

# Inconsistencies Within Biomarker Test Reports Provide Opportunities for Future Patient Education



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## ABSTRACT

Targeted therapy and associated biomarker testing for somatic (acquired) alterations and other types of non-genomic biomarkers are becoming more common for the treatment of patients with lung cancer. Yet, the reports of test findings for providers to use in discussion with patients are not always written with the patient in mind. To support shared decision making, increased patient education may be needed to explain test results and how patients can communicate with providers about results and next steps for treatment. The purpose of this study was to identify differences and commonalities within biomarker test reports to inform future patient educational interventions.

**METHODS:** An audit process was conducted for 16 biomarker reports from commercial, governmental, and academic entities received from December 2020 to May 2021. Qualitative coding conducted by a minimum of 2 researchers was used to structure and categorize the information in the reports.

**RESULTS:** The commercial/government report audit included 3 FDA companion diagnostic (CDx) reports and 9 laboratory-developed tests (LDTs). Overall, reports had a range of 3-37 pages in length; 3 of the 16 included a cover page including patient characteristics. Reports varied on what and how much patient information was included. Reports were inconsistent on including lab contact information, certification of results, as well as the information used to describe the sample collected. 14 reports included a results summary, but the information contained in the summaries varied widely, particularly between the commercial/government and academic reports. Reports used different terminology when describing therapeutic options; not all referenced FDA approval. Terms for biomarker were not standard: the terms “variant”, “mutation”, “biomarker”, “alteration”, and “gene” were used interchangeably. Only 4 reports included a glossary of terms. 12/16 reports contained clinical trial information, but there was variation in the placement and amount of trial information.

**CONCLUSIONS:** Biomarker testing results reports are inconsistent in the type of information they provide, raising the possibility of confusing patients and/or driving uncertainty about next steps. Developing education on interpreting biomarker test reports and communicating with providers about the significance of the results on a patient’s treatment decision is challenging, particularly for a patient audience that may not have sufficient health literacy. Specific recommendations for education will include consistent use of plain language terminology for biomarkers and treatment options, interpreting results, and engaging in next steps for clinical trials.

# OVERVIEW AND METHODOLOGY

Misunderstanding biomarker testing results reports often inhibits informed conversations between providers and NSCLC patients. The objective of this audit was to help identify the nature and number of report components that could be further explained in patient education materials on how to read and use a biomarker report in conversations with a healthcare provider. By learning more about the landscape of testing results reports, it will be possible to create comprehensive educational content that is structured around the variety of reports that patients may encounter. Ultimately, LUNGeivity aims to empower the lung cancer community to increase participation in shared decision-making with their multidisciplinary healthcare team by having a better understanding about what information is in their reports and how to ask providers about the report to get the answers to questions about their cancer and their care.

## Report Selection and Audit Process

LUNGeivity secured sample biomarker testing results reports from laboratories, testing companies, and a government research laboratory. The reports represented each organization’s most recent “template report”. For academic reports, patients and providers in the LUNGeivity network provided either personal reports or template reports from their hospital lab. Academic reports dated from 2020 and earlier.

A total of 16 biomarker reports were analyzed: 12 from commercial or governmental entities and 4 from academic organizations. Of the 12 commercial/government reports, there were 3 FDA companion diagnostic (CDx) reports and 9 laboratory-developed tests (LDTs) (Figure 1). Fourteen commercial lab reports were for tissue-based biomarker testing and 2 were for blood-based biomarker testing (liquid biopsy). All 4 academic reports were for tissue-based testing.

