Biologics and Psoriasis: The Beat Goes On

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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

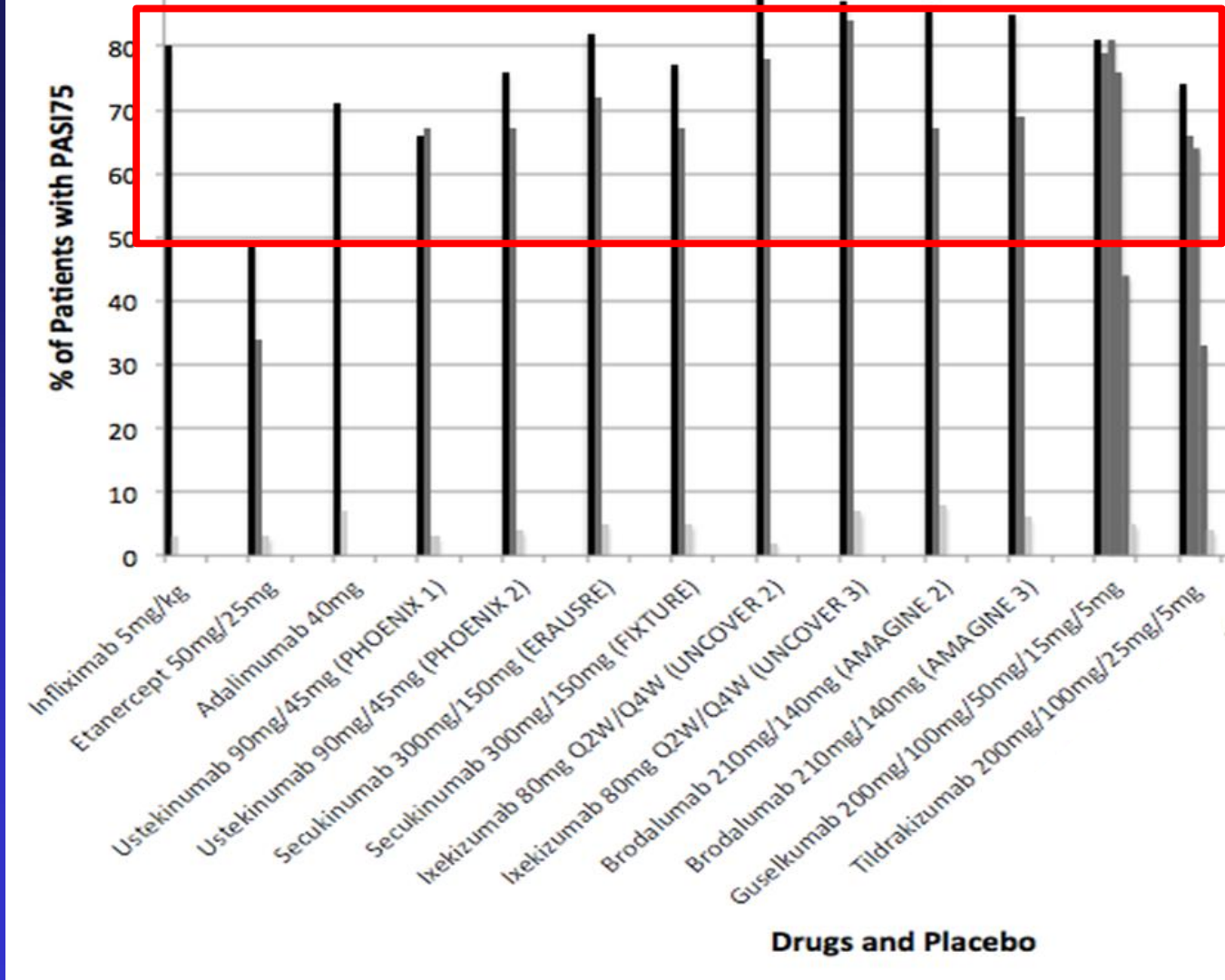
- Strong
- Few injections
- Fast
- durable
- Safe
- Safe in pregnancy
- Effective in obese patients
- Work for PsA
- Pill
- Cheap
- Grow hair and muscles, increase libido, lose weight

