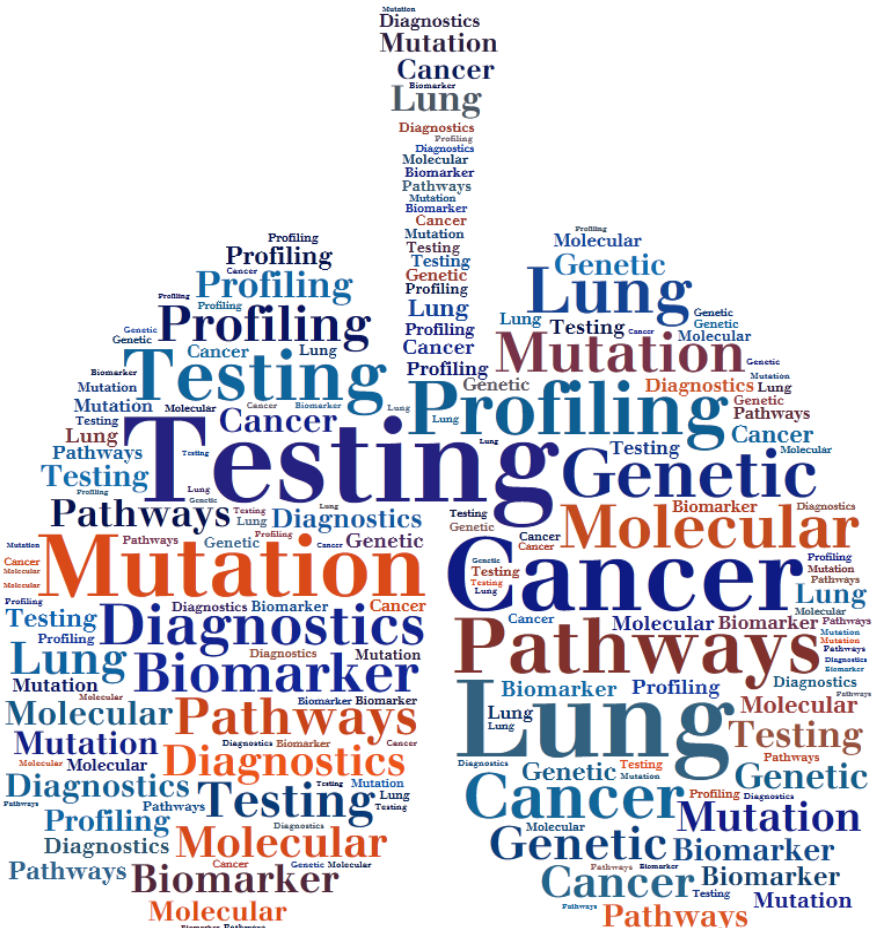


Molecular Testing in the Diagnosis and Treatment of Lung Cancer: A Communications Landscape Audit

June 12, 2015

LUNGEVITY

Contents

Introduction

In recent years, LUNGevity has observed increased conversation around the promise of targeted therapies for the treatment of lung cancer. These therapies work by focusing on an identifiable specific mutation that is driving or enabling growth of a patient's cancer. The testing to identify these mutations is the first step in determining if a patient can benefit from the targeted therapies currently approved or in development in clinical trials.

Despite the energy around the potential of targeted therapy in the treatment of lung cancer, evidence suggests that only a subset of eligible patients are benefitting from targeted therapy. Recognizing the complexity of the issue, as a first step we sought to understand how information around molecular mutation testing is being communicated and to what end. Questions included: How is testing being communicated? Who is talking to patients and who is talking to the medical community? Are there differences in the way the many organizations with a stake and interest in molecular testing and/or targeted therapy are communicating? And, if there are differences, what are the implications for patient and medical community understanding and application of, molecular testing for lung cancer?

To answer these questions we commissioned an audit of the online communications of 28 organizations ranging from pharmaceutical and biotech companies to cancer advocacy groups to general health sites. We also went straight to the patient, interviewing 15 people living with lung cancer about their awareness of and experience with molecular testing.

The Assignment

In early 2015 Edge Research was tasked with researching and analyzing how a cross-section of organizations are talking about molecular testing and its use in the diagnosis and treatment of lung cancer. The primary goals were to:

- Identify and inventory the various terms being used to reference molecular tumor testing;
- Identify the audiences organizations are addressing; and
- Catalog the message and calls to action.

Terms Inventoried

- Molecular Testing
- Molecular Diagnostics
- Biomarker Testing
- Molecular Pathways
- Personalized Medicine
- Genetic testing and/or genetic diagnostic
- Mutation testing/mutation profiling
- Targeted Therapies

In addition, in-depth interviews were conducted with 15 lung cancer patients to gain insights into their understanding and experiences with molecular testing and related procedures and therapies. The results of these interviews are reported as well. Where appropriate, verbatim quotes from the interviews are included, although unattributed, in order to protect respondents' anonymity and privacy.

NOTE TO READER: For the purposes of simplifying the report, we are using the term "molecular testing" as the summary term for all the labels used to refer to this type of tumor testing.

Executive Summary

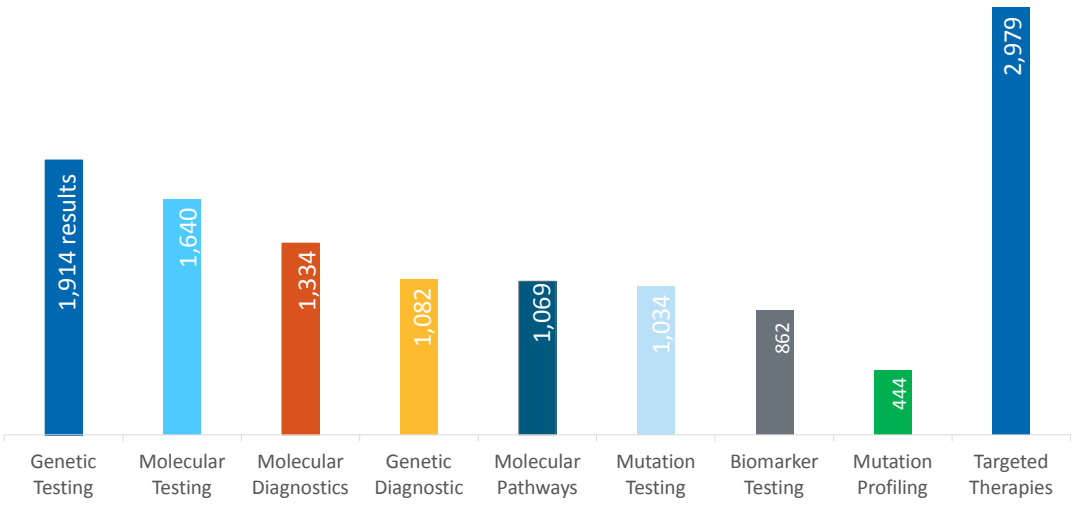
Over 9,000 (9,379) mentions of eight different terms to reference molecular testing and targeted therapy were inventoried, and the use of numerous other terms to reference this type of testing was uncovered. The findings highlight important considerations for the lung cancer and general cancer communities.

1. Content on cancer testing is dominated by the term "genetic testing." The use of this term in reference to testing for genetic mutations or the biomarkers for targeted therapies is confusing. Patients tell us that genetic testing is looking for hereditary indicators. When they hear it, they wonder if they could have inherited their lung cancer. Patients caution that language and terms that distinguish molecular testing from genetic testing for hereditary cancer is important.

Key Findings

1. Patient confusion created by use of term "genetic testing."
2. Overall there are too many terms, inconsistently used.
3. Divisions between terms used to talk to health care practitioners and those used to talk to patients – setting up a communications gap.
4. No clear or consistent call to action for testing – who, when and why.
5. Lack of information in the clinical setting means learning about and understanding of testing is often left to word-of-mouth.

Many Terms, None That Dominate

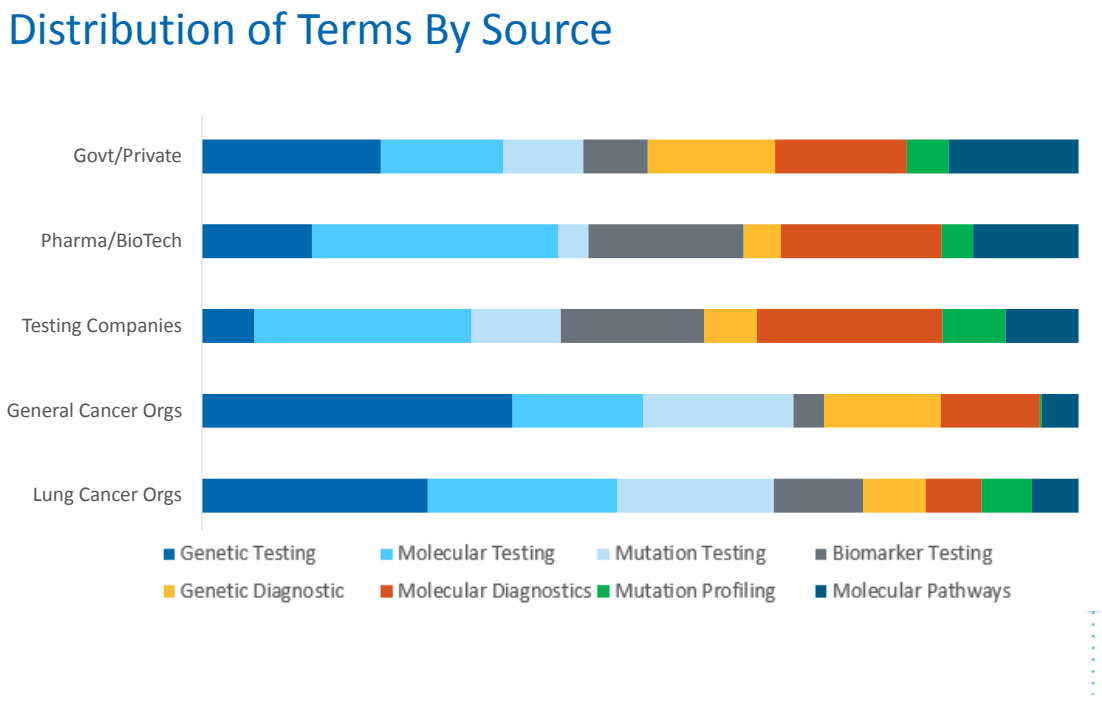


Graph: website search results

2. By far the greatest amount of content on molecular testing that is directed to patients comes from lung cancer advocacy groups. While many terms are used to refer to molecular testing, there is an effort to relate terms to one another and to define them as

they are used. The patient advocacy groups tend to focus on the terms “molecular testing,” “testing for genetic mutations” and “testing for biomarkers.” Among patients, the organic phrase seems to be “get your tumor tested.”

3. Of particular concern is that as the audit moved beyond patient advocacy communications to the terms used by the industries developing the tests and the targeted therapies, there is very little consistency in terminology. Even more terms are introduced, and terms are used with and without clear definitions. Sources use different terms to speak to different audiences – one set for the medical community and a different set for the patient. This lack of consistency has clear implications: If pharmaceutical and testing companies are talking to doctors about “genomic profiling” but patients are hearing about “molecular testing” from support groups, it sets the stage for unclear communication in the critical doctor-patient relationship.



4. There is a significant range in how molecular testing is framed, what it means for the patient, and the calls to action around it. Lung cancer patient advocacy groups tended to have a more unified voice around a strong call to action to patients to push for this type of testing without condition – in other words, to test at the outset of diagnosis or before standard care has been shown ineffective. The more general cancer groups are more likely to say “ask your doctor.” On the testing and pharma industry side there is also a call to establish molecular testing as a new standard of care. Some also advocate to establish tissue sampling protocols that allow for the expansion of the number and type of mutations for which the tumor can be tested. Lung cancer patients who know about molecular testing tell us they strongly urge all the patients they meet to get tested.

