LUNGMATCH: PERSONALIZED MOLECULAR TESTING AND CLINICAL TRIAL NAVIGATION FOR LUNG CANCER PATIENTS

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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.
- 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 established clinical guidelines (i.e. NCCN) that recommend all cancer patients be considered for clinical trials as part of standard care.
- We hypothesized that a personalized navigation program could increase molecular testing and clinical trial discussion rates.

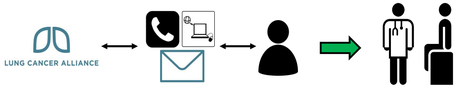
METHODS

Patients and caregivers accessing Lung Cancer Alliance's (LCA) support services (via phone/online) were asked if they had received molecular testing or considered clinical trial participation and 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 2 to 4 week intervals, to offer further support and collect outcomes information.

DEMOGRAPHICS – MOLECULAR TESTING

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. (Data collected Sept. 2016 to July 2017)

100 patients had been referred for molecular testing through LungMATCH from November 10th, 2016 to December 18, 2017. Callers were from throughout the United States with most from urban areas and non-academic practices.

	N (%)
Ethnicity (available for 73)	
Caucasian	62 (85%)
African American	5 (7%)
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

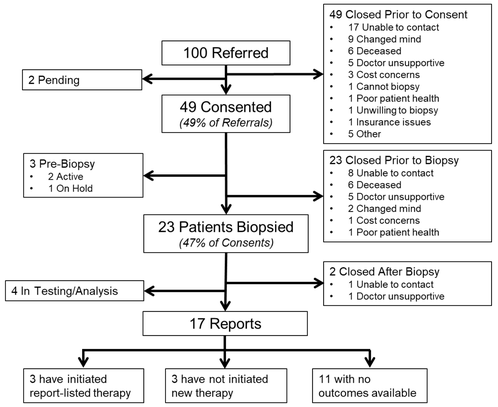


Figure 1. Referral and testing workflow and identified process barriers.

By next generation sequencing, 12/17 patients (71%) had at least one actionable genetic alteration including standard of care, off-label, and clinical trial options.

Gene	N (%)	Alterations	Implication
TP53	12 (71%)	G154fs*16, C176Y, H179R, C176F, H179R, C242S, G244S, M246V, R249M, P278R, P278L, Splice site, Q331*	WEE1 or CHEK1 inhibitor
CDKN2A	7 (41%)	Loss (4), G101W, D108Y, Rearrangement	CDK4/6 inhibitor
SOX2	4 (24%)	Amplification (4)	PD-1/PD-L1 inhibitor
CDKN2B	3 (18%)	Loss (3)	CDK4/6 inhibitor
FGFR1	3 (18%)	Amplification (3)	FGFR inhibitor
KRAS	3 (18%)	G13C, G13D, Amplification	MEK inhibitor
RB1	3 (18%)	Splice site (2), Q504*	CHEK1 inhibitor
EGFR	2 (12%)	Q1173*/amplification, L861Q	EGFR inhibitor
PIK3CA	2 (12%)	E545K, Amplification	PI3K/mTOR inhibitors
CCND1/2	2 (12%)	Amplification (2)	CDK4/6 inhibitor
STK11	2 (12%)	G56W, G276fs*11	mTOR inhibitor
ALK	1 (6%)	EML4-ALK fusion	ALK inhibitor
PD-L1 (CD274)	1 (6%)	Amplification	PD-1/PD-L1 inhibitor
CDK4	1 (6%)	R255C	CDK4/6 inhibitor
RET	1 (6%)	Amplification	Ret inhibitor
PTEN	1 (6%)	Splice site	PI3K/mTOR inhibitors
TSC1	1 (6%)	Loss	mTOR inhibitor
FAM123B	1 (6%)	E917*	Wnt inhibitor
SETD2	1 (6%)	Q1288*	WEE1 inhibitor

Table 2. NGS results and recommended therapy based on result. Changes in red were considered actionable.

In addition, mutational burden testing, ISH, and IHC results provided treatment recommendation information for patients. 82% of patients (9/11) with IHC/ISH testing had actionable alterations.

Tumor mutation burden (TMB)	N (%)
High	5 (31%)
Intermediate	7 (44%)
Low	2 (12.5%)
Unknown	2 (12.5%)

Table 3. Level of tumor mutation burden in the tissue biopsies by NGS. All 16 patients were microsatellite stable (MSS).

Marker	N (%)	Implication
Phospho-AKT	9 (82%)	PI3K/AKT/mTOR inhibitor
ERCC1 negative	4 (36%)	Platinum agents
EGFR amplified by ISH	3 (27%)	EGFR inhibitor
PD-L1 positive	3 (27%)	PD-1/PD-L1 inhibitor
RRM1 negative	2 (18%)	Gemcitabine

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

DEMOGRAPHICS – CLINICAL TRIAL MATCHING

70 total participants had received clinical trial navigation through the program from August 18th, 2016 to August 21st, 2018. 41% of participants were the patients themselves and 59% were caregivers acting on behalf of a patient. Most patients were diagnosed with NSCLC (74%); Stage IV (81%).

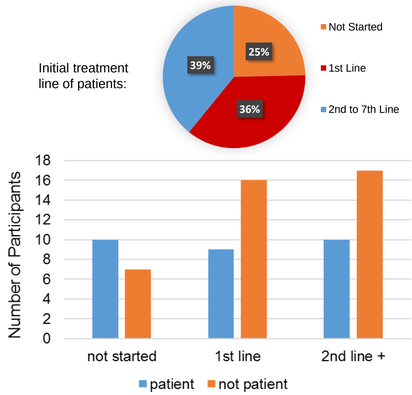


Figure 2. Initial treatment line of patients for whom navigation was performed and identity of participant by initial treatment line of patient

RESULTS – CLINICAL TRIAL MATCHING

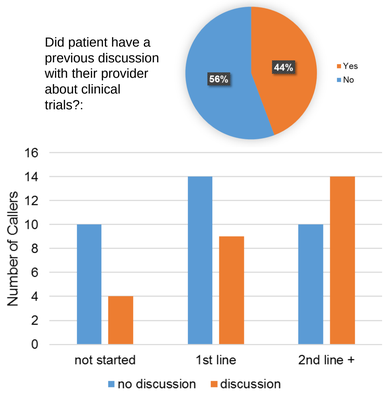


Figure 3. Occurrence of past discussions with providers about clinical trials among participants and timing of previous discussions by treatment line

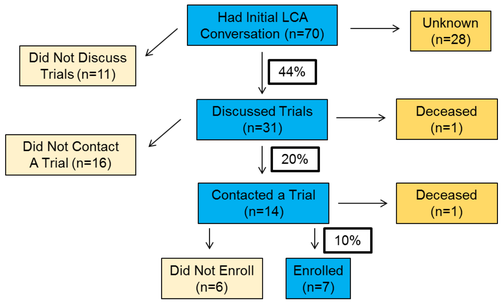


Figure 4. Navigation process and status of patients within program

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

- The molecular testing program is feasible and there is broad patient interest, particularly from those seen in non-academic settings.
- Testing barriers were identified, including cost concerns and physician and patient education.
- The majority (>70%) of patients receiving a molecular testing report had actionable alterations
- A majority (56%) of patients had not discussed clinical trials with providers and when discussions occurred they were delayed to later treatment lines
- Caregivers are the primary clinical trial information seekers during active treatment
- Navigation lead to subsequent discussions and trial enrollment while also identifying barriers to the trial enrollment process

CONTACT

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