



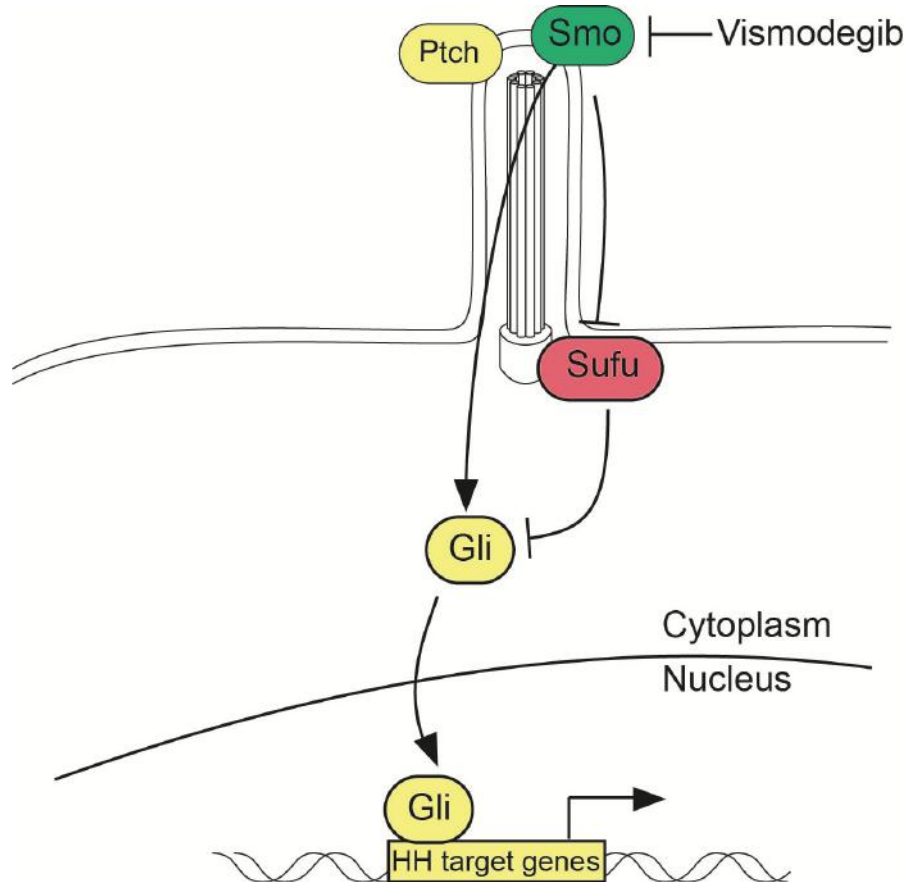
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# An Open-label Phase 2 Clinical Trial of Topical Retinostat for Basal Cell Carcinoma

