LUNGMATCH: A PERSONALIZED PROGRAM TO INCREASE MOLECULAR TESTING AND CLINICAL TRIAL PARTICIPATION IN LUNG CANCER PATIENTS

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BACKGROUND

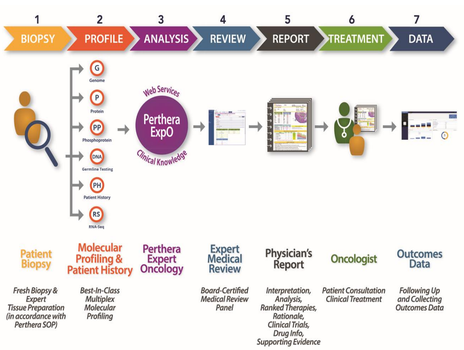
- For metastatic non-small cell lung cancer (NSCLC), guidelines include comprehensive testing for actionable biomarkers and considerations for enrollment into clinical trials. Yet previous studies indicate that not all patients with NSCLC are receiving testing, even for actionable mutations in EGFR, ALK, ROS, BRAF, and NTRK.
- In a previous survey of U.S. lung cancer patients, we found only 22% reported discussing clinical trial participation with their oncologist at the time of making treatment decisions (Fenton L, 2009), despite the established clinical guidelines (i.e. NCCN) recommending all cancer patients be considered for clinical trials as part of standard care.
- We hypothesized that a personalized navigation program could increase the number of patients receiving comprehensive biomarker testing and rates of clinical trial discussion.

METHODS

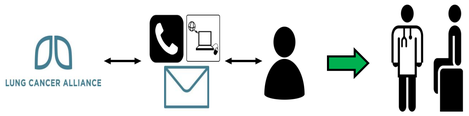
Patients and caregivers accessing Lung Cancer Alliance's support services (via phone/online) were asked if they had received molecular testing or considered clinical trial participation. Willing callers were referred to a LungMATCH navigator for further discussion.

Patients who had not received comprehensive testing, could be entered into a Program in partnership with the company Perthera, 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.



For patients considering clinical trials, navigators provided basic trial education and a personalized list of trial matches based on discussion. Patients were encouraged to discuss these trials with their treating oncologist. Navigators then regularly followed up with participants, via email or phone, at two to four-week intervals, to offer further support and collect outcomes information.

DEMOGRAPHICS – MOLECULAR TESTING

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.

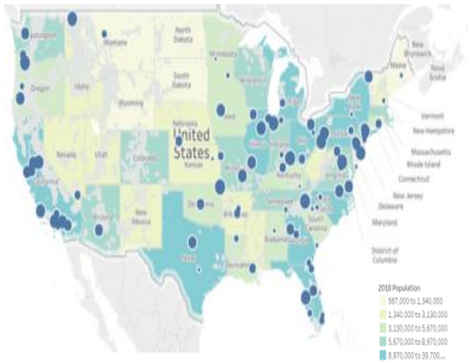


Figure 1. Geographic distribution of the 108 HelpLine callers referred for molecular testing, compared to U.S. population. Size of blue dot indicates number of referrals (One referral in Hawaii not shown)

	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

RESULTS – MOLECULAR TESTING

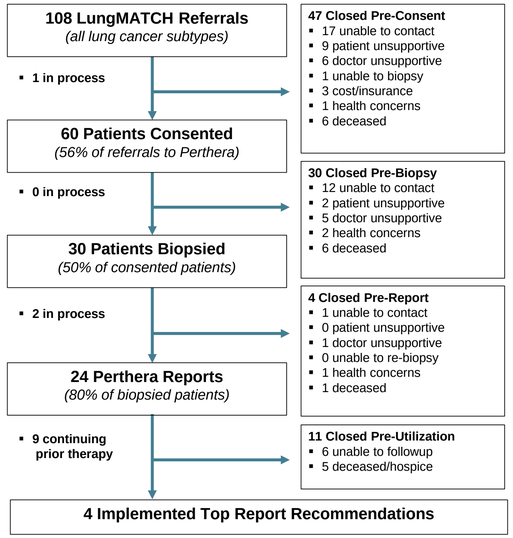


Figure 2. Referral and testing workflow and identified process barriers.