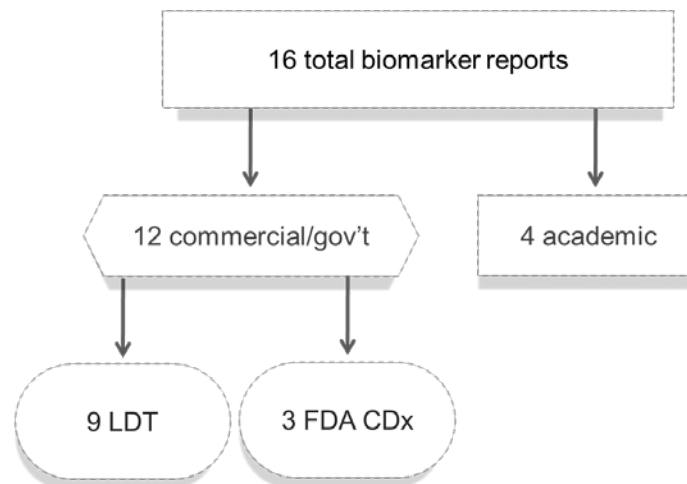


Figure 1. Biomarker reports included in this audit.

## **Analysis**

Qualitative coding was used to structure and categorize the information in the reports. Reports were coded by at least 2 researchers and differences were resolved prior to final report development. Analyses were used to understand potential pain points and/or barriers for both patients and healthcare providers to identify specific educational interventions that would be beneficial. Where appropriate, reports from the commercial/government entities and academic centers were compared.


## **Focus group verification**

Patient focus groups were conducted in October-November 2020 that created an opportunity to gather initial feedback from patients from varying socio-economic status, race/ethnicity, and regional backgrounds to provide input on how they are using the reports currently with providers. Additional focus groups with a similar cohort of patient participants and multi-disciplinary clinician team members were conducted after the audit in June 2021 to validate and provide context for the audit results.

This paper highlights the results of the report audit, focusing on 5 main themes: 1) an overview of the characteristics of the reports, 2) how the reports summarize biomarker testing results, 3) how the reports summarize therapeutic implications, 4) differences in terminology between reports, and 5) clinical trial information provided.

# REPORT CHARACTERISTICS

Overall, reports of biomarker testing results varied in total length of pages, whether they contained a patient cover page, and inclusion of reference page(s) (Table 1). The longest report was 37 pages and the shortest was 3; on average, reports from commercial/government organizations were twice as long as those from academic institutions. Only 3 reports included a patient cover page. Nine reports include reference pages; those that did contained an average of 3.5 pages of reference.




“I wish there was a patient version. Take all that external information out and just provide the patient with a small not 10, 12 pages, but just with patient information. So it's easy for them to read.”

ONCOLOGY NURSE PRACTITIONER

Only 7 reports indicated if they were “final” or not (Table 1), potentially giving healthcare providers uncertainty on whether additional reporting would be provided.

Only half of the commercial/government reports and 3 academic reports included a section on Surgical Pathology indicating the characteristics of the sample used (ie, specimen site, date/time collected, tumor cellularity, etc.) (Table 1). One commercial report contained an image of the tumor stain on a slide for additional context. There was little consistency on the tissue attributes described in this section in each report. Information missing from this section could mislead healthcare providers on the reliability of the report, including whether there was biopsy degradation due to time gaps from collection to testing delivery or details on the sample quality/quantity.



“The results usually come in as a 14-page or 20-page reports that are PDFs and they're downloadable from a web link or they're faxed to you and hard to read is just not the way to do this.”

THORACIC MEDICAL ONCOLOGIST

**Table 1:** Overview of report details

|                              | Commercial/gov't (n = 12) | Academic (n = 4) |
|------------------------------|---------------------------|------------------|
| Page length (mean, range)    | 15 pages (6-37)           | 7 pages (3-12)   |
| Contains patient cover page? | 3/12                      | 0/4              |
| Contains reference page?     | 9/12                      | 4/4              |
| Report indicates “final”?    | 5/12                      | 2/4              |
| Surgical pathology section   | 6/12                      | 3/4              |

Reports varied considerably on the type and quantity of patient information provided, such as the disease type, patient characteristics (eg, age, gender, address, phone number), cancer stage, medical record number, current therapies, and the name of the ordering physician (Table 2). Not all the reports included a patient identifier on all pages of the report.