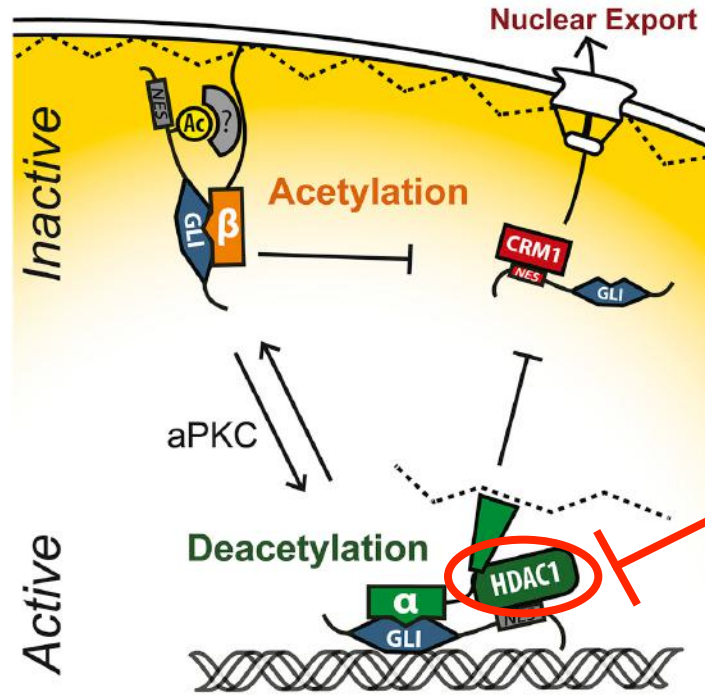
Nicole Urman

May 11, 2019

# The conventional Hedgehog signaling pathway:



# Nuclear Hedgehog proteins offer new targets for therapeutic intervention



## Remetinostat

- Pan-HDAC inhibitor
- Other HDAC inhibitors are approved for late-stage CTCL

Mirza et al, *Cell* 2019

# Study Protocol

Eligibility/Week 0: subjects with BCC  $5 < x < 25$  mm

Week 0: Begin applying retinostat gel 3x/day under bandage occlusion

Week 4: 15 minute check-in appointment, assess AEs

Week 8: AE and tumor response assessment (ORR). Participant finishes with dermatologic surgery for surgical assessment.

- 6 weeks of retinostat
- Assess primary outcome at 8 weeks
- Primary outcome: ORR defined by at least a 30% decrease in longest diameter

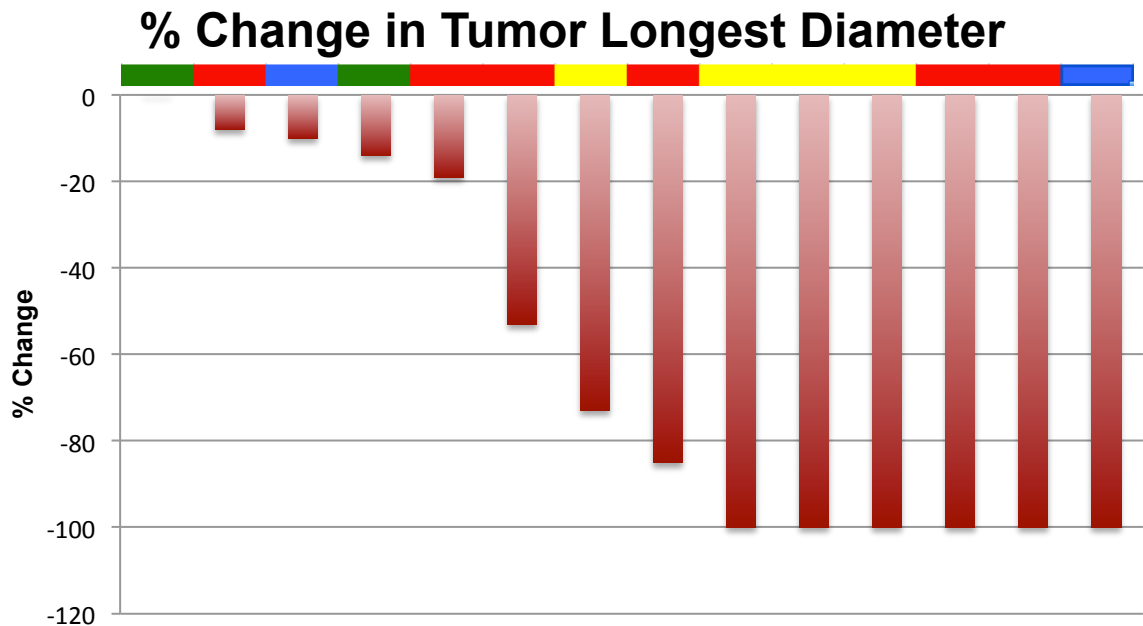
# Study Enrollment and Excluded Subjects

	Tumors	Subjects
Enrolled	30	14
<i>Removed/lost</i>	<i>-15</i>	<i>-3</i>
Remaining in study	15	11
Completed study	14	10
Currently enrolled	1	1

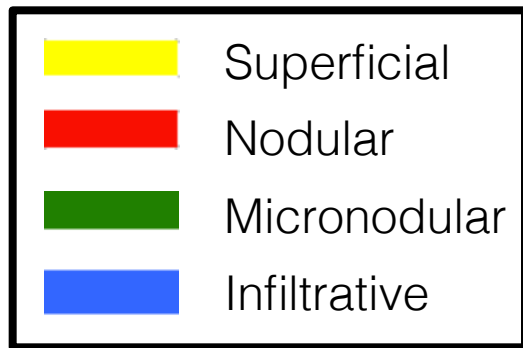
# Study Results by Tumor Type

Tumor Type (pre-Tx)	Number of Per-Protocol Tumors	Number with $\geq$ 30% decrease in longest diameter	Average decrease in tumor area	Number with residual BCC	Number with full tumor clearance	% with a complete clinical response
All Tumors	14	9	70%	8	6	43%
Superficial	4	4	99%	1	3	75%
Nodular	6	4	70%	4	2	33%
Infiltrative	2	1	68%	1	1	50%
Micronodular	2	0	17%	2	0	0%