5. When it comes to what the testing is looking for, there is heavy emphasis on mutations linked to existing FDA-approved targeted therapies. The most commonly cited are the EGFR and ALK mutations and related inhibitor drugs. While these are the tests covered by insurance, a risk here is that less informed doctors may not order tests for other mutations being studied in clinical trials.

6. Further, patients tell us that doctors do not always discuss clinical trials with them and that is another area of treatment they learn about through word-of-mouth. This raises important questions about when and why patients should be tested. Solely to be matched to treatments that are FDA-approved? Or to find all possible means of treatment when the current standard of care is not working?

7. Despite the volume of information about targeted therapies and the use of molecular testing to identify patient candidates, this information is not necessarily reaching patients. In fact, learning about this critical step in diagnosis and treatment can easily be hit or miss. Information is not easy to find at many of the treatment sites and patients tell us they hear about it through word of mouth.

8. Patients flag that there is little information about mutation testing available or given to them in the clinical setting – the very place where they get most of their information about their cancer and their treatment. Explanations given to patients about testing by members of their medical team vary widely.

Finally, new terms are emerging as this report is being released. In the time it took to conduct the audit, some sources shifted language. Most apparent is a shift from “personalized medicine” to “precision medicine” and the emergence of “comprehensive genomic profiling.”

To best serve the needs of lung cancer patients who are extremely vulnerable and often overwhelmed by their diagnosis and treatment, consideration must be given to defining the communications terms and the goals of molecular testing. It is incumbent on the testing companies as the originators of the tests themselves, the pharmaceutical industry as the developers and marketers of the relevant therapies, and the patient advocacy community that serves patients directly to develop clear and consistent information. A more unified voice and message will help the medical community and patients achieve common understanding about the use and potential impact of molecular testing and targeted therapies, as well as increase patient empowerment and satisfaction.

Pharmaceutical, Bio-Tech & Industry Associations

Overview

Although most of the pharmaceutical and bio-tech company websites included in the research contained content about testing and lung cancer, this content was not easily accessible. Generally speaking there was no obvious path for patients or, if there was, there was no specific path to lung cancer-focused testing information at the corporate websites. In the case of AstraZeneca, there was no path other than searching by specific drugs. The majority of the content we assembled for this group of sources was the result of running site searches on the terms of interest as opposed to content collected from the home page or through a clear navigation path. To be fair, however, patient communication is not the main focus of these sites.

Sources Reviewed

- Abbot
- AstraZeneca
- Boehringer Ingelheim & Let's Test
- Genentech & Right Test Right Time
- Novartis
- Pfizer & LungCancerProfiles.com
- BIO (Association)
- PhRMA (Association)

Three companies are notable for developing microsites devoted specifically to molecular testing: Pfizer's *Lung Cancer Profiles*; Genentech's *Right Test Right Time*; and Boehringer Ingelheim's *Let's Test*. Of these, *Lung Cancer Profiles* and *Right Test Right Time* are directed toward patients, while Boehringer Ingelheim's *Let's Test* is focused on the medical community.

Microsite	Focus	Audience	Home Page Message
Pfizer's *Lung Cancer Profiles*	Molecular Testing for Lung Cancer	Patient	*Molecular profiling — testing your tumor for molecular biomarkers — is changing the way some lung cancers are diagnosed and treated based on their genetic differences.*
Genentech's *Right Test Right Time*	Molecular Testing for Cancer	Patient	*An important part of your cancer experience may be biomarker testing. Whether cancer has just been diagnosed or it has recurred, biomarker testing may help determine if you may benefit from a medicine that specifically targets your type of cancer.*
Boehringer Ingelheim's *Let's Test*	Molecular Testing for Lung Cancer	Medical Community	*Let's Test is dedicated to helping you make a difference in the lives of patients with lung cancer by providing you with relevant information and educational resources on biomarker testing in NSCLC.*

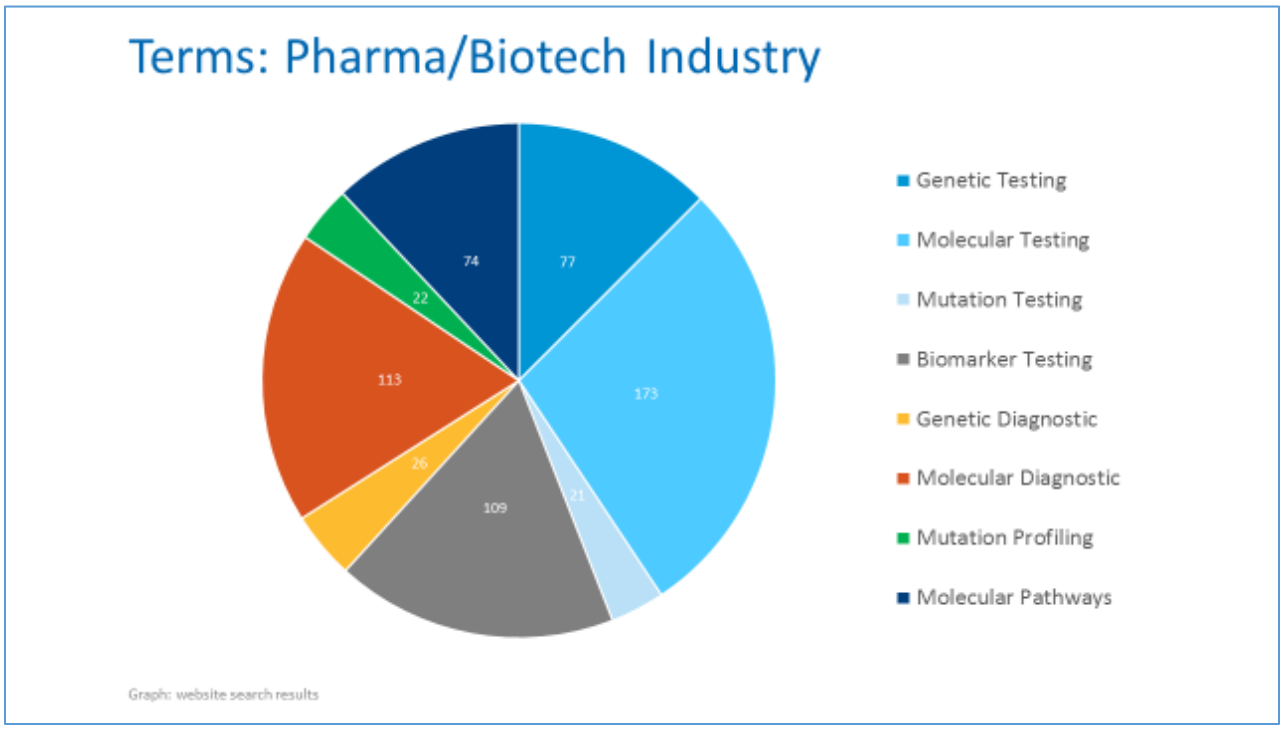
Focus of Communications

As with testing companies, there are several audiences being addressed, including patients, clinicians and investors. In this case, we prioritized content that was directed to patients or had patients as one of the target audiences.

The tone and detail of the content is extremely varied, with the Pfizer and Genentech microsite content being the most structured toward patients in both tone and content. For example, Pfizer content included an explanation of molecular profiling similar to the explanations found at lung cancer advocacy organization websites; in contrast the content most relevant to this audit from Novartis was announcements about drug testing results or information about relevant drugs. Boehringer Ingelheim fell in-between these two approaches, with some more accessible patient content, as well as more technical detail about the targeted therapies at their main site.

Across the corporate and industry association (BIO, PhRMA) web sites, there is a consistent focus on the deadly statistics of lung cancer, with added emphasis on the future of treatment and the momentum behind drugs "targeted at the molecular level."

Terms Used and Context



Search Terms	Pfizer	Lung Cancer Profiles (Pfizer)	Genen-tech	Right Test Right Time (Gen)	Novartis	BI	Let's Test (BI)	Abbott Labs	Astra Zeneca	Total for Industry
Molecular Testing	102	23	0	3	0	30	0	15	0	173
Molecular Diagnostics	7	1	0	2	55	16	0	32	0	113
Biomarker Testing	4	2	2	9	1	8	76	7	0	109
Molecular Pathways	1	0	0	1	55	16	1	0	0	74
Genetic Testing	20	2	0	4	10	18	3	20	0	77
Mutation Profiling	3	0	0	0	0	3	15	1	0	22
Mutation Testing	0	0	1	3	0	16	0	1	0	21
Genetic Diagnostic	3	0	0	1	0	15	0	7	0	26
Targeted Therapies	17	3	16	5	45	45	8	10	0	149

- As seen by the highlighting in the table above, there is variation across sources in the terms used to refer to *molecular testing*, without a seeming trend toward any one term. The sites themselves vary pretty widely in how much content they have on the topic.
- Review of the content shows that while *biomarker testing* is not a common reference, discussion and explanation of *biomarkers* is. The exception is Boehringer Ingelheim's *Let's Test Now* which uses the term biomarker testing as the main way in which they refer to molecular testing.
- In addition, the terms *molecular profiling* and *companion diagnostic* are frequently used.
- Compared to general cancer and lung cancer organizations, there is less use of the term *targeted therapies*; however, the same focus remains on the use of test to match the patient's cancer to drugs that will help.

The examples below also highlight the plethora of terms being used alone and in combination to explain the purpose and value of molecular testing.

> *Personalized Medicine is defined as the customization of healthcare, where medical decisions are tailored to the individual patient based on their susceptibility to disease or response to a particular treatment. A key component of personalized medicine includes advanced testing of a patient's genetic information to help identify targeted treatment options. The practice of personalized*

medicine is based on the premise that for many diseases, including cancer, there is no "one-size-fits-all" treatment. In personalized medicine, diagnostic tests are used to help tailor disease prevention, diagnosis, and treatment based on the genetic makeup of a particular patient. (Abbott)

Molecular profiling — testing your tumor for molecular biomarkers — can help doctors tailor treatment plans for certain patients based on the genetic makeup of their tumors. It may also help determine some tumors' potential for spreading or recurring. (Pfizer)

In the past, cancer was defined by and even named for its location: breast cancer, kidney cancer, lung cancer. Scientists now know that cancer is largely a disease of the genome. And two patients with the same "type" of cancer can have tumors with different genetic roots. Breast cancer, for example, is actually a collection of diseases, each caused by specific genetic mutations. The ultimate goal is to stratify patients to therapy based on the individual genetics of their disease. This targeted approach could help finally fulfill the promise of personalized medicine and have significant implications for the way cancer is treated across the globe. (Novartis)

Depending on the source, there is more or less discussion of the genetic mutations and biomarkers for which there are existing targeted drugs vs. the biomarkers for which there are drugs in development. Abbott and Pfizer offer explanations of the EGFR and ALK mutations. In addition, companies such as Genentech and Abbott discuss *companion diagnostics* and *biomarker panels* as important new forms of testing.

