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

Nicole Urman

May 11, 2019
The conventional Hedgehog signaling pathway:
Nuclear Hedgehog proteins offer new targets for therapeutic intervention

Mirza et al, *Cell* 2019

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

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

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

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


- 6 weeks of remetinostat
- Assess primary outcome at 8 weeks
- Primary outcome: ORR defined by at least a 30% decrease in longest diameter
## Study Enrollment and Excluded Subjects

<table>
<thead>
<tr>
<th></th>
<th>Tumors</th>
<th>Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled</td>
<td>30</td>
<td>14</td>
</tr>
<tr>
<td><strong>Removed/lost</strong></td>
<td>-15</td>
<td>-3</td>
</tr>
<tr>
<td>Remaining in study</td>
<td>15</td>
<td>11</td>
</tr>
<tr>
<td><strong>Completed study</strong></td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>Currently enrolled</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
# Study Results by Tumor Type

<table>
<thead>
<tr>
<th>Tumor Type (pre-Tx)</th>
<th>Number of Per-Protocol Tumors</th>
<th>Number with ≥ 30% decrease in longest diameter</th>
<th>Average decrease in tumor area</th>
<th>Number with residual BCC</th>
<th>Number with full tumor clearance</th>
<th>% with a complete clinical response</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Tumors</td>
<td>14</td>
<td>9</td>
<td>70%</td>
<td>8</td>
<td>6</td>
<td>43%</td>
</tr>
<tr>
<td>Superficial</td>
<td>4</td>
<td>4</td>
<td>99%</td>
<td>1</td>
<td>3</td>
<td>75%</td>
</tr>
<tr>
<td>Nodular</td>
<td>6</td>
<td>4</td>
<td>70%</td>
<td>4</td>
<td>2</td>
<td>33%</td>
</tr>
<tr>
<td>Infiltrative</td>
<td>2</td>
<td>1</td>
<td>68%</td>
<td>1</td>
<td>1</td>
<td>50%</td>
</tr>
<tr>
<td>Micronodular</td>
<td>2</td>
<td>0</td>
<td>17%</td>
<td>2</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>
Results

% Change in Tumor Longest Diameter

Mean % change: 62% decrease

- Superficial
- Nodular
- Micronodular
- Infiltrative
Results

Mean % change: 70% decrease

% Change in Tumor Area

-120
-100
-80
-60
-40
-20
0
20
40
60
80
100
120

% Change

Superficial
Nodular
Micronodular
Infiltrative
Week 0

Subtype: superficial and nodular

Outcome: 83% decrease in tumor area

Week 8

Subtype: nodular

Outcome: clinical resolution, Mohs was clear
**Subtype:** infiltrative

**Outcome:** clinical resolution, mohs was clear

---

**Subtype:** superficial and nodular

**Outcome:** clinical resolution, mohs was clear
Adverse Events*

<table>
<thead>
<tr>
<th>Adverse Event (AE)</th>
<th>Severity of AE (Grade)</th>
<th>Number of subjects reporting AE (% patients, total n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eczema</td>
<td>1-2</td>
<td>10 (71%)</td>
</tr>
<tr>
<td>Pain</td>
<td>1-2</td>
<td>5 (36%)</td>
</tr>
</tbody>
</table>

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
Subtype: superficial
AE: grade 2 eczematous reaction
Outcome: clinical resolution

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
Acknowledgements

- **Sarin Lab**
  - Kavita Sarin, MD, PhD
  - Shaundra Eichstadt, MD
  - Hanh Do
  - Irene Bailey

- **Oro Lab**
  - Anthony Oro, MD, PhD
  - Amar Mirza
  - Siegen McKellar

- **Stanford Dermatology**
  - Jean Tang, MD, PhD
  - Paul Khavari, MD, PhD
  - Sumaira Aasi, MD

- **Funding:**
  - Medivir
  - American Skin Association
  - Stanford Medical Scholars
  - Albert M. Kligman Travel Fellowship
# Study Results by Tumor