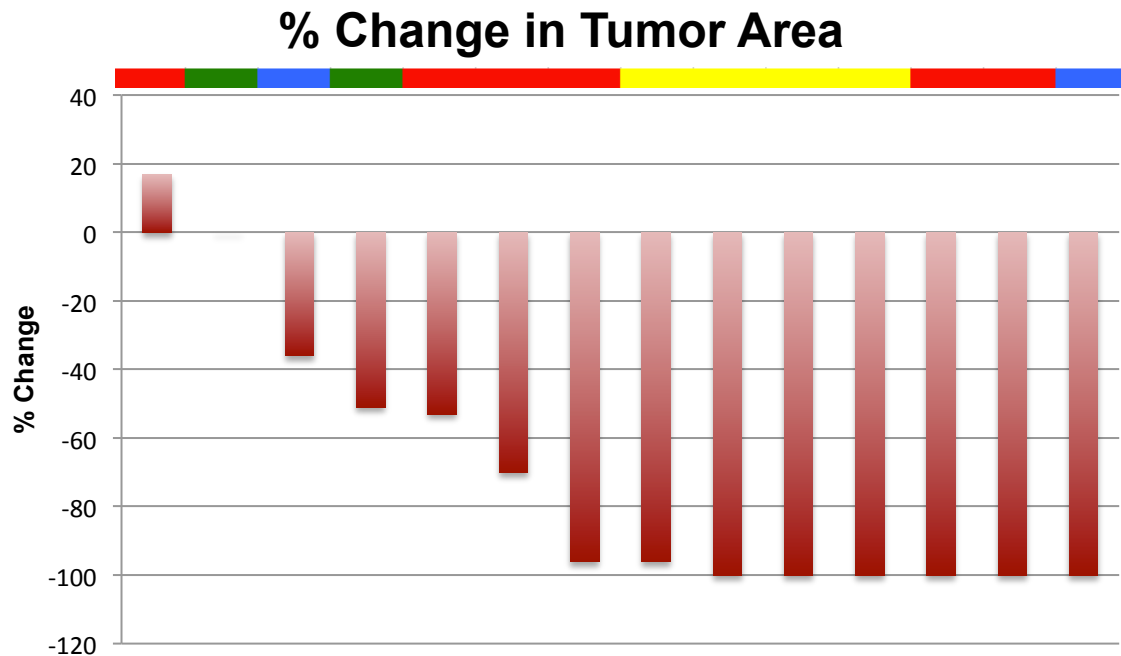
# Results



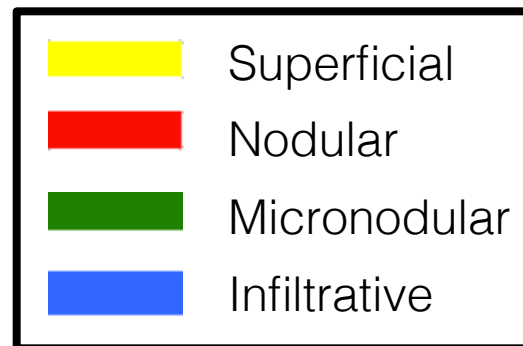
Mean % change: 62% decrease



# Results



Mean % change: 70% decrease





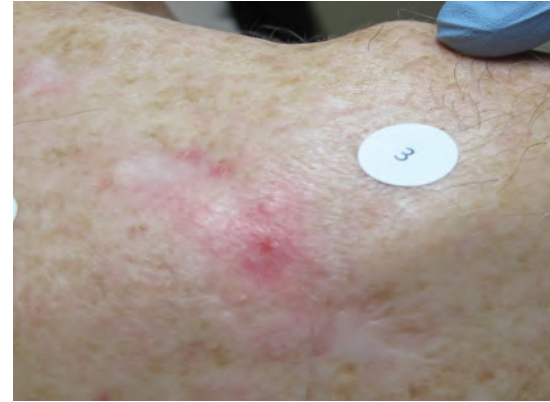
Subtype:  
superficial and  
nodular

Outcome: 83%  
decrease in  
tumor area

Week 0



Week 8



Subtype: nodular

Outcome: clinical  
resolution, mohs  
was clear



Subtype:  
infiltrative

Outcome: clinical  
resolution, mohs  
was clear

Week 0



Week 8



Subtype:  
superficial and  
nodular

Outcome: clinical  
resolution, mohs  
was clear



# Adverse Events\*

Adverse Event (AE)	Severity of AE (Grade)	Number of subjects reporting AE (% patients, total n=14)
Eczema	1-2	10 (71%)
Pain	1-2	5 (36%)

**2 of 14** subjects had their study drug temporarily discontinued (for 1-3 days) due to AEs.

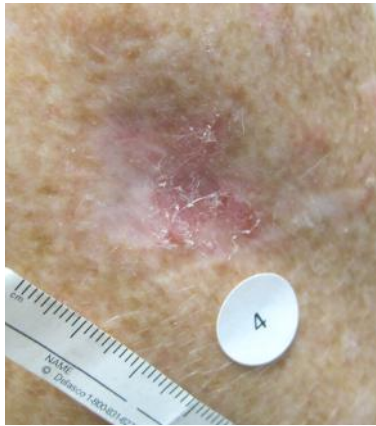
\* includes AEs in all patients at all time points, not just for those who have completed study

