab vs. infliximab
Etanercept vs. infliximab
Previous anti-TNFα failure vs. naïve

(b) Cumulative probability of drug survival

Time (months)

Br J Dermatol. 2011 May;164(5):1091-6
Worse with Previous Failure

(a) Anti-TNFα naïve
(b) Previous lack of anti-TNFα efficacy

Br J Dermatol. 2011 May;164(5):1091-6
• Worse persistence in obese patients
BioCAPTURE: Happy drug survival

- Still on drug
- DLQI<5

Interpreting Long Term Response

- 424 of 463 = 92%

https://www.tremfyahcp.com/efficacy/open-label-extension-data
As Observed May Be Misleading

- 95 / 150 = 63%
- 66% ACR20 of 63% still in the study = 42%

https://www.otezlapro.com/psoriatic-arthritis/efficacy/
Managing Psoriatic Arthritis

• Screen for it
  – Can be your pertinent review of systems item
  – Ask about: Joint pain, joint stiffness, back pain

• Refer to rheumatology for evaluation
  – Complete assessment of tenderness and range of motion in joints
  – X-rays to evaluate for joint destruction
  – Comprehensive treatment options

## Psoriatic Arthritis Efficacy

<table>
<thead>
<tr>
<th>Treatment</th>
<th>ACR20 at Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etanercept</td>
<td>50%</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>57%</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>42-44%</td>
</tr>
<tr>
<td>Secukinumab 300mg</td>
<td>50-54%</td>
</tr>
<tr>
<td>Ixekizumab (every 4 weeks)</td>
<td>58%</td>
</tr>
<tr>
<td>Gusekumab (every 2 months)</td>
<td>58%</td>
</tr>
<tr>
<td>Apremilast (30mg twice a day)</td>
<td>38%</td>
</tr>
</tbody>
</table>
Cochrane Review of Biologic Safety

• Biologics had a higher rate of total adverse events (odds ratio 1.19, NNTH = 30), withdrawals due to adverse events (OR 1.32, NNTH = 37) and risk of TB reactivation (OR 4.68, NNTH = 681) compared to control.

• The rate of SAEs, serious infections, lymphoma, and congestive heart failure were not statistically significantly different between biologics and control treatment.

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>UST (N=3474)</th>
<th>IFX (N=1151)</th>
<th>ETAN (N=1854)</th>
<th>ADA (N=2675)</th>
<th>MTX Non-biologics (N=490)</th>
<th>Non-MTX Non-biologic (N=1610)</th>
<th>All (N=11466)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [years], mean ± SD</td>
<td>47.2 ± 13.09</td>
<td>48.5 ± 13.45</td>
<td>48.7 ± 13.65</td>
<td>47.6 ± 13.26</td>
<td>55.1 ± 13.82</td>
<td>50.1 ± 15.82</td>
<td>48.5 ± 13.82</td>
</tr>
<tr>
<td>Males, n (%)</td>
<td>1999 (57.5)</td>
<td>655 (56.9)</td>
<td>1038 (56.0)</td>
<td>1505 (56.3)</td>
<td>207 (42.2)</td>
<td>830 (51.6)</td>
<td>6321 (55.1)</td>
</tr>
<tr>
<td>Caucasian, n (%)</td>
<td>3002 (86.4)</td>
<td>966 (83.9)</td>
<td>1482 (80.0)</td>
<td>2138 (79.9)</td>
<td>395 (80.6)</td>
<td>1357 (84.3)</td>
<td>9508 (82.9)</td>
</tr>
<tr>
<td>BMI [kg/m²], mean (SD)</td>
<td>31.3 ± 7.17</td>
<td>32.2 ± 8.23</td>
<td>30.4 ± 7.10</td>
<td>31.0 ± 7.00</td>
<td>30.1 ± 6.95</td>
<td>29.9 ± 6.88</td>
<td>30.9 ± 7.23</td>
</tr>
<tr>
<td>Duration of psoriasis, years, mean ± SD</td>
<td>19.4 ± 12.80</td>
<td>18.4 ± 12.68</td>
<td>17.4 ± 13.35</td>
<td>17.2 ± 13.07</td>
<td>14.3 ± 14.80</td>
<td>14.3 ± 14.62</td>
<td>17.5 ± 13.43</td>
</tr>
<tr>
<td>Physician’s Global Assessment (PGA), mean ± SD</td>
<td>2.0 ± 1.25</td>
<td>1.8 ± 1.23</td>
<td>1.9 ± 1.14</td>
<td>1.9 ± 1.22</td>
<td>2.1 ± 1.17</td>
<td>2.3 ± 1.06</td>
<td>2.0 ± 1.21</td>
</tr>
<tr>
<td>Psoriatic arthritis (self-reported), n (%)</td>
<td>1134 (32.6)</td>
<td>601 (52.2)</td>
<td>785 (42.3)</td>
<td>1112 (41.6)</td>
<td>140 (28.6)</td>
<td>237 (14.7)</td>
<td>4098 (35.7)</td>
</tr>
<tr>
<td>History of treated Infections 3 years prior to enrollment, n (%)</td>
<td>802 (23.2)</td>
<td>350 (30.5)</td>
<td>467 (25.2)</td>
<td>660 (24.7)</td>
<td>116 (23.7)</td>
<td>337 (21.0)</td>
<td>2791 (24.4)</td>
</tr>
</tbody>
</table>
Adverse Event Rates

