Shortening time from diagnosis to treatment in NSCLC: Are blood-based biopsies the answer?

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BACKGROUND

Recent technological advances have led to the development of blood-based diagnostics or "liquid biopsies" in NSCLC. This approach allows for the prognosis of outcomes, identification of genetic alterations to guide targeted therapy, and real-time monitoring of treatment response.

The limitations of tumor biopsies have recently been supported by a study that demonstrated up to 30% of patients at a community-based academic center did not undergo guideline recommended molecular testing, despite an institutional reflex testing policy for tissue.[1]

In a recent ELCC survey (N=562 oncologists/pulmonologists)[2], 16% of patients were tested, but results were not available to make a first-line treatment decision. Furthermore, a recent study found the median turn-around time for tissue-based mutation results was 12 days (range 1-54) for newly diagnosed patients and 27 days (range 1-146) for patients with acquired TKI resistance.[3]

Biodesix Lung Reflex™ is a blood-based testing pathway that integrates GeneStrat™ mutation testing (EGFR sensitizing & resistance, EML4-ALK, KRAS, BRAF; concordance to tissue, 97%) with reflex to VeriStrat® testing (predictive of response to EGFR-TKI therapy and indicator of tumor aggressiveness through the measure of chronic activation of proteomic pathways)

METHODS

In this study, we compared standard molecular testing strategies with the Biodesix lung reflex testing strategy in advanced lung cancer patients:

- Order data from 5 multidisciplinary thoracic oncology programs (Gundersen Lutheran, CHI Memorial Hospital, Pinehurst Medical Clinic, 21st Century Oncology, Leo Jenkins Cancer Center) were included
- Tests were ordered as part of normal clinical practice for recently or newly diagnosed lung cancer patients
- In all five centers, we evaluated the time to mutation results and reported the detected mutation rates for Biodesix Lung Reflex
- Time to results were calculated from the receipt of sample and all necessary patient information required for testing to the receipt of a patient report
- In one large cancer program (Leo Jenkins Cancer Center), we also evaluated the availability of results at time of next oncology visit where a treatment decision is made

Information on molecular testing strategies and real-world usage of both the Biodesix Lung Reflex strategy and other molecular tests was collected through a multi-disciplinary advisory board and a review of published evidence.

RESULTS: EARLY BLOOD BASED REFLEX TESTING STRATEGY
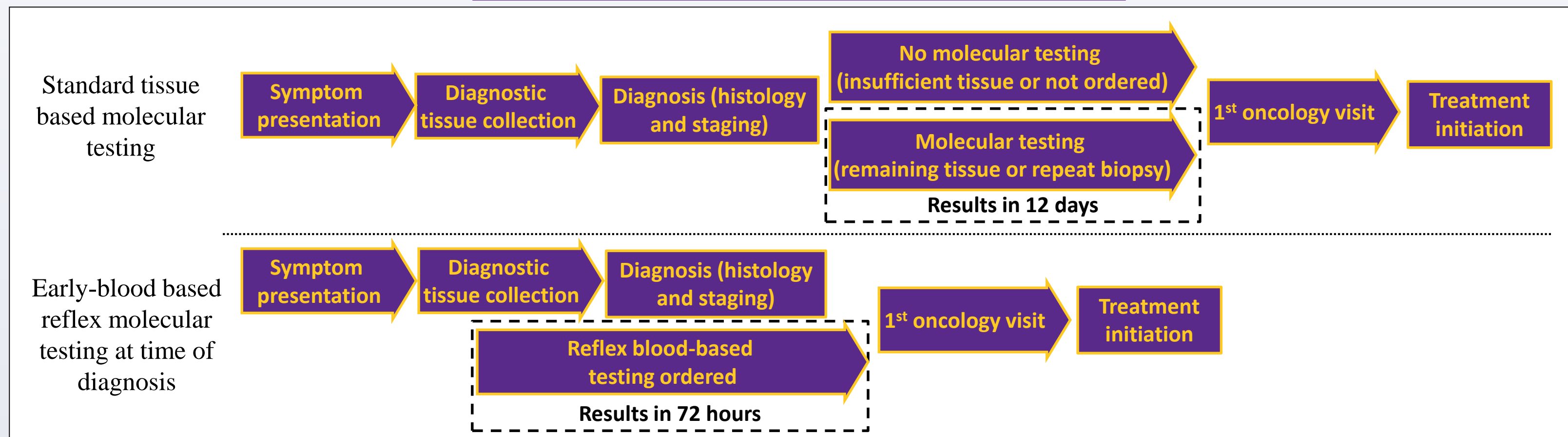
In standard practice, remaining tissue (if sufficient) from the diagnostic tissue block may be used for molecular testing. Re-biopsy may be necessary when insufficient tissue remains. As shown in Table 3, tissue molecular pathology, whether prior to treatment start or to evaluate response and acquired resistance to treatments, have slow turn around times. This can result in either delays in treatment start or treatment without biomarker information which could lead to sub-optimal treatment for patients with driver mutations.