Biologics for Psoriasis and Psoriatic Arthritis

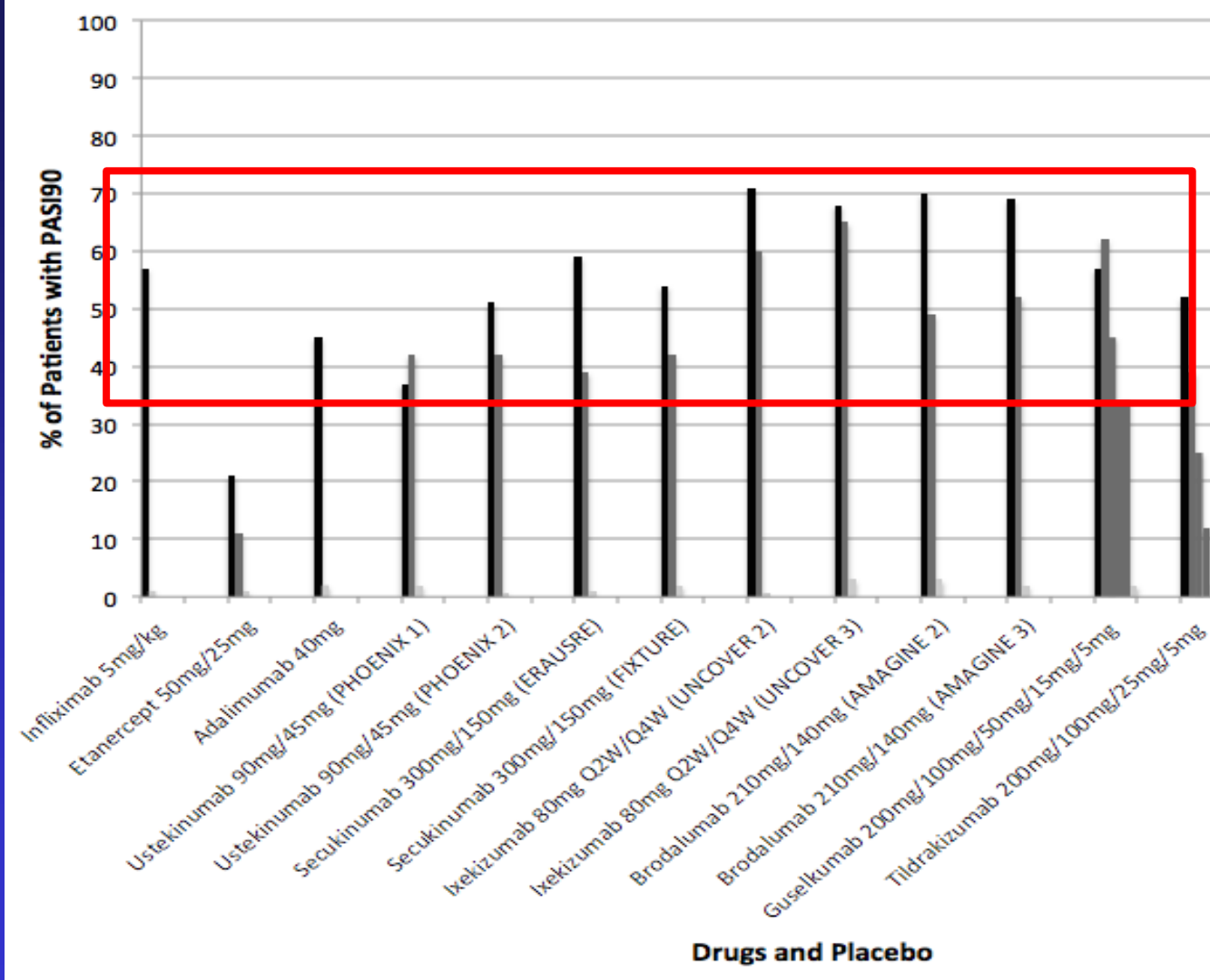
STRONG

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

PASI 75


% of Patients with PASI75
0
10
20
30
40
50
60
70
80
Infliximab 5mg/kg
Etanercept 50mg/25mg
Adalimumab 40mg
Ustekinumab 90mg/45mg (PHOENIX 1)
Ustekinumab 90mg/45mg (PHOENIX 2)
Secukinumab 300mg/150mg (ERAUSRE)
Secukinumab 300mg/150mg (FIXTURE)
Ixekizumab 80mg Q2W/Q4W (UNCOVER 2)
Ixekizumab 80mg Q2W/Q4W (UNCOVER 3)
Brodalumab 210mg/140mg (AMAGINE 2)
Brodalumab 210mg/140mg (AMAGINE 3)
Guselkumab 200mg/100mg/50mg/15mg/5mg
Tildrakizumab 200mg/100mg/25mg/5mg
Drugs and Placebo

PASI 90


100
90
80
70
60
50
40
30
20
10
0
% of Patients with PASI90
Infliximab 5mg/kg
Etanercept 50mg/25mg
Adalimumab 40mg
Ustekinumab 90mg/45mg (PHOENIX 1)
Ustekinumab 90mg/45mg (PHOENIX 2)
Secukinumab 300mg/150mg (ERAUSRE)
Secukinumab 300mg/150mg (FIXTURE)
Ixekizumab 80mg Q2W/Q4W (UNCOVER 2)
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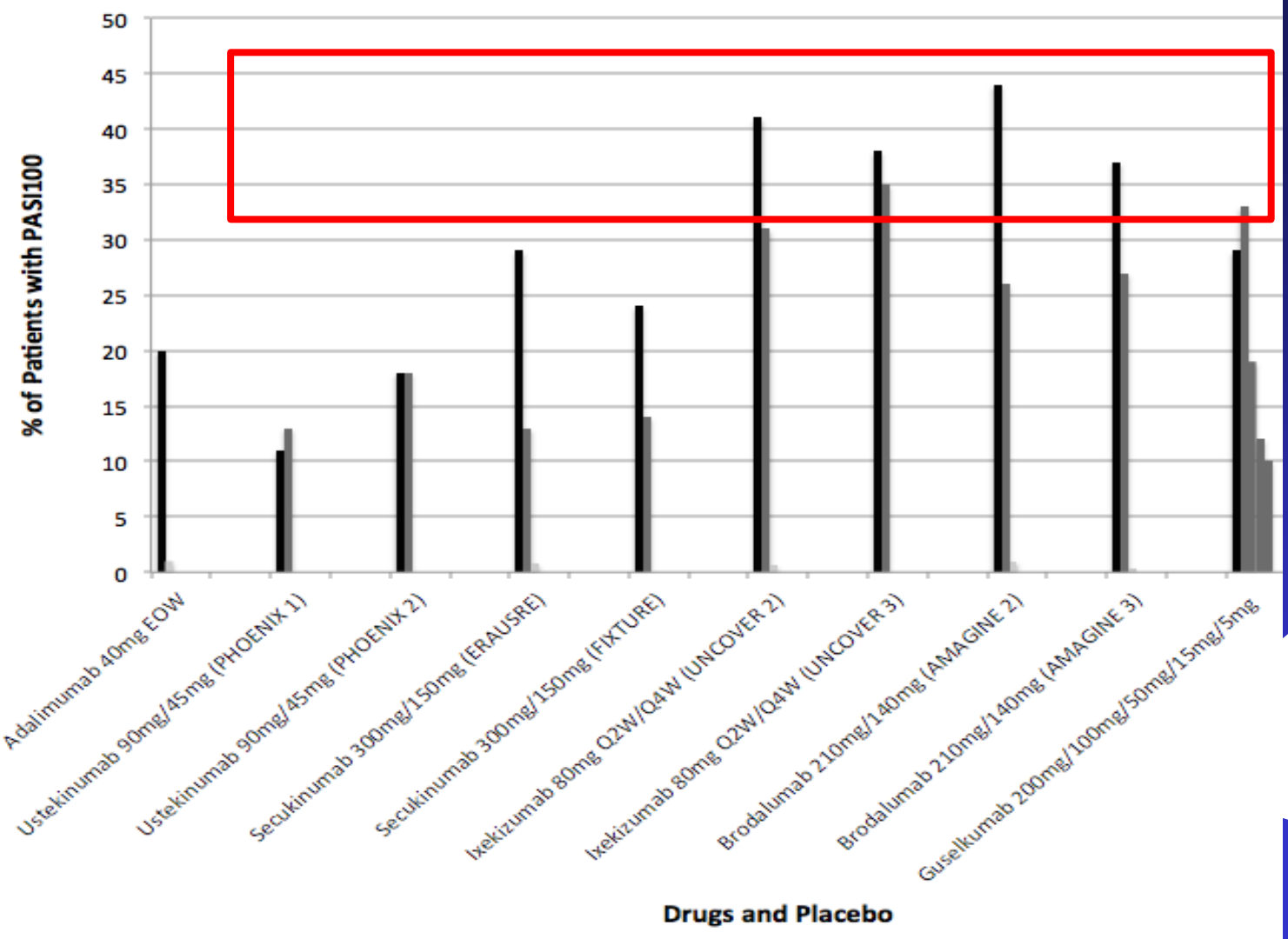
Brodalumab 210mg/140mg (AMAGINE 3)
Guselkumab 200mg/100mg/50mg/15mg/5mg
Tildrakizumab 200mg/100mg/25mg/5mg
Drugs and Placebo