At Genentech, we're already spearheading efforts to help medical professionals navigate the complexity of the testing process. We are educating pathologists and surgeons about quality biomarker testing, and we have experts in diagnostics working on a "biomarker panel" for lung cancer. (Genentech)

Personalized medicine and targeted therapies such as these hold immense potential to improve patient care, and more genetically targeted cancer drugs are on the way. The field is advancing at an astonishing pace for a broad range of medical conditions, infectious diseases – and in oncology. As a consequence of this tremendous growth in personalized medicine technologies, Abbott has recently signed agreements with Abbvie, Epizyme, GlaxoSmithKline, and Janssen Pharmaceuticals to develop molecular companion diagnostic tests that will work hand-in-hand with their new cancer drugs. (Abbott)

Call to Action

While there is a lot of explanation about testing and its link to treatment, there is not a consistent call for tumor testing across all industry sites– in part because few of the organizations have communications solely focused on patients. Pfizer and Boehringer Ingelheim are the two sources that specifically advocate for patient testing in content at their main corporate sites:

"Boehringer Ingelheim is honored to be supporting the Bonnie J. Addario Lung Cancer Foundation to help communicate the importance of immediate biomarker testing for patients diagnosed with advanced non-small cell lung cancer," said Kevin Lokay, vice president and business unit head,

Oncology, Boehringer Ingelheim Pharmaceuticals, Inc. "It's about a more detailed diagnosis as early as possible to help physicians more immediately match each patient with the most appropriate course of treatment." The sponsorship from BI to promote genetic biomarker testing in advanced NSCLC also complements ALCF's Patient 360 Community Hospital Program that aims to create a new standard of care for lung cancer patients in the community hospital setting. One of the requirements of the ALCF's Patient 360 Community Hospital Program is administering genetic biomarker testing for all patients in the program. (Boehringer Ingelheim)

If you have NSCLC, molecular profiling could give your doctors information that may guide your treatment plan or determine your eligibility for clinical trials. Talk to your doctor and ask if molecular profiling is right for you. This Interactive Discussion Guide can help you start the conversation. (Pfizer)

In contrast the testing microsites are very clear in their advocacy for the use of molecular testing in cancer and lung cancer, including calls for adequate tissue sampling at the time of initial diagnostics.

Performing tests to determine the presence of biomarkers is dependent on the collection of tissue that is adequate in both quality and quantity. In the past, adequate tissue acquisition was not a priority as only a small sample size was necessary to confirm histology. Now that molecular markers are being incorporated into the treatment of NSCLC, understanding the details of the testing process from tissue acquisition to assay techniques is of utmost importance. Therefore, it is often recommended that a multidisciplinary team, including thoracic surgeons, radiologists, and pulmonologists, be called upon to obtain the tissue to be used in testing. (Let's Test)

Targeted medicines represent a personalized way to treat disease. Scientists continue to research how cancer cells work in order to develop new ways to test for biomarkers and new targeted medicines. If you test positive for a biomarker, you may be eligible for treatment with a targeted treatment. Ask your healthcare team for more information. (Right Test Right Time)

Join Lung Cancer Profiles in making the United We Test Quest pledge! (Lung Cancer Profiles)

"When people are diagnosed, they don't know any of these terms…. We don't go around studying cancer and what to do when it hits us, because we don't think it will ever happen to us. Then all of a sudden we are faced with a life threatening disease. We need to find answers, and we need to find them quick. It makes it difficult that there is not standard terminology." (Patient)

Testing Companies

Overview

The content of communications from testing companies is focused on the support of both treatment decisions and development of new therapies. While not exclusive to lung cancer, all the sites reviewed had some content geared toward lung cancer specifically. Content covers both testing for diagnosis and treatment, as well as testing to predict response to treatment and longer-term prognosis.

Sources Reviewed

- Biodesix
- Caris & MyCancer.com
- Foundation Medicine & MyCancerIsUnique.com
- Myriad

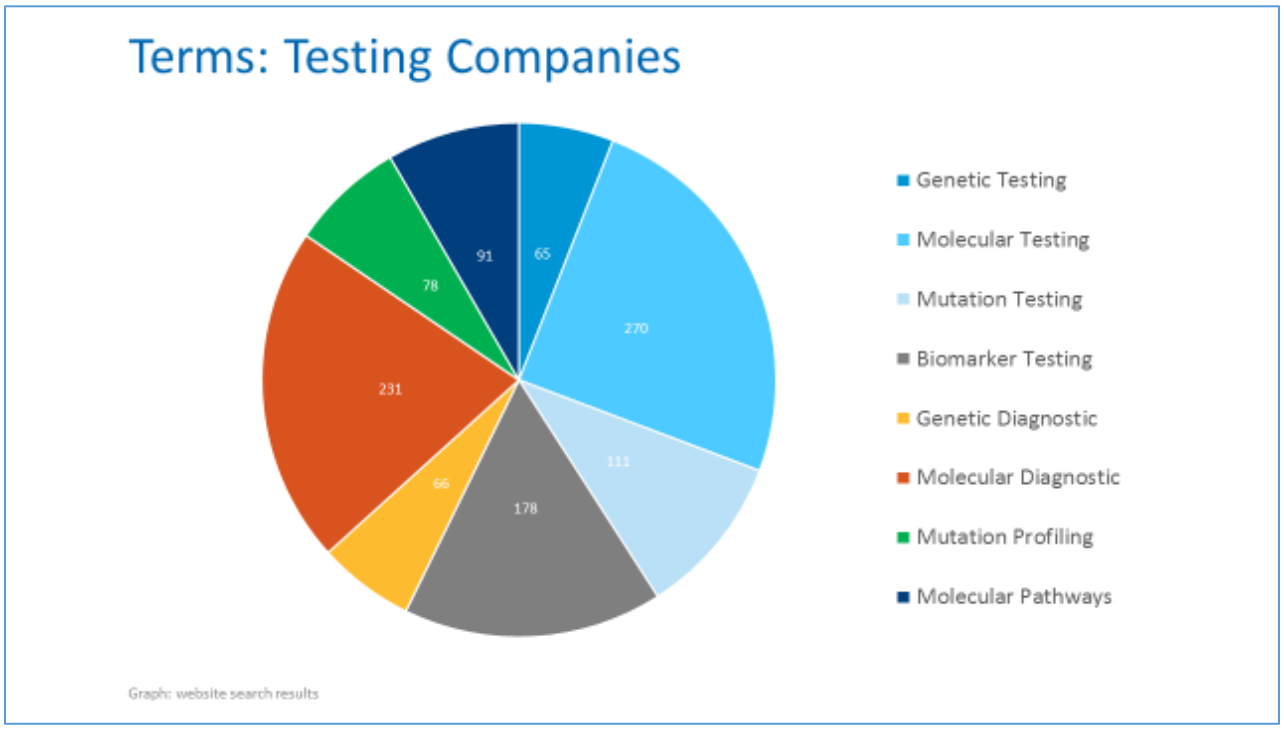
Focus of Communications

The companies address several audiences on their websites, most notably clinicians and investors. That said, all except Foundation Medicine have a menu navigation path clearly directed at patients at the home page (i.e., menu navigation labeled "Patients"). Foundation Medicine has navigation to patient-focused information under a tab called "Connect."

As we see with some of the pharmaceutical companies, two of the testing companies have developed microsites or companion sites that are geared specifically to patients.

Microsite	Focus	Audience	Home Page Message
Foundation Medicine's *MyCancerIsUnique.com*	How "genomic profiling" through Foundation One can help you	Guided "patient" path to Foundation's offering	*Learn more about cancer and available treatment options*
Caris' *MyCancer.com*	A personal guide to transforming your treatment	Guided "patient" path by where in cancer journey-- just diagnosed, in treatment, treatments not working	*New research about cancer biomarkers is reshaping cancer care*

Terms Used and Context



Search Terms	Foundation Medicine	Caris	Myriad	Biodesix/Veristrat	TOTAL FOR TESTING COMPANIES
Molecular Testing	45	218	6	1	270
Molecular Diagnostics	8	182	5	36	231
Biomarker Testing	0	172	6	0	178
Molecular Pathways	0	91	0	0	91
Genetic Testing	0	54	11	0	65
Genetic Diagnostic	0	58	8	0	66
Mutation Testing	0	61	50	0	111
Mutation Profiling	0	78	0	0	78
Targeted Therapies	46	71	2	16	135

- Among the testing companies, with the exception of Caris, there are just a couple of the search terms that generate significant content relevant for lung cancer – *molecular testing*, *molecular diagnostics* and *targeted therapies*.
- That said, the sites reference a number of other terms not included in our search, most frequently:
    - Molecular profiling
    - Comprehensive genomic profiling
    - Companion diagnostics

Interestingly, the two testing microsites do not use many of the "testing" terms included in this audit (i.e. genetic testing, genetic diagnostic, mutation profiling). Each site consistently uses a single term – Caris' MyCancer.com uses *molecular profiling (to identify cancer biomarkers)* and Foundation Medicine's MyCancerIsUnique.com uses *comprehensive genomic profiling*.

Testing sites may be among the most difficult for lung cancer patients to navigate and from which to draw conclusions about molecular testing for lung cancer, versus other testing related to cancer diagnosis and treatment. The use of terminology is inconsistent across sites and generally intended to highlight the specific testing products of the company:

- Biodesix promotes its Veristrat test for patients with NSCLC directly from the home page referring to it as, "A serum proteomic test that helps physicians guide treatment for **advanced non-small cell lung cancer patients**"
- Myriad is focused on genetic testing with a message of "what's my **hereditary risk**?" While molecular diagnostics is promoted at the home page, a lung cancer patient must click into the Patients & Caregivers menu to find his disease in a list that heavily emphasizes hereditary testing:
    - *Hereditary Breast Cancer*
    - *Hereditary Colon Cancer*
    - *Lung Cancer*
    - *Melanoma*
    - *Hereditary Ovarian Cancer*
    - *Hereditary Pancreatic Cancer*
    - *Prostate Cancer*
    - *Rheumatoid Arthritis*
    - *Hereditary Uterine Cancer*
- At the main Caris site, a lung cancer patient would need to click into Patients and read general information to find (below "the fold") that "**Biomarker testing** has become standard of care before treatment for some cancer types, including certain types of lung, stomach, colon, skin and breast cancers. But for most cancer types, this type of upfront testing is not yet standard."
- At the main Foundation Medicine site the initial message is, "Foundation Medicine is leading a transformation in cancer care, where each patient's treatment is informed by a deep understanding of the **molecular changes that contribute to their disease**."

"Molecular profiling? I would say it's what your tumor is made up of.
Again, it's not a phrase I use." (Patient)
"Companion diagnostic? In ten years as a patient, I've never heard that term." (Patient)

Although each company has differences on how they talk about their testing products, the prevailing message is a more comprehensive understanding of the genetics of the tumor, leading to better decision-making:

> ***Biodesix**: Tests for precise medical decisions: Biodesix is changing the paradigm of companion diagnostics development. Our hypothesis-independent approach has demonstrated its ability to classify patients into groups correlated with specific clinical outcomes using mass spectra obtained from serum or plasma samples.*
>
> ***Myriad**: The Myriad myPlan™ Lung Cancer score can be used in combination with information about cancer stage to better predict the five-year risk of lung cancer-specific death. Gaining insight into tumor aggressiveness will also help determine if surgery alone is sufficient, or if more aggressive treatment is needed.*
>
> ***Caris**: Provides oncologists with the most relevant, clinically actionable and individualized treatment information to personalize cancer care for all solid tumors. Our suite of tumor profiling services allows the physician to customize the level of profiling they deem necessary for each patient.*
>
> ***Foundation Medicine**: A comprehensive approach to genomic profiling enables a physician to get a broad view of the targeted treatment options available in a single test. The comprehensive approach to genomic profiling saves time and precious tissue and enables physicians to make informed decisions more efficiently than standard molecular tests. Comprehensive genomic profiling has also been shown to detect targetable alterations that were missed or would never have been found by standard testing.*

Call to Action

Although the implied call to action from each company is to use the tests they have developed or are developing, the testing companies have cross-cutting messages that are not evident in content from other sources.