Table 1. time to test results and results (all centers combined)

Total number of lung reflex tests	179
Number of GeneStrat tests	179
Percentage of patients with VeriStrat Results	95%
Average time to results (95% CI)	33.0 hours (30.4-35.6)
% delivered under 72 hrs	95.0%
GeneStrat test results	
EGFR sensitizing or resistance (N detected)	14
ALK mutation (N detected)*	2
BRAF (N detected)	2
KRAS (N detected)	20
% of patients with impactful mutation**	20.1%
VeriStrat test results	
VeriStrat (% VS Poor)	21.2%

*ALK testing became available 1/1/2016. 153 of the 179 GeneStrat tests ordered in 2016 had ALK results available.
**Mutations which impact treatment decisions or patient management were deemed as impactful or actionable mutations

Within Leo Jenkins Cancer center, 69 patients underwent the Biodesix Lung reflex test during the data collection period between March 1st 2016 and July 10th 2016.
- 97 % had results available within 72 hours
- All patients had results available prior to their next physician consultation
- All patients returned for treatment decisions and initiated treatment within 7 days of the initial diagnostic biopsy or blood draw (for previously diagnosed patients)

179 tests from the 5 thoracic oncology programs were ordered for lung cancer patients since 2015:

- 20% of patients had actionable mutations (mutations which impact treatment decisions)
- Of patients with VeriStrat test results, 21% received a result of VS-Poor, meaning patients have relatively poor prognosis and EGFR-TKI therapy should not be considered
- The average time to results was 33 hours
- Results were available within 72 hours for 95% of patients (170/179 tests)
- Mutation results affecting patient management were found in 20% of patients (1/5).
  - These patients presented with either a driver mutation leading to treatment with a targeted therapy, or a detected KRAS mutation which can impact patient management[4] and radiotherapy decisions.

Table 2. Test turn-around time (TAT) and results (ECU only)

Total number of lung reflex tests	69
average TAT (95% CI) in hours	35.99 (31.83 - 40.15)
median TAT	32.47
% delivered below 72 hrs	97.1%
% delivered prior to next patient visit	100.0%

Table 3. Review of tissue-based pathology turn-around time.

Study	Testing type	Turn around time
Sequis et al. 2011 [5]	Tissue based testing, PCR assay (SNaPshot)	Median of 2.8 weeks from requisition to results finalizations
Sacher et al. 2016 [3]	Tissue based testing (EGFR and KRAS only)	Medians of 12 and 27 business days for newly diagnosed and pre-treated patients respectively. Measured from tissue collection to result delivery
Fiore et al. 2016 [6]	Tissue based testing, (general biomarker panel)	Expected TAT: 14 days as performed by Personal Genome Diagnostics or Personalis, Inc.

DISCUSSION

For advanced non-small cell lung cancer patients in whom the disease has metastasized, goals of treatment are no longer curative, but focused on extending overall survival and improving quality of life.

Studies show delays in treatment initiation have a negative impact on a patients health.[7] Studies on patient pathways from first diagnosis and treatment initiation have found inefficiencies surrounding late molecular testing. In cases where a reflex testing strategy is encouraged alongside diagnosis, tissue based methodologies still delay the start of treatment due to long turn around times.

The five participating multi-disciplinary cancer programs within this analysis have adopted an early blood-based reflex molecular testing strategy shifting molecular testing earlier in the continuum of care. Study results show that the Biodesix Lung Reflex strategy provides mutation and molecular information to physicians in 72 hours. On the other hand, tissue pathology turn around times for mutation testing are much longer. In the example of the Leo Jenkins Cancer Center, early testing has resulted in patients starting treatment within 7 days of initial diagnostic biopsy or blood draw as informed by the patients molecular profile.

Early intervention has been shown in recent studies to improve overall survival for NSCLC. Utilizing a blood-based reflex strategy with rapid results for genomic and proteomic testing earlier in the continuum of care can help patients receive appropriate treatment faster.

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