Overview Photography and Short-term Mole Monitoring in Patients Taking a BRAF Inhibitor

Patients taking BRAF inhibitors develop new primary melanomas and nevi. Many of these neoplasms are BRAF wild-type, which may be due to the paradoxical activation of the RAF/MEK/ERK pathway via an alternative driver mutation, similar to the mechanism involved in inducing the development of squamous cell carcinomas in these patients. In addition, some nevi in these individuals involute, and many of these involuting lesions harbor a BRAF<sup>V600E</sup> (OMIM *164757) mutation.

Baseline-overview photographs allow for the detection of new melanocytic lesions (MLs) and permit monitoring for morphologic changes. This study was designed to investigate the magnitude of the volatility of these MLs. We used overview photography and dermoscopy to determine the extent of melanocytic changes in patients taking a BRAF inhibitor and described their dermoscopic morphology.

Methods | A formal review and waiver were obtained from the Memorial Sloan Kettering Cancer Center Institutional Review Board. Patients taking BRAF inhibitor therapy seen by the dermatology department at Memorial Sloan-Kettering Cancer Center between January 2009 and December 2012 were identified. Patients with baseline photographs within one year of the initiation of BRAF inhibitor therapy and subsequent follow-up overview photographs of their torso were included in the study. Information on each patient’s age, sex, initial and follow-up photography date, date patient started inhibitor therapy, and date of last treatment with a BRAF inhibitor was collected.

Overview photographs of the upper back, lower back, chest, and abdomen were retrospectively obtained from the MIRROR Body Mapping software (Canfield Scientific, Inc.). Color mode and zoom were used, as necessary, to facilitate comparison, and initial and follow-up images were compared. Photographic reviewers (A.A.M. and S.Y.) were not masked to the dates of the photos.

A total count of new, growing and/or darkening, and involuting MLs was determined. Growing and darkening observations were made by objective side-by-side comparison. Any anatomic area that had not been photographed at the follow-up photography visit was excluded. Dermoscopic images of all biopsied MLs were evaluated for pattern and melanoma-specific features. The pathologic diagnosis of each lesion was recorded.

The incidence rate of new melanomas was determined as the total number of new melanomas divided by the total number of study days of BRAF inhibitor therapy (calculated as the days from initial to final treatment, or date of final visit during the study period).

Descriptive and comparative statistical analyses were performed using Stata software (version 12.1; StataCorp LP).

Results | Thirteen men and 9 women (mean age, 53 years) taking BRAF inhibitors were identified. The mean length of photography follow-up and therapy were 319 and 332 days, respectively. Baseline and follow-up images of at least 1 anatomic area were available for 13 (59%) patients. The mean number of combined new and growing and/or darkening ML across anatomic locations was between 6.1 and 16.4, and the mean number of involuting MLs across anatomic locations was between 3.4 and 8.0 (Table 1).

Of 42 MLs, 35 (83%) were benign and 7 (17%) were melanoma. There was no difference in exposure times to inhibitor between patients who developed melanomas and those who did not (P = .42). In addition, there was no positive correlation between the number of melanomas developing with the length of exposure to the BRAF inhibitor (P = .11). All melanomas had at least 1 melanoma-specific dermoscopic structure, with negative network being the most common, followed by crystalline structures (P < .05) (Table 2). The incidence rate of new melanomas was 435 per 1000 person-years of BRAF inhibitor therapy (eFigure 1 in the Supplement).

Discussion | The increased volatility of MLs in patients on BRAF inhibition results in a complex background on which to find

### Table 1. Melanocytic Lesion Counts From Overview Photographs

<table>
<thead>
<tr>
<th>Anatomic Area</th>
<th>New&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Growing and/or Darkening&lt;sup&gt;a&lt;/sup&gt;</th>
<th>New and Growing and/or Darkening</th>
<th>Involuting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper posterior trunk (n = 9)</td>
<td>4.3</td>
<td>8.8</td>
<td>13.1</td>
<td>8.0</td>
</tr>
<tr>
<td>Lower posterior trunk (n = 5)</td>
<td>6.8</td>
<td>9.6</td>
<td>16.4</td>
<td>4.0</td>
</tr>
<tr>
<td>Upper anterior trunk (n = 8)</td>
<td>4.3</td>
<td>5.3</td>
<td>9.5</td>
<td>4.3</td>
</tr>
<tr>
<td>Lower anterior trunk (n = 7)</td>
<td>3.3</td>
<td>2.9</td>
<td>6.1</td>
<td>3.4</td>
</tr>
</tbody>
</table>

<sup>a</sup> Any anatomic area that had not been photographed at baseline or at follow-up visits was excluded.

