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Long-term outcome of pigmented lesions clinically suspicious for melanoma previously tested with the Pigmented Lesion Assay (PLA): results from the TRUST Study

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James Rock[1], Maral K. Skelsey[2,3], Gary Peck[2], Simone McKitty[4], Brook Brouha[5], Tana Frumento[6], S. Sasha Jazayeri[7], Zuxu Yao[1], Michael D. Howell[1], Burkhard Jansen[1]

1. DermTech Inc, La Jolla, CA 2. Dermatologic Surgery Center of Washington, Chevy Chase, MD 3. Dermatology, Georgetown University, Washington, DC
4. McKitty Dermatology, Torrance, CA 5. West Dermatology, San Diego, CA 6. Omni Dermatology, Tempe, AZ 7. Alliance Dermatology and Mohs Center, Phoenix, AZ

DermTech

Abstract

The assessment of pigmented lesions suspicious for melanoma remains a challenge. The non-invasive Pigmented Lesion Assay (PLA) guides biopsy decisions and detects melanoma at its earliest stages based on genomic atypia. The TRUST Study was designed to determine the proportion of true negative lesions among those that initially tested negative. Of the 1781 lesions in the long-term follow-up screening cohort, there were no known melanoma deaths or late-stage melanoma detected. Of the 1233 cases that returned for follow-up evaluation to the clinic, ten lesions received a melanoma diagnosis after the initial PLA test with four (0.3%) at Stage 0 (in situ) and six (0.5%) at Stage 1a. The negative predictive value (NPV) calculated from this subset of 1233 lesions with confirmed follow-up evaluations, but not repeated tested, was 99.2% (CI = 98.5 - 99.6). Of the 302 lesions assessed by means of repeat testing with the PLA, none (0%) were found to have clinically obvious melanoma upon the subject's return to the clinic, confirming the results of the initial chart review. Of these 302 lesions, 88.7% percent (268 lesions) were negative on repeat testing with the PLA and 34 (11.3%) were positive. All 34 lesions (100%) were surgically biopsied, with 3 (1%) diagnosed as Stage 0 (in situ), identified 13, 14 and 19 months after the initial PLA (NPV = 99.0% [CI = 97.1 - 99.8]). This long-term repeat-testing study confirmed the NPV of the PLA and found no adverse outcomes related to the test's routine use.

Objective

The objective of the study was to determine the proportion of true negative lesions among those that previously tested negative with the DermTech Pigmented Lesion Assay (PLA).

Methods

Five geographically dispersed trial sites that routinely use the PLA in clinical practice were recruited to participate in this trial. Samples were to be collected from patients who previously had a PLA negative result and retested over an approximate 12- to 24-month period. In addition, patient charts were reviewed over up to a 36-month period to determine:

- Did the patient returned to the trial site post-PLA
  - If yes, was the PLA- lesion biopsied
  - If biopsied, was melanoma diagnosed
  - Evidence of mortality
  - Evidence of mortality caused by melanoma

All samples were processed in DermTech's CLIA commercial laboratory located in La Jolla, CA. The DermTech PLA is a non-invasive adhesive patch test to sample lesions clinically suspicious for melanoma.

The test assesses the expression of two genes associate with melanoma, LINC00518 (long intergenic noncoding RNA 518) and/or PRAME (preferentially expressed antigen in melanoma). The PLA is used to guide biopsy decision and rule out melanoma based on the gene expression results.

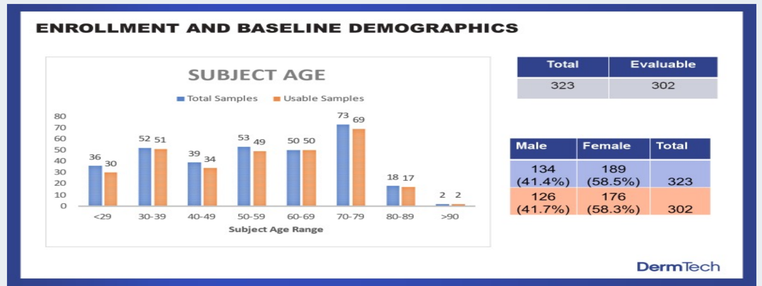
Results

The results of the chart review from 2575 lesions is depicted below in Figure 1.