Week 0

Subtype: superficial

AE: grade 2  
eczematous reaction

Outcome: clinical  
resolution



Week 4



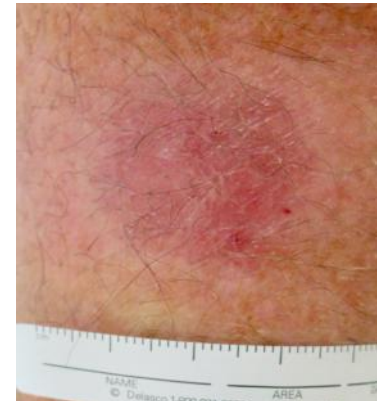
Week 8



Subtype: superficial

AE: grade 2  
eczematous reaction

Outcome: clinical  
resolution, mohs was  
clear



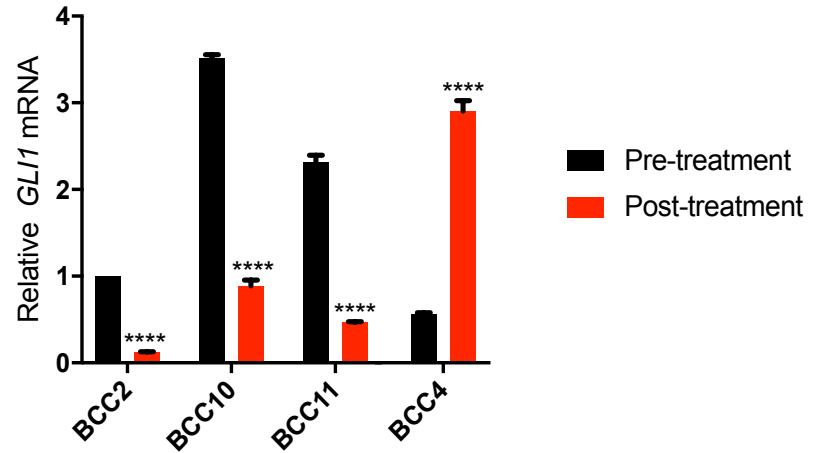
# Limitations of Treatment with Remetinostat

- Inflammatory reaction – eczema, pain
- Medication refrigeration
- 3x/day treatment
- Bandage occlusion for 6 week duration

# Preliminary qPCR Results: GLI1

- Strong decrease in signaling:
  - 2 (superficial): no residual BCC
  - 10 (nodular): residual BCC
  - 11 (infiltrative): residual BCC
- Increase in signaling:
  - 4 (micronodular): residual BCC
  - Correlates with increase in tumor size

hBCC GLI1 Pre/Post Treatment



# Acknowledgements

- **Sarin Lab**
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  - Stanford Medical Scholars
  - Albert M. Kligman Travel Fellowship