**Table 2:** Patient information contained within reports

|                           | Commercial/gov't (n = 12) | Academic (n = 4) |
|---------------------------|---------------------------|------------------|
| Patient date of birth/age | 11/12                     | 4/4              |
| Cancer stage              | 9/12                      | 4/4              |
| Medical record #          | 2/12                      | 4/4              |
| Disease type              | 12/12                     | 3/4              |
| Sex/gender                | 11/12                     | 3/4              |
| Ordering physician name   | 6/12                      | 3/4              |
| Tissue collection date    | 2/12                      | 2/4              |
| Accession date            | 0/12                      | 2/4              |
| Date reported/completed   | 0/12                      | 2/4              |
| Patient address           | 9/12                      | 0/4              |
| Phone number              | 2/12                      | 0/4              |

While most, but not all, biomarker reports contained the name of the lab or center performing the testing, information varied on the location, contact information, results certification, signature of the lab director, and contact information for the certifying pathologist (Table 3).

**Table 3:** Laboratory information contained within reports

|  | Commercial/gov't (n = 12) | Academic (n = 4) |
|--|---------------------------|------------------|
| Lab/Center name                                | 12/12                     | 3/4              |
| Location                                       | 10/12                     | 3/4              |
| Contact information (any)                      | 10/12                     | 3/4              |
| Certification of results                       | 9/12                      | 1/4              |
| Lab director signature                         | 9/12                      | 2/4              |
| Contact information for certifying pathologist | 5/12                      | 3/4              |

Only 4 of the commercial/government reports and 1 academic report clearly indicated the intended audience for the reports. While these reports will likely go directly to the ordering physician, data from the focus groups suggest that some patients want to receive, read, and understand all reports themselves. Some want the physician to read the report and only provide them with information the physician deems relevant.

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Contact information of the testing laboratory and certifying pathologist puts the impetus on the healthcare provider to track down this information if they have any questions about the report. In some limited circumstances a patient may have questions about their results and want to contact the certifying pathologist directly, particularly if they are unable to secure adequate information from their oncologist. Including the contact information for the certifying pathologist will facilitate this process for the patient/caregiver at a time when they want clear answers as quickly as possible.

Even if patients are not the intended audience, biomarker reports would benefit from including more patient friendly language as the assumption should be that at some point a patient or caregiver will end up seeing this document.

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# RESULTS SUMMARIES

Among commercial/government reports, 10 of the 12 sample reports included a summary of the results in the first page or two of the report. The information contained in these summaries varied widely (Figure 2). Common elements found in most report summaries included a review of drugs that could be used with a particular biomarker (10 of 12 reports) and clinical trials relevant to the particular patient (8/12). Elements not commonly included in report summaries include drugs that should NOT be used for the patient and levels/tiers of evidence. Five reports contained information on only the mutations that were found and 4 included information on all the mutations that were tested.

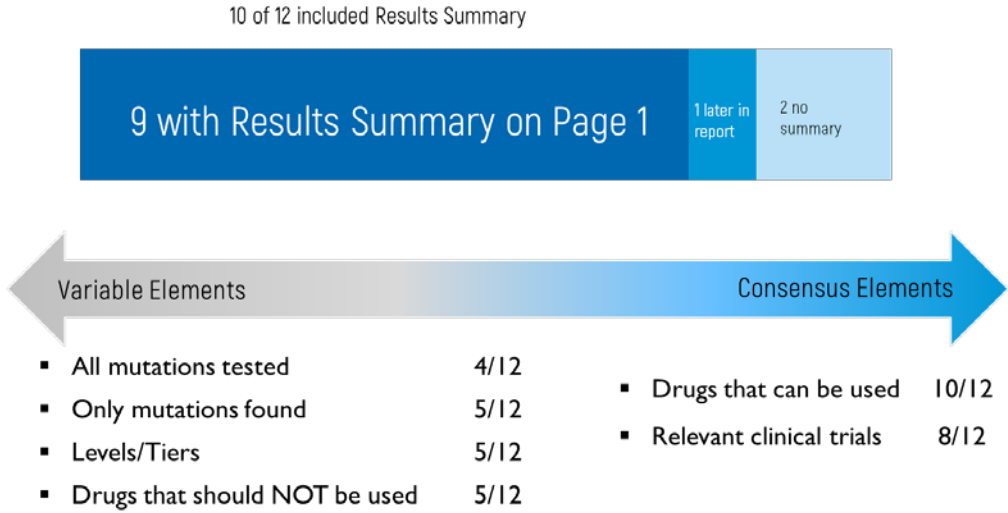



Figure 2. Ten of twelve commercial/government reports included a results summary.