- **Push for "comprehensive" profiling** – communications recommend more comprehensive profiling, rather than risk piecemeal testing for specific known mutations.
  Comprehensive genomic testing detects all types of alterations in all the regions where they can occur, and it does so for all the genes that are known to be associated with cancer. The NCCN now endorses the use of broader molecular profiling for the identification of rare driver mutations that may inform the use of an approved targeted therapy or one in clinical trials. (Foundation Medicine)

- **Value of testing to match therapies and patients** – another distinct message from testing companies is the development of testing to better predict patient outcomes.
  Today, the co-development of drugs and companion diagnostics has captured the imagination of the healthcare industry, regulators and payers to a point where these institutions are aligning around improving outcomes for patients. More than 50 percent of oncology drugs in development are proceeding with some form of companion diagnostic. The evolution of this complex ecosystem has been rapid and reflects a shift in industry focus from the old school "trial and error" drug

development process to understanding the molecular basis of a given disease, the isolation of a biological target and development of specific therapies for that target. (Myriad)

"I understood that they wanted to do this testing, because they wanted to see what type of cancer I had. Afterward, they explained the gene mutation that I had, but nobody ever really explained to me what the different mutations were or what it would mean to me." (Patient)

Government and Private Sector Online Sources

Overview

All three sources in the group have a clear path for patients to get information on lung cancer, and within that content, to find some mention of molecular testing. The volume and detail of content varies dramatically, however, with the National Cancer Institute having the greatest amount of information on lung cancer and the use of testing.

Sources Reviewed

- National Cancer Institute / cancer.gov (NCI)
- Mayo Clinic
- WebMd

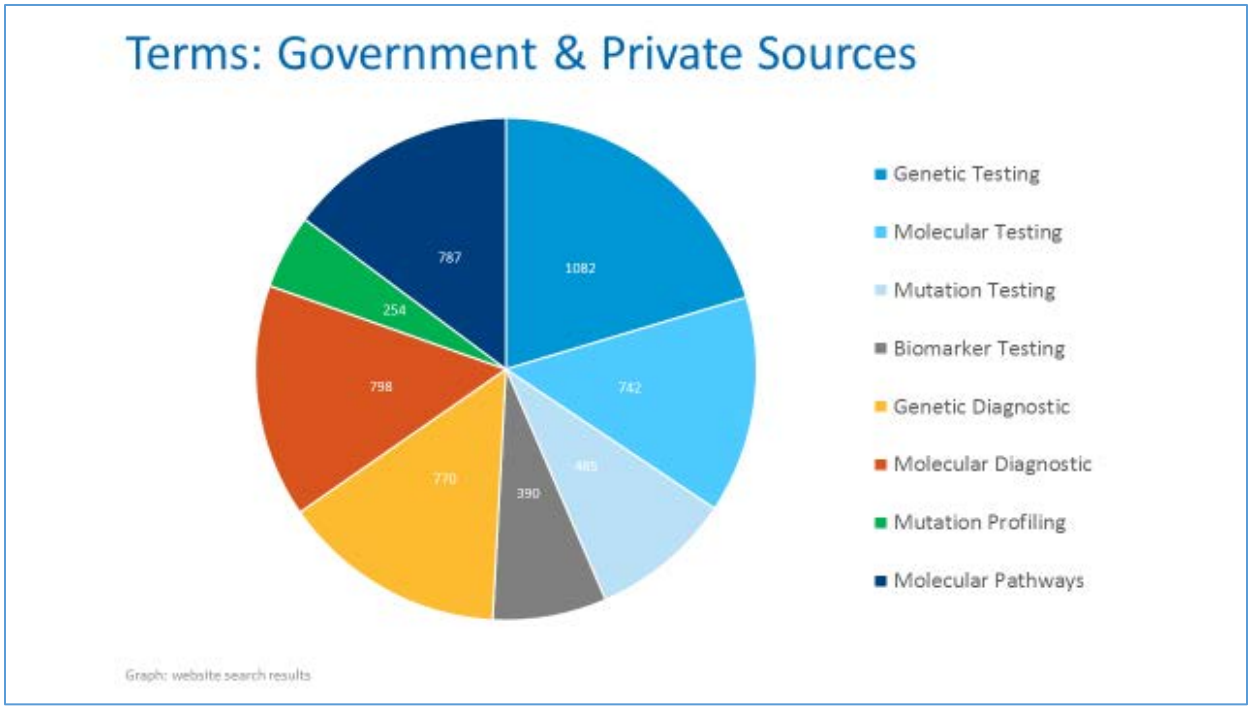
Focus of Communications

These sources focus their communications for both patients and the medical community. As such there are layperson definitions of terms as well as the use of more detailed and technical language. Of note, the explanations of targeted therapies are not always consistent, at times including angiogenesis inhibitors despite the lack of a test to identify responders. This may further confuse patient understanding of molecular testing. Examples of patient-focused explanations include:

> *Targeted Therapies are a newer form of cancer treatment that can be used together with chemotherapy or when other therapies don't work. One type prevents the growth of new blood vessels that feed cancer cells. It may help people with advanced lung cancer live longer. Other targeted therapies interrupt the signals that cause lung cancer cells to multiply. (WebMD)*

> *For years, researchers and oncologists have been making discoveries about genetic mutations that drive the growth of certain cancers. Much work has been done to discover and create drugs that can target specific genetic mutations and shut down their ability to keep the tumor alive and growing. It's this collection of known cancer genes (oncogenes) and targeted agents that are the background for the creation of the gene panel test. (Mayo Clinic)*

Terms Used and Context



Search Terms	National Cancer Institute	WebMD	Mayo Clinic	TOTAL ONLINE SOURCES
count of results, filtered for "lung cancer"				
Genetic Testing	631	45	406	1082
Molecular Diagnostics	659	18	121	798
Molecular Pathways	686	17	84	787
Molecular Testing	556	15	171	742
Genetic Diagnostic	579	31	160	770
Mutation Testing	370	21	94	485
Mutation Profiling	175	6	73	254
Biomarker Testing	265	9	116	390
Targeted Therapies	647	70	208	925

- There are significant differences in the volume of testing-related content at these sites, making it difficult to draw conclusions about use of terminology. Among the most frequently used terms is genetic testing, although this term often appears in the context of propensity to develop a particular cancer.
- Targeted drug therapy is given varying levels of attention and is characterized as an emerging field in some Mayo Clinic content; it is discussed in the context of specific drugs by WebMD; and is mentioned yet more specifically in content about particular trials by NCI.

- There are many more layers of content available at NCI, and those layers correspond to trends we see in other sources – for example, discussion of specific mutations (EGFR and ALK) but on a more technical level, along with content about the related drug therapies.

What the search count does not show is the number of additional terms used by these sources to refer to testing and the value of testing. As in the pharma/bio-tech sector, many more terms are being coined and different terms can be found within the same source depending on whether the content is original or articles drawn from other sources. The Lung-MAP project gets significant attention at the NCI website (and was mentioned by some of the pharma/bio-tech sites as well). Information about Lung-MAP also introduces numerous terms.

Among the terms we found:

- Tumor marker tests
- Tumor gene panel testing
- Individualized medicine
- Precision medicine

This description from NCI content underscores the point that many terms are being referenced without definition at once:

> *Lung-MAP is a multi-drug, multi-arm, **biomarker-driven** clinical trial for patients with advanced squamous cell lung cancer. Squamous cell carcinoma represents about a quarter of all lung cancer diagnoses, but there are currently few treatment options beyond surgery for the disease. The trial will use **genomic profiling** to match patients to one of several different investigational treatments that are designed to target the genomic alterations found to be driving the growth of their cancer. The trial will initially test five experimental drugs—four **targeted therapies** and an anti-PD-L1 **immunotherapy**. It is anticipated that between 500 and 1,000 patients will be screened per year for over **200 cancer-related genes** for **genomic alterations**. The results of this test will be used to assign each patient to the trial arm that is best matched to their **tumor's genomic profile**. (NCI)*

Call to Action

There is no unified call to action across the content evaluated from these sites. Content at the sites is presented as informative and sourced to research studies and experts. In particular, there was not readily-accessible content about tumor testing as a standard of care for lung cancer.

"Once I learned more about testing, I was disappointed that it wasn't standard, that it wasn't automatically done. I talk with a lot of patients, all over the United States, and come in contact with people that are newly diagnosed and haven't had it done. It is a much easier treatment than standard chemotherapy and people still aren't getting the testing done." (Patient)

General Cancer Organizations

Overview

Recognizing that the organizations that focus on all types of cancer will naturally have less content specific to lung cancer, we see some similarities in the content related to molecular testing and a few marked departures.

Sources Reviewed

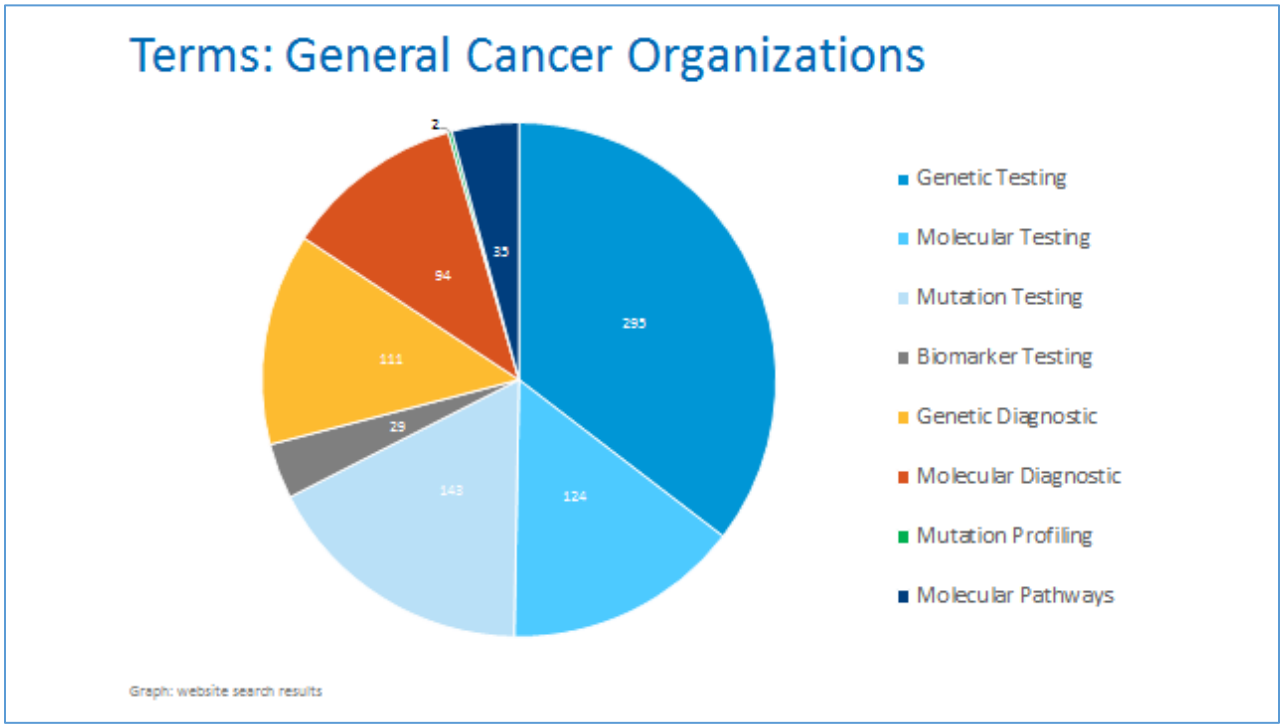
- American Cancer Society (ACS)
- American Society of Clinical Oncology (ASCO) & the related site Cancer.net
- Cancer Support Community (CSC)
- CancerCare (CC)

Most notable for this analysis is the relative lack of emphasis on molecular testing. While lung cancer sites tend to talk about testing first as part of a whole picture of the patient journey, the general cancer sites are more high level and start with the treatments that are available, rather than how patient treatment is determined. In addition, immuno-therapy is more likely to be presented along with targeted therapies as the important new approaches to treating lung cancer.

