June 22, 2020

Re: DermTech's Pigmented Lesion Assay /NCCN

Submitted by:
Name: Daniel M. Siegel MD, MS
Company/Organization: SUNY Downstate
Address: Basic Sci Bldg 849 450 Clarkson Avenue, Box46, Brooklyn 11203
Phone: 718 270 1229
Email: Daniel.siegel@downstate.edu
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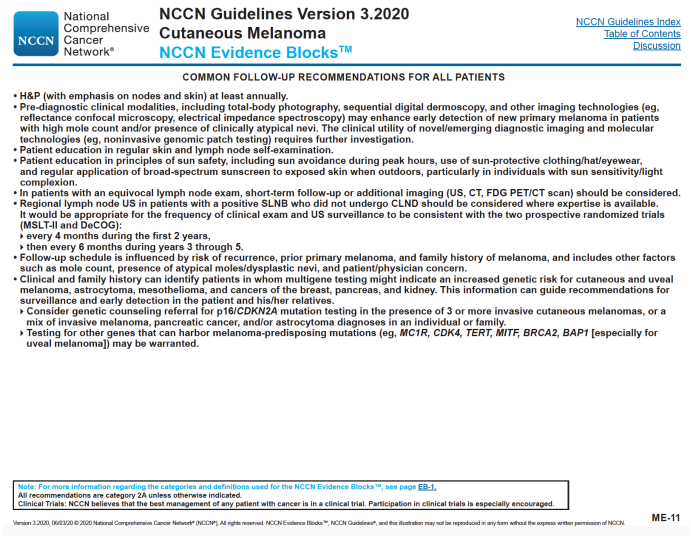
NCCN Guidelines Panel: Cutaneous Melanoma

Dear Cutaneous Melanoma Panel Members:

As a clinician and clinical researcher, I've not only studied and published, but also incorporated the use of DermTech's Pigmented Lesion Assay (PLA) into my practice to rule out melanoma by guiding biopsy decisions via molecular risk factors. I find this non-invasive CLIA test useful, because its biopsy guidance and its NPV of over 99% that allows me to miss fewer melanomas and find them earlier. Recent work by Conic et al. (JAAD, 2018; 78(1):40-46 e.7) highlights, that even a relatively small delay in managing primary melanomas (which the PLA helps minimize) negatively impacts survival of stage I melanoma patients. Problems inherent to the practice of dermatology include access to specialty care, a shortage of dermatologists dependent on geography, and lack of tools supporting providers in the assessment of often difficult to ascertain pigmented skin lesions. This situation has not been helped by COVID-19 and related closures or limited access to dermatology offices. Additionally, in this period where telemedicine in general and teledermatology in particular have been a lifeline for many patients, the PLA has been a lifesaver for many patients who could obtain the sample necessary for testing while sheltering at home and either obtain a sense of relief of make it to a high priority waiting list for further evaluation or treatment as guided by the PLA and clinical circumstances. When the pandemic ends, the PLA will still paly a valuable role in expediting the management of potential high-risk lesions and be especially useful for those qualified health care providers who have very high numbers to needed to biopsy to find a melanoma.

Following the required format, I provide information in the requested categories:

Specific Changes: Please see below regarding the requested specific change over Version 3.2020 (Page 19, ME-11, Bullet Point 2, Pre-Diagnostic Clinical Modalities, Screen Shot):



National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2020
Cutaneous Melanoma
NCCN Evidence Blocks™

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Discussion

COMMON FOLLOW-UP RECOMMENDATIONS FOR ALL PATIENTS

- **H&P (with emphasis on nodes and skin) at least annually.**
- **Pre-diagnostic clinical modalities, including total-body photography, sequential digital dermoscopy, and other imaging technologies (eg, reflectance confocal microscopy, electrical impedance spectroscopy) may enhance early detection of new primary melanoma in patients with high mole count and/or presence of clinically atypical nevi. The clinical utility of novel/emerging diagnostic imaging and molecular technologies (eg, noninvasive genomic patch testing) requires further investigation.**
- **Patient education in regular skin and lymph node self-examination.**
- **Patient education in principles of sun safety, including sun avoidance during peak hours, use of sun-protective clothing/hat/eyewear, and regular application of broad-spectrum sunscreen to exposed skin when outdoors, particularly in individuals with sun sensitivity/light complexion.**
- **In patients with an equivocal lymph node exam, short-term follow-up or additional imaging (US, CT, FDG PET/CT scan) should be considered.**
- **Regional lymph node US in patients with a positive SLNB who did not undergo CLND should be considered where expertise is available. It would be appropriate for the frequency of clinical exam and US surveillance to be consistent with the two prospective randomized trials (MSLT-II and DeCOG):**
  - **every 4 months during the first 2 years,**
  - **then every 6 months during years 3 through 5.**
- **Follow-up schedule is influenced by risk of recurrence, prior primary melanoma, and family history of melanoma, and includes other factors such as mole count, presence of atypical moles/dysplastic nevi, and patient/physician concern.**
- **Clinical and family history can identify patients in whom multigene testing might indicate an increased genetic risk for cutaneous and uveal melanoma, astrocytoma, mesothelioma, and cancers of the breast, pancreas, and kidney. This information can guide recommendations for surveillance and early detection in the patient and his/her relatives.**
  - **Consider genetic counseling referral for p16/*CDKN2A* mutation testing in the presence of 3 or more invasive cutaneous melanomas, or a mix of invasive melanoma, pancreatic cancer, and/or astrocytoma diagnoses in an individual or family.**
  - **Testing for other genes that can harbor melanoma-predisposing mutations (eg, *MC1R, CDK4, TERT, MITF, BRCA2, BAP1* [especially for uveal melanoma]) may be warranted.**

Note: For more information regarding the categories and definitions used for the NCCN Evidence Blocks™, see page EB-1.
All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

ME-11

I recommend the following changes: … ~~The clinical utility of novel/emerging diagnostic imaging and molecular technologies (e.g. non-invasive genomic patch testing) requires further investigation.~~ … Pre-diagnostic molecular genomic patch testing to help guide biopsy decisions on pigmented skin lesions should be considered.

FDA Clearance: This is a CLIA administered laboratory developed test.

Rationale: Solid evidence from multiple utility studies demonstrates biopsy guidance of this pre-diagnostic, pre-biopsy test with a negative predictive value of over 99% that allows clinicians to miss fewer melanomas and find them earlier.

From a portfolio of about 20 peer reviewed PLA publications in the public domain, I am attaching 3 most recent PDFs on the PLA's clinical utility, a measure that appeared in question in earlier versions of the Cutaneous Melanoma Guidelines.

1. Ferris et al., DOJ 2019: No missed melanomas during 12 months of follow-up.
2. Brouha et al. JDD 2020: Real-world registry study of 3,418 cases, 90% reduction in biopsies, clinicians follow the guidance of the test in over 98% of cases.
3. Robinson et al. SKIN 2020: Physician-guided PLA home sample collection is feasible.

I sincerely hope the panel recognizes the abundance of peer reviewed data including on clinical utility available for the PLA (about 20 publications total) and recommends its use as a biopsy-guiding pre-diagnostic technology in pigmented lesion management in the latest version of our 2020 NCCN Cutaneous Melanoma Guidelines.

Thank you,

Daniel Mark Siegel MD, MS (Management and Policy)
Clinical Professor of Dermatology, SUNY Downstate
Former President, American Academy of Dermatology