Differences in the report summaries highlight differences in the perception each organization has on the importance of information, such as whether showing all tested mutations shows thoroughness or if this level of detail is unnecessary. There is no consensus or standardization on the types of information found in results summaries, which could cause confusion for a healthcare provider. Further, reports differed on how they are presenting summaries. While most generally used a table format, the types of information highlighted within in was variable (Figure 3). For example, some reports named biomarkers broadly while others highlighted specific nucleotide changes that resulted in the formation of a specific pathogenic variant.



“I would want more simplification. So what actually benefits me specifically? I'd rather it be more detailed for me personally and leave whatever's irrelevant out.”

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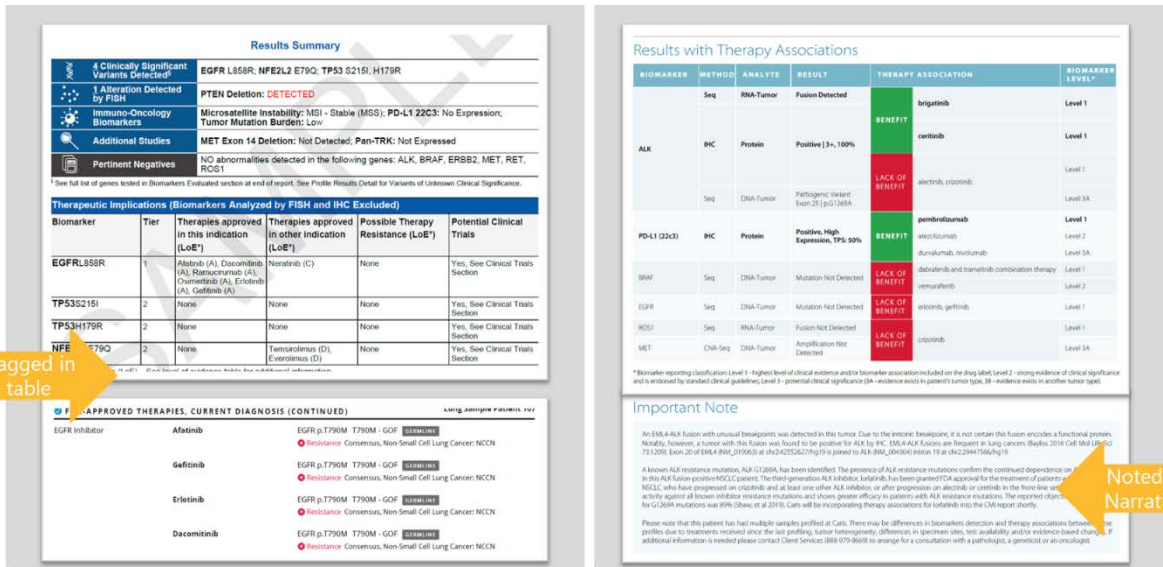


Figure 4. Reports summaries varied in how they described therapeutic implications.

All four academic reports included a results summary on the first page, but they contained much less information compared to the LDT and CDx reports (Figure 5). Of the common elements in most commercial/government reports, only 1 academic report contained information on the drugs that can be used and one contained information on relevant clinical trials. Three of the academic reports provided information only on the mutations that were found and 1 included information on all tested mutations.

