Mark Lebwohl is an employee of Mount Sinai which receives research funds from: Abbvie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen / Johnson & Johnson, Kadmon, Medimmune/Astra Zeneca, Novartis, Pfizer and ViDac.

Dr. Lebwohl is also a consultant for Allergan, Leopharma, and Promius.
• Tildrakizumab
• Guselkumab – Tremfya ®
• Brodalumab – Siliq ®
• Ixekizumab – Taltz ®
• Secukinumab – Cosentyx ®
• Ustekinumab – Stelara ®
• Adalimumab – Humira®
• Etanercept – Enbrel ®
• Certolizumab - Cimzia ®
• Risankizumab/Mirikizumab
The Ideal Biologic for Psoriasis

- Strong
- Few injections
- Fast
- durable
- Safe
- Safe in pregnancy
- Effective in obese patients
- Work for PsA
- Pill
- Cheap
- Grow hair and muscles, increase libido, lose weight
Biologics for Psoriasis and Psoriatic Arthritis

STRONG

• ETANERCEPT
• ADALIMUMAB
• INFliximab
• CERTOLIZUMAB
• GOLIMUMAB
• USTEKINUMAB
• SECUKINUMAB
• IXEKIZUMAB
• BRODALUMAB
• GUSELKUMAB

• TILDRAKIZUMAB
• RISANKIZUMAB
• MIRIKIZUMAB
PASI 75
PASI 90
PASI 100
Biologics for Psoriasis and Psoriatic Arthritis - FEW INJECTIONS

- ETANERCEPT
- ADALIMUMAB
- INFLIXIMAB
- CERTOLIZUMAB
- GOLIMUMAB
- USTEKINUMAB
- SECUKINUMAB
- IXEKIZUMAB
- APREMILAST
- METHOTREXATE
- CYCLOSPORINE
- ACITRETIN
- BRODALUMAB
- GUSELKUMAB
- TILDRAKIZUMAB
- RISANKIZUMAB
- MIRIKIZUMAB
Biologics for Psoriasis and Psoriatic Arthritis - FAST

- ETANERCEPT
- ADALIMUMAB
- INFliximab
- CERTOLIZUMAB
- GOLIMUMAB
- USTEKINUMAB
- SECUKINUMAB
- IXEKIZUMAB
- BRODALUMAB
- GUSELKUMAB
- TILDRAKIZUMAB
- RISANKIZUMAB
- MIRIKIZUMAB

SPEED
Time to achieve 50% improvement in baseline PASI scores (NRI) in induction phase (baseline to week 12). Time estimates based on linear progression. Comparative biologics shown as weighted means based on individual study published results.
Biologics for Psoriasis and Psoriatic Arthritis

DURABLE

• ETANERCEPT
• ADALIMUMAB
• INFLIXIMAB
• CERTOLIZUMAB
• GOLIMUMAB
• USTEKINUMAB
• SECUKINUMAB
• IXEKIZUMAB
• BRODALUMAB
• GUSELKUMAB

• TILDRAKIZUMAB
• RISANKIZUMAB
• MIRIKIZUMAB
Secukinumab Delivers High and Long-lasting Skin Improvement Through 5 Years

LOCF, last observation carried forward; MI, multiple imputation; n, number of evaluable patients in the as-observed analysis (the number of evaluable patients in the MI and LOCF analyses was 168 at each time point); PASI, Psoriasis Area and Severity Index

<table>
<thead>
<tr>
<th>Year</th>
<th>As observed</th>
<th>MI</th>
<th>LOCF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>n = 162</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>n = 152</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>n = 139</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>n = 132</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>n = 122</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$\Delta = \approx 8\%$

$\Delta = \approx 7\%$

$\Delta = \approx 5\%$
UNCOVER-1, 2, 3: PASI responses up to Week 60 for initial non/partial responders to ixekizumab

- By Week 20 and Week 24, more than 60% of non/partial responders at Week 12 maintained PASI 50 response and more than 30% had PASI 75 response