Focus of Communications

Similar to the lung cancer advocacy and support groups reviewed, the general cancer organizations included in this review tend to have a primary focus on patients and caregivers, with some additional focus on fundraising for research. Cancer Support Community expands this audience to include patients, social workers, and HCPs simultaneously. The exception is American Society of Clinical Oncologists (ASCO), which has a primary focus on practitioners and standards of care; as a result, much of the content is highly technical. For that reason, the ASCO-developed patient-focused site, Cancer.net was also included in the audit.

Terms Used and Context



1. The search term counts reveal some interesting similarities and departures from the lung cancer-specific sites:

Search Terms	American Cancer Society	CancerCare	Cancer Support Community*	ASCO	Cancer.net	Total for General Cancer Orgs
Genetic Testing	121	28	10	7	129	295
Genetic Diagnostic	0	40	2	7	62	111
Molecular Testing	12	11	0	16	85	124
Mutation Testing	6	16	5	12	104	143
Molecular Diagnostics	0	21	0	9	64	94
Molecular Pathways	6	1	1	18	9	35
Biomarker Testing	0	11	1	8	9	29
Mutation Profiling	0	0	0	0	2	2
Targeted Therapies	156	123	53	27	238	597
	most relevant content was within webinars					

- There is far less coalescence around terms – the different sources place very different emphasis on specific terminology such as *molecular testing*, *molecular diagnostics*, *mutation testing*, and so on.

- Again, of the testing-related terms, *genetic testing* is by far the most commonly found, although this is driven by two sources – American Cancer Society and Cancer.net. This is due in part to content that addresses diseases other than lung cancer and in part by using the term "genetic" when explaining molecular testing.

Like the lung cancer specific organizations, a variety of terms are used interchangeably or referenced to one another when defining molecular testing.

> *When a tumor is biopsied (a small portion removed), a pathologist examines the tissue and its cells closely. This determines what type of lung cancer it is: small cell or non-small cell. Now more detailed testing can be done on your tumor if your doctor requests it. These tests are sometimes referred to as molecular testing or biomarker testing. They look for changes (mutations) in the DNA of the tumor and levels of specific proteins present in the tumor. (ACS)*

> *Testing specific features of cancer cells (biomarker testing, also called tumor marker testing) helps oncologists identify whether or not available targeted therapy options will work for an individual's treatment – thereby "personalizing" treatment based on the best available knowledge. (CSC)*

In the case of Cancer.net, the most easily accessible explanations of the testing (within a couple clicks of the home page) avoid any technical terms, referring to it simply as "testing."

> *To find the most effective treatment, your doctor may run tests to identify the genes, proteins, and other factors in your tumor. For some lung cancers, abnormal proteins are found in unusually large amounts in the cancer cells. Running tests to find these proteins can help doctors better match each patient with the most effective treatment whenever possible. (Cancer.net)*

Even more so than with lung-cancer focused sources, these sources link testing to targeted therapies. In fact, they do not tend to have a navigation path that includes *testing* as a specific content area; instead information about molecular testing is found in content related to treatment standards and options. For example, a good deal of the content from both the American Cancer Society and Cancer.net on how targeted therapies work and how they are administered did not use the term "molecular testing" at all.

> *"I don't think a lot of people understand the science, nor are they interested. I would like information to be more in layman's terms. You start to care after you know your mutation, when you know 'I'm ALK positive.' People want to know this is the cancer I have, this is the subset, and then they want to know the targeted therapies." (Patient)*

Similar to lung cancer specific organizations, there is relative emphasis on explaining testing in the context of the genetic mutations for which there are targeted therapies in use and/or in clinical trials, with emphasis on EGFR and the ALK gene changes and related drugs. The ASCO website goes further with highly technical content aimed at

practitioners that encompasses both the current standards of care and what might be likely in the future.

> *Epidermal growth factor receptor (EGFR) is a protein found on the surface of cells. It normally helps the cells to grow and divide. Some NSCLC cells have too much EGFR, which causes them to grow faster. Drugs that target EGFR and used to treat non-small cell lung cancer (NSCLC) include Erlotinib (Tarceva®) and Afatinib (Gilotrif®) (American Cancer Society)*

> *Knowledge of histology (squamous versus nonsquamous) and molecular markers (EGFR, ALK, ROS, RET, etc.) are essential for making appropriate choices for treatment in advanced disease. (ASCO)*

Call to Action

While there is some call to action for molecular testing of lung cancer tumors, it is not as strong and clear within the general cancer organization content. The sites tend to provide an overview of likely treatment approaches and leave the call to action around testing and target therapies as "your doctor may recommend a test" or "ask your doctor." ASCO makes the strongest call and it is aimed at clinicians:

> *It has been recommended that all lung adenocarcinomas be tested for EML4-ALK fusion and EGFR mutation, while squamous cell carcinomas should be tested for other gene abnormalities (DDR2 mutation and FGFR1 amplification). On the other hand, our growing understanding of the cancer biology of NSCLC, particularly the molecular evolution of tumors during local progression and metastasis and the identification of molecular abnormalities contributing to resistance to TK inhibitor therapies, emphasizes the importance of characterizing the molecular abnormalities of the disease at every stage of its evolution. For molecular testing of advanced metastatic NSCLC, it is important to sample and analyze the tumors' sample at each time point of clinical decision making. (ASCO)*

Lung Cancer Advocacy & Support Organizations

Overview

We reviewed content from nine lung cancer-focused organizations and found all contain significant amounts of content on the topic of molecular testing.

On many of these organizations' websites, there are navigation paths directed to patients that will bring them to information about molecular testing within a few clicks. So even if a patient is completely unaware of this type of testing or any terms, content is discover-able. That said, a few of the sources bring testing information to the forefront, among them the Lung Cancer Mutation Consortium and Lung Cancer

Sources Reviewed

- American Lung Association
- Bonnie J. Addario Foundation
- Free To Breathe
- International Association for the Study of Lung Cancer (IASLC)
- Lung Cancer Alliance
- Lung Cancer Foundation of America (LCFA)
- Lung Cancer Mutation Consortium (LCMC)
- LUNGevity
- Uniting Against Lung Cancer

Foundation of America, which both had information visible on the home page at the time of the review. On other sites, there is a less clear path and information is nested within many pages of content on treatment. The bottom line is that these sources offer a great deal of online information for a lung cancer patient to navigate. Whether and how much patients learn about molecular testing will depend at least in part on their navigation savvy and ability to process a lot of written content.

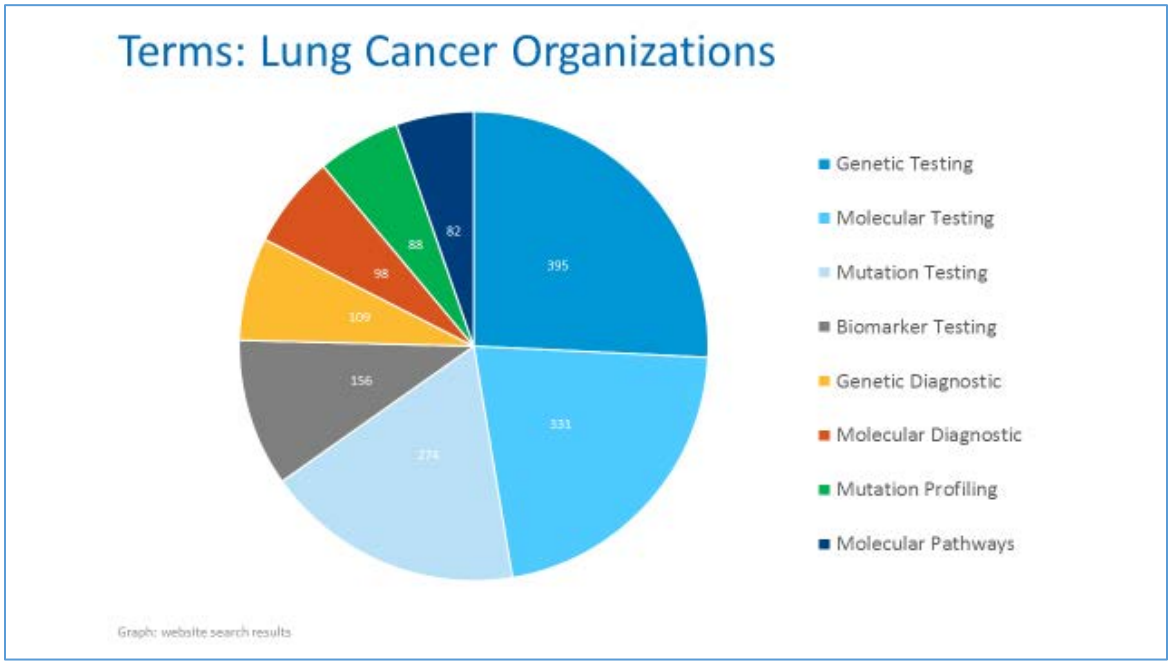
Focus of Communications

All of these sources have a clear focus on the patient as the target of their communications regarding lung cancer diagnosis, treatment and support resources. To varying degrees they also direct communication to a wider audience of interested parties and potential donors, with a couple of sources seeming to have a primary communications focus on fundraising for research. However, two organizations – IASLC and LCMC – have a stronger focus on researchers and the medical community and less communication directed to patients themselves.

Positive momentum and hopeful themes are the message of the day. Across lung cancer advocacy and patient support organizations, communication about molecular testing stresses that the science and medicine are developing rapidly. All these sites include extensive content on the treatment of lung cancer, and they introduce newer treatment options of targeted therapies and immunotherapy alongside surgery, chemotherapy and radiation. While they make the point that there is not a cure, sites also imply that more and more people in the US are living, and living longer, with a lung cancer diagnosis. Advances in the understanding and treatment of the disease are presented as reasons to hope.

> *There are more lung cancer treatments today than ever before, including surgery, radiation therapy, chemotherapy, and "targeted therapies," and new drugs being tested in clinical trials are also available to many patients. (Free To Breathe)*

Testing Terms Used



Among the lung cancer organization sites there are some notable trends:

Search Terms	BJA	LUNG	ALA	UALC	LCMC	LCFA	FTB	LCA	IASLC	Total for Lung Cancer Orgs
Genetic Testing	39	16	248	42	8	24	8	4	6	395
Molecular Testing	22	44	74	41	3	59	19	7	62	331
Mutation Testing	3	36	75	45	15	75	12	6	7	274
Biomarker Testing	2	13	63	37	3	27	2	6	3	156
Genetic Diagnostic	0	4	42	36	6	17	0	4	0	109
Molecular Diagnostics	4	7	29	36	1	4	0	3	14	98
Mutation Profiling	0	3	20	33	14	15	1	1	1	88
Molecular Pathways	2	2	30	35	2	6	1	0	4	82
Targeted Therapies	235	71	137	51	10	200	24	30	415	1173

- *Genetic testing* is the most commonly found testing-related term, driven mainly by American Lung Association's site, where the term comes up not only in relation to lung cancer but to other types of lung-related diseases. Among the lung cancer-related sites, the term genetic testing generally overlaps with content on *molecular testing*, *mutation testing*, etc. In other words, the term "genetic" is being used as part of the explanation for what molecular testing is and what it is looking for.