PASI 100


% of Patients with PASI100
50
45
40
35
30
25
20
15
10
5
0
Adalimumab 40mg EOW
Ustekinumab 90mg/45mg (PHOENIX 1)
Ustekinumab 90mg/45mg (PHOENIX 2)
Secukinumab 300mg/150mg (ERAUSRE)
Secukinumab 300mg/150mg (FIXTURE)
Ixekizumab 80mg Q2W/Q4W (UNCOVER 2)
Ixekizumab 80mg Q2W/Q4W (UNCOVER 3)
Brodalumab 210mg/140mg (AMAGINE 2)
Brodalumab 210mg/140mg (AMAGINE 3)
Guselkumab 200mg/100mg/50mg/15mg/5mg
Drugs and Placebo

Biologics for Psoriasis and Psoriatic Arthritis- FEW INJECTIONS

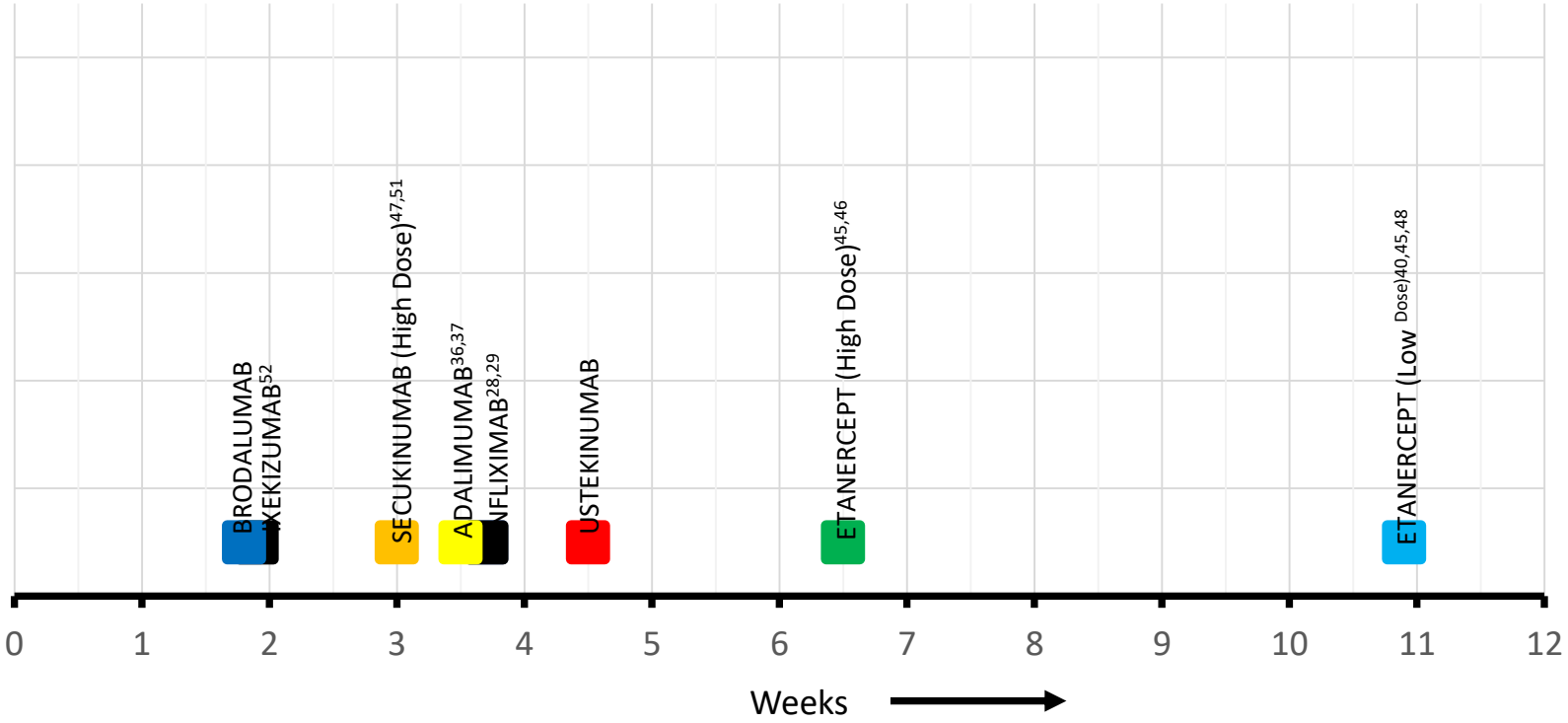
- **ETANERCEPT**
- **ADALIMUMAB**
- **INFLIXIMAB**
- **CERTOLIZUMAB**
- **GOLIMUMAB**
- **USTEKINUMAB**
- **SECUKINUMAB**
- **IXEKIZUMAB**
- **APREMILAST**
- **METHOTREXATE**
- **CYCLOSPORINE**
- **ACITRETIN**
- **BRODALUMAB**
- **GUSELKUMAB**
- **TILDRAKIZUMAB**
- **RISANKIZUMAB**
- **MIRIKIZUMAB**

Biologics for Psoriasis and Psoriatic Arthritis- FAST

- **ETANERCEPT**
- **ADALIMUMAB**
- **INFLIXIMAB**
- **CERTOLIZUMAB**
- **GOLIMUMAB**
- **USTEKINUMAB**
- **SECUKINUMAB**
- **IXEKIZUMAB**

- **BRODALUMAB**
- **GUSELKUMAB**
- **TILDRAKIZUMAB**
- **RISANKIZUMAB**
- **MIRIKIZUMAB**

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.

