

## Top 5 Tips to be in the Know!

Dermatology Updates Cynthia Griffith, MPAS, PA-C

### #5 – New Melanoma Guidelines

- The American Joint Committee on Cancer (AJCC) updated the staging system for classification of melanoma.
- 8<sup>th</sup> edition.
- Background: the AJCC is a classification system developed by the for describing the extent of disease progression in cancer patients. It utilizes in part the TNM scoring system: Tumor Size, Lymph Nodes affected and metastases.







### AJCC Melanoma of the Skin Staging

#### Definitions

#### Primary Tumor (T)

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T3 Melanoras 21-43 mm

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#### Regional Lymph Nodes (N)

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#### Distant Metastasis (M)

MD. No detectable systems of distant metastases.

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M15 Metabacerology

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#### Notes

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# Change in T1 classification of Melanoma

### 7<sup>th</sup> edition AJCC guidelines

- Melanoma is classified as T1 if:
  - Less than for equal to 1mm thickness
- Tla- nonulcerated and had a mitosis rate of less than 1/mm2
- T1b-ulcerated or had at least 1 mitosis/mm2

### 8<sup>th</sup> edition AJCC guidelines

- Tla nonulcerated and less than 0.8 mm in thickness
- T1b is 0.8-1.0 mm thick or less than 0.8 mm with ulceration

■ Tumor mitotic rate has been dropped as a staging criterion for T1 tumors.

### + Example:

56 year old Asian American male with a 0.9 mm melanoma with no ulceration or mitotic figures on the back.

7<sup>th</sup> edition guidelines this would be: Tla

8th edition guidelines this would be: T1b

Updated 2017 NCCN guidelines: Sentinel Lymph Node Biopsy (SLNB)

- Not recommended in melanoma in Situ
- If 0.76-1.mm thickness without ulceration or mitotic rate of at least 1 per mm2 → discuss and consider SLNB
  - Evidence suggests that roughly 7% probability of positive result
- If 0.76-1.mm thickness with ulceration or mitotic rate of at least 1 per mm2 → discuss and OFFER SLNB
  - Evidence suggests that roughly 35% probability of positive result



# New treatment options for melanoma stage III and IV

- Combination therapies BRAF + MEK inhibitors work better than individual therapies (Dabrafenib + Trametinib)
- Immunomodulator drugs (CTLA4 and PD1 inhibitors) are most effective at treating melanoma (Combo>PD1>CTLA4)
  - CTLA4 inhibition (Ipilimumab), PD1 inhibition (Pembrolizumab)

Long GV, et al, Adjuvant Dabrafenib plus Trametinib in Stage III BRAF-mutated Melanoma, The New England Journal of Medicine. 2017; 377;19

Lancet Oncology, Vol 17, No 11, p 1558-1568, Nov 2016

# #4 - Advances in Atopic Dermatitis (AD) Treatment

- Atopic Dermatitis aka: Eczema
  - Common skin disease affecting children and adults
  - Manifests as itchy red scaly patches on the cheeks of children, antecubital and popliteal fossae of children and adults

■ Part of the Atopy Triad: Atopic Dermatitis, Allergic rhinitis and

**Asthma** 











# **Current Tx of Atopic Dermatitis**

#### ■ Topical Treatments

- Topical Steroids like Desonide (for use on the face or body fold areas), Triamcinolone (for use on the body), Clobetasol (for use on thick plaques)
- Topical Calcinuerin inhibitors (Steroid Sparing medications) –
   Tacrolimus and Pimecrolimus

### ■ Phototherapy

Most commonly Narrow Band UVB

### ■ Immunosuppressants

Methotrexate, Mycophenolate mofetil, Cyclosporine, Azathioprine



### New Medications for use in AD

- New non steroidal topical medication
  - Crisaborole approved late 2016
  - Topical PDE4 inhibitor
  - PDE4 is part of the inflammatory cascade
  - Approved for mild to moderate AD in ages 2 and up
  - Formulated as a 2% ointment applied BID with results seen in 28 days



## New Medications for use in AD

- Dupilumab First biologic medication approved for AD
- What is a biologic?
  - It's ALIVE!
    - Given IV or Injections biologics are proteins derived from living tissue or cells cultured in a lab

Body contains interleukins (IL) that fight against viruses/bacteria as part of immune system but in AD these are overactive and they result in chronic inflammation

■ Dupilumab blocks IL-4 and IL-13 from binding to their cell receptors limiting overreaction of the immune cascade and limiting inflammatory symptoms of AD

### + Dupilumab

- Loading dose two injections (600 mg)
- One injection (300 mg) every other week
- Most common adverse reactions: conjunctivitis, injection site reaction, cold sores
- Also note can cause transient elevation in eosinophils so good to have a baseline
- No starting or routine recommended lab testing

# Drugs coming down the pipeline

- Nemolizumab Phase 2b trials IL-31 blocker receptor A (Late 2019-2020)
- Tralokinumab Phase 3 trials IL13 (Target) Launch 2020

