IMPLEMENTATION OF A DEMOCRATIZED APPROACH TO MULTI-OMIC MOLECULAR PROFILING VIA THE LUNGMATCH PROGRAM

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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

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.

PATIENT DEMOGRAPHICS

108 patients had been referred for molecular testing through LungMATCH as of September 14, 2018. Callers were from throughout the United States with most from urban areas and non-academic practices.

Figure 1. Geographic distribution of the 108 HelpLine callers referred for molecular testing, compared to U.S. population. Size of blue dot indicates number of referrals (One referral in Hawaii not shown)

	N (%)
Ethnicity (available for 78)	
Caucasian	67 (86%)
African American	5 (6%)
Hispanic	1 (1%)
Asian	1 (1%)
Other	4 (5%)
Rural/urban (available for 81)	
Urban	65 (80%)
Rural	16 (20%)
Practice type (available for 61)	
Academic	17 (28%)
Community	44 (72%)

Table 1. Demographic information for patients referred for molecular testing through LungMATCH.

PROCESS RESULTS

As of September 14, 2018, 24 patients have completed the Perthera program and received a Perthera Report. A number of barriers to informed consent and biopsy/testing have been identified. Workflows are being continually adjusted and process improvements have included additional communication, lung-cancer specific patient coordinators, more information about cost, and revised language explaining the process to physicians.

PROCESS RESULTS

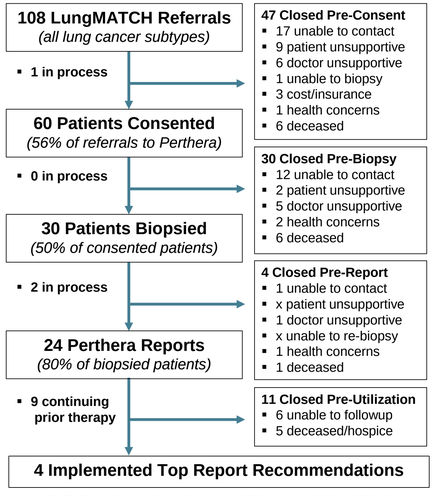

Figure 2. Referral and testing workflow and identified process barriers.

Patient ID	Tissue	NGS	IHC/ISH
lca-1567	L5 vertebra, excision	Success	Success
lca-1628	Lung, left upper lobectomy	Success	Success
lca-1718	Liquid biopsy	Success	N/A
lca-1723	Lung, right lower lobe, FNA	Success	QNS
lca-1740	Right station 4 lymph node	Success	QNS
lca-1761	Lung, left, core biopsy	Success	QNS
lca-1791	Lung, right, core biopsy	Success	QNS
lca-1875	Lung, right lower lobe, core biopsy	Success	Success
lca-1997	Chest wall	Success	Success
lca-2013	Brain	Success	Success
lca-2025	Lung, right, core biopsy	Success	QNS
lca-2099	Right supraclavicular lymph node	Success	Success
lca-2300	Lung, left upper lobe, core biopsy	Success	Success
lca-2494	Lung, left upper lobe, wedge resection	Success	Success
lca-2495	Right station 4 lymph node	Success	Success
lca-2510	Lung, right upper lobectomy	Success	Success
lca-2539	Liquid biopsy	Success	N/A
lca-2854	Lung, right, core biopsy	Success	QNS
lca-3020	Brain	Success	Success
lca-3145	Liquid biopsy	Success	N/A
lca-3292	Lung, left lower lobe, FNA [TBNA/Wang]	Success	QNS
lca-3325	Lung, left upper lobe, core biopsy	Success	Success
lca-3337	Lung, left upper lobectomy	Success	Success

Table 2. Source of tissue and testing success rates.

TESTING RESULTS

By next generation sequencing and IHC/ISH, 19/24 patients (79%) had at least one moderately or highly actionable genetic alteration including standard of care, off-label, and clinical trial options.

Marker	Alterations	N (%)	Implications
p53	H179R(2); C176F; C242S; C275S; G154fs*16; G244S; I255T; M237K; M246V; P278L; P278R; Q104*; Q331*; R273H; R65*; splice site 560-2A>T; V157F	18 (75%)	Wee1 inhibitors, CHK1 inhibitors
TMB	Intermediate(10); High(6)	16 (66.67%)	Immunotherapy
CDKN2A	Loss(4); D108Y; G101W; Rearrangement intron 1	7 (29.17%)	CDK4/6 inhibitors
KRAS	Amplification(3); G12D; G13C; G13D; Q61H	7 (29.17%)	MEK/ERK inhibitors
CDKN2B	Loss(4)	4 (16.67%)	CDK4/6 inhibitors
RB1	Q504*; splice site 1050-1G>C; splice site 1216-2A>G; Y813*	4 (16.67%)	CHK1 inhibitors
EGFR	Amplification; E746_A750del; L861Q; Q1173*	4 (16.67%)	EGFR inhibitors
SOX2	Amplification(3); Amplification equivocal	4 (16.67%)	Hedgehog inhibitors
ARID1A	G838*; Q404*; S571*; S617*	4 (16.67%)	PI3K/AKT/mTOR inhibitors
MCL1	Amplification(2); Amplification equivocal	3 (12.5%)	Bcl-2 inhibitors
FGFR1	Amplification(2); Amplification equivocal	3 (12.5%)	FGFR inhibitors
PIK3CA	Amplification(2); E545K	3 (12.5%)	PI3K/AKT/mTOR inhibitors
AMER1	E282*; E917*; Q1019*	3 (12.5%)	Wnt inhibitors
ZNF703	Amplification; Amplification equivocal	2 (8.33%)	mTOR inhibitors
CDK4	Amplification(2)	2 (8.33%)	CDK4/6 inhibitors
MYC	Amplification; Amplification equivocal	2 (8.33%)	CHK1 inhibitors
FRS2	Amplification; Amplification equivocal	2 (8.33%)	FGFR inhibitors
NOTCH1	E44*; G1320fs*125	2 (8.33%)	HDAC inhibitors
STK11	G276fs*11; G56W	2 (8.33%)	mTOR inhibitors
NTRK1	Amplification; G595R	2 (8.33%)	NTRK inhibitors
PTEN	M35V; splice site 493-1G>T	2 (8.33%)	PI3K/AKT/mTOR inhibitors
CRKL	Amplification; Amplification equivocal	2 (8.33%)	SRC inhibitors

Table 3. Common NGS findings in two or more patients and possible therapeutic implications based on result. Notable changes in single patients included EML4-ALK rearrangement, MET amplification, and RET amplification.

Marker	N (%)	Implication
Phospho-AKT	11 (79%)	PI3K/AKT/mTOR inhibitor
ERCC1 negative	6 (43%)	Platinum agents
PD-L1 positive	6 (43%)	PD-1/PD-L1 inhibitor
RRM1 negative	5 (36%)	Gemcitabine

Table 4. Immunohistochemistry and in situ hybridization results and recommended therapy based on result.

CONCLUSIONS

There is broad patient interest in accessing precision medicine information but still many barriers to widespread adoption. The LungMATCH program provides a turn-key solution to help provide a facile means to "democratize" access to precision medicine information unbound by geography or community/academic setting. Importantly, the majority of patients who received a completed profiling report had actionable molecular alterations, which underscores the potential impact of testing. Treatment decisions and patient outcomes continue to be followed.

Importantly, the program demonstrated that the majority of patients who received the Perthera Report (79%) had actionable molecular alterations, underscoring the critical importance of multi-omic testing for treatment decision making.

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 precision 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 Perthera Reports.

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