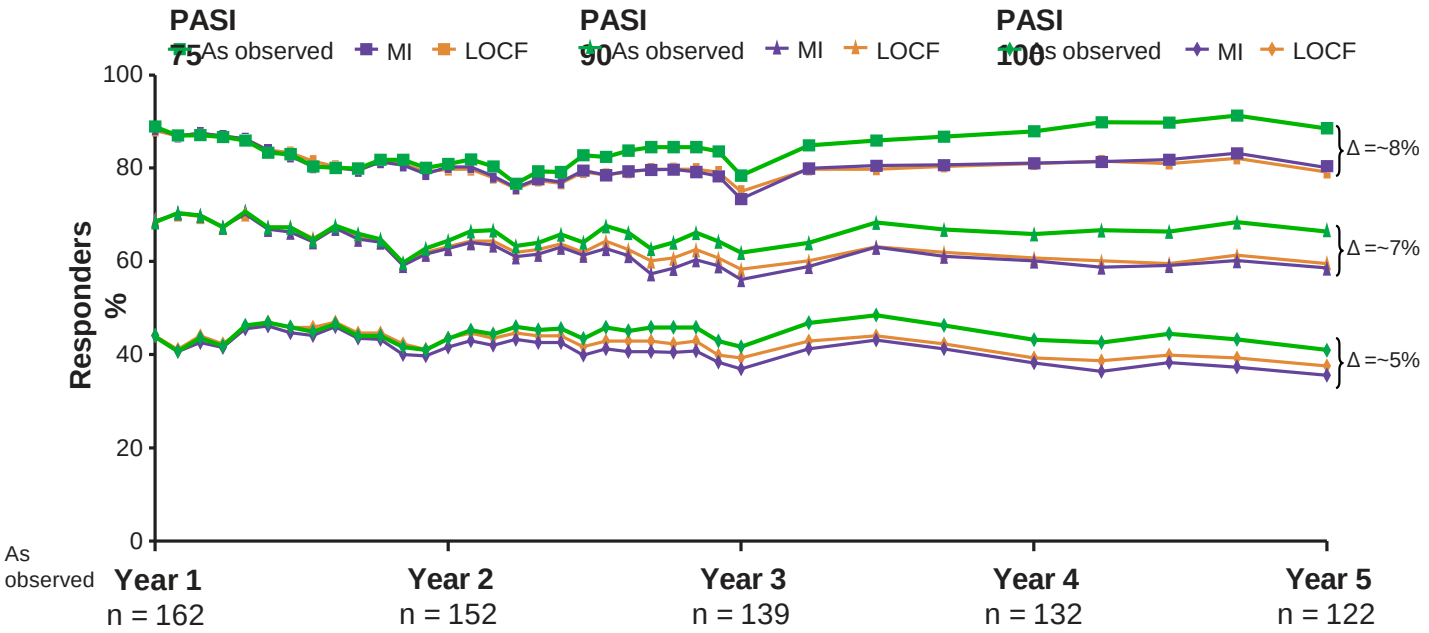


Biologics for Psoriasis and Psoriatic Arthritis

DURABLE

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

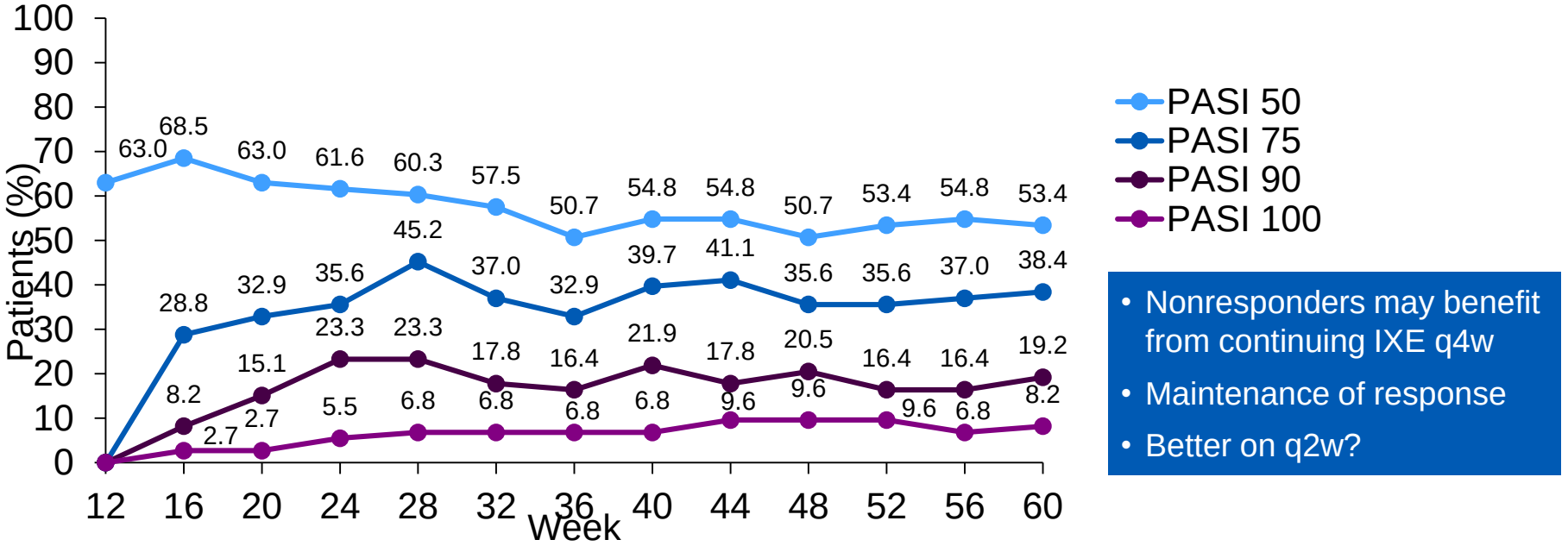
Secukinumab Delivers High and Long-lasting Skin Improvement Through 5 Years