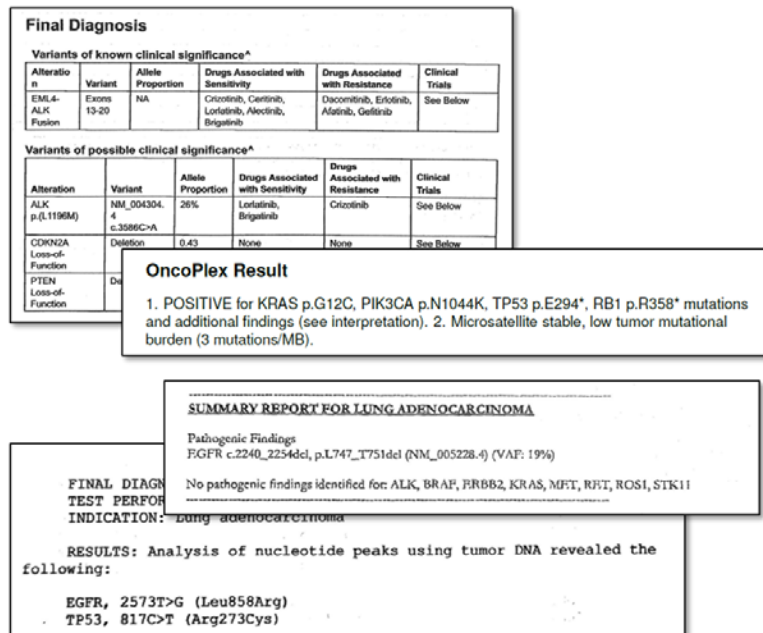


Figure 5. All 4 academic reports included a results summary on the first page, but they contained much less information compared to the LDT and CDx reports.



“The best thing was it broke down which ones they found, so I had four that they found. And it told me how much amplification it was, whether it's low, high or medium, and the therapies that were available for each one. And then it also said that I had 73 genes tested. So, the first page they gave me, which they call the therapy finder page, was the most interesting because it has everything I need in one shot.”

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Lack of consensus on the information provided in these summaries and varying methods used to highlight results implies differences in priority and perceived importance and may lead to increased healthcare provider and patient confusion.

Further research may be needed to determine whether less information is more useful for the oncologist and the patient, or if additional context and explanation of the findings would make these summaries clearer.

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# THERAPEUTIC IMPLICATIONS

All of the audited biomarker reports contained information on available or preferred treatment options based on the testing results, however these results organized the options differently, by characteristics such as the detected biomarker, level of evidence, and specific therapy (Figure 6). Most commercial/government reports (9/12) included therapeutic options for NSCLC as well as other disease states, while the other 3 only included options for NSCLC. Three reports also included clinical trial information in the same section of the report as the therapeutic options.



Figure 6. The commercial/government reports provided treatment options differently, organized by the detected biomarker, level of evidence, and/or therapy.



“There were parts of the report that there was some treatment on some of it, and on other parts, it said there was no treatment. So, I wanted to know, were they working on treatments? What were they doing with that?”

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Several of the commercial/government biomarker testing reports, but not all, included disclaimers, referencing that treatment decisions are the responsibility of the physician (8/12 reports), the provided options have no guaranteed clinical benefit (5/12), and there is no guarantee of insurance reimbursement (2/12).

Only 1 of 4 academic reports audited included therapeutic implications, reporting on the therapeutic options for patient's disease state (and other disease states), as well as disclaimers that the treatment decisions are the physician's responsibility.

The amount of explanatory information included about the results, what is known about the biomarkers, possible treatment responses, and new findings from clinical trials varied widely. More typical inclusions consisted of an explanation of the test or tests used to determine the mutation, a brief explanation of the mutation or note of why it is significant/known to be oncogenic, and a note of any associated therapies. Less frequent topics explained included clinical trial results on potentially relevant therapies and recommendations for patient treatment.

One report included over 4 pages solely on EGFR, explaining the background of the gene, effects of mutations, FDA-approved therapies in both the specific tumor type as well as other tumors, and relevant clinical trials.

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Like many of the other sections, the type of therapeutic information varies from report to report, prompting questions on the usefulness of the information provided. How much background information on the individual genes is necessary? Is the purpose of the report to inform clinicians about the mutations in an individual patient or teach about biomarkers and associated therapies? Is there value in including therapies outside of NSCLC for patient/provider conversations or does that distract from the focus?