  The use of testing for genetic abnormalities in tumor tissue is helping to advance…treatment. (IASLC)

  Your cancer care team may take a sample of your tumor and test it for changes or mutations that drive its growth. This process can be called molecular, biomarker, genetic or mutation testing. (Free To Breathe)

  Note that other names for genetic mutation testing include: Biomarker testing, Genetic testing, Molecular testing. (LUNGevity)

- Of the terms, *molecular testing* and *mutation testing* are emerging as the most common and frequently interchangeable terms. To a lesser extent, *mutation profiling* is being used.

"'Molecular testing' I understand. It's called everything from gene mutation analysis to biomarker testing." (Patient)

Now, more detailed testing can be done on your tumor if your doctor requests it. These tests are sometimes referred to as molecular testing, and may involve…looking for changes (mutations) in the DNA make-up of the tumor. (LCMC)

Although the search counts reveal many terms are being used, review of the content shows that multiple terms are being used simultaneously as organizations seek to define and describe the purpose, process and value of molecular testing. A small sampling underscores the point:

Molecular testing, also called assays or profiles, can help your treatment team identify specific biomarkers that are in your tumor. (Bonnie J Addario Foundation)

These tests, sometimes referred to as molecular testing, look for changes (mutations) in the DNA of the tumor and levels of specific proteins present in the tumor. When doctors have this information, they may choose to administer specialized therapies that target the mutation in the cells. (American Lung Association)

To know whether a patient will respond to a particular targeted therapy, doctors will conduct molecular testing (also called genetic or genomic testing, or profiling) on the tumor, to match patients to the appropriate targeted therapy. (Uniting Against Lung Cancer)

The context of molecular testing is very firmly rooted in the potential identification of mutations for which targeted therapeutic drugs are ***already*** available. In most content, molecular testing is presented as the first step in ultimately discovering if a patient is either a candidate for an approved targeted therapy or, alternately, eligible for a clinical trial.

Researchers have learned about the cell pathways involved in the development of many types of cancers and have developed drugs that block those pathways. These drugs are known as targeted drugs, and treatment is known as targeted therapy. (IASLC)

These mutant proteins in cancer cells are good "targets" for new drugs. These drugs are known as targeted therapies. Targeted therapies work by blocking these mutant proteins, which prevents them from growing and spreading, while not harming normal cells. (LCFA)

Effective targeted therapy depends on two factors: identifying targets that play an important role in the growth and survival of cancer cells, and developing agents that can attack those targets… Targeted therapy, in combination with chemotherapy, is currently approved for advanced non-small cell lung cancers. (IASLC)

When particular tumor characteristics are found through molecular testing, targeted therapies—special lung cancer treatments designed to "target" these characteristics—may be offered to you as an option for treatment. It is important to know if you have a tumor with one of these characteristics so you and your doctor can make well-informed decisions about your treatment. (Free to Breathe)

As researchers have learned more about the gene changes that cause cancer in cells, they have been able to develop drugs that target some of these changes. Targeted cancer therapies are a type of biological therapy that aims to target cancer cells directly. They target certain parts of cells

and the signals that cause cancer cells to grow uncontrollably and thrive. These drugs are often grouped by how they work or what part of the cell they target. (LUNGevity)

Similarly, molecular testing and related targeted therapies are sometimes presented in the context of the larger trend of personalized medicine in cancer treatment broadly, and lung cancer specifically. Phrases such as "no one's cancer is the same as another person's" and moving away from "one size fits all" treatment are often used.

Within the discussion of molecular testing, mutations and biomarkers, there is relatively more content emphasis on explaining two specific mutations – EGFR and ALK – and describing how the targeted therapies for those mutations work.

Characteristics that can be targeted with treatments currently available include Epidermal Growth Factor Receptor (EGFR) mutation and Anaplastic Lymphoma Kinase (ALK). Gene rearrangement EGFR and ALK mutations turn on processes in tumors that make cancer cells uncontrollably grow and divide. Targeted therapies work by turning off these processes. Testing for EGFR and ALK mutations is particularly recommended if you have the adenocarcinoma sub-type of NSCLC, though other sub-types can also contain these characteristics. Generally, if one of these tumor characteristics is present, the other is not. (Free To Breathe)

One signaling pathway involved in the development of many different kinds of cancer, including non-small cell lung cancer, is directed by the epidermal growth factor receptor (EGFR) protein, which is made by the EGFR gene. Abnormalities (mutations) in this gene activate the EGFR protein, which in turn triggers a complex process that leads to increased growth and division of cancer cells and allows the tumor to spread. Targeted therapy drugs have been developed to block the activity of EGFR, and these drugs are known as "EGFR inhibitors." (IASLC)

This trend and information presented is similar across sites, with nearly all integrating more detailed information on the drugs themselves.

Tarceva® (Erlotinib), Gilograf® (Afatanib), Xalkori® (Crizotinib) and Zykadia® (Ceritinib) are examples of FDA-approved drugs that target the mutated proteins, some of which are referred to as "receptors" that are driving the cancer cells out of control. (LCFA)

Researchers have found that EGFR genetic mutation tumors are sensitive to gefitinib (Iressa™) and erlotinib (Tarceva®) – that is, the growth of EGFR tumors may be slowed by these drugs. On the other hand, tumors with the KRAS mutation are resistant to these drugs and they will not work for these tumors. By doing molecular testing, your doctor will be able to determine if your tumor is sensitive or resistant to these drugs. (Bonnie J Addario Foundation)

In other areas, the lung cancer sites are far less consistent in the additional detail they provide or the context provided around molecular testing and the efficacy of targeted therapies. Notably there is:

- Inconsistent use of statistics, with only some sites presenting information about the percentage of lung cancer patients who will have these mutations.

- Discussion of mutations for which the targeted therapies are not developed or that do not respond to existing drugs. KRAS is the most commonly referenced, although several sites (including Lung Cancer Foundation of America, Lung Cancer Mutation Consortium and LUNGevity include longer list of the mutations currently being studied as candidates for targeted therapies (including BRAF, HER2, MEK1, MET, RET, ROS1, FGFR1, PIK3CA)

- Discussion of resistance to targeted therapy is not universally raised within the same content about its potential. We found some language about resistance at a few sites, usually in the context of developing even newer drugs:

  The biggest challenge of TKIs is that patients with lung cancer who initially benefit from them eventually develop resistance. Acquired resistance is defined as disease progression after initial benefit with a targeted cancer therapy. Cancer cells are clever enough to bypass roadblocks to their survival and often mutate to overcome the effects of targeted drugs. The most common way adenocarcinomas become resistant to EGFR inhibitors is by mutating to a drug-resistant state that stops the drugs from working. (LUNGevity)

  Unfortunately, cancer always finds a way to get around targeted therapies and they eventually stop working. Research efforts are underway to find new treatments to overcome this "resistance." Two drugs in particular show promise and are expected to be FDA approved in 2015. (Lung Cancer Alliance)

  One of the most important problems associated with both chemotherapy and targeted therapy is that cancer cells often become resistant to the drugs, which become less effective over time. Researchers continue to explore ways to overcome resistance, identify new pathways to target, and develop new drugs to interrupt the growth of lung cancer cells. (IASLC)

  A patient being treated with a targeted therapy lung cancer drug can develop resistance to that drug after a period of time. This means that the drug stops working because the tumor cells develop new mutations that effectively "outsmart" the drug, allowing the cells to grow. "Second and third generation treatments" are often available in clinical trials that overcome this drug resistance, and tumor cell growth can once again be contained. (LCFA)

- How targeted therapies are used in relation to radiation and chemotherapy was another area that either had less information or the information was not always clear. Sometimes they were presented as instead of chemo, other times as alternatives when radiation and chemotherapy are not effective, and still other times without any reference to other treatments.

  Early stage lung cancer may be treated with surgery, chemotherapy or radiation therapy. If surgery is no longer an option, a doctor may prescribe other kinds of chemotherapy or targeted therapy to fight the tumor. (Uniting Against Lung Cancer)

  But newer drugs and other substances known collectively as "targeted therapy" are different from traditional chemotherapy. They zero in on molecular processes that allow cancer cells to grow and spread, and may work better than chemo while causing fewer side effects. (LCFA)

Call to Action

"Every time a new person comes into the community asking, 'What should we do?' 'What should we ask?'everybody tells them how important it is to have this testing done. It really is lifesaving… This could be a game changer." (Patient)

While the lung cancer advocacy and support organizations universally encourage patients to get tested, they do so with varying degrees of urgency. Among the stronger calls are those that alert patients to question a doctor who is unfamiliar with molecular testing:

> *If your doctor doesn't recommend tumor testing for you, it is okay for you to ask why not. Testing may not be appropriate in all cases, but it is best for you to know as much as you can about your disease so you and your doctors can be full partners in your care. If you have questions about the response you receive from your doctor, it is okay to ask for a second opinion from another doctor. (Free To Breathe)*

More typical is to present testing as a decision to be made with your medical team or doctor:

> *Ultimately, any decision to test for mutations should be made together by you and your physician(s). This should be a part of the discussion with both your oncologist and surgeon. Your oncologist may recommend additional testing at different points of your treatment process. (LUNGevity)*

Content around this call to action can vary even within the same site:

> *The role of molecular testing in lung cancer has grown in the past year.* ***Ask your doctor if molecular testing is available to you****. If not, contact us at 1-650-598-2857 to learn how to have your lung cancer tested. (Bonnie J Addario Foundation)*

> *Targeted therapies are a relatively new line of research.* ***If your oncologist is not familiar with molecular testing and targeted therapies, it is acceptable and advisable to get a second opinion*** *about your treatment options. (Bonnie J Addario Foundation)*

The call for testing regardless of certain patient characteristics was strong in the content of IASLC and the Lung Cancer Foundation of America:

> *It is also important for patients of any race, age and smoking history diagnosed with advanced adenocarcinoma to receive tumor testing conducted by pathology experts to determine if they can benefit from these treatments. Patients should speak with their oncologist to receive more information about personalized medicine and reach out to lung cancer patient advocacy organizations for support. (IASLC)*

> ***All*** *metastatic adenocarcinoma tumors should be tested for EGFR and ALK, as should some squamous tumors. (LCFA)*

For IASLC, the call is also geared to the medical community:

> *All patients with advanced lung adenocarcinoma should be tested for EGFR and ALK abnormalities that would qualify them for tyrosine kinase inhibitor therapy, regardless of their clinical variables, such as smoking history, gender, or ethnicity. (IASLC)*

Finally some sites emphasize the value of testing not only to identify candidacy for approved therapies, but for purposes of identifying possible mutations that are currently under study or have treatments in clinical trials.