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

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

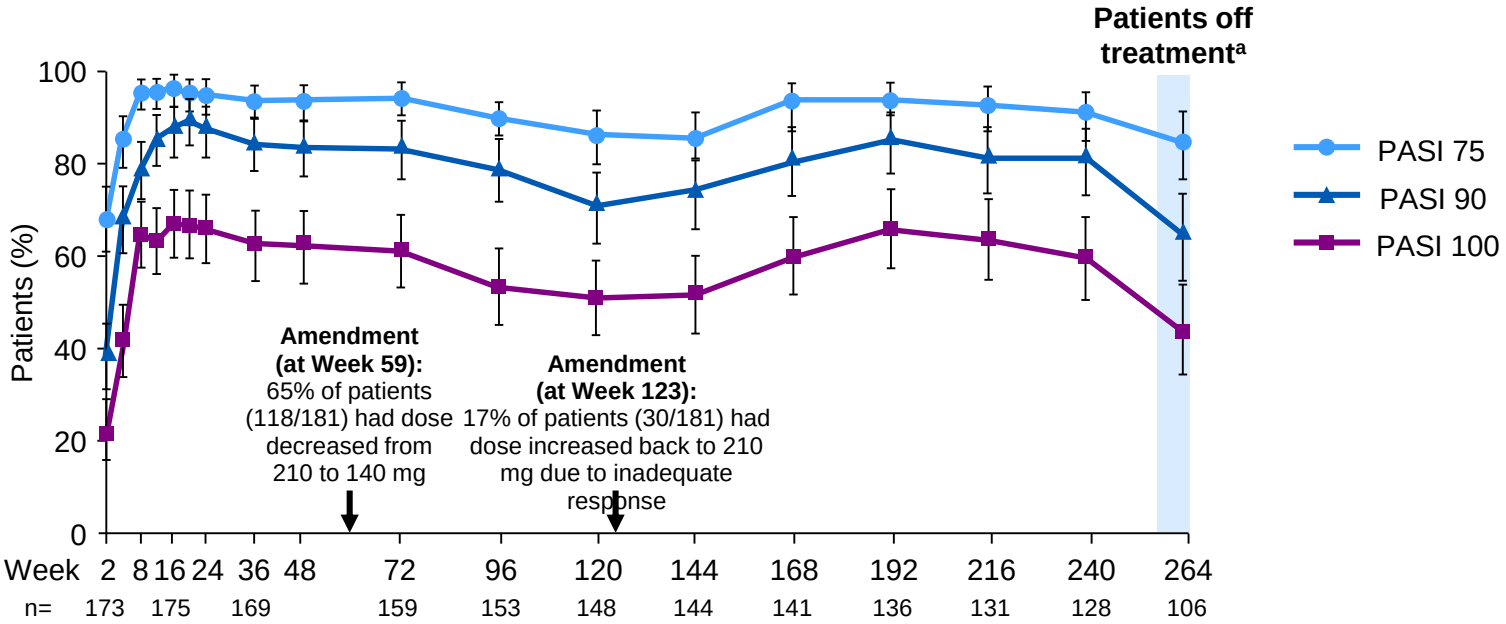


- Nonresponders may benefit from continuing IXE q4w
- Maintenance of response
- Better on q2w?

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

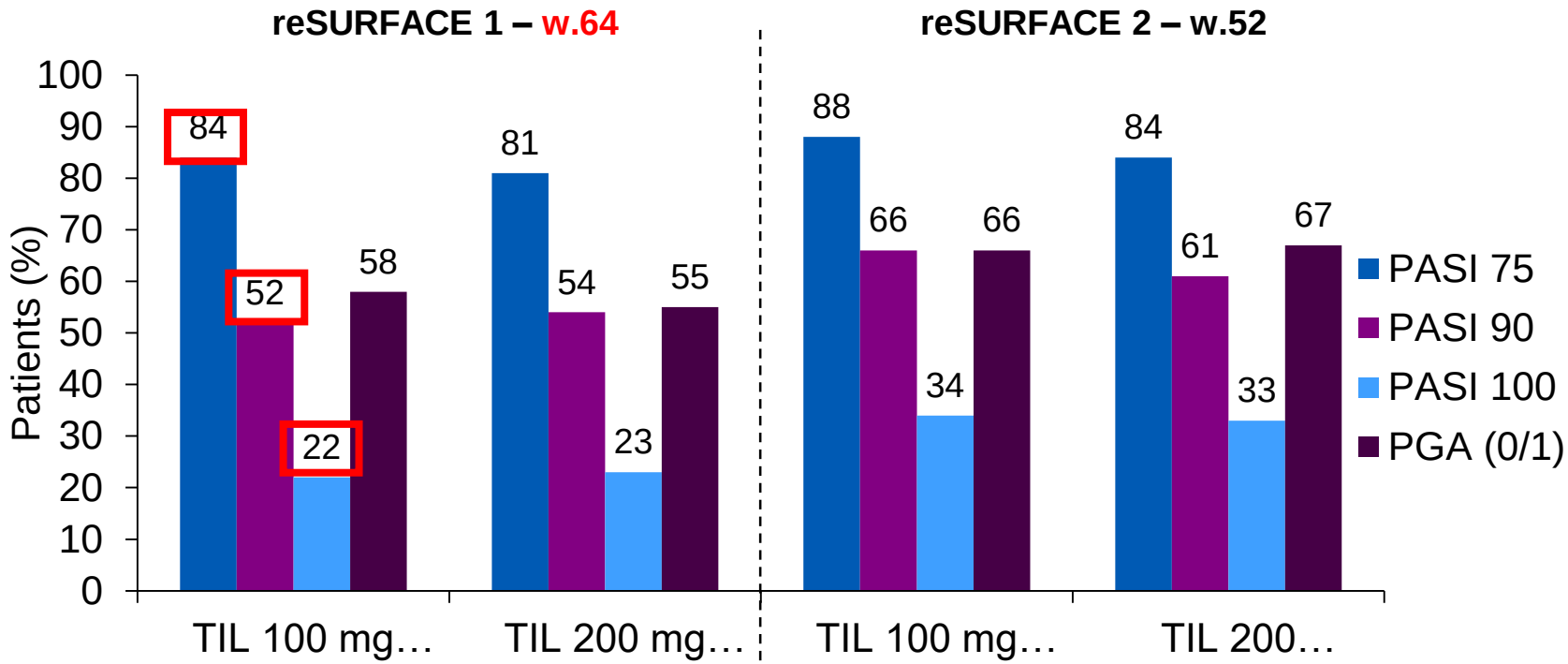
PASI responses with brodalumab over 5 years



