Letters

COMMENT & RESPONSE

In Reply We appreciate the comments by Beatson and Weinstock on our analysis of the pigmented lesion assay (PLA).[1] We agree that it is important to develop tools that have the potential to help decrease biopsies of benign pigmented skin lesions such as the PLA, a gene expression melanoma rule-out test based on obtaining skin samples noninvasively via adhesive patches.[1-4] We believe that it is important to view the PLA's performance relative to the performance of histopathologic diagnosis. In a large and recent study based on data from 10 US states,[5] the sensitivity of standard histopathologic assessment in comparable in situ and early invasive melanomas was 65% ([Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis [MPATH-Dx] classes III and IV; 908 + 113 + 11+717 + 928 + 198 = 2875; 2875 of 4416 = 0.65). Even the best dermatopathologist cannot see and describe molecular changes that have yet to develop morphological correlates, thereby highlighting the limitations of our current care standard. Thus, the authors' concerns that the PLA sensitivity is low at 91% should be viewed in this comparative context.[1-6] In light of this concern, it is also helpful to mention recent follow-up studies that support a PLA sensitivity in real-world settings of 95%.[3]

The authors also present concerns that the negative predictive value (NPV) of the PLA may not be as high as reported citing that the prevalence of melanoma in the validation study was higher than the 7% used in the NPV calculation.[2] A number of real-world US practice scenarios place the prevalence of melanoma in biopsied pigmented lesions (biopsied to rule out melanoma) at between 3.7% and 6.0% (149 of 4039 = 0.037,[6] 19 of 381 = 0.050,[3] and 179 000/3 000 000 = 0.060[3]). These figures are all below the conservatively chosen 7% biopsy population prevalence used in Gerami et al,[2] which was selected to understand the true NPV (above 99%) in the clinical setting and not simply in a research validation setting. Again, by way of comparison with the current histopathologic pathway using a 7% prevalence, the calculated NPV from Elmore et al[5] for early-stage melanoma based on the sensitivity described herein is well below 83%.[1,4,5] It is also important to note that 708 PLA-evaluated real-world lesions have now been followed up for over a year, and no missed melanomas have been identified (D.M.S. and Laura K. Ferris, MD, PhD, unpublished observations), further supporting the high NPV of the PLA.

We agree that it is important to carefully test new technologies such as the PLA. To date, the performance of the PLA has been established and corroborated by over 40 investigators, and findings have been summarized in over 10 peer-reviewed publications including the references found in Gerami et al,[2] Ferris et al,[3] Hornberger and Siegel,[1] and Rivers et al.[4] Additional corroborating data sets come from over 1350 clinicians in 40 US states who have used the PLA on over 20 000 patients. If used as intended, the PLA improves the current diagnostic paradigm of ruling out melanoma by reducing the number needed to biopsy about 10-fold from about 25[6] to 2.7,[4] while significantly increasing the NPV to 99%. This in turn drives cost savings for the health care system (−47% at the PLA selling price reference point of $500) and demonstrates that the PLA is a new technology that can deliver better care at a lower cost.[1-4]

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Published Online: January 30, 2019. doi:10.1001/jamadermatol.2018.4377

Conflict of Interest Disclosures: Dr Siegel is a member of DermTech's Scientific Advisory Board and a stockholder in DermTech; Dr Hornberger is a consultant to DermTech.

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