IDENTIFYING AND ADDRESSING GAPS IN MOLECULAR TESTING FOR PATIENTS WITH LUNG CANCER

JENNIFER C. KING[1], ANDREW CIUPEK[1], TARA PERLOFF[1], ASHLEY BLANCHARD[2], KIMBERLY MASON[2], EDIK BLAIS[2], DAVID HALVERSON[2], JOSEPH BENDER[2], SUBHA MADHAVAN[2], EMANUEL PETRICOIN[2]
[1]LUNG CANCER ALLIANCE, WASHINGTON, DC, U.S.A [2]PERTHERA, INC., MCLEAN, VA, U.S.A.

BACKGROUND

For metastatic non-small cell lung cancer (NSCLC), guidelines include molecular testing for actionable biomarkers and recommend broad profile testing. Yet previous studies indicate that not all patients with NSCLC are receiving testing, even for actionable mutations in EGFR, ALK, ROS, and BRAF.

We hypothesized that rates of molecular testing would be low for patients calling a community HelpLine and that we could potentially increase testing rates with one-on-one caller education and providing free precision medicine services.

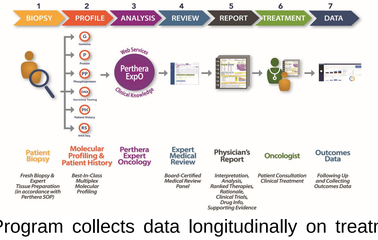
METHODS

Caller statistics were collected during treatment discussions on the toll-free Lung Cancer Alliance (LCA) HelpLine from September 1, 2016 – July 31, 2017.

Recruitment to the LungMATCH molecular testing program began November 10, 2016.

Patients are recruited through conversations on the LCA HelpLine, then entered into the Perthera Program to receive a Perthera Report (PR) through consent into an IRB-approved registry protocol.

The Program includes tissue acquisition, multi-omic molecular profiling, and collection of patient treatment history followed by integration into a computational pipeline with extensive drug and clinical trial databases to provide ranked therapeutic options matched to the patient. An every-patient, real-time medical review board then reviews and approves the PR. PRs are returned to both treatment physicians and patients.



The Program collects data longitudinally on treatment decisions, patient outcomes including progression-free and overall survival, and patient experience.

HELPLINE STATISTICS

When asked if they had received molecular testing, 54% of LCA HelpLine callers (155/288) said "No", indicating a lack of widespread testing in the community.

Of 58 patients who were tested and knew the results, patients had lung cancers with many potentially actionable genomic and proteomic changes.

Biomarker	# of pts
EGFR	32
PD-L1	10
ALK	9
KRAS	4
MET	2
RET	1
BRAF	1
HER2	1

Table 1. Patient-reported molecular alterations

Taken together, these data suggest that increasing multi-omic testing for lung cancer patients in the community setting could have a positive impact on patient outcomes.

PATIENT DEMOGRAPHICS

72 patients had been referred for molecular testing through LungMATCH as of July 31, 2017. Callers were from throughout the United States but tended to be from more urban settings. Most referred patients were receiving care in a non-academic oncology practice.

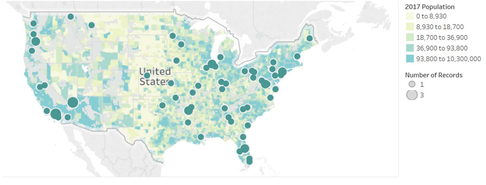


Figure 1. Geographic distribution of the 72 HelpLine callers referred for molecular testing.

	N (%)
Ethnicity (available for 52)	
Caucasian	46 (88%)
African American	2 (4%)
Hispanic	1 (2%)
Other	3 (6%)
Rural/urban (available for 58)	
Urban	46 (79%)
Rural	12 (21%)
Practice type (available for 50)	
Academic	12 (24%)
Community	38 (76%)

Table 2. Demographic information for patients referred for molecular testing through LungMATCH

PROCESS RESULTS

As of August 31st, 11 patients have completed the Perthera Program and received a PR. A number of barriers to informed consent and biopsy/testing have been identified. Workflows are being continually adjusted in response to identified barriers and process improvements have included additional communication, lung-cancer specific patient coordinators, more information about cost, and revised language explaining the process to physicians.

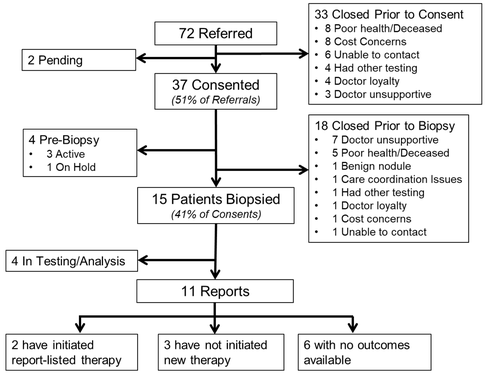


Figure 2. Referral and testing workflow and identified process barriers

Of the patients who received the reports, all 11 received information from next generation sequencing. Insufficient tissue was a significant problem for completing immunohistochemistry/in-situ hybridization.