IL-23 genes protect against IBD

- 3 loss of function mutations in IL-23R linked to protection against the development of Crohn disease and ulcerative colitis in humans
- These 3 IL23R variants cause a reduction in IL23 receptor activation-mediated phosphorylation of the STAT3 & STAT4
Flares of psoriasis with IBD treatment

• Seen with TNF inhibitors
  – Poorly explained process
  – 21 of 1294 patients with IBD treated with anti-TNF developed drug-induced psoriasis
    • 14 patients with infliximab
    • 7 with adalimumab
  – The onset varied (mean 13±8 doses).
  – Plaque psoriasis (57%), scalp (14%), palmoplantar pustulosis (14%), generalized pustular psoriasis (5%), guttate (5%) and inverse (5%)
Worsening IBD with anti-IL17

- Roughly 1 in 300 patients without screening
- Confirmed in IBD patients
  - 59 IBD patients randomized 2:1 to secukinumab vs placebo
  - Primary end point analysis estimated <0.1% probability that secukinumab reduces CDAI by >50 points more than placebo
  - Secondary showed a significant difference in favor of placebo.

Gut. 2012 Dec;61(12):1693-700
Confirmed with Brodalumab

- Patients randomized receive brodalumab (210, 350, or 700 mg or placebo).
- Study terminated early based on an imbalance in worsening CD in active treatment groups.
- Mean change in CDAI at week 6 was -8.7 (210 mg), -35.4 (350 mg), -0.6 (700 mg), and -28.2 (placebo).
- Brodalumab resulted in more cases of worsening CD in patients with active CD and no evidence of meaningful efficacy.

Demyelination with a TNF inhibitor

- Proportion of patients remaining exacerbation free
  - Placebo ——
  - Lenercept 10 mg - - - -
  - Lenercept 50 mg - - - -
  - Lenercept 100 mg ——

Do Safety Differences Matter?

Incidents per flight

- JetBlue
- American Airlines
- United
- Delta
- Continental
- US Airways
- Southwest
- AirTran
Rates of Serious Infections per 100 Patient-years

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Rates per 100PY (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UST (N=49)</td>
<td>0.83</td>
</tr>
<tr>
<td>IFX (N=56)</td>
<td>2.49</td>
</tr>
<tr>
<td>ETAN (N=55)</td>
<td>1.47</td>
</tr>
<tr>
<td>ADA (N=102)</td>
<td>1.97</td>
</tr>
<tr>
<td>MTX Non-biologic (N=16)</td>
<td>1.28</td>
</tr>
<tr>
<td>Non-MTX Non-biologic (N=40)</td>
<td>1.05</td>
</tr>
<tr>
<td>All (N=323)</td>
<td>1.45</td>
</tr>
</tbody>
</table>

N = number of serious infections per treatment group

No Infection in 99 or 98 out of 100

- How patients perceive it depends on how you spin it

Visual communication of numeric information: adalimumab treatment in long-standing RA patients

Graphically representing risk in selected patient groups
Risk of selected serious adverse events after one year of exposure in a clinical trial setting

- All patients exposed to Adalimumab in 1-year period: 1,000 patients
- Patients presenting with serious infections: 46 /1,000 patient-years
- Opportunistic Infections: 0.9/1,000 patient-years
- Tuberculosis: 2.9/1,000 patient-years

Use images to communicate risks in perspective

Biologic Monitoring from AAD Guidelines

• “There is no specific guideline or single way of taking care of any patient”

• “There are some tests that many dermatologists obtain in patients with psoriasis before commencing systemic therapies including biologics.”
  – Blood chemistries with liver function tests
  – CBC, Hepatitis panel and TB testing

Expected Findings With Lab Testing

- Prospective study over 5 years
- 162 patients treated with etanercept and/or adalimumab
  - 370 patient-years of follow up
- 26% of etanercept and 14% of adalimumab patients had grade 3 or 4 lab abnormalities
- Laboratory abnormalities did not lead to permanent discontinuation of biologic treatment in any patient

<table>
<thead>
<tr>
<th>Chemistry</th>
<th>Haematology</th>
<th>Additional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>Haemoglobin</td>
<td>Antinuclear antibodies*</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>Haematocrit</td>
<td>Hepatitis B/C serology*</td>
</tr>
<tr>
<td>Direct bilirubin</td>
<td>White blood cell count</td>
<td></td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>White blood cell</td>
<td>Serum pregnancy test*</td>
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<tr>
<td>Alkaline phosphatase</td>
<td>differentiation</td>
<td></td>
</tr>
<tr>
<td>Alanine aminotransferase</td>
<td>Platelet count</td>
<td></td>
</tr>
<tr>
<td>γ-Glutamyl transferase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholesterol*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglycerides*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinalysis*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*These laboratory tests were only performed at pretreatment. The other tests were performed at pretreatment, weeks 6 and 12 and every 12 weeks afterwards.