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**Table 4:** Variability in biomarker terms used in reports

| Term             | Variations of term  | Commercial/gov't<br>(n = 12) | Academic<br>(n = 4) |
|------------------|---|------------------------------|---------------------|
| Variant          | Variant of uncertain significance,<br>Variant of unknown significance,<br>Genomic variants, Somatic variant | 6/12                         | 1/4                 |
| Mutation         | Mutations of interest, Mutation<br>frequency  | 6/12                         | 3/4                 |
| Biomarker        | Clinically significant biomarker,<br>Immunotherapy biomarker, Immuno-<br>oncology biomarker                 | 6/12                         | 1/4                 |
| Alteration       | Genomic alteration, Somatic<br>alteration   | 4/12                         | 2/4                 |
| Marker           | Clinical trial markers,<br>Immunotherapy markers, Targeted<br>therapy markers                               | 2/12                         | 0/4                 |
| Gene             |   | 2/12                         | 3/4                 |
| Genomic findings |   | 2/12                         | 1/4                 |

*Terms used in only one report: Germline, allele fraction, mutant fraction, fusion*

Seven out of the 16 audited reports referenced “levels of evidence” but only 5 included a definition. Six reports used the term “level” and 2 reports used the term “tier” (one report used both “level” and “tier” terminology).



“I had to figure out on my own that your three top terms, biomarker, molecular and genomic, were all the same thing.”

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Using a variety of terms, both across reports and within the same report, may cause confusion. Some terms (clinically significant vs. unknown significance) are more specific, while others (genomic alteration, mutations of interest) are less clear.

For physicians who may be receiving reports from multiple labs, the lack of standardized language may make interpreting results more difficult. Do descriptors like “benefit” have an impact on treatment decisions?

For patients, terminology that is unclear about the benefit or unclear if the therapy is beneficial for their indication or relevant to other cancers may be confusing.

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# CLINICAL TRIALS

Twelve of the 16 audited reports provided information on clinical trials (11/12 commercial/government reports and 1/4 academic reports). As with other data points, elements varied in this section of the biomarker testing reports. Items found in most clinical trial sections included the trial ID and name, targeted biomarkers of each trial, the trial study phase, trial location, and a disclaimer that all trials may not be included (Figure 8). Items not commonly found were websites with more information, a phone number/email to contact a trial site, and a disclaimer that the healthcare provider has a responsibility to research trials.

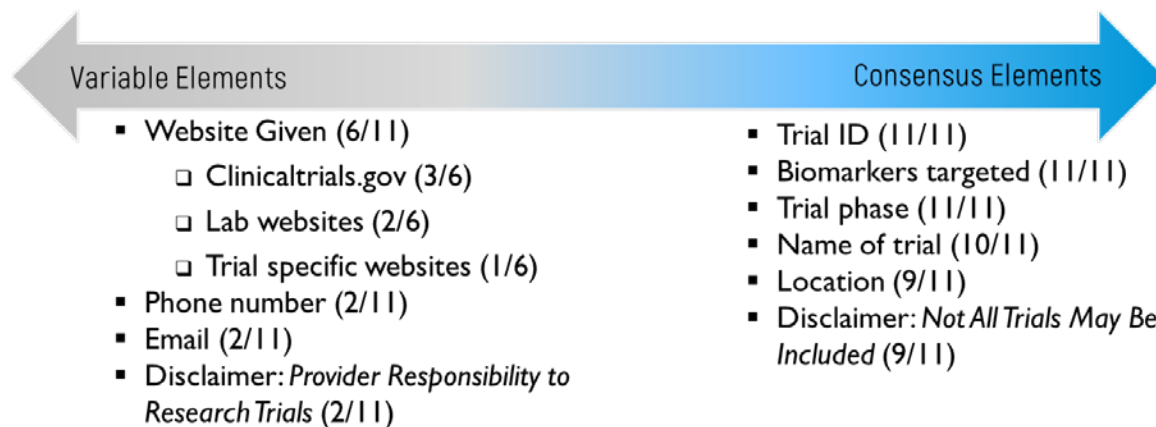


Figure 8. In the commercial/government reports, 11/12 included clinical trial information of some kind, however the specific type of information varied by report.



