



Memorial Sloan Kettering
Cancer Center

Skin Care Pearls

Erdheim Chester Disease Management

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Oct 27th 2017

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
 - BRAF^{V600E} mutation more common with skin involvement (p=0.005)*
- Treatment: Difficult!
 - Laser treatments, excision
 - Systemic disease treatments

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*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)



Papulonodular/hyperkeratotic lesions



Skin Care during ECD treatment

BRAF inhibitors – Vemurafinib,
Dabrafinib

- 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

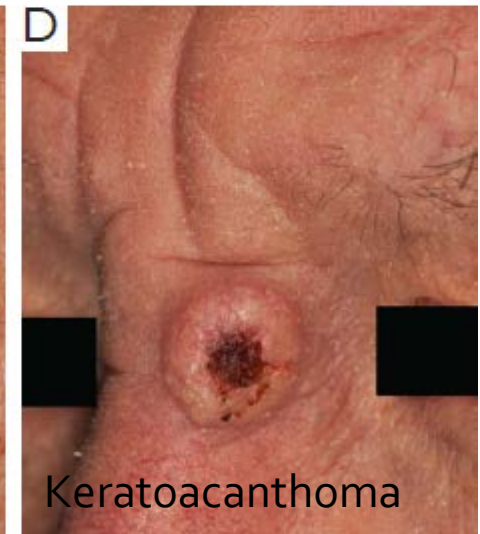
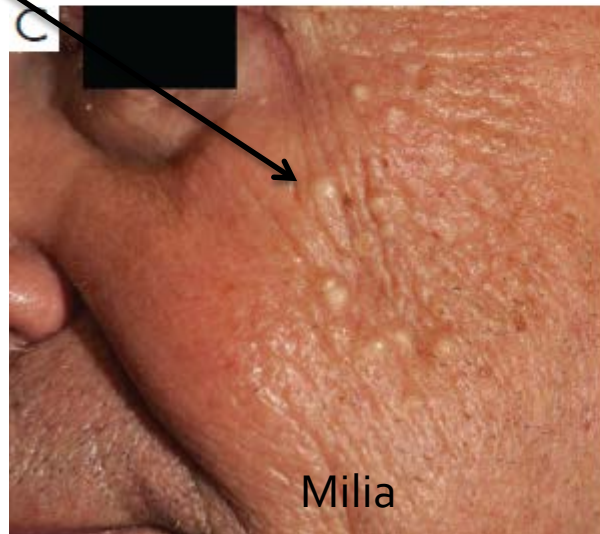
- Acneiform rash
- Pruritis (itching)
- Dry skin/tenderness
- Alopecia (hair loss)

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



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



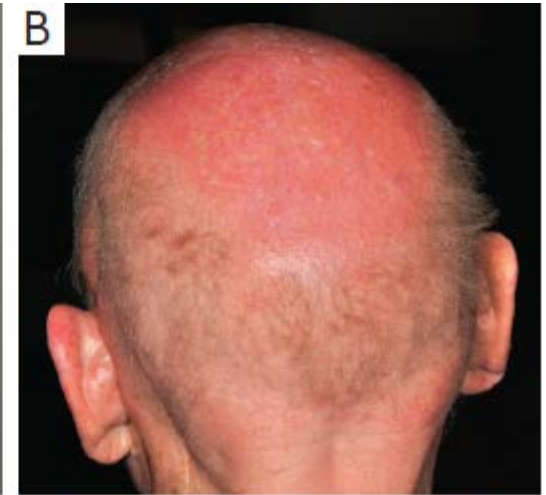
Additional skin changes from BRAFi: A Rasopathy

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**



Sunscreens

Physical Blockers:

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

Chemical Blockers

- Broad spectrum sun screens – avobenzene, homosalate, octisalate, oxybenzone
- Pros: apply clear
- Cons: slightly less effective in their coverage
- Can be irritating to the skin, though most people tolerate well.