# #3 - Advances in Psoriasis Management

#### ■ Psoriasis

- An immune mediated skin disease that causes raised red scaly plaques commonly on the extensor elbows, knees, scalp, lower back/buttock but can be on any body surface area.
- Itchy
- Associated with other conditions: diabetes, metabolic syndrome, heart disease, depression
- Men and women can develop psoriasis in equal rates, all races

About 30% of people will develop psoriatic arthritis an inflammatory form of arthritis



## Current treatment options

#### ■ Topical Treatments

- Topical Steroids like Desonide (for use on the face or body fold areas), Triamcinolone (for use on the body), Clobetasol (for use on thick plaques)
- Vitamin D topicals -> Calcipotriene
- Vitamin A derivative → Tazarotene

### Phototherapy

- Narrow Band UVB
- Psoralens + UVA
- Excimer Laser

### ■ Immunosuppressants

■ Methotrexate, Cyclosporine, Azathioprine, Acitretin

# New Oral Medication for use in Psoriasis

- Unlike traditional treatments for Psoriasis recent medications target specific parts of immune system pathways selectively
- Apremilast
  - Inhibits an enzyme known as phosphodiesterase 4 (PDE4) that controls inflammatory action within cells and effects inflammation
  - 30 mg twice daily dosing, after a 5 day start taper
  - Meant to be taken continuously to maintain improvement
  - Adverse effects: Diarrhea, Nausea, URI, Headache,
    - More rare depression, weight decrease
  - Think about using it in combination with phototherapy or topicals



# New Biologics for use in Psoriasis

- What is a biologic?
  - It's ALIVE!
    - Given IV or Injections biologics are proteins derived from living tissue or cells cultured in a lab



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Treatment type	Indication	Mechanism of Action	Method of Delivery	Dosage and Frequency	Possible Side Effects•	Warning and Precautions**
Secukinumab	Psoriasis (Adults) Psoriatic arthritis (Adults)	Blocks interleukin 17 (IL-17)	Subcutaneous self-injection	Psoriasis and/or psoriatic arthritis: Week 0, 1, 2, 3 and 4, then every four weeks	Cold or flu-like symptoms Diarrhea Upper respiratory infection	Serious infection Tuberculosis (TB) testing before starting Cosentyx Inflammatory bowel disease (IBD) Serious allergic reaction
Etanercept  Biosimilar to	Psoriasis (People over 4 yrs) Psoriatic arthritis (Adults)	Blocks TNF-Alpha	Subcutaneous self-injection	Adult psoriasis: Twice weekly for 3 months, then once weekly Pediatric psoriasis: Once weekly Adult psoriatic arthritis: Once weekly	Infection Injection site reaction	Serious infection Fungal infection Nervous system problem Lymphoma New or worsening heart failure Low blood count Hepatitis B reactivation Serious allergic reaction Lupus-like syndrome
Adalimumab  Biosimilar to  Adalimumab	Psoriasis (Adults) Psoriatic arthritis (Adults)	Blocks TNF-Alpha	Subcutaneous self-injection	Psoriasis and/or psoriatic arthritis: Once every other week	Infection (including upper respiratory and sinus) Injection site reaction Headache Rash	Serious infection Fungal infection Malignancies Serious allergic reaction Hepatitis B reactivation Nervous system problem Low blood count New or worsening heart failure Lupus-like syndrome

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Biologic treatments							
Treatment type	Indication	Mechanism of Action	Method of Delivery	Dosage and Frequency	Possible Side Effects•	Warning and Precautions**	
Infliximab  Biosimilar to Infliximab  Biosimilar to Infliximab	Psoriasis (Adults) Psoriatic arthritis (Adults)	Blocks TNF-Alpha	IV infusion by a health care provider	Psoriasis and/or psoriatic arthritis: Week 0, 2, and 6, then every 8 weeks	Infections (including upper respiratory, sinus and throat) Infusion-related reaction Headache Stomach pain	Serious infection (especially when switching between biologics) Fungal infection Malignancies Hepatitis B reactivation Liver problem (including hepatotoxicity) New or worsening heart failure Low blood count Nervous system problem Lupus-like syndrome Special consideration when receiving a live vaccine Serious allergic reaction	
Infliximab  Brodalumab	Psoriasis (Adults)	Blocks IL-17	Subcutaneous self-injection	Psoriasis: Week 0, 1, 2, then every 2 weeks	Joint pain Headache Fatigue Diarrhea Throat pain Nausea Muscle pain Injection site reaction Cold or flu-like symptoms Low blood count Fungal infection	Suicidal ideation and behavior Serious infection TB testing before starting Siliq Crohn's disease Special consideration when receiving a live vaccine	

