Skin Care Pearls
Erdheim Chester Disease Management

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Dermatology Service
Skin and ECD

- Skin can be a presenting site in up to 30% of cases*

- Skin lesions associated with ECD spectrum
  - Most frequent - Xanthelasma like lesions (XLL) – 25% of cases
  - Patches or papulonodular lesions
  - \( \text{BRAF}^{V600E} \) mutation more common with skin involvement (\( p=0.005 \))*

- Treatment: Difficult!
  - Laser treatments, excision
  - Systemic disease treatments

*Chasset F et al. JAAD. 2016 Mar;74(3);513-20
**Estrada-Veras JI et al. Blood Adv. Feb 14; 1 (6);357-366
Xanthelasma like lesions (XLL)

Chasset F et al. JAAD. 2016 Mar;74(3);513-20
Papulonodular/hyperkeratotic lesions

Chasset F et al. JAAD. 2016 Mar;74(3);513-20
Skin Care during ECD treatment

BRAF inhibitors – Vemurafenib, Dabrafenib
- Keratosis Pilaris (prickly skin)
- Xerosis (Dry skin)
- Photosensitivity
- Eczema
- Keratoacanthomas (early skin cancer)
- Nevi (mole) changes
- Hand foot syndrome (palmoplantar dysesthesia)
- Alopecia (Hair loss)

MEK inhibitors – Trametinib, Cobimetinib
- Acneiform rash
- Pruritis (itching)
- Dry skin/tenderness
- Alopecia (hair loss)

Anakinra – injection site reactions
Skin changes from BRAFi: A Rasopathy

• Keratosis Pilaris
• Hyperkeratotic changes on the nipple
• Cysts or milia on face
• Keratoacanthomas
• Extreme photosensitivity

* Elisabeth Livingstone et al. Chin Clin Oncol. 2014 Sep;3(3):29
KA/cutaneous SCC from BRAFi: A Rasopathy

- Keratoacanthoma Incidence: lower with MEK inhibitors
  - Dabrafenib: 9%
    - Dab+trametinib: 3%
  - Vemurafenib: 21%
    - Vem+cobimetinib: 2%

- Time to development
  - Median 6.5 mos
  - Range 0.9-43 mos

- Treatment
  - Surgical or destructive
  - No reports of metastasis
  - Dose mod infrequent

Lacouture et al, Oncologist 2012; Robert et al, NEJM 2015 – Slide courtesy of Dr. Lacouture
Additional skin changes from BRAFi: A Rasopathy

Extreme photosensitivity
- Sunburns in shorter than expected times
- Burns in unusual times of the year ex: Fall/spring
- Can develop blisters

Treatment
- Broad spectrum sun screens
  - Re-apply every 80 mins; sooner if in the water
- Use UPF protective clothing: Coolibar
- Consider Heliocare

* Elisabeth Livingstone et al. Chin Clin Oncol. 2014 Sep;3(3):29
Sunscreens

Physical Blockers:
- Contain Zinc Oxide or Titanium dioxide
- “baby sunscreen”
- Pros: Less irritating and more protective
- Cons: Leave a while film on the face

Chemical Blockers
- Broad spectrum sunscreens – avobenzone, homosalate, octisalate, oxybenzone
- Pros: Apply clear
- Cons: Slightly less effective in their coverage
- Can be irritating to the skin, though most people tolerate well.
Polypodium leucotomos extract*

METHODS:
22 subjects with Fitzpatrick skin phototype I to III were enrolled.

On day 1, subjects were irradiated with visible light, ultraviolet (UV) A1, and UVB (using 308-nm excimer laser).

Evaluation was done immediately and 24 hours after irradiation. On days 3 and 4, irradiation and evaluation process was repeated after ingestion of PLE.

CONCLUSION:
The results suggest that PLE can potentially be used as an adjunctive agent to lessen the negative photobiologic effects of UVB.