- "As observed" data
- Efficacy is maintained for up to 5 years

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

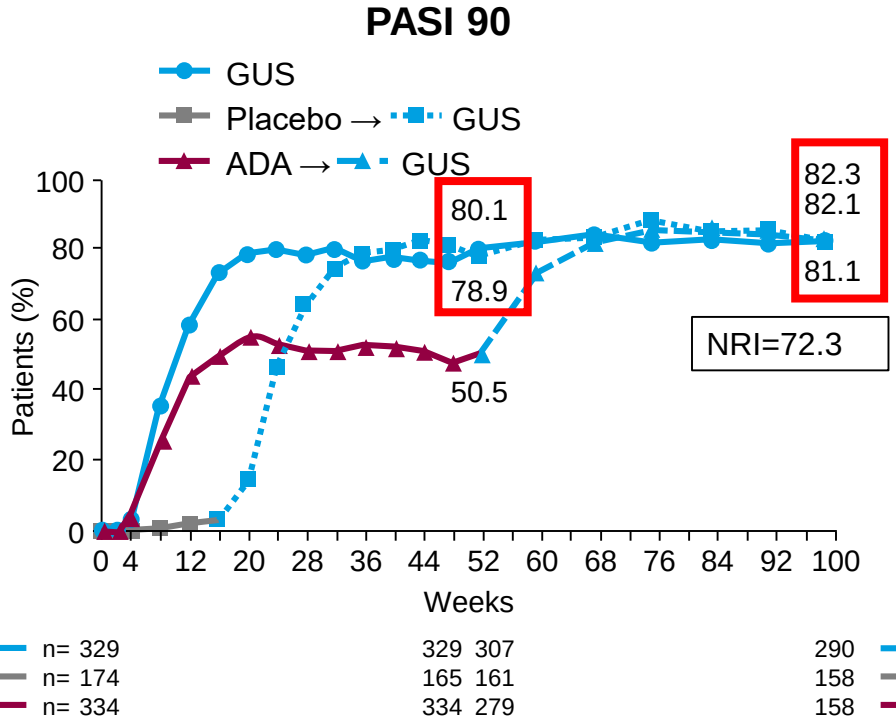
Papp K, et al. EADV 2017, P1798 Sponsored by LEO Pharma

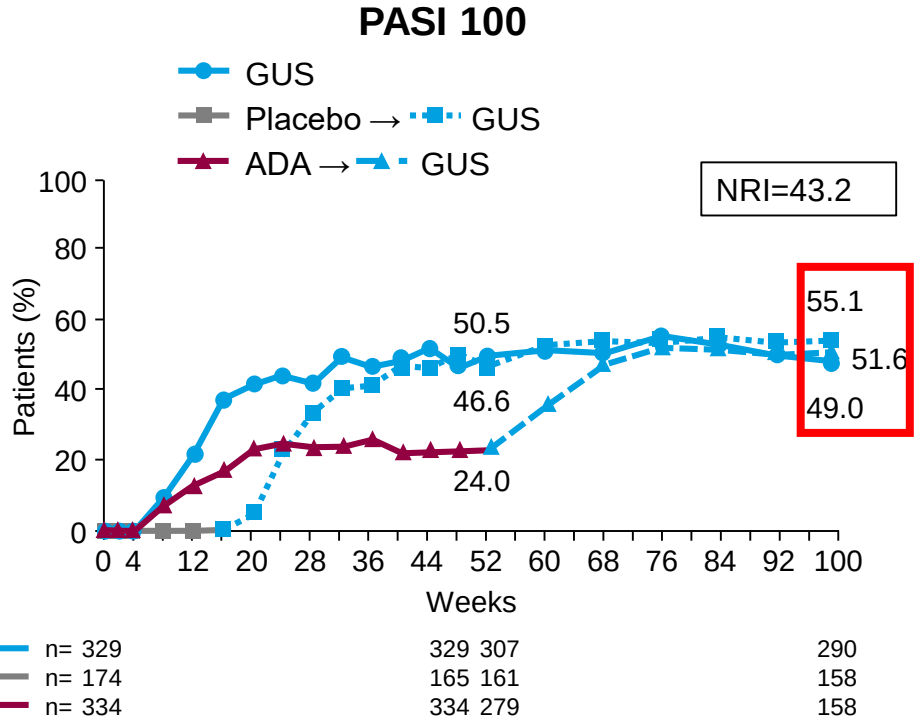


FAS (full analysis set; subjects with ≥1 dose of extension treatment based on assigned treatment); as observed data
Patients entering OLE after 64 weeks (reSURFACE 1) or 52 weeks (reSURFACE 2) were at least partial responders (PASI ≥50).
For reSURFACE 1, patients had to have received active drug within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

Papp K, et al. EADV 2017, D3T01.1H Sponsored by Merck & Co., Inc.

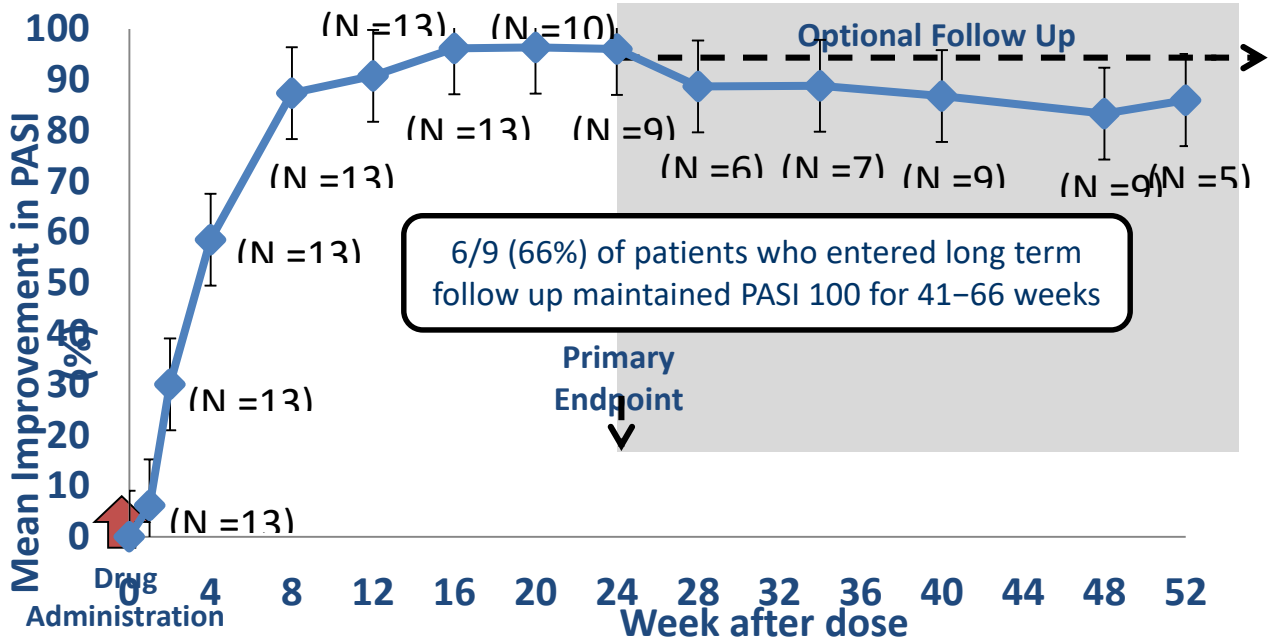
VOYAGE1: PASI 90 & PASI 100 response with guselkumab through 2 years





Griffiths CEM, et al. EADV 2017, D3T01.I Sponsored by Janssen Research and Development LLC

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



Krueger et al. J. Allergy Clinical Immunology. Published on line 12 March 2015

Biologic drug survival in Israeli psoriasis patients.. Shalom G, et al;J Am Acad Dermatol. 2017;4(76):662-9.

