**ABSTRACT**

Tools that reduce the number of surgical biopsies performed on benign skin lesions have the potential to improve patient care. The non-invasive pigmented lesion assay (PLA) gene expression test is such a tool. It helps rule out melanoma and the need for surgical biopsies of atypical pigmented skin lesions with a NPV >99%. Analyses of ~15,000 PLA samples in the real-world routine use setting of over 600 US dermatology offices demonstrated that ~88% were PLA(-). A real-world utility study in 381 cases demonstrated that 99% of PLA(-) cases were monitored, while all PLA(+) cases were surgically biopsied demonstrating that clinicians follow the guidance of the test. With efforts to validate the PLA beyond histopathology, we found that we can identify somatic mutations in three genes known to be drivers of melanoma development (BRAF, NRAS, and the TERT promoter) in PLA samples. Mutations in adhesive patch PLA samples were concordant with mutations in biopsies. The frequency of mutations in melanoma samples was 77% and statistically higher than the 14% found in non-melanoma samples (p=0.0001). TERT promoter mutations were the most prevalent mutation type in PLA(+) melanomas (79%). Eighty-six percent of non-melanomas had no mutations and 97% of histopathologically confirmed melanomas were PLA and/or mutation positive (n=103). Mutation frequencies were similar in 519 additional prospectively collected real-world PLA samples, with 88% of PLA(-) samples having no mutations. Combining gene expression and mutation analyses enhances the ability to non-invasively detect early melanoma.

**OBJECTIVES**

- To assess the real-world utility of the PLA and determine, if physicians follow the guidance of the test
- To determine if BRAF, NRAS and TERT promoter mutations can be used as additional validation for PLA gene expression analysis

**METHODS**

All studies were IRB approved. Gene expression analyses were performed as described. (Ref. 1-5) Mutation analyses were performed by Sanger sequencing of adhesive patch and FFPE tissue block samples.

**RESULTS**

A total of 381 real-world use cases were analyzed, 330 in the PLA(-) cohort and 51 in the PLA(+) cohort. Table 1 shows the summary of the clinical management for these 2 cohorts.

<table>
<thead>
<tr>
<th>Melanoma</th>
<th>Non-Melanoma</th>
<th>Clinical Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLA(+)</td>
<td>10 (12 MIS, 7 INvasive)</td>
<td>32</td>
</tr>
<tr>
<td>PLA(+)</td>
<td>1**</td>
<td>329* (3 follow-up biopsies, all non-melanoma)</td>
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**REFERENCES**