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Tumor Type (pre-Tx)</th>
<th>Compliance</th>
<th>Week 0 Size (mm)</th>
<th>Week 8 Size (mm)</th>
<th>% Change Longest Diameter</th>
<th>% Change Tumor Area</th>
<th>Pathology Available?</th>
<th>Residual tumor on pathology?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>superficial</td>
<td>100%</td>
<td>13x8</td>
<td>2x2</td>
<td>85%</td>
<td>96%</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>1.2</td>
<td>superficial and nodular</td>
<td>100%</td>
<td>15x14</td>
<td>Two lesions: 2x2, 2x2</td>
<td>73%</td>
<td>96%</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>1.3</td>
<td>superficial and nodular</td>
<td>100%</td>
<td>16x14</td>
<td>Two lesions: 8x6, 4x5</td>
<td>19%</td>
<td>70%</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>1.4</td>
<td>superficial</td>
<td>100%</td>
<td>15x12</td>
<td>0x0</td>
<td>100%</td>
<td>100%</td>
<td>No</td>
<td>/</td>
</tr>
<tr>
<td>2.1</td>
<td>superficial</td>
<td>100%</td>
<td>10.5x8</td>
<td>0x0</td>
<td>100%</td>
<td>100%</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>4.1</td>
<td>nodular and micronodular</td>
<td>95%</td>
<td>12x7</td>
<td>11x9</td>
<td>8%</td>
<td>-17%</td>
<td>No</td>
<td>/</td>
</tr>
<tr>
<td>5.1</td>
<td>superficial and nodular</td>
<td>100%</td>
<td>14x12</td>
<td>0x0</td>
<td>100%</td>
<td>100%</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>6.1</td>
<td>nodular</td>
<td>95%</td>
<td>8x9</td>
<td>0x0</td>
<td>100%</td>
<td>100%</td>
<td>No</td>
<td>/</td>
</tr>
<tr>
<td>Tumor</td>
<td>Tumor Type (pre-Tx)</td>
<td>Compliance</td>
<td>Week 0 Size (mm)</td>
<td>Week 8 Size (mm)</td>
<td>% Change Longest Diameter</td>
<td>% Change Tumor Area</td>
<td>Pathology Available?</td>
<td>Residual tumor on pathology?</td>
</tr>
<tr>
<td>-------</td>
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<td>----------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>9.1</td>
<td>nodular and micronodular</td>
<td>95%</td>
<td>7x7</td>
<td>6x4</td>
<td>14%</td>
<td>51%</td>
<td>No</td>
<td>/</td>
</tr>
<tr>
<td>10.1</td>
<td>nodular</td>
<td>99%</td>
<td>15x5</td>
<td>7x5</td>
<td>53%</td>
<td>53%</td>
<td>No</td>
<td>/</td>
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<tr>
<td>10.2</td>
<td>nodular</td>
<td>99%</td>
<td>7x5</td>
<td>7x5</td>
<td>0%</td>
<td>0%</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>11.1</td>
<td>nodular and infiltrative</td>
<td>97%</td>
<td>7x10</td>
<td>5x9</td>
<td>10%</td>
<td>36%</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>12.1</td>
<td>superficial</td>
<td>95%</td>
<td>7x5</td>
<td>0x0</td>
<td>100%</td>
<td>100%</td>
<td>No</td>
<td>/</td>
</tr>
<tr>
<td>13.1</td>
<td>infiltrative</td>
<td>99%</td>
<td>10x12</td>
<td>Unable to determine</td>
<td>100%</td>
<td>100%</td>
<td>Yes</td>
<td>No</td>
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<tr>
<td>14.1</td>
<td>nodular</td>
<td></td>
<td>6x9</td>
<td></td>
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</tbody>
</table>
Paired Research Biopsy Samples

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Tumor Type (pre-Tx)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>superficial</td>
</tr>
<tr>
<td>4.1</td>
<td>nodular and micronodular</td>
</tr>
<tr>
<td>7.1</td>
<td>superficial and nodular</td>
</tr>
<tr>
<td>10.1</td>
<td>nodular</td>
</tr>
<tr>
<td>11.1</td>
<td>nodular and infiltrative</td>
</tr>
</tbody>
</table>
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