OFF LABEL BIOLOGICS IN DERMATOLOGY

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DISCLOSURES

- Consultant, Speaker, Investigator:
  - Abbvie, Amgen, Brickell Biotech, Dermavant, DS Biopharma, Eli Lilly & Co., Foamix, Incyte, Janssen, Merck/Serono, Novartis

- Employee/Stockholder(ended Sept 2014):
  - Eli Lilly & Co.
Probity Medical Research

- International Consortium of Dermatology Researchers
- Adding research sites all across the US
Objectives

- Understand how new biologic therapies will dramatically change dermatology.
- Understand how the MOA of the biologic determines which Derm diseases will be successfully treated.
ARS: Which Disease has the Highest Need for a Biologic?

1. Severe Atopic Dermatitis
2. Hidradenitis Suppurativa
3. Plaque Psoriasis
4. Pemphigus Vulgaris
5. Pyoderma Gangrenosa
6. Chronic Urticaria
Our Current Biologics

- **Anti-TNF**
  - Receptor: Etanercept
  - Antibody: Adalimumab, Infliximab, Certolizumab
- **Anti-IL-12/23**: Ustekinumab
- **Anti-IL-17**: Secukinumab, Ixekizumab
- **Anti-IL-17RA**: Brodalumab
- **Anti-IL-23**: Gusekumab, Tildrakizumab
- **IL-1 RA**: Anakinra
- **Anti-IL-1B**: Canakinumab
- **Anti-IgE**: Omalizumab
- **Anti-CD20**: Rituximab
- **Anti-IL-4/13**: Dupilumab
Tumor Necrosis Factor (TNF)

- TNF has myriad upstream and effector roles in TH1 inflammation
- Receptor binds free TNF
- Antibodies bind free and bound TNF
- Both approved for PSO, PSA, RA, AS
- Antibodies approved for Crohns, UC and Adalimumab is approved for HS
TNF Mediated Derm Diseases

- FDA Approved:
  - Psoriasis
  - Hidradenitis Suppurativa

- Off Label:
  - Sarcoid
  - GA/NLD
  - Pyoderma Gangrenosa
  - TEN
  - Pityriasis Rubra Pilaris
Sarcoid

- Effective: Infliximab, Adalimumab
- Ineffective: Etanercept, Ustekinumab, Golimumab

Sarcoid (Cont.)


Sarcoid (cont.)


Granuloma Annulare

- Effective: Adalimumab, Infliximab
- Ineffective: Etanercept
- Min M, Lebwohl M. Treatment of recalcitrant granuloma annulare (GA) with adalimumab: A single-center, observational study. JAAD: 74(1) 127-133 (7 cases)
Hidradenitis Suppurativa

- FDA Approved: Adalimumab
- Effective: Infliximab, Adalimumab
- Possible: Ustekinumab, Anakinra
- Ineffective: Etanercept


Pyoderma Gangrenosa

- Effective: Infliximab(104), Adalimumab(15)
- Maybe: Ustekinumab (3), Canakinumab(6)
- Ineffective: Etanercept (7)
- The Future: anti-IL-17???

Toxic Epidermal Necrolysis

- Thalidomide trial worsened TEN
- Infliximab: 15 Case Reports 14/15 survive
- Etanercept: 12 Case Reports 11/12 survive
Pityriasis Rubra Pilaris

- Effective: Adalimumab, Infliximab, Ustekinumab
B Cell Derm Diseases

- Pemphigus Vulgaris
- Pemphigus Foliaceous
- Paraneoplastic Pemphigus
- Bullous Pemphigoid
- Mucous Membrane Pemphigoid
- Epidermolyis Bullosa Acquisita
- Vasculitis
Anti CD20: Rituximab

- CD20 is present on mature B cells. Anti-CD20 leads to sustained reduction in mature B cells
- FDA approved for Lymphoma, Rheumatoid Arthritis
Rituximab for Pemphigus

- Lymphoma: 375mg/m2 weekly x4
- RA Protocol: 1000mg x 2
- CR: 66.6% (L) vs. 75% (R)
- PR: 12.78% (L) vs. 23.91% (R)
- Relapse: 22.78% (L) vs. 35.87% (R)
- Ser. Infxn: 3.9% (L) vs. 15.2% (R)
- Mortality: 2.2% (L) vs. 1.1% (R)
Rituximab for Pemphigus

- 578 patients
- 76% Complete Response
- 5.8mos mean time to remission
- 40% Relapse Rate
- 3.3% Serious Adverse Events
Key Takeaways

- We have several Biologic Medications that target specific parts of the immune system.
- In addition to the FDA approved indications (Psoriasis and HS), the anti-TNF antibodies (Adalimumab and Infliximab) work well for Pyoderma Gangrenosa, PRP, Granuloma Annulare and Cutaneous Sarcoid.
- Rituximab targets B cells and is the first line agent for pemphigus vulgaris and other AIBD’s.
The Future

- Biosimilars
- The Payor Decides Everything!!!
- Ask me about Probity