Subgroup of patients who did not respond/partially responded (sPGA ≥2 and no PASI 75 response) to IXE q2w during the 12-week induction period and who were assigned to IXE q4w (n=73)

Kemény L, et al. EADV 2017, FC04.04 Sponsored by Eli Lilly and Company
At week 264, patients had been off treatment for ≥6 weeks. Error bars represent 95% CI

Papp K, et al. EADV 2017, P1798 Sponsored by LEO Pharma

- PASI responses with brodalumab over 5 years
- As observed data
- Efficacy is maintained for up to 5 years

At week 264, patients had been off treatment for ≥6 weeks. Error bars represent 95% CI

Papp K, et al. EADV 2017, P1798 Sponsored by LEO Pharma
FAS (full analysis set; subjects with ≥1 dose of extension treatment based on assigned treatment); as observed data.
Patients entering OLE after 64 weeks (reSURFACE 1) or 52 weeks (reSURFACE 2) were at least partial responders (PASI ≥50).
For reSURFACE 1, patients had to have received active drug within 12 weeks of end of base study.

Papp K, et al. EADV 2017, D3T01.1H Sponsored by Merck & Co., Inc.
VOYAGE1: PASI 90 & PASI 100 response with guselkumab through 2 years

**PASI 90**

- **GUS**
- **Placebo → GUS**
- **ADA → GUS**

- **n= 329**
- **n= 174**
- **n= 334**

**Patients (%)**

- Week 0: 0%
- Week 28: 50.5%
- Week 52: 80.1%
- Week 100: 82.3%

**NRI=72.3**

**PASI 100**

- **GUS**
- **Placebo → GUS**
- **ADA → GUS**

- **n= 329**
- **n= 174**
- **n= 334**

**Patients (%)**

- Week 0: 0%
- Week 28: 24.0%
- Week 52: 50.5%
- Week 100: 55.1%

**NRI=43.2**
Mean PASI Improvement in Patients Treated with Subcutaneous RISANKIZUMAB (0.25 and 1.0 mg/kg)

6/9 (66%) of patients who entered long term follow up maintained PASI 100 for 41−66 weeks.

<table>
<thead>
<tr>
<th>Week after dose (N)</th>
<th>Mean Improvement in PASI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>(N =13)</td>
</tr>
<tr>
<td>4</td>
<td>(N =10)</td>
</tr>
<tr>
<td>8</td>
<td>(N =6)</td>
</tr>
<tr>
<td>12</td>
<td>(N =7)</td>
</tr>
<tr>
<td>16</td>
<td>(N =9)</td>
</tr>
<tr>
<td>20</td>
<td>(N =9)</td>
</tr>
<tr>
<td>24</td>
<td>(N =5)</td>
</tr>
<tr>
<td>28</td>
<td></td>
</tr>
<tr>
<td>32</td>
<td></td>
</tr>
<tr>
<td>36</td>
<td></td>
</tr>
<tr>
<td>40</td>
<td></td>
</tr>
<tr>
<td>44</td>
<td></td>
</tr>
<tr>
<td>48</td>
<td></td>
</tr>
<tr>
<td>52</td>
<td></td>
</tr>
</tbody>
</table>

Krueger et al. J. Allergy Clinical Immunology. Published online 12 March 2015
Fig 1. Kaplan-Meier drug survival analysis for each systemic agent.
Biologics for Psoriasis and Psoriatic Arthritis
SAFE

- ETANERCEPT
- ADALIMUMAB
- INFLIXIMAB
- CERTOLIZUMAB
- GOLIMUMAB
- USTEKINUMAB
- SECUKINUMAB
- IXEKIZUMAB
- BRODALUMAB
- GUSELKUMAB

- TILDRAKIZUMAB
- RISANKIZUMAB
- MIRIKIZUMAB
Methotrexate Boxed Warning

• Fetal death/congenital anomalies
• bone marrow suppression and GI toxicity with concomitant NSAIDs
• hepatotoxicity, fibrosis, and cirrhosis
• Lung disease
• malignant melanomas
• infections
• Severe, occasionally fatal, skin reactions
Boxed Warning: Etanercept, Adalimumumab, Golimumumab