BRAF inhibitors: Digital Dermoscopy Followup

Vemurafenib →

Patients on vem (n=42)
- Lesions/pt: 51
- Follow up: 6.7 mo

Lesions (2,155)
- Change: 56%
- Color (↑): 15%
- Globules: 14%
- Excised: 36 lesions
- Melanoma: 14 (1.2%)
- 21% risk of secondary melanoma in Vem pts
  (vs 5% in general melanoma population)

Perier-Muzet et al, *J Invest Dermatol* 2014 - Slide courtesy of Dr. Lacouture
Hand Foot Skin Reaction: BRAFi

- **Symptoms**
  - Within the first 12 weeks
  - Pain, irritation
  - Decreased QOL
  - Limits ADL

- **Incidence**
  - Vemurafenib: 27%
    - V+Cobi: 10%
  - Dabrafenib: 33%
    - D+Trame: 6%

- **Prevention/treatment**
  - Grade 0/1: Salicylic acid, urea
  - Grade 2/3: Lidocaine, topical steroid creams

Slide courtesy of Dr. Lacouture
Skin Care during ECD treatment

MEK inhibitors – Trametinib, Cobimetinib
- Acneiform rash – similar to EGFR inhibitors used for colorectal cancer
- Pruritis (itching)
- Dry skin/tenderness
- Alopecia (hair loss)
Skin Care during ECD treatment

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Acneiform Rash: MEK inhibitors

- Pruritus and tenderness in 62%

- Trametinib
  - All grade: 57% (+D: 23%)
  - Grade 3: 8% (+D: 1%)

- Cobimetinib
  - All grade: 61% (+V: 38%)
  - Grade 3: 13% (+V: 6%)

Slide courtesy of Dr. Lacouture
STEPP Trial:
Phase 2 study of pre-emptive vs reactive skin toxicity treatment in mCRC

Prophylactic arm: Doxycycline 100mg bid and topical steroids, moisturizers for 6w

<table>
<thead>
<tr>
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<th>Prophylactic ( n = 48 )</th>
<th>Reactive ( n = 47 )</th>
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<tbody>
<tr>
<td>Patients with ≥grade 2 skin toxicity – n (%)</td>
<td>14 (29)</td>
<td>29 (62)</td>
</tr>
<tr>
<td>Odds Ratio (95% CL)</td>
<td>0.3 (0.1, 0.6)</td>
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</tbody>
</table>
**ARCHER Trial:**
Phase 2 study of pre-emptive vs reactive skin toxicity/diarrhea in NSCLC

**Dacomitinib in NSCLC**

- **Randomize**
  - **Placebo**
    - N=58
    - Skin tox: 46.6%
    - Diarrhea: 41.4%
  - **Doxycycline**
    - N=56
    - Skin tox: 23.2%*
    - Diarrhea: 33.9%
  - **Top Steroid+Probiotic**
    - N=59
    - Skin tox: 35.6%
    - Diarrhea: 39.0%

*Skin tox: 23.2%*

Slide courtesy of Dr. Lacouture
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MEK inhibitors - dry skin/eczema/dermatitis

Patient on trametinib

Noted increased dry skin → itching → scratching → Rash

Applied bacitracin → Blisters!

No prior history of bacitracin allergies

Treatment:
1. Topical steroid creams
2. Excellent skin care
3. Daily moisturizers
4. Gentle soap
5. Avoid fragrances
6. For the itching – daily zyrtec 10 mgs can help
   *15% of patients feel drowsy
MEK inhibitors - dry skin/eczema/dermatitis

- Soap
  - Dove Gentle skin care

- Moisturizers
  - Ceramides
    - Eucerin eczema relief
    - Cera ve

- Avoid TIDE and other fragranced detergents

- Avoid dryer sheets
Skin Care during ECD treatment

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  – Alopecia (hair loss)
## Alopecia to BRAF/MEK inhibition

<table>
<thead>
<tr>
<th>Target</th>
<th>Agent</th>
<th>Incidence %</th>
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<tbody>
<tr>
<td>BRAF Inhibitor(s)</td>
<td>Vemurafenib</td>
<td>23.7%</td>
</tr>
<tr>
<td></td>
<td>Dabrafenib</td>
<td>18.9%</td>
</tr>
<tr>
<td>MEK Inhibitor</td>
<td>Trametinib</td>
<td>13.3%</td>
</tr>
<tr>
<td>BRAF/MEK Inhibitors</td>
<td>Vemurafenib/Cobimetinib</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td>Dabrafenib/Trametinib</td>
<td>6%</td>
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Alopecia to BRAF/MEK inhibition

- No great treatments

- Important to rule out other causes – other drugs, severe iron or vit D deficiency, hypothyroidism

- Consider Minoxidil (Rogaine foam/solution) once or twice a day respectively

- Consider Biotin 2500-5000 micrograms daily if hair is brittle or dry

- Unclear safety of cosmetic practices – Ex Fresh frozen plasma

- Consider hair pieces
Questions? Comments?

Thank you!