Patient ID	Tissue	NGS	IHC/ISH	Prior Targeted or Immunotherapy
Ica-1567	L5 vertebra, excision	Success	Success	Immunotherapy
Ica-1628	Lung, left upper lobectomy	Success	Success	--
Ica-1718	Liquid biopsy	Success	N/A	Immunotherapy
Ica-1723	Lung, right lower lobe, FNA	Success	QNS	--
Ica-1740	Right station 4 lymph node	Success	QNS	--
Ica-1761	Lung, left, core biopsy	Success	QNS	Immunotherapy
Ica-1791	Lung, right, core biopsy	Success	QNS	Immunotherapy
Ica-1875	Lung, right lower lobe, core biopsy	Success	Success	--
Ica-2013	Brain	Success	Success	--
Ica-2025	Lung, right, core biopsy	Success	QNS	ALK inhibitor
Ica-2099	Right supraclavicular lymph node	Success	Success	Immunotherapy

Table 3. Source of tissue and testing success rates for the 11 patients that completed the program. (NGS = next generation sequencing. IHC = immunohistochemistry. ISH = in situ hybridization. QNS = quantity not sufficient)

TESTING RESULTS

By next generation sequencing, 9/11 patients (82%) had at least one genetic alteration that was actionable including standard of care, off-label, and clinical trial options.

Gene	N (%)	Alterations	Implication
TP53	8 (73%)	G154fs*16, C176F, C176Y, H179R, C242S, G244S, P278L, Splice site	WEE1 or CHEK1 inhibitor
CDKN2A	6 (55%)	Loss (4), G101W, Rearrangement	CDK4/6 inhibitor
CDKN2B	3 (27%)	Loss (3)	CDK4/6 inhibitor
SOX2	3 (27%)	Amplification (3)	PD-1/PD-L1 inhibitor
KRAS	2 (18%)	G13C, Amplification	MEK inhibitor
PIK3CA	2 (18%)	E545K, Amplification	PI3K/mTOR inhibitors
FGFR1	2 (18%)	Amplification (2)	FGFR inhibitor
CCND1/2	2 (18%)	Amplification (2)	CDK4/6 inhibitor
ALK	1 (9%)	EML4-ALK fusion	ALK inhibitor
EGFR	1 (9%)	Q1173*/amplification	EGFR inhibitor
PD-L1 (CD274)	1 (9%)	Amplification	PD-1/PD-L1 inhibitor
APC	1 (9%)	R213*	Wnt inhibitor
RET	1 (9%)	Amplification	Ret inhibitor
STK11	1 (9%)	G56W	mTOR inhibitor
RB1	1 (9%)	Splice site	CHEK1 inhibitor
PTEN	1 (9%)	Splice site	PI3K/mTOR inhibitors
TSC1	1 (9%)	Loss	mTOR inhibitor
FAM123B	1 (9%)	E917*	Wnt inhibitor
SETD2	1 (9%)	Q1288*	WEE1 inhibitor

Table 4. NGS results and recommended therapy based on result. Changes in red were considered actionable.

In addition, mutational burden testing, in situ hybridization (ISH), and immunohistochemistry (IHC) provided additional treatment recommendation information for patients. All patients (5/5) with IHC/ISH testing had actionable alterations.

Tumor mutation burden (TMB)	N (%)
High	2 (20%)
Intermediate	4 (40%)
Low	2 (20%)
Unknown	2 (20%)

Table 5. Level of tumor mutation burden in the tissue biopsies by NGS. All 10 patients were microsatellite stable (MSS).

Marker	N (%)	Implication
Phospho-AKT	3 (60%)	PI3K/AKT/mTOR inhibitor
PD-L1 positive	1 (20%)	PD-1/PD-L1 inhibitor
RRM1 negative	2 (40%)	Gemcitabine
ERCC1 negative	2 (40%)	Platinum agents
EGFR amplified by ISH	1 (20%)	EGFR inhibitor

Table 6. Immunohistochemistry and in situ hybridization results and recommended therapy based on result. Five of five patients had actionable IHC/ISH markers.

CONCLUSIONS

Caller data indicated that patients with lung cancer are not receiving molecular testing in accordance to guidelines. To address this problem, we introduced a program through a nonprofit-corporate partnership that navigates patients and their physicians through a comprehensive precision therapy program.

We have demonstrated that this type of program is feasible and there is broad patient interest, particularly from those seen in non-academic settings. A number of barriers were identified and are being addressed including cost concerns and physician and patient education. Additional barriers such as insufficient amounts of biopsy tissue for testing and patient discomfort with advocating for testing remain concerns.

Importantly, the program demonstrated that the majority of patients who received the PR (82%) had actionable molecular alterations, underscoring the critical importance of multi-omic testing, treatment history, and integration into a computational pipeline with extensive drug and clinical trial databases to obtain matched and ranked targeted therapies in lung cancer.

FUTURE DIRECTIONS

The program continues to enroll with ongoing improvements in:

- Patient educational information at time of referral and additional patient follow-up calls
- Working with community oncology practices/health systems to facilitate patient enrollment

Our goal is to give all patients with lung cancer an opportunity for precise therapy matching based on multi-omic testing, treatment history and drug targeting regardless of where they receive their care. Future research efforts will include updated analyses of molecular alterations as well as decisional and health outcome analyses of those who have received PRs.

CONTACT

JENNIFER C. KING, PHD
Director of Science and Research
LUNG CANCER ALLIANCE
jking@lungcanceralliance.org

FOR PATIENTS TO ENROLL

1-800-298-2436