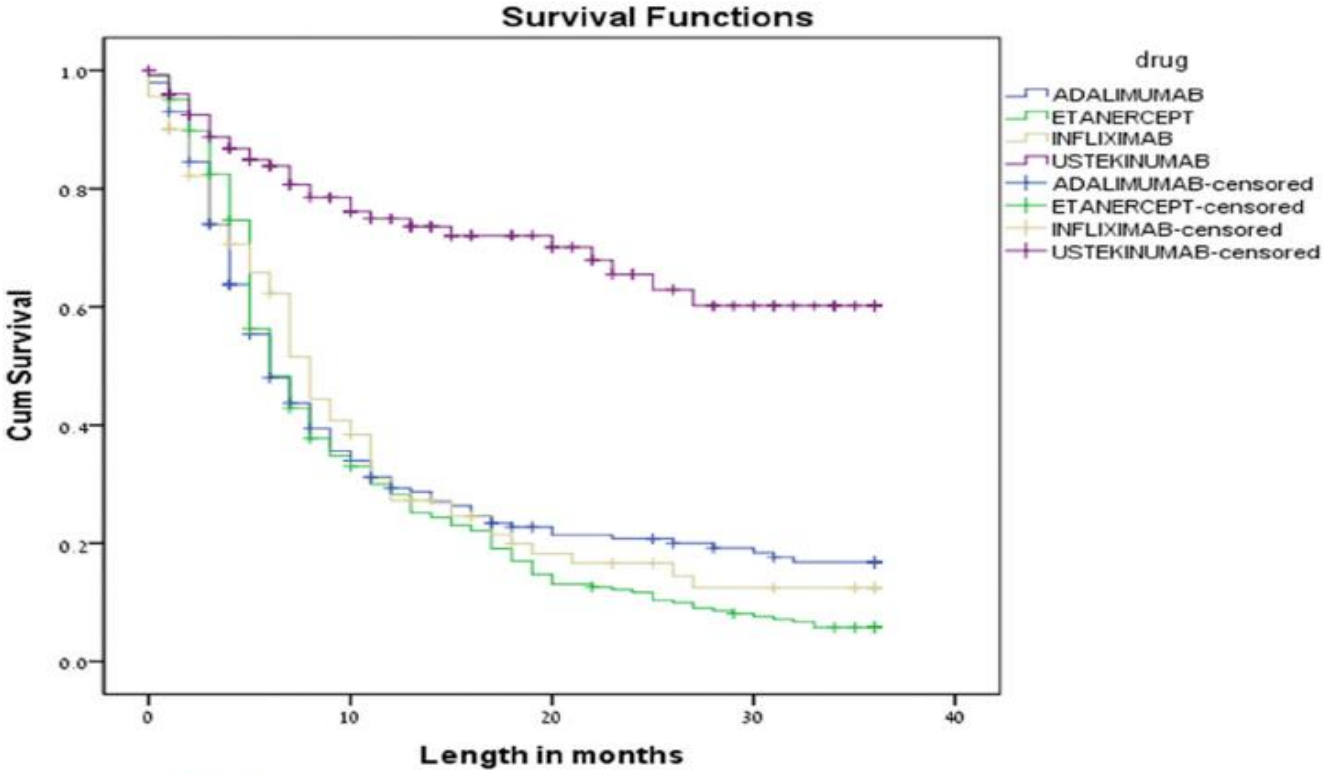


Fig 1. Kaplan-Meier drug survival analysis for each systemic agent.

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, Adalimumab, Golimumab

- 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

Ann Rheum Dis. 2013;72:517-24

Treatment with TNF blockers and mortality risk in patients with rheumatoid arthritis.

Jacobsson LT et al.

Ann Rheum Dis. 2007;66:670-675.

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

Treatment with tumor necrosis factor blockers is associated with a lower incidence of first cardiovascular events in patients with rheumatoid arthritis.

Jacobsson LT et al.

J Rheumatol. 2005;32:1213-8.

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.

Dixon WG, Watson KD, Lunt M, Hyrich KL; British Society for Rheumatology Biologics Register Control Centre Consortium, Silman AJ, Symmons DP; British Society for Rheumatology Biologics Register. Arthritis Rheum. 2007;56(9):2905-12.

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

Wu JJ, Poon KY, Channual JC, Shen AY.
Arch Dermatol. 2012 Aug 20:1-7.

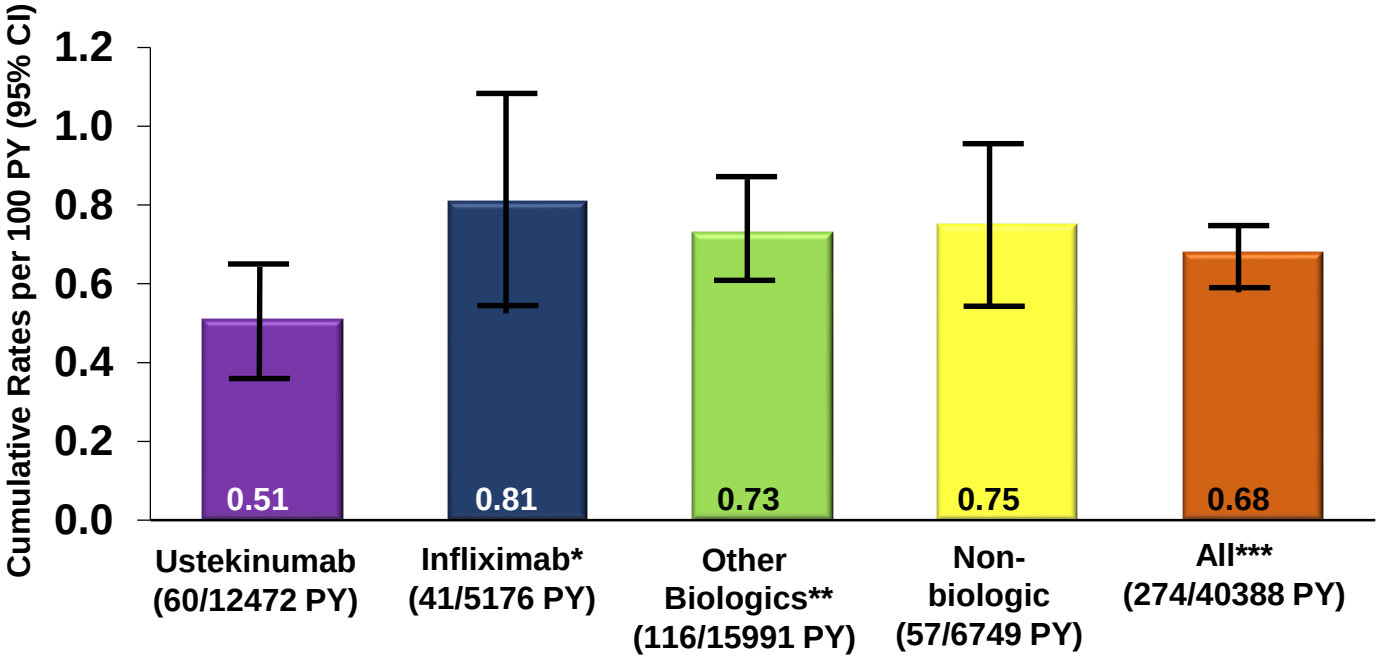
- MI incidence TNF inhibitor/ oral or photoRx /topical: 3.05, 3.85, and 6.73 per 1000 patient-years
- adjusted HR 0.50 vs topical Rx 95% CI, 0.32-0.7