<sup>b</sup> Incidence rates of new and growing and/or darkening nevi are 53 and 77 per 1000 person-years of BRAF inhibitor therapy, respectively.
inconspicuous new primary melanomas. The rate of new primary melanomas is approximately 17 times higher than has been reported in a high-risk atypical-mole syndrome population with a history of melanoma.5

BRAF inhibitor therapy can theoretically cure patients of their BRAFV600Emutated melanoma, but BRAF wild-type melanomas remain a challenge. As yet, the underlying driver mutation in these changing MLs remains to be elucidated, although NRAS (OMIM *164790) mutations have occasionally been found.1 Dermoscopy helps identify melanoma, and all melanomas in our series demonstrated at least 1 melanocytic specific feature.

A limitation of our study was patient selection bias, as only patients undergoing BRAF inhibitor therapy and seen by the dermatology department were assessed. Many of these patients had a high-risk phenotype with many nevi and dysplastic nevi. Further studies are needed to determine the extent of changes in all patients taking BRAF inhibitors. In addition, it remains to be seen if melanocytic changes are less dynamic in the setting of combined therapy with a MEK inhibitor, as was the case with squamous cell carcinomas.6

We support total-body photography and short-term mole monitoring with dermoscopy as a method for monitoring atypical-pigmented lesions in the setting of highly volatile melanocytic changes in patients taking a BRAF inhibitor.

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**Author Contributions:** Drs Marghoob and Lacouture had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Yagerman, Flores, Lacouture, Marghoob.

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### Table 2. Summary of Dermoscopic Features of New and Changing Suspicious Lesions

<table>
<thead>
<tr>
<th>Dermoscopic Feature</th>
<th>Benign (n = 35)</th>
<th>Melanoma (n = 7)</th>
<th>Benign vs Melanoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative network</td>
<td>3 (9)</td>
<td>4 (57)</td>
<td>0.002*</td>
</tr>
<tr>
<td>Atypical network</td>
<td>14 (40)</td>
<td>4 (57)</td>
<td>0.403</td>
</tr>
<tr>
<td>Atypical dots/globules</td>
<td>8 (23)</td>
<td>3 (43)</td>
<td>0.272</td>
</tr>
<tr>
<td>Off-center blotches</td>
<td>9 (26)</td>
<td>2 (29)</td>
<td>0.875</td>
</tr>
<tr>
<td>Blue-white veil over raised areas</td>
<td>5 (14)</td>
<td>2 (29)</td>
<td>0.355</td>
</tr>
<tr>
<td>Blue-white veil over flat areas</td>
<td>3 (9)</td>
<td>1 (14)</td>
<td>0.638</td>
</tr>
<tr>
<td>Streaks/pseudopods</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Polymorphous vessels/vascular blush</td>
<td>5 (14)</td>
<td>3 (43)</td>
<td>0.079</td>
</tr>
<tr>
<td>Peripheral structureless</td>
<td>4 (11)</td>
<td>2 (29)</td>
<td>0.237</td>
</tr>
<tr>
<td>Chrystaline structures</td>
<td>0</td>
<td>1 (14)</td>
<td>0.024</td>
</tr>
</tbody>
</table>

**Abbreviation:** NA, not applicable.

*P < .05 using a proportion test.

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Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Yagerman, Flores, Marghoob, Lacouture.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Yagerman, Flores.

Administrative, technical, or material support: Yagerman, Flores, Lacouture, Marghoob.

Study supervision: Yagerman, Flores, Lacouture, Marghoob.

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### Portable Shade Structure Use at a Youth Soccer Camp

More than 3 million nonmelanoma skin cancers (NMSCs) are diagnosed annually in the United States.1,2 The incidence of malignant melanoma (MM) has increased annually by 2.4%.3 Open field activities in youth are a major source of sun exposure, which leads to skin cancer later in life.4-6 Few studies exist on the use of shade structures in open field sports, particularly soccer. In this pilot study, we assess the rate of use of portable shade structures among soccer-playing youths.

**Methods** The Virginia Commonwealth University (VCU) institutional review board approved this study, waiving participant written informed consent. A summer soccer camp for boys and girls in metropolitan Richmond, Virginia, consisted of...