Neutrogena® Pure and Free® Baby Faces Ultra Gentle Sunblock

- Waterproof, sweatproof
- Oil-free, PABA free
- Hypoallergenic
- Fragrance free

Drug Facts

Active ingredients Titanium Dioxide 5.1%, Zinc Oxide 2.9%	} Purpose Sunscreen
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Uses • helps prevent sunburn • if used as directed with other sun protection measures (see **Directions**), decreases the risk of skin cancer and early skin aging caused by the sun



Drug Facts

Active ingredients Avobenzene 3%, Homosalate 15%, Octisalate 5%, Octocrylene 10%, Oxybenzone 6%	} Purpose Sunscreen
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Uses • helps prevent sunburn • if used as directed with other sun protection measures (see **Directions**), decreases the risk of skin cancer and early skin aging caused by the sun

Warnings • For external use only • Do not use on damaged or broken skin



Additional skin changes from BRAFi: PHOTSENSITIVITY

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.



*Kohli et al. [J Am Acad Dermatol.](#) 2017 Jul;77(1):33-41



BRAF inhibitors: Digital Dermoscopy Followup

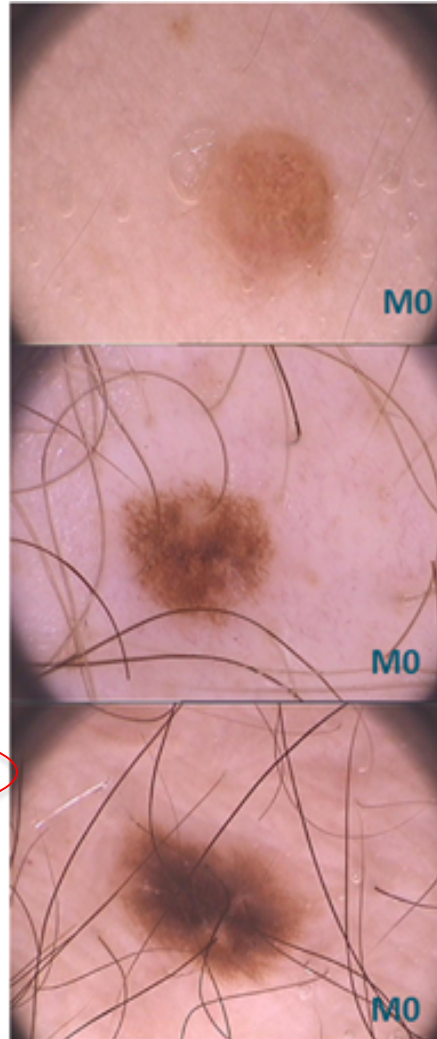
Vemurafenib →

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)



Hand Foot Skin Reaction: BRAFi

- **Symptoms**

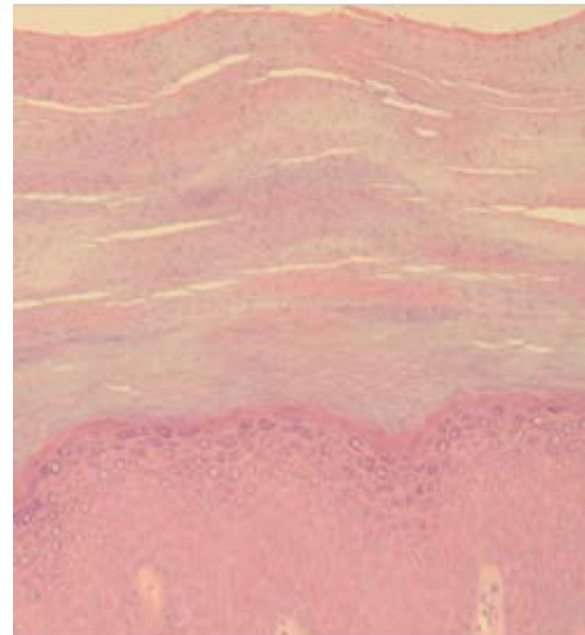
- Within the first 12 weeks
- Pain, irritation
- Decreased QOL
- Limits ADL

- **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



Lacouture et al, *Oncologist* 2012; Long et al, *Lancet* 2015;

Ascierto et al, *Lancet Oncol* 2016

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

MEK inhibitors – Trametinib, Cobimetinib

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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%)