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)

Figure 1. Cumulative Rates of Malignancies



*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.

Fiorentino D, et al. AAD 2015. P1631.

Inborn errors of human IL-17 immunity underlie chronic mucocutaneous candidiasis.

Puel A, et al.

Allergy Clin Immunol. 2012;12:616-22.

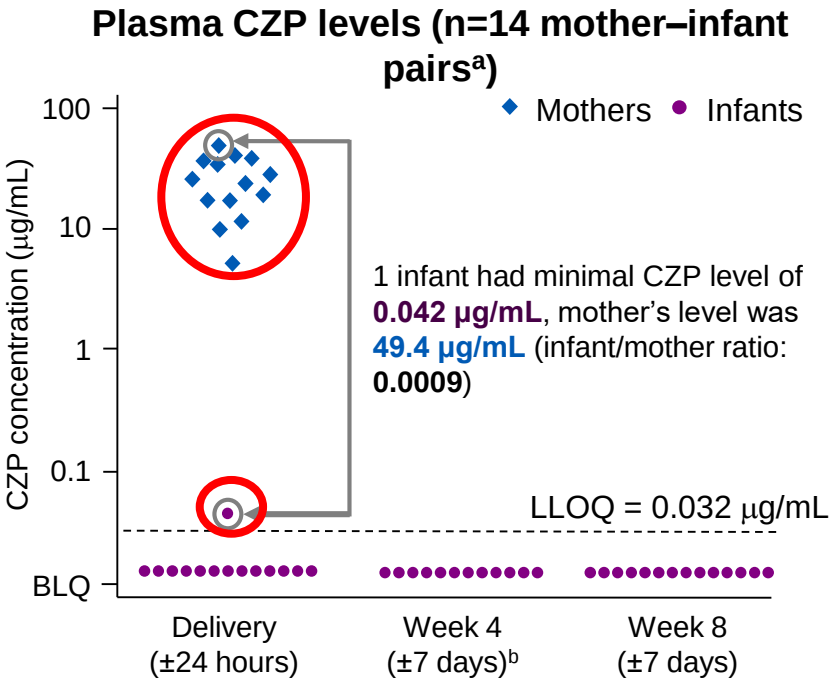
Immunity to infection in IL-17-deficient mice and humans.
Cypowyj S, Picard C, Maródi L, et al
Eur J Immunol. 2012;42:2246-2254.

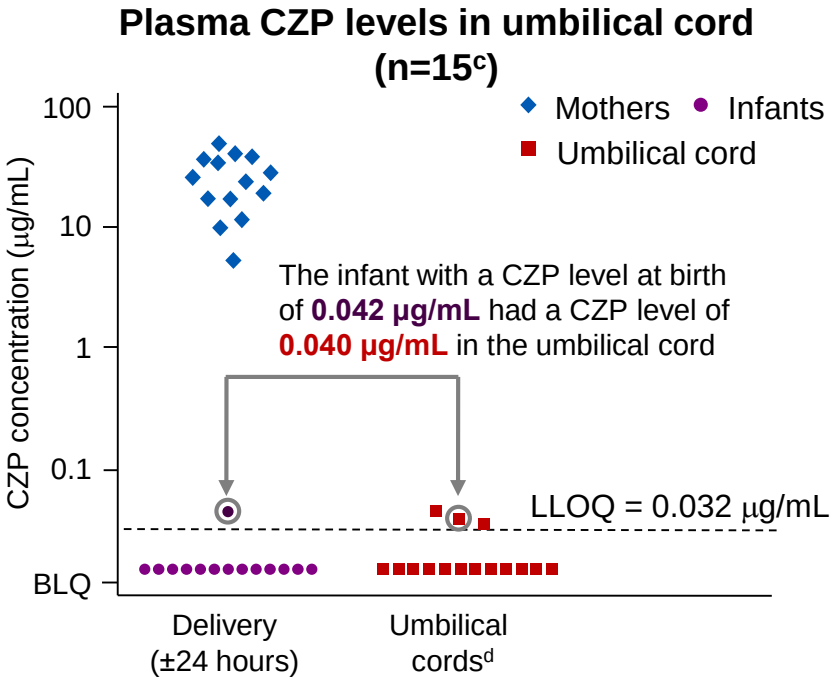
Chronic mucocutaneous candidiasis in humans with inborn errors of interleukin-17 immunity.
Puel A, Cypowyj S, Bustamante J, et al.
Science. 2011;332(6025):65-68.

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





[a]2/16 infant samples excluded from per protocol analysis set (1 missing data at birth, 1 due to implausible PK data [ie, data not consistent with pediatric CZP PK model, based on expected range of clearance, volume of distribution, and subsequent elimination $t_{½}$]); [b]2 samples not collected; [c]1 umbilical cord excluded due to missing data; [d]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**
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- **IXEKIZUMAB**
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- **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**
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- **CERTOLIZUMAB**
- **GOLIMUMAB**
- **USTEKINUMAB**
- **SECUKINUMAB**
- **IXEKIZUMAB**
- **BRODALUMAB**
- **GUSELKUMAB**

- **TILDRAKIZUMAB**
- **RISANKIZUMAB**
- **MIRIKIZUMAB**