“It’s impossible for a lay person to follow this. It’s just not reasonable and not possible. But these reports actually can be misleading because for example, it listed the EGFR mutation with links to trials. That’s reasonable, but then it also listed for the p53 and the NFE2L2. So, a patient will see this and, oh, that NFE2L2 has a catchy name. Why don’t I try the clinical trial for that instead of taking osimertinib? That would be a huge mistake. So really this is more misleading than helpful in this patient.”

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While most report categorized clinical trials by biomarker, one categorized it by treatment. Some reports further organized by location, target therapy vs. immunotherapy, or age range inclusion criteria for pediatric patients (Figure 9).

**2.1.6 BIOMARKER-MATCHED CLINICAL TRIALS**  
Trials Prioritized By Clinical Specificity\*

| Markers | Trial ID    | Title  | Phase   | Targets         | Locations/contact  |
|---------|-------------|--|---------|-----------------|--|
| 1 EGFR  | NCT03076164 | A Phase 1/2 Trial of Trametinib and Erlotinib in Patients With EGFR-Mutant Lung Adenocarcinomas and Acquired Resistance to Erlotinib | Phase 1 | EGFR            | Overall contact: Helena Yu, MD, yuh@mskcc.org, 646-888-4274<br>NJ (3), NY (4)  |
| 2 EGFR  | NCT03944772 | Phase 2 Platform Study in  | Phase 2 | CD24, EGFR, MET | Overall contact: AstraZeneca Clinical Study Information Center, information.center@astrazeneca.com, 1-877-240-9479<br>CA (5), MA (3), MD (1), NY (1), TX (1), WA (1), Denmark (2), Japan (6), Korea, Republic of (4), Netherlands (5), Norway (2), Spain (5), Sweden (2) |

**By Variant & Disease** (Left side of image)

**Including Location** (Middle of image, pointing to Locations/contact)

**Including Contact** (Right side of image, pointing to Targets)

Figure 9. Some reports further organized by location, target therapy vs. immunotherapy, or age range inclusion criteria for pediatric patients.

Differences in elements contained within the clinical trial section lead to increased patient and provider confusion. Are all potential clinical trials included? How do the organizations that develop these reports keep up-to-date with available trials? When were databases accessed to know if the provided trials are up-to-date?

Additional details would be useful to help an oncologist determine whether to proceed with FDA-approved therapy or try to quickly move a patient to a clinical trial.

# CONCLUSIONS AND EDUCATIONAL RECOMMENDATIONS

Biomarker testing results reports are inconsistent in the type of information they provide, raising the possibility of confusing patients and/or driving uncertainty about next steps. Based on the results of this audit on biomarker testing, the following would be beneficial for future educational initiatives:

- The lack of standardized language might make interpreting results more difficult if physicians are receiving reports from multiple labs. For patients, unclear terminology could make information confusing.
- It is uncertain whether longer report lengths help or hinder the oncology team with determining a treatment plan. Differing levels of information contained within the report could indicate that how these reports are used is not well understood.
- A lack of contact information for the lab or pathologist could create a significant clinician time burden if there are any questions about the report results.
- Consistent inclusion of surgical pathology and tumor percentage information could be a useful feedback loop to the physician who performed the lung biopsy.

Developing education on interpreting biomarker test reports and communicating with providers about the significance of the results on a patient's treatment decision is challenging, particularly for a patient audience that may not have sufficient health literacy. Development of a *How to Read Your Biomarker Testing Results Report* educational guide will make the information in the report about their biomarker status accessible and comprehensible, having positive implications on treatment discussions between patients and their doctors.

Finally, creation of a patient-provider tear pad may be useful, including features such as:

- Plain language terminology for biomarkers and treatment options,
- Key points to call out in patient-provider conversations when interpreting results,
- Addressing how/whether to engage in next steps for clinical trials.



## CONTACT

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**ACKNOWLEDGEMENTS:** This study was supported by LUNgevity Foundation. Edge Research performed the audit of the biomarker testing reports. Professional medical writing and editorial assistance were provided by CE Outcomes, LLC. Special thanks to the Association of Community Cancer Centers (ACCC), the Association for Molecular Pathology (AMP), the Advanced Practitioner Society for Hematology and Oncology (APSHO), and the International Association for the Study of Lung Cancer (IASLC) for their engagement in this effort.



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