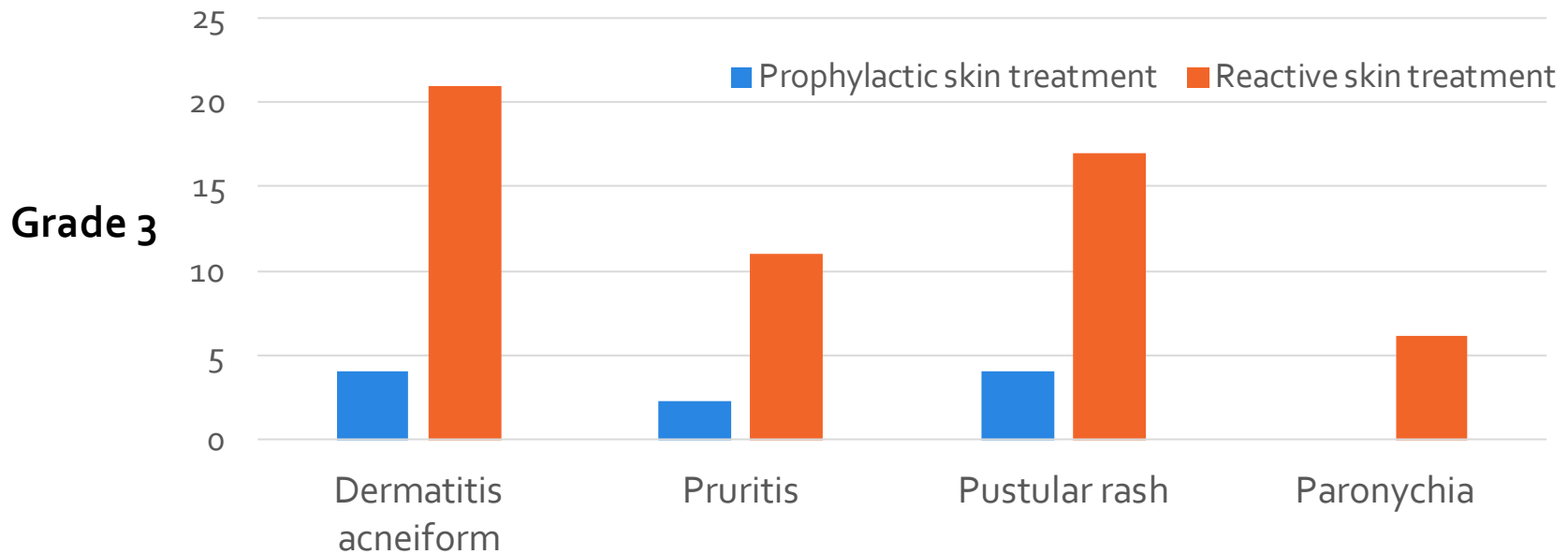


STEPP Trial:

Phase 2 study of pre-emptive vs reactive skin toxicity treatment in mCRC

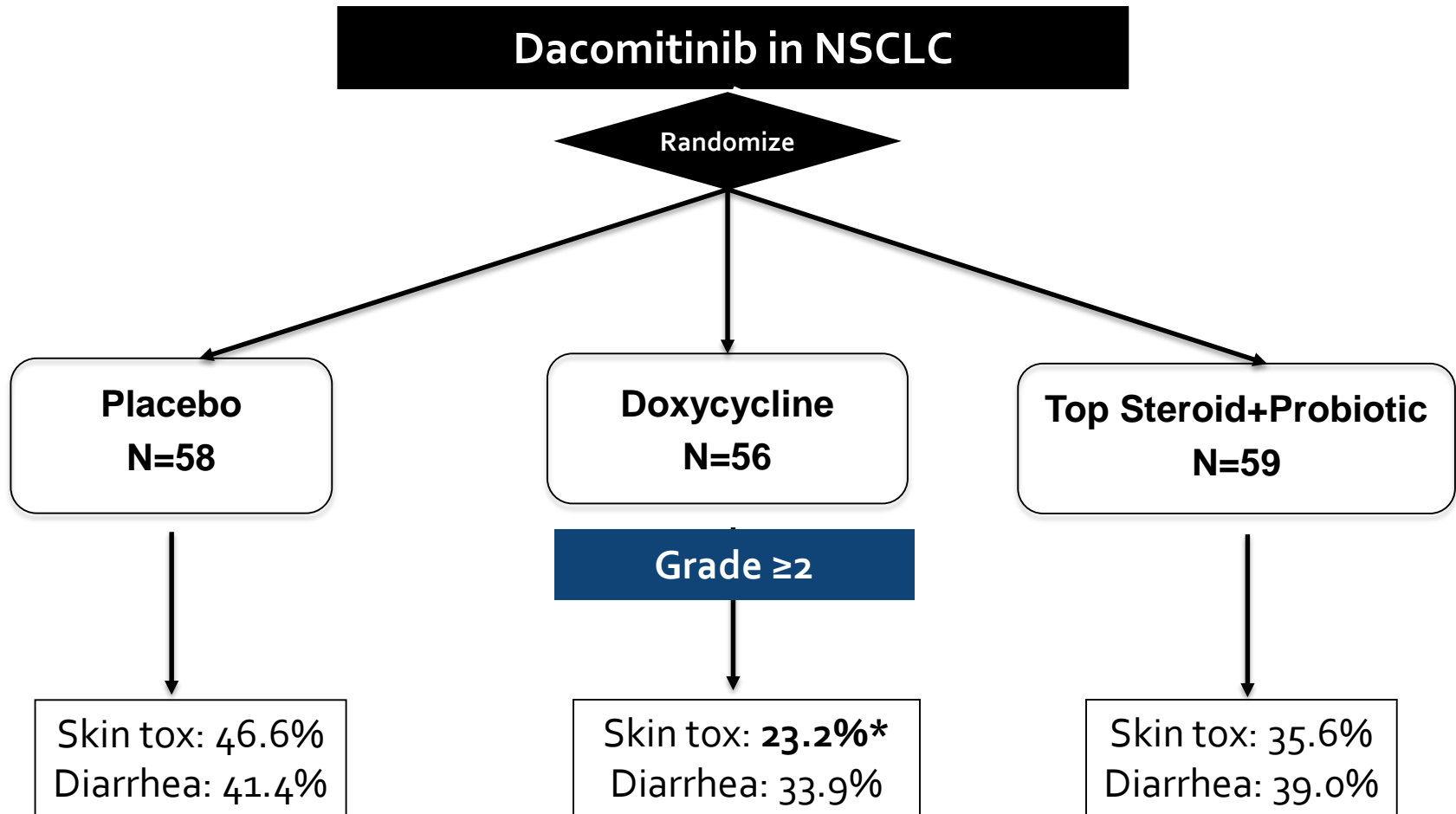
Prophylactic arm: Doxycycline 100mg bid and topical steroids, moisturizers for 6w

	Prophylactic n = 48	Reactive n = 47
Patients with \geq grade 2 skin toxicity – n (%)	14 (29)	29 (62)
Odds Ratio (95% CL)	0.3 (0.1, 0.6)	



ARCHER Trial:

Phase 2 study of pre-emptive vs reactive skin toxicity/diarrhea in NSCLC



Skin Care during ECD treatment

MEK inhibitors – Trametinib, Cobimetinib

- Acneiform rash – similar to EGFR inhibitors used for colorectal, lung cancers
- **Pruritis (itching)**
- **Dry skin/tenderness**
- Alopecia (hair loss)



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

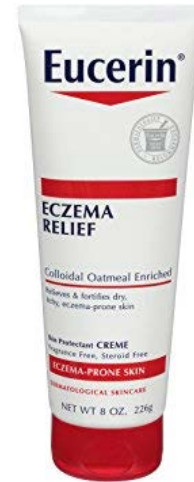
Treatment:

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

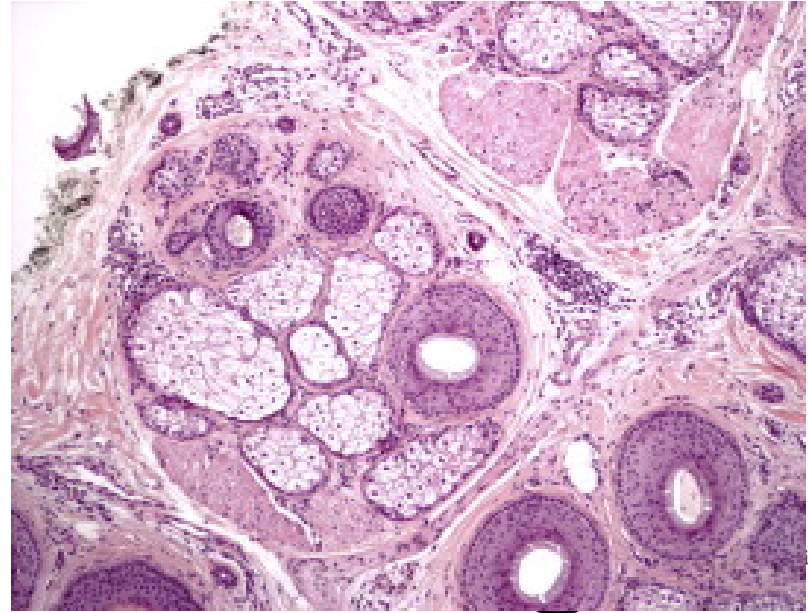
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Alopecia to BRAF/MEK inhibition

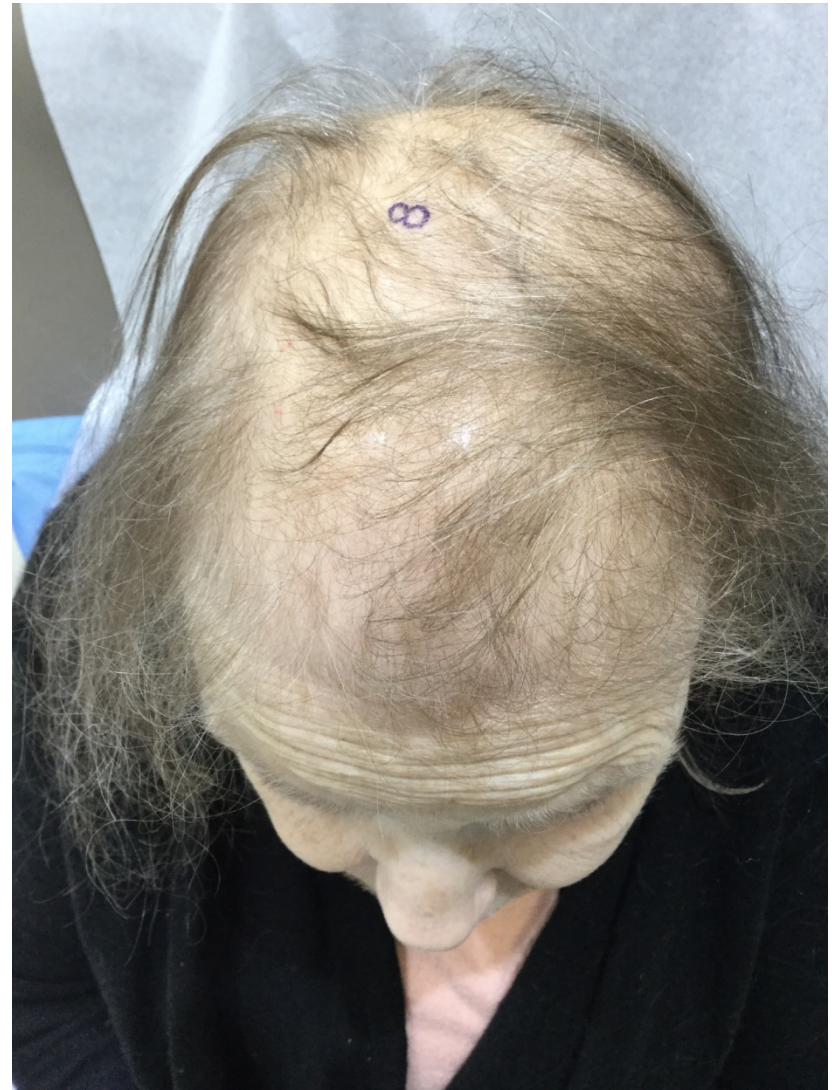
Target	Agent	Incidence %
BRAF Inhibitor(s)	Vemurafenib	23.7%
	Dabrafenib	18.9%
MEK Inhibitor	Trametinib	13.3%
BRAF/MEK Inhibitors	Vemurafenib/ Cobimetinib	13%
	Dabrafenib/ Trametinib	6%



Belum et al, *Ann Oncol* 2015; Piraccini et al, *JAAD* 2015

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!