> *When deciding whether to have your tumor tested, you may also want to consider that mutations in genes other than ALK and EGFR have been found in both adenocarcinoma and squamous cell carcinoma. Testing to identify other possible mutations in the tumor may help you find clinical research studies. These studies are testing new treatments for mutations in other types of lung cancer. Therefore, you may consider molecular testing for other mutations even if you don't fit into the ALK or EGFR testing categories. (LUNGevity)*

> *Even though we only have a few FDA-approved targeted therapies, many more mutations have been identified and are being studied in ongoing clinical trials for use in these other mutations. (LCFA)*

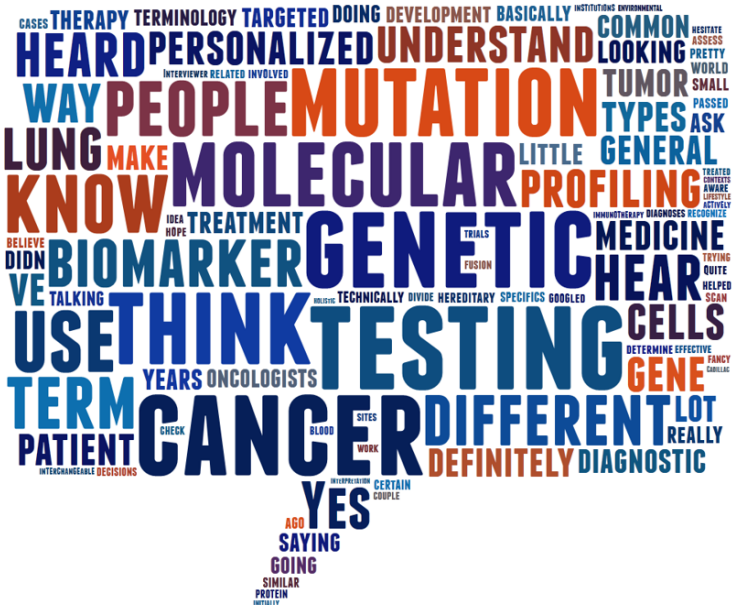
"I remember waiting for the PET scan to find out the stage of cancer. I couldn't stop crying. My doctor never said, 'Here's a support group,' I had to go out and find one. Those ladies have helped get me through… The support group is where I've seen information about testing." (Patient)

Patient Perspectives

Overview

Perhaps the most important source consulted in this audit is lung cancer patients themselves. They must navigate a communications landscape crowded with terminology at a time when mentally and emotionally they may be least able to process all the information coming at them. To get insight, LUNGevity provided patient contacts who are part of the LUNGevity community and who agreed to be interviewed. They ranged from people who had been living with lung cancer for many years to those much newer in their diagnosis and treatment. As well, they had a range of knowledge and direct experience with molecular testing. All the interviewees were open and thoughtful in their comments and generous with their time. To them, we are deeply grateful.

- According to patients, the dialogue includes a lot of competing terms
- Mentions of "genetic testing" are as common as references to "cancer"
- Advice to "know your cancer" is a major theme right now in the patient support community



Familiarity with Terms

In their own words, patients used a variety of terms to refer to the types of testing they experienced with their tumors. Their lack of consistency illustrates that there is no preferred term in the healthcare community. Instead, patients are hearing many technical terms and required to have a high degree of health literacy. Across the interviews, patients referred to the topic as:

- "Making sure my biopsy was analyzed"
- "Gene testing"
- "Genetic testing"
- "Mutation testing"
- "Molecular testing"
- "Biomarker testing"
- "Geno-typing"

When we asked about specific testing terms, patients were most familiar with "testing" nomenclatures. Of all the variations, the most familiar terms were molecular testing, biomarker testing and genetic testing.

- Molecular testing – all sources seemed to understand this term as it related to their experience;

  "I hear it called a lot of different things - everything from gene mutation analysis, to molecular testing, to biomarker testing - but I think molecular testing is a good way to put it."

- Biomarker testing – perceived to be used more in medical field, by scientists/researchers/oncologists, but patients felt they understood it.

  "I think biomarker testing is pretty much the same as molecular testing. That terminology is used more in the medical field. Most patients wouldn't say that. Medical institutions, your doctors, your hospitals, they tend to use more technical language."

Genetic testing is a term that patients hear frequently, which has some advantages and one major disadvantage. On the one hand, the term is relatable and makes the topic of testing more approachable. Patients understand that genes can dictate health or risk of disease, and they appreciate that each person has her own collection and combination of genes. The value of genetic testing is a given, it has some public awareness, and patients found this terminology used in the dialogue about cancer in general (not lung cancer specifically).

"I think genetic testing applies to cancer in general. I think people are aware of that. They have just discovered these things in lung cancer, but they've been around a lot longer in breast cancer, ovarian cancer and some others."

"Yes, I hear genetic testing more than the other terms. It has become a known term with the lung cancer community… I'm still using that term."

On the other hand, the term genetic testing can be confusing to use in the same context as molecular testing. Conventional wisdom on genes and genetics is that they are inherited from your parents. Patients told us that they heard "genetic testing" and assumed the tests were looking for something hereditary. This leads to a new series of questions, and can add another layer of stress for patients, to understand if their lung cancer is something that will be shared within the family. The mental noise this creates seems very counterproductive for patients and their healthcare teams.

"I think genetic testing is becoming a known term, for all cancers. To me it was confusing how something 'genetic' could not be passed down to my children and grandchildren. That was one of the first things I worried about."

"I've had to rethink my own language. I use 'biomarker testing' when I'm talking to people not familiar with it. I was saying 'genetic testing,' but it was confusing, because people think of that as

what's passed down from one generation to the next. For me, 'molecular' sounds too clinical. People can relate to having markers or biomarkers."

"I make the joke that I'm a mutant, a Mutant Ninja Turtle. Truthfully, the word mutant makes me feel weird. It's definitely an easier term than genetic testing. When I say genetic testing, the first thing people say is, 'Oh, so you got this from your family?' I quit using genetic testing altogether. It's just too confusing."

"Cancer is rampant in my family. My daughter was just diagnosed with thyroid cancer. She had the gene testing done. If it comes back positive, I will get tested…. Everyone in the family is very concerned now. They would like to know if lung cancer is genetic, especially since our father had lung cancer [and now I have it]."

When it comes to other terms, mutation testing, molecular testing, and biomarker testing seem to be interchangeable to most respondents:

"Mutation testing definitely is the most used. If you ask an informed patient anyway, they will know what that terminology means."

"I think biomarker testing is really similar to molecular testing. The biomarker is just a particular marker that the scientist, researcher or oncologist will monitor. For example, I get tested every 3 months and they look for change."

The terms that patients were least familiar with tended to be those that are more common among the testing, pharma and bio-tech companies and are less likely to be used in patient resources. These terms include: molecular profiling; molecular diagnostics; companion diagnostic – a term with which they were totally unfamiliar. This poses an interesting challenge to communication between doctors and patients if doctors are using the language of industry and patient are using different terms.

Becoming Aware of Testing

Most of the patients interviewed were diagnosed and had initial treatment without having any molecular testing of their tumor. Among 15 interviewees, 4 recalled testing at the time of their initial diagnosis. The other patient experiences with testing were extremely varied.

- *Plan B or C* – Some patients found out about this type of testing only after other treatments failed or stopped working.

"The doctor raised it after my treatment failed, but he didn't call it molecular testing. He just said it was important to get a sample and find the best treatment for me. We found out I am 'ALK positive', but I don't think he ever said 'ALK positive' -- he just launched into the treatment."

"It came up for me after treatment failed. The doctor thought I was likely to be EGFR, because I was a female non-smoker. He didn't call it molecular testing. He just said it was important to sample and find out the best treatment for me."

- *Doctor Driven* – Some patients were completely in the dark about what they were being tested for until the result came back and they found out they have a mutation.

  "The only thing I understood was that they wanted to do the test. Nobody explained what they were looking for or what it would mean."

  "For me it was part of the protocol. It was part of the process. As I said, my whole upper lobe was removed and the tumor was sent off for testing. I don't remember if a family member or I was asked. I don't remember anybody asking me."

- *Patients Advocating* – Some patients appeared to drive the process, they asked and even had to push their doctors to order the tests.

  "I had a biopsy at the hospital and started chemotherapy. I found out about molecular testing on my own through an online support group. When I brought it up the doctor said, 'let's just wait'… Eventually I switched doctors. The new doctor thought it was so important, they did a full chest open to remove the tissue for testing. It was in a hard place to access. Afterward, the doctor called me at 10pm at night and said he was very excited I had a mutation."

  "I was at [a large academic institution] for my initial line of therapy…. It is considered the best cancer center in the world. They did not test me for ALK mutation until I asked. They do more research than any other cancer center, and my wife is convinced that I would not be here today if I had not asked to have testing done, and she is probably right."

Along the way we heard some of the "best" and "worst" experiences that these lung cancer patients have had with their doctors.

> *" I started going to Tampa for my treatments, because my local doctor was basically telling me to go home until I didn't feel well and then come back to see him. My husband said, 'that is not an option.' So we went down to Tampa and that's when they requested my records. They did the gene testing on me and found out that I had the K-ras mutation. "*
>
> *"My primary care doctor was very proactive. He called me within an hour of the scan. My surgeon was wonderful. She explained everything, and I was nervous but felt informed. With the oncologist, it's been a different story. I couldn't get the tumor markers from him, or I had to fight with them to get a copy. When I asked what it meant he said, 'I don't know. I'll have to look it up.' And he's supposed to be one of the top people at [a center for cancer treatment and research]."*

All in all, there is not consistent communication coming to patients regarding testing. They are getting piecemeal information from their personal networks, their own web research and doctors who may or may not explain the testing or what it means. Feedback suggests that patient support groups are filling an information void. Patients in the interviews said that their understanding about molecular testing advanced after they connected with lung cancer advocacy and patient support organizations. LUNGevity, Bonnie J. Addario, INSPIRE, SurviveIt, GRACE and Livestrong are among the resources mentioned.

"I do think the terminology is a problem…I really feel that the doctors don't have enough time to explain properly. Once I found out I had this KRAS mutation, I didn't really understand it so I Googled it to read about it and find out if there were other treatments that other places have found that maybe [major academic center] was not doing, because this is the other thing, too. Don't forget that the different cancer centers you go to don't all offer the same types of treatment."

Why Test?

Patients underscore the point that the test itself is not the goal. The goal is to find another, more effective line of treatment. Patients perceive that molecular testing and targeted therapies hold the promise of "more accurate" treatments, of care that is "personalized" and more effective.

"It was a gamechanger. I was a year and a half into the lung cancer journey. I went from being a sick cancer patient to having a relatively normal life. It's incredible…. Sometimes I get frustrated that it was not discovered earlier, but everything I've been through makes me who I am."

"There's just one message I'm hearing and one message to it: having your tumor tested for genetic mutations could identify what is driving your cancer. Once that driver is identified, that will determine what kind of treatment you should receive. Certain drugs work better with certain mutations. It's vital. If you know what's causing your particular strain of lung cancer then it narrows down the drugs that should be used to fight it."

"Using chemo, a treatment that's 40 or 50 years old, was not going to work for me. To me, that was the standard stuff that they had on the shelf at the hospital. As far as the difference with targeted therapy, it's amazing. That's what I always tell people in my support group. If you find out you have a mutation, there are other drugs that have less side effects. You've got more choices."

Keeping the end goal in sight seems important for any communication around molecular testing. While testing is the quickest way to the endpoint of effective therapy, it is not the only way. We had one particularly interesting source in the interviews. This patient heard about targeted treatments from a friend and started emailing his doctor to request a brand name drug. Fast forward to today and his cancer is now stable on Tarceva, and they are assuming he has an EGFR mutation. The oncologist says there is no point in testing now as all the tissue sample is dead and cancers can mutate.

"If I have a change, the minute it starts spreading, I will go have genetic testing. It's the first thing I'll do, and I know where I'm going to get it done. We have to assume I have an EFGR mutation, because Tarceva is effective if you have that mutation. But my oncologist says there is no point in testing right now."

Feedback suggests that the "diagnosis" stage is a confusing time for every patient and that patients vary in appetite for doing a lot of research on their own. Sources in these interviews stress that information is needed in multiple formats, at different reading levels, with some repetition and consistency.