# Treatment Comparison

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Treatment type	Indication	Mechanism of Action	Method of Delivery	Dosage and Frequency	Possible Side Effects*	Warning and Precautions**
Ixekizumab	Psoriasis (Adults) Psoriatic arthritis (Adults)		Subcutaneous self-injection	Psoriasis: Week 0 and every 2 weeks for 3 months, then every 4 weeks Psoriatic arthritis: Week 0, then every 4 weeks	Injection site reaction Upper respiratory infection Nausea Fungal infection	Serious infection TB testing before starting Taltz Serious allergic reaction Inflammatory bowel disease
Guselkumab	Psoriasis (Adults)	Blocks interleukin 23 (IL-23)	Subcutaneous self-injection	Psoriasis: Week 0 and 4, then every 8 weeks	Upper respiratory infection Headache Injection site reaction Joint pain Diarrhea Stomach flu Fungal infection Herpes simplex infection	Serious infection TB testing before starting Tremfya
Ustekinumab	Psoriasis (People over 12 yrs) Psoriatic arthritis (Adults)	Blocks interleukin 12 and 23 (IL-12/23)	Subcutaneous self-injection	Psoriasis and/or psoriatic arthritis: Week 0 and 4, then every 12 weeks	Cold or flu-like symptoms Upper respiratory infection Headache Fatigue	Serious infection (especially from mycobacteria, salmonella and Bacillus Calmette-Guerin (BCG) vaccinations) TB testing before starting Stelara Malignancies Serious allergic reaction Reversible posterior leukoencephalopati syndrome

# Hidradenitis suppurativa (HS)

- HS is a chronic inflammatory disorder of the apocrine glands
- Follicular occlusion leads to trapped follicular contents, rupture, inflammation of the dermis and superinfection
- Adalimumab has new indication to treat moderate to severe HS in people 12 years of age and older







# #2 – New medication for the treatment of Urticaria

- Urticaria, Hives, are raised edematous wheals caused by histamine release from mast cells
- Triggers by a variety of mechanisms both allergic and non allergic in half the cases the inciting factor never identified
- 40% associated with URI, 9% drug, 1% food
- Pruritus (itch), stinging, pain
- Acute (less than 6 weeks)
  - MC children
- Chronic (more than 6 weeks)
  - MC in women, middle aged
  - Resolves in 12 months in approx 50% of adults with idiopathic urticaria



# Triggers for Urticaria

#### Drugs

- Aspirin, NSAIDs, morphine, codeine, PCN, Cephalosporins, Sulfa, Tetracyclines, blood products, radiographic contrast, Angiotensinconverting enzyme inhibitors,
- Infection
- Insect bits (papular urticaria)
- Pregnancy
- Foods
- Heat, cold, solar, pressure, water



• Acute vs Chronic:  $\rightarrow$  Acute usually resolves

 Is anaphylaxis present (hypotension, respiratory distress, throat scratchiness, swelling of mucous membranes (tongue,

throat, lips))? → epinephrine

■ Can we identify triggers → if so avoid



# Current Management/treatment of Urticaria

- Nonsedating H1 antagonists:
  - Cetirizine 10 mg QHS, BID
  - Fexofenadine 120 -180 mg
- Sedating Antihistamines:
  - Diphenhydramine 10-25 mg up to 4 times daily
  - Hydroxyzine 10-25 mg up to 4 times daily
  - Doxepin 10-50 mg up to 3 times daily
- Leukotriene inhibitors can be used in combination with antihistamines
  - Montelukast 10 mg daily



### Omalizumab for Urticaria

- This is a humanized monoclonal IgG antibody against IgE
  - Approved for adults and children 12 and up for urticaria symptomatic on H1 antihistamines
  - 150 or 300 mg subcutaneous injections every 4 weeks
  - No routine baseline or monitoring labs
  - Commonly reported Adverse effects:
    - Headache, tired feeling, joint/muscle pain, rash, injection site reaction, hair loss, URI symptoms, dizziness

# #1 – Topical prescription strength Retinol now available OTC

- Adapelene Gel 0.1% for over the counter use to treat acne.
- First retinoid approved for OTC use.
- Indications:
  - Comedonal acne (treatment of choice)
  - Fine line and wrinkle prevention, it decreases collagen resorption
  - Evens skin tone





# Adapelene gel 0.1%

- Comparable to Tretinoin 0.025% cream in efficacy and slightly better than Tretinoin 0.025% in tolerability.
- Good for use in men and women all ages except women who are pregnant
- Common adverse effect: dryness, redness, peeling, photosensitivity → this can be alleviated by decreasing the amount used and applying moisturizer



## Bonus: Sunscreen Primer

- What do you need to know about sunscreen?
- Broad spectrum → Protective against UVA and UVB
  - UVA  $\rightarrow$  rays that cause tans, aging (brown spots, wrinkles),
  - UVB → rays that cause burning
- SPF 30-50 SPF 15 is not considered protective enough.
- Use daily on the face, neck, upper chest, backs of the hands