- 2575 — 2575 PLA lesions; ~2400 patients
- 1781 — Excludes PLA+, QNS, enrolled subjects, and those not reviewed
- 1233 — 69.2% returned to the clinic post-PLA
- 808 — 45.4% returned in the last year
- 158 — 12.8% hx of melanoma
- 10 — 0.81% PLA- lesions melanoma+
- 2 — Known deaths – neither melanoma related

Of the reviewed charts, there were 10 PLA- lesions histopathologically assessed as melanoma. Of the 10 melanoma diagnoses 6 (0.5%) were noted to be Stage 1A and 4 (0.3%) melanoma *in situ*. The time from the PLA- result to the date of melanoma diagnosis ranged from 1 to 33 months after the initial PLA test with an average of 15.1 months (5 - less than 12 months, 2 – 12 to 24 months and 3 – greater than 24 months. The negative predictive value calculated from this cohort was 99.2% (CI95%= 98.5 - 99.6) based on the 1233 reviewed charts.

Of the patients who underwent repeat testing of the lesion with the PLA, basic demographic data is presented in Figure 2.



Enrollment was higher for females versus males with patients aged 70-79 representing the largest age cohort. There was virtually no difference in the sex of patients between those enrolled and those with a repeat PLA result. Data for 21 (6.5%) of the 323 enrolled subjects was not analyzed due to off-label use, and quantity not sufficient for analysis (QNS).

PLA positive results for the 302 retested lesions by site are presented below in Table 1.

SITE	PRAME +	LINC +	DOUBLE+	TOTAL
01	0	5	1	79
02	1	0	0	21
03	0	3	1	19
04	4	9	7	166
05	1	2	0	17
Total	6 (2.0%)	19 (6.3%)	9 (3.0%)	302

Overall LINC+ results were the most frequent positive finding with PRAME+ and DOUBLE+ results occur less frequently. All 34 of these lesions went on to surgical biopsy and those results are presented below in Table 2.

PLA+ repeat testing	PLA+ surgical Bx	Melanoma Diagnosis initial PLA-	Proportion of melanoma (NPV)	95% CI
34/302 (9.9%)	34/34 (100%)	3 (1%)	299/302 (99.0%)	(0.971 – 0.998)

Three Stage 0 (MIS) melanoma were detected in these repeat PLA+ lesions including 1 PRAME+ and 2 DOUBLE+. Repeat testing on these lesions occurred 13, 14 and 19 months after the initial PLA test.

Conclusions

- Ten lesions from the screening cohort (1233) received a melanoma diagnosis. Four (0.3%) at Stage 0 (*in situ*) six (0.5%) at Stage 1a
- NPV of the 1233 lesions with confirmed follow-up evaluations was 99.2% (CI95%= 98.5 - 99.6)
- Of the 323 enrolled subjects, 34 lesions were PLA+ and all went on to surgically biopsied with 3 (1%) diagnosed as Stage 0 (in situ) melanoma
- NPV of the 302 lesions was 99.0% (CI95% = 97.1 - 99.8)
- No adverse outcomes related to the test's routine use

Reference

Gerami P, Yao Z, Polsky D, et al. Development and validation of a noninvasive 2-gene molecular assay for cutaneous melanoma. J Am Acad Dermatol. 2017 Jan;76(1):114-20 e2.

Disclosures

J Rock, Z Yao, MD Howell, and B Jansen are employees and shareholders at DermTech, Inc. MK Skelsey, G Peck, B Brouha are consultants for DermTech