- Infections
- Malignancy
Infliximab Boxed Warning

- Bone marrow suppression, corticosteroid therapy, diabetes mellitus, fungal infection, herpes infection, immunosuppression, infection, mycobacterial infection, sepsis, tuberculosis, viral infection
- Cervical cancer, lymphoma, neoplastic disease, secondary malignancy, skin cancer
Efficacy and Safety of up to 10 years of Etanercept Therapy in North American Patients with Early and Longstanding Rheumatoid Arthritis

- Open label extensions of etanercept trials
- 1272 patients

Poster presented at AAD, March 6-10 2009
San Francisco
Adalimumab: long-term safety in 23,458 patients from global clinical trials in rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis and Crohn’s disease

G. Burmester, Panaccione R, Gordon KB, McIlraith MJ, Lacerda AP
Treatment with TNF blockers and mortality risk in patients with rheumatoid arthritis.


- Anti-TNF: 51 deaths/3177 pt yrs
- Controls: 137 deaths/3900 pt yrs

First cardiac event: anti-TNF - 14.0/1000 pt yrs controls - 35.4/1000 pt yrs
Reduction in the incidence of myocardial infarction in patients with rheumatoid arthritis who respond to anti-tumor necrosis factor alpha therapy: results from the British Society for Rheumatology Biologics Register.

Association Between Tumor Necrosis Factor Inhibitor Therapy and Myocardial Infarction Risk in Patients With Psoriasis.


- MI incidence TNF inhibitor/oral or photoRx/topical: 3.05, 3.85, and 6.73 per 1000 patient-years
- adjusted HR 0.50 vs topical Rx 95% CI, 0.32-0.7
Ustekinumab, Secukinumab, Ixekizumab, Brodalumab, Guselkumab: NO BOXED WARNING
Results: Age and Gender Adjusted Cumulative Rates of Malignancies (excluding NMSC) per 100 Patient-Years (PY) Based on Any Exposure to Therapy (Figure 1)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cumulative Rates per 100 PY (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ustekinumab (60/12472 PY)</td>
<td>0.51</td>
</tr>
<tr>
<td>Infliximab* (41/5176 PY)</td>
<td>0.81</td>
</tr>
<tr>
<td>Other Biologics** (116/15991 PY)</td>
<td>0.73</td>
</tr>
<tr>
<td>Non-biologic (57/6749 PY)</td>
<td>0.75</td>
</tr>
<tr>
<td>All*** (274/40388 PY)</td>
<td>0.68</td>
</tr>
</tbody>
</table>

*This group includes (n=36) patients exposed to golimumab only.
**95.7% (n=4067) are adalimumab &/or etanercept patients, with the remainder exposed to other biologics.
***Adjustment used All population as reference.

Figure 1. Cumulative Rates of Malignancies

Inborn errors of human IL-17 immunity underlie chronic mucocutaneous candidiasis.
Puel A, et al.
Immunity to infection in IL-17-deficient mice and humans.

Chronic mucocutaneous candidiasis in humans with inborn errors of interleukin-17 immunity.
Biologics for Psoriasis and Psoriatic Arthritis

SAFE IN PREGNANCY

- ETANERCEPT
-adalimumab
- infliximab
- certolizumab
- golimumab
- ustekinumab
- secukinumab
- ixekizumab
- brodalumab
- guselkumab

- tildrakizumab
- risankizumab
- mirikizumab
CRIB: Maternal and infant plasma and umbilical cord levels of certolizumab pegol

**Plasma CZP levels (n=14 mother–infant pairs)**

<table>
<thead>
<tr>
<th>CZP concentration (µg/mL)</th>
<th>Delivery (±24 hours)</th>
<th>Week 4 (±7 days)</th>
<th>Week 8 (±7 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLQ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 infant had a minimal CZP level of 0.042 µg/mL, mother’s level was 49.4 µg/mL (infant/mother ratio: 0.0009)

