Molecular recurrence risk profiles in patients with early-stage NSCLC: Current standard of care compared to a prognostic and predictive 14-gene expression assay

ABSTRACT #98
POSTER XXXX

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BACKGROUND

The National Comprehensive Cancer Network (NCCN) Guidelines recommend patients with stage IB-IIA non-small cell lung cancer (NSCLC) receive adjuvant therapy post-surgical resection if they have clinicopathologic features that are considered high-risk.[1] These features are not validated to stratify risk or predict therapy benefit. NCCN recommends observation for stage IA patients, despite a 26% recurrence rate for stage I adenocarcinomas post-resection[2], with no guidelines to stratify which IA patients could benefit from additional management. This study reports utilization of a commercial CLIA-certified 14-gene qPCR expression assay (DetermaRx), validated to evaluate recurrence risk and predict chemotherapy benefit in early-stage non-squamous NSCLC.[3] This report analyzes the benefit of assessing molecular risk compared to NCCN high-risk features alone. The study expands a previously published report of 250 cases to a review of over 2000 cases.[4]

METHODS

All non-squamous NSCLC specimens received between 2/2020 and 8/2022 were tested with DetermaRx in a CLIA-certified laboratory (Oncocyte).
Pathologic stage, type, and number of NCCN high-risk features[1] (poorly differentiated tumor, vascular invasion, wedge resection, tumor size >4cm, visceral pleural involvement, unknown lymph node status) were obtained from pathology reports submitted with the specimens and compared to the molecular risk profile.
Inclusion criteria for this analysis were cases with single tumors of NSCLC adenocarcinoma stage IB-IIA, when all NCCN clinicopathologic features were available. Number of NCCN high-risk features were not analyzed in stage IA cases.

RESULTS

2003 cases were available for analysis at the time of abstract submission. The analysis has since been expanded to 2257 cases. Specimens were sent from a total of 219 community and academic medical centers; most cases came from a community setting. Eighty percent (80%) of tests were ordered by thoracic surgeons, and 20% by medical oncologists. Forty three percent (43%) of cases were resulted as molecular high- or intermediate-risk by the 14-gene expression assay. 67% of all specimens received were stage IA according to AJCC 8th edition staging criteria, and about one-fourth of these stage IA cases were found to be molecular high/intermediate-risk. Detailed comparison of molecular profiling and NCCN high-risk features was performed for 566 stage IB & IIA cases (Figure 1). Visceral Pleural Involvement was the most frequent NCCN high-risk feature in 68% of Stage IB & IIA cases.
In stages IB & IIA, 36% of cases that would have been considered high-risk by NCCN (defined as having at least one high-risk feature) were reclassified as low-risk by the molecular assay, and at the same time 8% of cases that had no NCCN high-risk features were reclassified as molecular high or intermediate-risk. The intermediate- & high-risk cases are both considered candidates to benefit from adjuvant therapy.

Table 1: Stage by Molecular Risk Results All Samples Reported

	Stage IA	Stage IB	Stage IIA	Total
Low	988 *(44%)*	271 *(12%)*	35 *(2%)*	1294 *(57%)*
Intermediate	340 *(15%)*	204 *(9%)*	29 *(1%)*	573 *(25%)*
High	174 *(8%)*	165 *(7%)*	21 *(2%)*	390 *(17%)*
Total	**1502** *(67%)*	**640** *(28%)*	**115** *(5%)*	**2257** *(100%)*

Table 2: Number NCCN High-Risk Features vs. Stage

# NCCN	Stage IB	Stage IIA	Total
0	89 *(16%)*	0 *(0%)*	**89** *(16%)*
1	246 *(43%)*	40 *(7%)*	**286** *(51%)*
2	100 *(18%)*	26 *(5%)*	**126** *(22%)*
3+	48 *(8%)*	17 *(3%)*	**65** *(11%)*
Total	**483** *(85%)*	**83** *(15%)*	**566** *(100%)*

Table 3: Number NCCN High-Risk Features vs. Molecular Risk

# NCCN	Low	Intermediate	High	Total
0	42 *(7%)*	25 *(4%)*	22 *(4%)*	**89** *(16%)*
1	133 *(23%)*	90 *(16%)*	63 *(11%)*	**286** *(51%)*
2	49 *(9%)*	39 *(7%)*	38 *(7%)*	**126** *(22%)*
3+	20 *(4%)*	14 *(2%)*	31 *(5%)*	**65** *(11%)*
Total	**244** *(43%)*	**168** *(30%)*	**154** *(27%)*	**566** *(100%)*

Figure 1: Inclusion for NCCN High-Risk Comparison

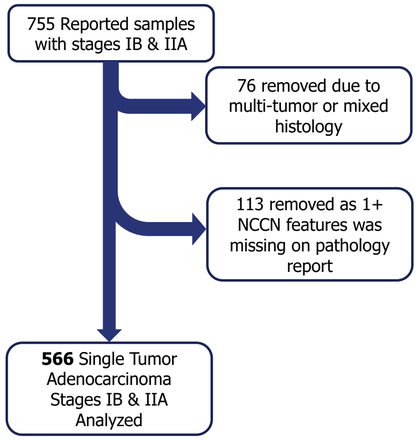
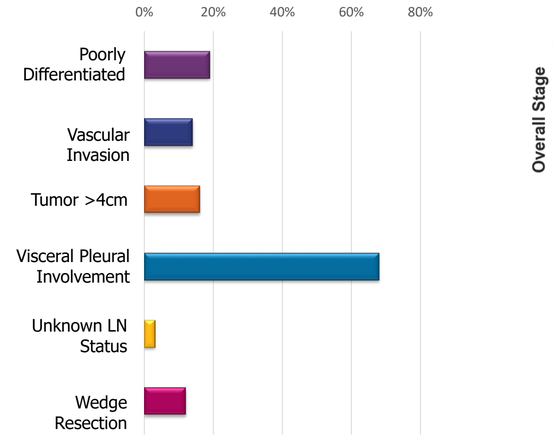
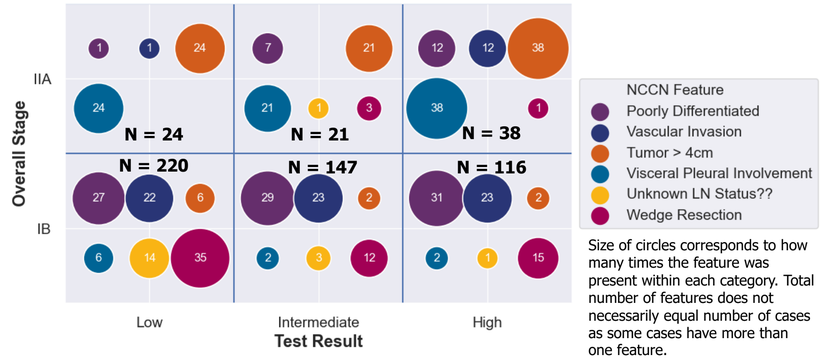


Figure 2: % Cases by NCCN High-Risk Feature





Size of circles corresponds to how many times the feature was present within each category. Total number of features does not necessarily equal number of cases as some cases have more than one feature.

CONCLUSION

Molecular risk classification may improve outcomes for early-stage NSCLC patients, particularly for stage IA patients, who may be at higher risk for recurrence and could benefit from additional treatment post-resection. Use of clinicopathologic features alone may lead to overtreatment by the current paradigm. A validated 14-gene expression assay assessing recurrence risk is a powerful tool for reclassifying recurrence risk for many early-stage patients in the clinical setting.

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