Vulvovaginal vs. Cutaneous Melanoma: A Retrospective Cohort Study on Cutaneous Immune-Related Adverse Events

Sheida Naderi-Azad,1 Faisal Sickandar,2 Rossanna C. Pezo2,3,4

1 University of Toronto Faculty of Medicine, Toronto, ON, Canada
2 Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada
3 Division of Medical Oncology and Hematology, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada
4 Department of Medicine, University of Toronto, Toronto, ON, Canada
Background

• Immune Checkpoint Inhibitors (ICIs) have been at the forefront of metastatic melanoma\(^1\)

• The use of ICIs in vulvovaginal melanoma has been studied less extensively compared to cutaneous melanoma\(^2,3,4\)

• Consistent with their mechanism of action, common toxicities associated with ICI therapy occur as a result of inflammatory dysregulation
Background

• These inflammatory reactions range from colitis, dermatitis, and hepatitis, to respiratory diseases and endocrinopathies\textsuperscript{5,6}

• While Cutaneous immune-related Adverse Events (CAEs) are some of the most common toxicities in metastatic melanoma, they have not been examined comprehensively in patients with vulvovaginal and cutaneous melanoma on ICIs
1. Examine the clinical and morphological characteristics of CAEs in patients with vulvovaginal and cutaneous melanoma

2. Determine associations between CAEs and treatment outcome
• Retrospectively analyzed 169 patients with advanced-stage vulvovaginal or cutaneous melanoma who received at least one dose of an ICI including PD-1 and CTLA-4 inhibitors between June 2012 to December 2018

• **Descriptive statistics**: summarize the baseline characteristics, disease outcomes, and toxicity profiles

• **Chi-square statistical**: examine associations between irAEs and treatment response

PD-1: Programmed Cell-Death Protein-1
CTLA-4: Cytotoxic T-Lymphocyte Associated Protein-4
Results

- CAEs were the most common immune-related adverse events, occurring in 28/156 patients with cutaneous melanoma and 1/13 patients with vulvovaginal melanoma.

- CAEs were significantly associated with patient response to ICIs, in patients for whom response was recorded (p = 0.01).

<table>
<thead>
<tr>
<th>Treatment Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAE status</td>
</tr>
<tr>
<td>CAE Present</td>
</tr>
<tr>
<td>CAE Absent</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Table 1. ICI treatment outcome in patients with and without CAEs.
Results

Figure 1. CAE Morphology for vulvovaginal and cutaneous melanoma

Figure 2. CAE Anatomical location for vulvovaginal and cutaneous melanoma.
Most patients had associated autoimmune comorbidities prior to initiation of ICIs (89.8% patients with cutaneous melanoma and 91.7% patients with vulvovaginal melanoma).

Topical and systemic steroid therapy were not used in the patient with vulvovaginal melanoma with CAEs, yet was used in 50% of patients with cutaneous melanoma with CAEs.
Conclusion

• CAEs were significantly associated with response to ICIs in patients with metastatic melanoma

• Furthermore, the nuanced differences in the clinical, morphological, and treatment modalities for CAEs in patients with vulvovaginal vs. cutaneous melanoma are important considerations for initiating ICIs in accordance with melanoma type


Vulvovaginal vs. Cutaneous Melanoma: 
A Retrospective Cohort Study on Cutaneous Immune-Related Adverse Events

Sheida Naderi-Azad,1 Faisal Sickandar,2 Rossanna C. Pezo2,3,4

1 University of Toronto Faculty of Medicine, Toronto, ON, Canada
2 Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada
3 Division of Medical Oncology and Hematology, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada
4 Department of Medicine, University of Toronto, Toronto, ON, Canada
Background

- Immune Checkpoint Inhibitors (ICIs) have been at the forefront of metastatic melanoma.
- The use of ICIs in vulvovaginal melanoma has been studied less extensively compared to cutaneous melanoma.
- Consistent with their mechanism of action, common toxicities associated with ICI therapy occur as a result of inflammatory dysregulation.
These inflammatory reactions range from colitis, dermatitis, and hepatitis, to respiratory diseases and endocrinopathies.

While Cutaneous immune-related Adverse Events (CAEs) are some of the most common toxicities in metastatic melanoma, they have not been examined comprehensively in patients with vulvovaginal and cutaneous melanoma on ICIs.
Objectives

1. Examine the clinical and morphological characteristics of CAEs in patients with vulvovaginal and cutaneous melanoma

2. Determine associations between CAEs and treatment outcome
Methods

• Retrospectively analyzed 169 patients with advanced-stage vulvovaginal or cutaneous melanoma who received at least one dose of an ICI including PD-1 and CTLA-4 inhibitors between June 2012 to December 2018

• **Descriptive statistics**: summarize the baseline characteristics, disease outcomes, and toxicity profiles

• **Chi-square statistical**: examine associations between irAEs and treatment response

PD-1: Programmed Cell-Death Protein-1
CTLA-4: Cytotoxic T-Lymphocyte Associated Protein-4
Results

- CAEs were the most common immune-related adverse events, occurring in 28/156 patients with cutaneous melanoma and 1/13 patients with vulvovaginal melanoma.

- CAEs were significantly associated with patient response to ICIs ($p = 0.01$)

<table>
<thead>
<tr>
<th>Treatment Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAE status</td>
</tr>
<tr>
<td>CAE Present</td>
</tr>
<tr>
<td>CAE Absent</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Table 1. ICI treatment outcome in patients with and without CAEs.
Results

Figure 1. CAE Morphology for vulvovaginal and cutaneous melanoma

Figure 2. CAE Anatomical location for vulvovaginal and cutaneous melanoma.
Results

• Most patients had associated autoimmune comorbidities prior to initiation of ICIs (89.8% patients with cutaneous melanoma and 91.7% patients with vulvovaginal melanoma)

• Topical and systemic steroid therapy were not used in the patient with vulvovaginal melanoma with CAEs, yet was used in 50% of patients with cutaneous melanoma with CAEs
Conclusion

• CAEs were significantly associated with response to ICIs in patients with metastatic melanoma

• Furthermore, the nuanced differences in the clinical, morphological, and treatment modalities for CAEs in patients with vulvovaginal vs. cutaneous melanoma are important considerations for initiating ICIs in accordance with melanoma type