Annual Cost of Treatment

- MTX 15 mg
- UVB
- PUVA
- Acitretin
- Cyclosporine 5 mg/kg
- Etanercept SQ 50 mg/wk
- Alefacept IM
- Infliximab IV 5 mg/kg

Expert Opin Pharmacother. 2003 Sep;4(9):1525-33
Annual Cost of Treatment

- Outpatient visits or services:
  - Apremilast: $4976
  - Biologics: $6458
  - Δ $1482 (p = NS)

- Outpatient pharmacy:
  - Apremilast: $23,171
  - Biologics: $42,090
  - Δ $18,919 (p < 0.001)

- Total costs:
  - Apremilast: $31,337
  - Biologics: $50,664
  - Δ $19,327 (p < 0.001)

*J Comp Eff Res. 2019 Jan;8(1):45-54*
Cost

- Doctors often don’t know the cost
- The payer does
- ICER suggests that all the treatments are cost effective
Biosimilars: To Complex To Duplicate

- ASA (21 atoms)
- ACE inhibitor (62 atoms)
- Insulin (790 atoms)
- Monoclonal Antibody (20,000 atoms)

Small molecules / large molecules
Deeper Complexity of Biologics
Etanercept is Not a Single Entity

Figure 3 Comparison of the different pre- and post-change batches of Enbrel. (a) Relative amounts of basic variants of the pre-change ($n = 6$) and the post-change ($n = 6$) batches as measured by CEX. (b) Relative amount of the G2F glycan of the pre-change ($n = 25$) and the post-change ($n = 9$) batches. (c) Exemplary CEX chromatograms. (d) Exemplary glycan mapping chromatograms.
Adalimumab Variation
Primary Structure is the Same

1: CT-P13, infliximab, biosimilar

2: US-licensed infliximab

3: EU-approved infliximab
Pharmacokinetics of Innovator and Biosimilar Adalimumab

Adherence to Biologics

Biologic Adherence

• Assessing adherence
  – “Are you keeping the extra syringes you’ve accumulated refrigerated like you are supposed to?”

• Putting patients’ minds at ease
  – “Biologic? Yes, this is an all-natural anti-inflammatory made in living cells that complements your body’s natural healing mechanisms because I like to take a holistic approach to treating skin disease”
## Comparison Table

<table>
<thead>
<tr>
<th></th>
<th>TNF</th>
<th>IL12 and/or IL23</th>
<th>IL17</th>
<th>JAK</th>
<th>PDE-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety</td>
<td>Etanercept, adalimumab, infliximab, certolizumab (golimumab)</td>
<td>Ustekinumab, guselkumab, tildrakizumab (risankizumab)</td>
<td>Secukinumab, ixekizumab, brodalumab</td>
<td>Tofacitinib</td>
<td>Apremilast</td>
</tr>
<tr>
<td>Safety</td>
<td>Some infection, rare MS</td>
<td>Clean</td>
<td>Candida risk Rare IBD</td>
<td>Possible viral reactivation</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Confidence</td>
<td>20 year safety record</td>
<td>3-10 years</td>
<td>3-5 years</td>
<td>Use in rheumatoid arthritis</td>
<td>Limited long term data</td>
</tr>
<tr>
<td>Efficacy</td>
<td>Moderate to high</td>
<td>High to highest</td>
<td>Highest</td>
<td>Moderate</td>
<td>Lowest</td>
</tr>
<tr>
<td>Convenience</td>
<td>Lots of shots</td>
<td>q2-3 months</td>
<td>Every month</td>
<td>Oral (BID)</td>
<td>Oral (BID)</td>
</tr>
<tr>
<td>Cost</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Cost**: Cost to patient may be low, cost to patients may be high
Give patients the risks & benefits of treatment in writing

• The National Psoriasis Foundation has terrific resources
• The Systemic Treatment brochure offers an overview of key points on many options

Other National Psoriasis Foundation Resources

- There are Fact Sheets on each of the biologics & a comparison table of all of them
- You can download them at no cost

https://www.psoriasis.org/about-psoriasis/treatments/biologics/resources
Standard Model

Psoriasis

Psychosocial

Joint Symptoms

Psoriasis Foundation

Rheumatology

Topicals

Promote good adherence

Yes

No

Localized?

Photo or systemic therapy

Phototherapy

Methotrexate

Biologics
Conclusions

• Use biologics for patients who need them
  – Offer the array of biologic options
• Statistically or clinically significant?
  – Comorbidities: demand absolute risk information
  – Efficacy differences
• Long term data: check who stays in the study
• Risk is subjective
  – Monitoring can be minimal or intensive as you see fit
• Give patients confidence & understanding
  – Have them use the medication regularly