Poor prognosis for thin ulcerated melanomas and implications for a more aggressive approach to treatment

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Melanoma Background

~91,270 New Cases in 2018 in the U.S.

5.3% of All New Cancer Cases in the U.S.

Melanoma in California:
• 3rd most common cancer in men
• 5th most common cancer in women

Figure 18. Trends in Melanoma Incidence Among Non-Hispanic Whites in California, 1988-2014

Note: Rates are per 100,000 and age-adjusted to the 2000 US standard population.
Source: California Cancer Registry, California Department of Public Health.
# Thin (<1mm) Tumors

Over 50% of melanoma tumors are <1mm.

Little is know about the survival differences among patients with thinner tumors.

All thin melanomas treated similarly (wide excision).

## 5-Year Survival
- Stage IA: 97%
- Stage IB: 92%

## 10-year Survival
- Stage IA: 95%
- Stage IB: 86%
<table>
<thead>
<tr>
<th>T1</th>
<th>AJCC 7th Ed.</th>
<th>AJCC 8th Ed.</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1.0</td>
<td>≤1.0 w/o ulceration and mitosis</td>
<td>&lt;0.8 mm w/o ulceration</td>
</tr>
<tr>
<td>T1a</td>
<td>≤1.0 w/o ulceration and mitosis</td>
<td>1) 0.8-1.0mm w/ or w/o ulceration</td>
</tr>
<tr>
<td>T1b</td>
<td>≤1.0 With ulceration or mitosis</td>
<td>2) &lt;0.8mm with ulceration</td>
</tr>
</tbody>
</table>

Actual data on survival differences in these two groups?
1. Investigate the variability in survival for thin tumors (T1a v T1b)
2. Describe the survival patterns by ulceration and nodal involvement

Identify tumor characteristics within thinner tumors to better guide clinical decision-making
Study Population

43,008 non-Hispanic whites (NHW) with cutaneous melanoma

Diagnosed between Jan 1, 2004 to Dec 31, 2013

Identified from California Cancer Registry (CCR)

Tumor Characteristics

Tumors were categorized by Breslow thickness and stage in accordance to AJCC staging

Tumor ulceration defined as “ulcerated” or “non-ulcerated”

Nodal involvement categorized as “without”, “with”, and “unknown”

Histologic type

Participant Characteristics

Socioeconomic status (SES) was determined using an index measure by Yost et al. and assigned on the basis of residence at diagnosis
Demographics

- <1mm, ulcerated: 2.5%
- Stage IIA: 5.0%
- Stage IIB: 5.5%
- Stage III: 7.3%
- Stage IV: 5.1%

n=43,008
Survival Outcomes

What We Looked At:

1. Risk of death and survival by thickness, ulceration, and stage
2. Risk of death and survival of thin melanomas by ulceration and nodal involvement
3. Demographic differences in thin melanomas by survival time
Risk for death by tumor thickness, ulceration and stage
### Survival by thickness, ulceration, and stage

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>&lt;1mm, non-ulcerated</td>
<td>98.0%</td>
<td>95.7%</td>
<td>93.4%</td>
<td>88.6%</td>
</tr>
<tr>
<td>Non-ulcerated</td>
<td>98.2%</td>
<td>96.1%</td>
<td>93.9%</td>
<td>89.1%</td>
</tr>
<tr>
<td>Ulcerated</td>
<td>92.5%</td>
<td>85.2%</td>
<td>81.7%</td>
<td>75.5%</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>94.5%</td>
<td>87.8%</td>
<td>80.3%</td>
<td>69.5%</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>92.7%</td>
<td>81.8%</td>
<td>72.2%</td>
<td>58.6%</td>
</tr>
<tr>
<td>Stage III</td>
<td>89.6%</td>
<td>74.3%</td>
<td>64.3%</td>
<td>53.9%</td>
</tr>
<tr>
<td>Stage IV</td>
<td>39.1%</td>
<td>25.5%</td>
<td>19.1%</td>
<td>14.9%</td>
</tr>
<tr>
<td>Condition</td>
<td>Without Nodal Invasion</td>
<td>With Unknown Nodal Invasion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>------------------------</td>
<td>-----------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1mm, non ulcerated w/o nodal inv. (reference)</td>
<td>96.8%</td>
<td>87.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1mm, non ulcerated w/ nodal inv.</td>
<td>1.9%</td>
<td>10.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1mm, ulcerated w/o nodal inv.</td>
<td>0.9%</td>
<td>2.3% 1.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1mm, ulcerated w/ nodal inv.</td>
<td>2.3%</td>
<td>0.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1mm, ulcerated w/ nodal inv.</td>
<td>96.8%</td>
<td>87.9%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Without Nodal Invasion: Non-Ulcerated 87.9%, Ulcerated 96.8%
With Unknown Nodal Invasion: Non-Ulcerated 10.2%, Ulcerated 2.3%
With Nodal Invasion: Non-Ulcerated 2.3%, Ulcerated 0.9%

The diagram illustrates the risk for death in <1mm by ulceration and nodal involvement, showing the percentage of patients in each category.
Survival of thin melanomas by ulceration and nodal involvement

<table>
<thead>
<tr>
<th>Tumor Classification</th>
<th>12 Mon.</th>
<th>24 Mon.</th>
<th>36 Mon.</th>
<th>60 Mon.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Ulcerated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>w/ nodal inv.</td>
<td>91.5%</td>
<td>80.6%</td>
<td>73.7%</td>
<td>66.7%</td>
</tr>
<tr>
<td>w/ unk. nodal inv.</td>
<td>97.4%</td>
<td>94.9%</td>
<td>92.4%</td>
<td>87.6%</td>
</tr>
<tr>
<td>Ulcerated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>w/ nodal inv.</td>
<td>79.8%</td>
<td>57.9%</td>
<td>50.8%</td>
<td>-</td>
</tr>
<tr>
<td>w/ unk. nodal inv.</td>
<td>84.7%</td>
<td>68.4%</td>
<td>58.6%</td>
<td>-</td>
</tr>
</tbody>
</table>
Demographics of thin melanomas (2004-2009)

≤ 26 months survival (n=112)
- Acral Lentiginous Melanoma 1%
- Superficial Spreading Melanoma 13.4%
- Lentigo Maligna Melanoma 3.4%
- Malignant Melanoma 59.8%

> 26 months survival (n=554)
- Acral Lentiginous Melanoma 0.4%
- Superficial Spreading Melanoma 29.8%
- Lentigo Maligna Melanoma 3.4%
- Malignant Melanoma 56.7%
Conclusion

• There is significant and substantial survival disadvantages for patients with thin ulcerated melanoma.

• Survival and risk of death for patients with thin ulcerated tumors is as poor as is experienced by patients with thicker lesions.

• Risk of death for thin melanomas is dramatically increased with ulceration and nodal involvement.
Clinical Relevance

(1) We are already distinguishing thin ulcerated tumors in AJCC 8:
• Now we know what to do with them!

(2) Identifying thin ulcerated tumors with LN positivity for more aggressive Tx approaches

New Clinical Trial
• NCT03405155 – Studying the benefit of more aggressive treatment of ulcerated tumors in Stage IIB and Stage IIC melanomas.

3. Is there something going on biologically (where do thin ulcerated tumors come from)?
Acknowledgements

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QUESTIONS?