"People are unique. Some want to do their own research. Some want to only think positive thoughts or avoid it. We need more than one way to define and explain this stuff. We need entry materials at 5th grade level, and then sources for people to get more details."

"I live and breathe cancer education. I spend hours, days, all the time on it. I feel like knowledge is power, especially in the beginning when it is so overwhelming. For me personally, I have to learn as much as I can. Some people don't want to know. I have to know everything."

For the patient advocates participating in these interviews, the message is simple: "Get your tumor tested." It is one of the first things they advise other patients. But they recognize that terminology and statistics of testing and mutations can overwhelm. What gets them engaged in testing are the resulting treatment options or the possibility of new options and the promise of potentially more effective treatments for them.

"When you're first diagnosed, you don't know what any of this means. That's when it's most confusing. Now I'm getting so many requests, I've put my key points into a form letter that I customize and send when I meet new patients."

"There is so much information, when you are a new patient it takes time to understand. I was lucky in a sense. I had a dad who was a doctor. I was educated. I was able to understand and had people around to help me."

"I have an EFGR mutation. There are numbers and categories involved, but I don't know all of that…. Everything I've learned because I wanted to know about lines of treatment. I Google a lot. I have a need to know everything."

Call to Action

The patients interviewed had two very strong calls to action for fellow cancer patients. First and foremost, they said, everyone needs to have testing and that testing should include ALL known mutations.

Patients who know about the types of mutations critique that their medical teams are typically focused on the more common types of mutations or are only testing for mutations that match FDA-approved drugs. This makes sense in practice, since these would be the only tests covered by insurance. However, patients feel it is short-sighted and they wish their doctors were more aware of drugs in clinical trials.

"We have to be prepared and be our own best advocate. Patients need a nice, easy document to request 'I'd like to have my tissue tested for these gene mutations.' That needs to be updated as they discover new mutations and be presented along with the targeted therapies."

"It's a huge deal. It's a game changer. If you're positive for a mutation, you can take a pill every day. It could extend your life. It's not curing me, but it's buying me time."

"It's important to get tested, because some cancer is resistant to chemotherapy. I get so aggravated when I think about the chemotherapy and how it was weakening my body."

Second, they want lung cancer patients to know that testing could extend their lives; it could change their outcome. Even though not all people will have a mutation for which there is an

approved therapy or a therapy in clinical trials, the science is advancing quickly (as is the medical practice that follows).

> *"Get your tumor tested. Knowing your specific mutation could save your life."*
>
> *"I didn't expect to be here 5 years later. In my opinion, it won't be long before lung cancer is not a terminal diagnosis. I'm excited about the future. I think the answers are going to be in immunotherapy and targeted therapy."*
>
> *"Targeted therapies mean a regular life. You never feel that sick. People need to know that to remain hopeful."*
>
> *"There needs to be more awareness. Here is what we currently know about different mutations. But that is not all; we're learning so fast. The message needs to be centered on the idea of hope…. I asked about the lifespan of this therapy I'm on, and the nurse said it's normally one year. I'm approaching that. It was an a-ha moment. Because I'm not scared. It would be inconvenient to have to find something else and change, but I'm not scared that I'm going to die. I don't worry anymore, because it's all changing so fast."*

Caveats to Consider

A question that we wanted to explore in the interviews was whether aggressively promoting testing could have negative consequences, if patients would see any risk in overpromising or offering false hope. Across the interviews, patients were definitive and consistent in their opinion that promoting testing would only be positive for patients. They said the tone of the message could be hopeful while acknowledging that a relatively small portion of the patient population will have an identifiable mutation.

> *"I think you can say it's worth a try, and that is not giving people false hope…. Very few people have the mutation, but you might be that one. You won't know until you have it tested."*
>
> *"A lot of people will say, 'I am not going to go through this or that, if I am going to die anyway.' People need to know that if you get this molecular testing and you have a mutation, your prognosis is a lot better. I think that messaging needs to be louder. The conversation needs to be started. Then it's up to the doctor to not get them overly excited but have a positive, upbeat conversation about testing."*

Another interesting consideration that emerged from the discussions is that patients told us molecular testing is not a practice that's "one and done." Those well versed in the topic said that testing was needed periodically. For example, one tumor may or may not have a mutation, and that result may not be the same if they get a new tumor. More than one source also makes the point that an individual's cancer can change over time. We also heard instances where multiple tests were needed before the mutation was identified.

"What I understand is that cancer can mutate. It can change your mutations. Is it because they change on their own or does treatment change your mutation? My doctor said that we don't know for sure. We know that mutations change over time, but we don't know why that is."

"Sometimes I get frustrated that [my mutation] wasn't discovered earlier. One theory is that it wasn't discovered because of the different samples being tested; there was my original biopsy and then the tumor tissue from my surgery. Another theory is that the testing got more sophisticated in the time between my original diagnosis and when it was finally discovered. I never got a clear answer as to why it wasn't discovered sooner."

A third consideration hinted at in these interviews is the issue of affordability. Only a few patients in these interviews touched on the issue of affordability and their awareness of what insurance will cover or not. Some clarity around this would be helpful as part of education and activating patients to seek out testing.

"I went on a clinical trial that I'm still on, and that is really important for a lot of reasons. First, because it obviously saved my life. Second, because Medicare doesn't cover targeted therapies, I wouldn't have been able to pay for a targeted therapy. So finding the trial was amazing. It saved my life twice, because I never could have paid for targeted therapy."

"I highly recommend tumor testing. I think for my daughter it only cost like $24."

Education Opportunities

These interviews support the notion that more education is needed so that lung cancer patients understand the issues and the value of molecular testing. A question for LUNGevity and partners is whether patients need to understand the basic science to know the importance of getting tested. From talking with these patients, we would say maybe not. According to these patients, the science is developing rapidly, it is very challenging information to digest, and the technicalities are only relevant if you have an identified mutation.

"Well, you have to realize that the cancer is not one disease. Everybody that has cancer has a separate cancer. It needs to be personalized. And in order to make it personalized, you've got to do molecular testing. You've got to do biomarker testing. That's the message that I would like organizations to tell."

"I think it should be simple. It should be something to the effect of get your tumor tested. The longer a statement is, the more people's eyes glaze over. 'Get your tumor tested.' That's right to the point. At least that would pique interest and maybe patients would ask for it."

A major finding from these interviews is that resources and information are lacking where they seem needed most, in the clinic setting as patients are learning of their lung cancer diagnosis.

"The one thing that I want to recommend is getting more information out to patients at clinics. At my care center the only information on the cancer billboard is from the American Cancer Society. I am not very fond of that organization. I would like to see a more equal representation of these advocacy groups."

"At my support center, they go all out for breast cancer. All the books and tapes are for breast cancer. They do nothing for lung cancer awareness month. It's awful. And lung cancer is killing more people."

Feedback suggests there is value in multiple formats, in traditional and new media. Patients weighed the pros and cons of different media in the interviews. Using a range of media, LUNGevity and others have the opportunity to create a surround sound effect.

- Print – *"I like handouts and written materials that I can carry with me. 'Crazy Sexy Cancer Tips' was a book that really helped me. It gave me the Cancer 101, helped me set up my binder, and helped me set some rules for myself. It was very empowering."*

- Fact sheets – *"Easy to read. Not too wordy. A one-page printout that talks about, 'Here are some resources that you can get to.'"*

- Video & webinars – *"What they did was they had webinars and they also had materials. They just help you understand how the research worked. You learned the basic science and that's all really that it is but you come out of it. What you do is you go through the webinars."*

- Blog & patient stories – *"Learning from other patients has probably been the most significant resource for me."*

Some patients expressed a preference for digital tools. They liked interacting directly with patients/advocates like themselves, telling their own stories. At least one source mentioned mobile-friendly information being important, easily accessible, up-to-date.

"I am always on my handheld or my iPad. For example, with the website INSPIRE, it might be a few days before I go in there to check to the message boards, because I have to be at my computer. It is too hard to do it on my iPhone or my iPad. It is just more cumbersome."

In addition to promoting testing and general education on the topic, LUNGevity and partners could serve this community by helping patients understand more about clinical trials. Sources told us that it was difficult to find information about lung cancer research. Patients also express some hesitations about participating. Shedding light in this area could benefit medical researchers and lung cancer patients themselves.

"It's extremely difficult to understand. Even oncologists have a difficult time keeping up with the latest clinical trials and qualification requirements to be able to enter into those trials."

"People with lung cancer run out of standard options, and they are looking for answers, whether it is an approved treatment or a clinical trial. I think streamlining the information, helping patients find new research and clinical trials would be one thing they could do to help patients."

"It is a little scary to be part of this clinical trial. The drug has only been tested on animals before, and you don't know that it's going to help."

"With the clinical trials, I don't understand it at all and am really nervous about it."

"It is pretty discouraging to read. If you go online, and read statistics, it is pretty discouraging." (Patient)

"I trust my local oncologist and the specialist. Both told me to stay offline. They said, 'Don't research this stuff. You'll drive yourself crazy.' There's a lot of misinformation online and bad advice. I've come to find out about testing through my mentoring with other patients." (Patient)

Appendix 1. Research Approach and Method

For each source Edge Research followed a standard procedure:

1. We first reviewed the home page of the site for any relevant terms and content related to lung cancer and/or lung cancer tumor testing to determine if an obvious path to relevant content was available for the user. If so, that content was included in the analysis.
2. Next we used the site's search function (using advanced search when available) to search each of the terms included in the analysis (see Figure 1).
    - In the case of lung cancer focused organizations, terms were searched as they appear.
    - In the case of organizations with a broader medical focus, terms were searched in conjunction with the term "lung cancer."
    - It is important to note that we took the approach of a layperson – typing the term into the search box or, where no search function was offered, doing a Google search of the site.
3. Material was included based on some expectation that it is intended for a patient or general audience – as opposed to technical information, information for journalists, investors, etc.
4. In conducting a site-search of terms for each site, we took note of the number of results returned, regardless of whether we included the content in the analysis. These search results reflect the gamut of content at the site from live pages to press releases to blog posts, etc.
5. Relevant content was pulled from the site (up to 10 pages) and then sorted and analyzed by:
    - Main idea/key points/terms used
    - Type of message (tone, explanation, benefits, any call to action)
    - Primary messenger
    - Intended audience
    - Examples of outreach inventoried
    - Bottom line (organization's position or intended action)

In addition, Edge Research also conducted a series of 15 in-depth interviews with lung cancer patients to gain insight to their understanding of and experiences with molecular testing and related procedures and therapies. The results of these interviews are reported along with the communications audit. Where appropriate we have included verbatim quotes from the interviews, but they are unattributed to protect respondents' anonymity and privacy.

Appendix 2. Summary of Terms

Search Terms in Use by Sector

Searched Terms	Pharma/BioTech	Testing	Gov't/Private	Cancer Orgs	Lung Cancer Orgs
Genetic Testing	77	65	1082	295	395
Molecular Testing	173	270	742	124	331
Mutation Testing	21	111	485	143	274
Biomarker Testing	109	172	390	29	156
Genetic Diagnostic	26	66	770	111	109
Molecular Diagnostics	113	231	798	94	98
Mutation Profiling	22	78	254	2	88
Molecular Pathways	74	91	787	35	88

Additional Terms Observed

Pharma/BioTech	Testing	Gov't/Private	Lung Cancer Orgs
Biomarker panel			
Companion diagnostic	Companion diagnostics		
	Comprehensive genomic profiling		
		Genomic profiling	Genomic testing
		Individualized medicine	
Molecular companion diagnostic tests			
Molecular profiling	Molecular profiling		
Personalized medicine		Precision medicine	Precision medicine
		Tumor gene panel testing	
		Tumor marker tests	