By Next Generation Sequencing,19/24 patients (79%) had at least one 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 2. Common NGS findings in two or more patients and possible therapeutic implications. 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 3. Immunohistochemistry and in situ hybridization results and recommended therapy based on result.

DEMOGRAPHICS – CLINICAL TRIAL MATCHING

84 total participants had received clinical trial navigation through the program from August 18th, 2016 to January 31st, 2019. 44% of participants were the patients themselves and 56% were caregivers acting on behalf of a patient. Most patients were diagnosed with NSCLC (75%); Stage IV (76%).

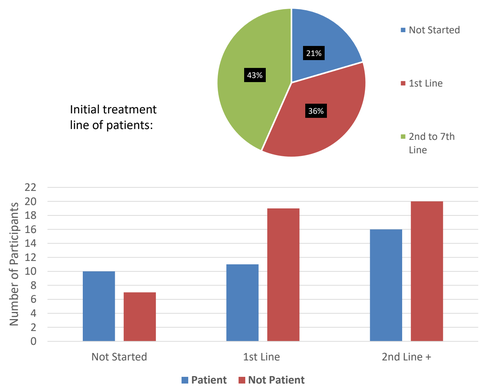


Figure 2. Initial treatment line of patients for whom navigation was performed and identity of participant by initial treatment line.

RESULTS – CLINICAL TRIAL MATCHING

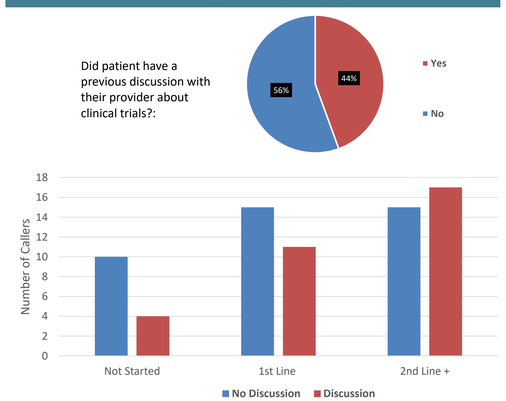


Figure 3. Occurrence of past discussions with providers about clinical trials among participants and timing of previous discussions by treatment line.

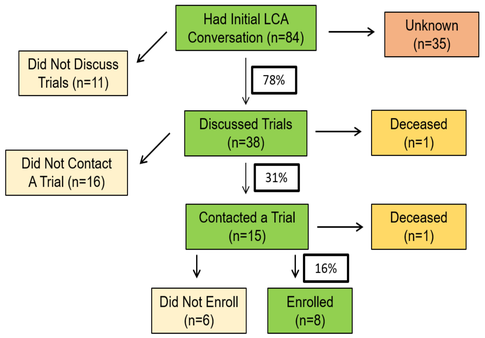


Figure 4. Navigation process and status of patients within program

Reasons For Not Discussing Trials (n=11)	
Stable on current treatment	3
Chose another treatment option	3
Waiting for appointment or test results	2
Progression	1
Not seeing a doctor	1
Needs more time to consider	1

Reasons For Not Contacting a Trial (n=16)	
Progression or Deceased	5
Chose another treatment option	5
Waiting for appointment or test results	3
Stable on current treatment	1
Lost to follow up	1
Doctor advised against trial	1

Reasons For Not Enrolling in a Trial (n=6)	
Publicly available trial information mismatch	2
Medically ineligible	2
Not Screened (Progression)	1
Not Screened (Chose another treatment option)	1

Table 5. Participant reported reasons/barriers during clinical trial navigation process

CONCLUSIONS

- There is broad patient interest in accessing molecular testing, particularly from those seen in non-academic settings.
- Testing barriers were identified, including cost concerns and physician and patient education.
- The majority (79%) of patients receiving a molecular testing report had actionable alterations, underscoring the importance of multi-omic testing for treatment decision making.
- Caregivers are the primary clinical trial information seekers during active treatment.
- A majority (56%) of patients had not discussed clinical trials with providers and when discussions occurred they were delayed to later treatment lines.
- Navigation lead to subsequent discussions and trial enrollment while also identifying barriers to the trial enrollment process.

CONTACT

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