LLOQ = 0.032 µg/mL

**Plasma CZP levels in umbilical cord (n=15)**

<table>
<thead>
<tr>
<th>CZP concentration (µg/mL)</th>
<th>Delivery (±24 hours)</th>
<th>Umbilical cords</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLQ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The infant with a CZP level at birth of 0.042 µg/mL had a CZP level of 0.040 µg/mL in the umbilical cord

LLOQ = 0.032 µg/mL

---

2/16 infant samples excluded from per protocol analysis set (1 missing data at birth, 1 due to implausible PK data (i.e., data not consistent with pediatric CZP PK model, based on expected range of clearance, volume of distribution, and subsequent elimination t½); 2 samples not collected; 1 umbilical cord excluded due to missing data; Umbilical cords were collected within 1 h of delivery. BLQ, below limits of quantitation of the assay; LLOQ, lower limit of quantitation

Kimball A, et al. EADV 2017, FC04.03 Sponsored by UCB Pharma
Biologics for Psoriasis and Psoriatic Arthritis –
OBESITY: ADJUST FOR WEIGHT

- ETANERCEPT
- ADALIMUMAB
- INFLIXIMAB
  - CERTOLIZUMAB
  - GOLIMUMAB
- USTEKINUMAB
  - SECUKINUMAB
  - IXEKIZUMAB
  - BRODALUMAB
  - GUSELKUMAB
- TILDRAKIZUMAB
- RISANKIZUMAB
- MIRIKIZUMAB
Biologics for Psoriasis and Psoriatic Arthritis – OBESITY: ADJUST FOR WEIGHT

- ETANERCEPT
- ADA'LIMUMAB

- INFLIXIMAB

- CERTOLIZUMAB
- GOLIMUMAB

- USTEKINUMAB

- SECUKINUMAB
- IXEKIZUMAB
- BRODALUMAB
- GUSELKUMAB

- TILDRAKIZUMAB
- RISANKIZUMAB
- MIRIKIZUMAB
Biologics for Psoriasis and Psoriatic Arthritis – OBESITY

- ETANERCEPT
- ADALIMUMAB
- INFliximab
- CERTOLIZUMAB
- GOLIMUMAB
- USTEKINUMAB
- SECUKINUMAB
- IXEKIZUMAB
- BRODALUMAB
- GUSELKUMAB
- TILDRAKIZUMAB
- RISANKIZUMAB
- MIRIKIZUMAB
Biologics for Psoriasis and Psoriatic Arthritis - PSA

- ETANERCEPT
- ADALIMUMAB
- INFLIXIMAB
- CERTOLIZUMAB
- GOLIMUMAB
  - USTEKINUMAB
  - SECUKINUMAB
  - IXEKIZUMAB
  - BRODALUMAB
  - GUSELKUMAB

- TILDRAKIZUMAB
- RISANKIZUMAB
- MIRIKIZUMAB
Biologics for Psoriasis and Psoriatic Arthritis - PSA

- ETANERCEPT
- ADALIMUMAB
- INFLIXIMAB
- CERTOLIZUMAB
- GOLIMUMAB
- USTEKINUMAB
- SECUKINUMAB
- IXEKIZUMAB
- BRODALUMAB
- GUSELKUMAB

- TILDRAKIZUMAB
- RISANKIZUMAB
- MIRIKIZUMAB
Biologics for Psoriasis and Psoriatic Arthritis - PSA

• ETANERCEPT
• ADALIMUMAB
• INFLIXIMAB
• CERTOLIZUMAB
• GOLIMUMAB
• USTEKINUMAB
• SECUKINUMAB
• IXEKIZUMAB
• BRODALUMAB
• GUSELKUMAB

• TILDRAKIZUMAB
• RISANKIZUMAB
• MIRIKIZUMAB