Blood-based Genomic and Proteomic Testing for Newly Diagnosed Lung Cancer Patients to Facilitate Rapid Treatment Decisions and Prognostic Conversations

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PURPOSE

Despite advances in the treatment of lung cancer, it remains a challenging disease to manage. While cure through surgical intervention is the desired goal, most patients present at an advanced stage where systemic therapy and biomarker testing are required. In studies analyzing turnaround time for biomarker results for patients with non small cell lung cancer (NSCLC), 21% of patients had biomarker results available at their initial oncology consultation which lead to shorter median time from consultation to treatment decision (0 vs. 22 days, p=0.0008) and time to treatment start (16 vs. 29 days, p=0.004)[1]. Of those patients with positive EGFR or ALK results, 19% started chemotherapy before biomarker results were available.[1]

Our institution's multi-disciplinary team used blood-based genomic (GeneStrat) and proteomic testing (VeriStrat) to expedite treatment decisions and facilitate more informed conversations with lung cancer patients. Here we present data on our clinical experience with GeneStrat and VeriStrat.

METHODS

Commercially-available, blood-based genomic and proteomic testing was ordered for all clinical patients with nodules at high risk for lung cancer. The GeneStrat genomic test included EGFR sensitizing and resistance mutations, ALK fusions, KRAS and BRAF mutations. The proteomic test, VeriStrat, provided prognostic information for outcomes and predictive information for TKI therapy benefit using a classification of Good or Poor. Testing results were used to make treatment decisions and to aid in prognostic conversations with patients.

Concordance and outcome analyses were performed to evaluate the utility of both tests. GeneStrat results were compared to mutation results obtained from tissue acquired at the time of blood draw. VeriStrat's ability to stratify patients according to progression free survival (PFS) and overall survival (OS) was analyzed using Cox proportional hazards and Kaplan Meier curves.

RESULTS

Of the patients (n= 84) submitted for genomic and proteomic testing, all were evaluable by either test and 100% of results were available within 72 hours of blood draw (average turnaround time (TAT)= 24.1 hours). Patients with sensitizing EGFR mutations did not have a VeriStrat test based on the standard reflex pathway.

Amongst the patients who had blood submitted for GeneStrat testing, 17.8% (n= 15) had a driver mutation (EGFR L858R= 1, EGFR del19= 1, EGFR T790M= 4, EML4-ALK= 3, KRAS G12C= 2, KRAS G12D= 5). When compared to tissue, GeneStrat had a sensitivity of 88%, specificity of 99% and overall concordance of 96% (Table 1). GeneStrat did not detect one exon 19 mutation and one exon 18 mutation. Exon 18 mutations are not included in the GeneStrat test so performance data were calculated with that variant excluded, leading to a final sensitivity of 93% (Table 2). An EML4-ALK mutation identified by blood-based testing was not detected by tissue-based testing most likely due to tissue heterogeneity. Interestingly, the patient with an EML4-ALK mutation missed by tissue also had an EGFR L858R mutation identified in both tissue and blood.

Table 1. GeneStrat concordance with tissue-based testing (all mutations)

	Tissue-based Mutation Results				Performance Data	
Blood-based Mutation Results	Status	+	-	Total		
	+	14	1	15	Sensitivity	88%
	-	2	67	69	Specificity	99%
Total		16	68	84	Concordance	96%

Table 2. GeneStrat concordance with tissue-based testing (w/o EGFR exon 18)

	Tissue-based Mutation Results				Performance Data	
Blood-based Mutation Results	Status	+	-	Total		
	+	14	1	15	Sensitivity	93%
	-	1	67	68	Specificity	99%
Total		15	68	83	Concordance	96%

VeriStrat testing was performed on most patients in this cohort (n=82). Of those patients, 41 had at least 3 months of clinical follow up data (stage 1= 10, stage 2= 6, stage 3= 6, stage 4= 18, NA= 1) and were included in outcome analyses. PFS and OS were calculated for VeriStrat Good and Poor patients across all stages of disease (Figure 1 and 2) and for patients with advanced-stage disease only (Figure 3 and 4). In the analysis of all disease stages, VeriStrat Good and Poor patients had significantly different PFS (not reached vs. 1.5 mo., Cox HR= .11, p<.001) and OS (not reached vs. 2.5 mo., Cox HR= .15, p<.001). In the analysis of advanced disease stages, VeriStrat Good and Poor patients had significantly different PFS (not reached vs. 1.25 mo., Cox HR= .15, p=.016) and OS (4.0 mo. vs. 2.0 mo., Cox HR= .34, p=.05).

Figure 1. All Patients

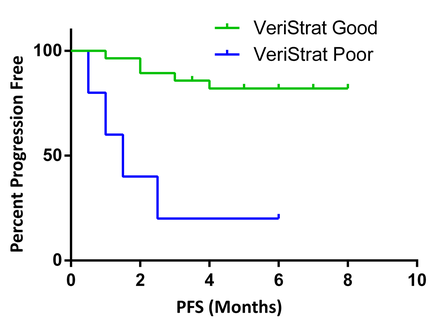


Figure 2. All Patients

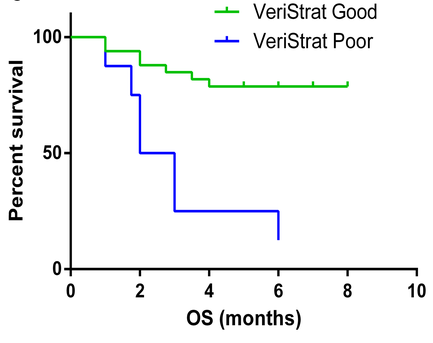


Figure 3. Advanced Stage Disease

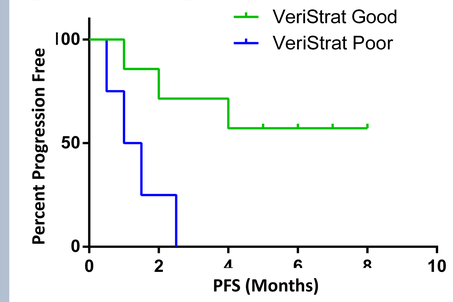
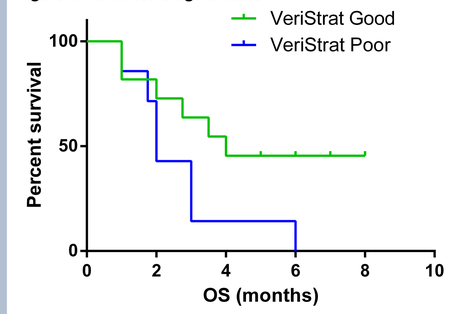


Figure 4. Advanced Stage Disease



CONCLUSIONS

- Blood-based genomic and proteomic testing results were all available within 72 hours (average TAT 24.1 hours)
- GeneStrat results were highly concordant with tissue-based mutation results
- VeriStrat was prognostic for PFS and OS across all stages of lung cancer

CLINICAL IMPLICATIONS

For patients with lung cancer, blood-based genomic and proteomic testing can provide results to aid multi-disciplinary teams in expediting treatment decisions and facilitating more informed prognostic conversations with patients.

REFERENCES

1. Lim, C., et.al. 2015. Biomarker Testing and Time to Treatment Decision in Patients with Advanced Non-Small Cell Lung Cancer. Ann Oncol first published online April 28, 2015