

## EDITORIAL – LETTER TO THE EDITOR

**Response to “Prediction of Sentinel Node Positivity Risk in Melanoma Patients: When Appropriate Statistical Methodology was Employed an i31-GEP Test Did Not Outperform a Tool that Uses Clinicopathologic Features Only”**

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*Response:* We thank Dr. Lo and colleagues for their interest our paper. The analysis by [Zakria et al](#)<sup>1</sup> reiterates the challenges of using the MIA nomogram in the clinical setting and the pitfalls of relying solely on clinicopathologic factors without considering a tumor’s molecular profile. Lo and colleagues assert that a flawed statistical analysis may have been used to compare the Melanoma Institute Australia (MIA) nomogram and the i31-GEP for sentinel lymph node biopsy (i31-SLNB).<sup>1</sup> Lo et al suggest that the comparison was performed without regard for the fact that different methods were used to calculate confidence intervals (CI) for the nomogram and GEP test. Although the compared tests were developed using different methods of CI determination, in fact, they were evaluated within the study according to the procedures that are available to physicians for clinical use to guide patient care. The i31-GEP for SLNB provided an SLNB positivity prediction with higher confidence and precision (possibly due to the inclusion of genomic factors in the model). It is surprising that the developers of the MIA tool would make the

The cost of a tool does not necessarily relate to its clinical utility and accuracy. The more relevant question is whether the test adds benefit to current guidance surrounding SLNB. Decision curve analysis for SLNB returns two outcomes at various risk thresholds: 1) net benefit, which considers how many true positive SLNs a test can identify for every 100 patients, and 2) interventions avoided, which considers how many SLNBs could be avoided per 100 patients without missing a biopsy for any patient with a positive SLN.<sup>2</sup> A recent analysis of the MIA nomogram demonstrated net harm at risk thresholds of 5-8% and 10%, with a small net benefit at a 9% risk threshold. Moreover, at each risk threshold, the interventions able to be avoided per 100 patients without missing biopsy for a patient with a positive SLN was zero at 5-8% and 10% risk thresholds and <1 at a 9% risk threshold.<sup>3</sup> A second analysis has shown similar results.<sup>4</sup> In contrast, Marchetti et al. demonstrated that the i31-GEP for SLNB provided a positive net benefit compared to SLNB for all patients, with the greatest benefit in T1b tumors with 23 interventions avoided per 100 patients.<sup>5</sup>

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Given all of the above analyses and facts, when clinicians choose which test can better identify patients who may or may not benefit from SLNB, they might consider the demonstrated benefit of the i31-GEP test and that the MIA nomogram has not shown a net benefit over performing SLNB for everyone and may potentially do net harm.

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