**MEDIVIR**

American Skin Association



# Study Results by Tumor

Tumor	Tumor Type (pre-Tx)	Compliance	Week 0 Size (mm)	Week 8 Size (mm)	% Change Longest Diameter	% Change Tumor Area	Pathology Available?	Residual tumor on pathology?
1.1	superficial	100%	13x8	2x2	85%	96%	Yes	Yes
1.2	superficial and nodular	100%	15x14	Two lesions: 2x2, 2x2	73%	96%	Yes	Yes
1.3	superficial and nodular	100%	16x14	Two lesions: 8x6, 4x5	19%	70%	Yes	Yes
1.4	superficial	100%	15x12	0x0	100%	100%	No	/
2.1	superficial	100%	10.5x8	0x0	100%	100%	Yes	No
4.1	nodular and micronodular	95%	12x7	11x9	8%	-17%	No	/
5.1	superficial and nodular	100%	14x12	0x0	100%	100%	Yes	No
6.1	nodular	95%	8x9	0x0	100%	100%	No	/



# Study Results by Tumor (continued)

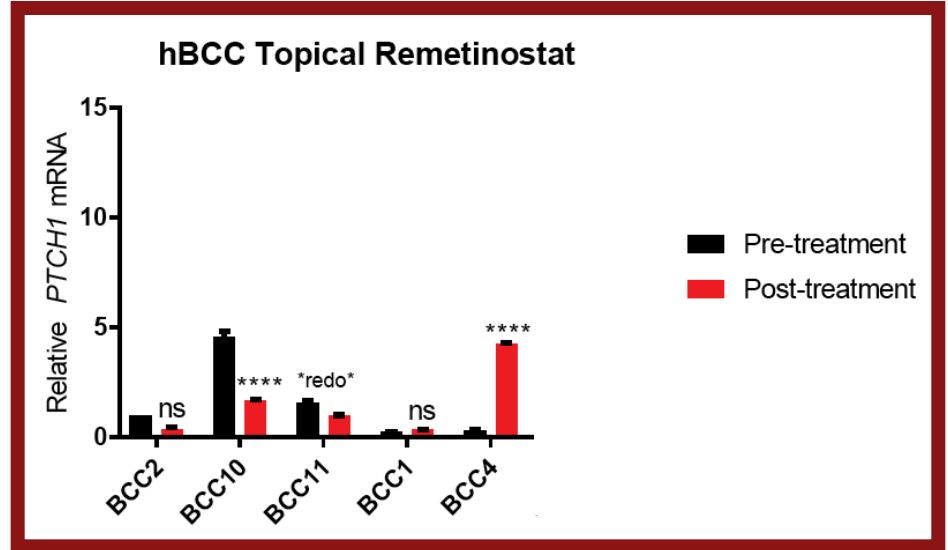
Tumor	Tumor Type (pre-Tx)	Compliance	Week 0 Size (mm)	Week 8 Size (mm)	% Change Longest Diameter	% Change Tumor Area	Pathology Available?	Residual tumor on pathology?
9.1	nodular and micronodular	95%	7x7	6x4	14%	51%	No	/
10.1	nodular	99%	15x5	7x5	53%	53%	No	/
10.2	nodular	99%	7x5	7x5	0%	0%	Yes	Yes
11.1	nodular and infiltrative	97%	7x10	5x9	10%	36%	Yes	Yes
12.1	superficial	95%	7x5	0x0	100%	100%	No	/
13.1	infiltrative	99%	10x12	Unable to determine	100%	100%	Yes	No
14.1	<i>nodular</i>		<i>6x9</i>					

# Paired Research Biopsy Samples

Tumor	Tumor Type (pre-Tx)
2.1	superficial
4.1	nodular and micronodular
7.1	superficial and nodular
10.1	nodular
11.1	nodular and infiltrative

# Preliminary qPCR Results: PTCH

- Strong decrease in signaling:
  - 10.1 (nodular): residual tumor
- Pre-treatment biopsy likely normal skin:
  - 1.1 (superficial): residual BCC
- Increase in signaling:
  - 4.1 (micronodular): residual BCC





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