Lung Cancer Outcome Improvement through Genotype-Specific Care

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Summary

Lung cancer is the leading cause of cancer-related death for men and women in the state of Indiana and across the country. While earlier diagnosis and new pharmaceutical innovations have improved five-year survival rates, disparities in access and responsiveness to new therapeutics continue to prevent major improvements in lung cancer prognosis. A more personalized approach to treatment comes from genetically characterizing the tumors of lung cancer patients through the most comprehensive genetic screening available. Biomarker-guided treatment for lung cancer patients shows markedly improved responsiveness to treatment compared to traditional therapeutics. While many states, including Indiana, have passed legislation to mandate insurance reimbursement of biomarker testing, the policy does not explicitly include the most advanced and meaningful screening. Biomarker screening to date is driven by determining eligibility for specific targeted therapies, but its true power could be realized by including more comprehensive characterizing to allow correlation between genetic abnormalities of tumors, disease progression, and responsiveness to treatment. Utilizing this broader-based strategy will improve treatment and prognosis for current patients and provide data for the discovery of new potential therapeutic targets.

Biomarker testing for lung cancer can provide more personalized treatment and better prognosis for patients, but available technology is underutilized.

Prior to the early 2000s, treatment for lung cancer was largely determined based on the origin of the cells involved (squamous vs. nonsquamous) and tumor node metastasis (TMN) stage (Spiro & Silvestri, 2005). Using these diagnostic benchmarks, combination therapies —including platinum-based chemotherapies — were the standard of care (Schiller et al., 2002). While genetic analysis was emerging, it was not used to guide differential diagnosis (Lynch et al., 2004). Prognosis following diagnosis of lung cancer, particularly late stage, was bleak. Response rates ranged from 19–32%, with a median survival rate of less than 8 months, and a 1-year survival rate of around 30% (Schiller et al., 2002).

The early 2000s saw the beginning of the biomarker era in treatment of all cancer types. Following FDA approval of drugs to target genetic abnormalities within lung tumors accompanied by biomarker testing to guide treatment, dramatically improved responsiveness (70% vs. 47%) was achieved (Johnson et al., 2005). This historic event marked the first step toward personalized cancer treatment. The dramatic increase in response to treatment was impressive, but the translation into increased progression free survival (PFS) has been less pronounced. The largest PFS reported is less than 4 months (Solomon et al., 2014). The lack of major improvements in PFS largely stems from the late TMN stage at which lung cancer is typically diagnosed. Thus far, biomarker testing affects treatment choice and can be predictive of outcome but has not shifted the TMN stage at diagnosis.

While biomarker screening has provided a movement toward more personalized medicine, accessibility to this type of testing remains uneven. While many patients are receiving some biomarker screening, the testing is to determine if a certain drug is indicated by the presence of a specific mutation. That approach, however, limits not only the personalization (as it is only based on a single mutation, not the repertoire of tumor mutations) but also restricts the ongoing improvement of targeted therapy.

Current biomarker screening does not provide guidance for treating all lung cancer patients.

From 2004 until the present, the number of lung cancer patients receiving at least single gene biomarker scanning has increased but the percentage of eligible patients has not increased proportionately (Figure 1). This is driven largely by the expanded repertoire of pharmaceutics that target specific mutations and the advancement of biotechnology.

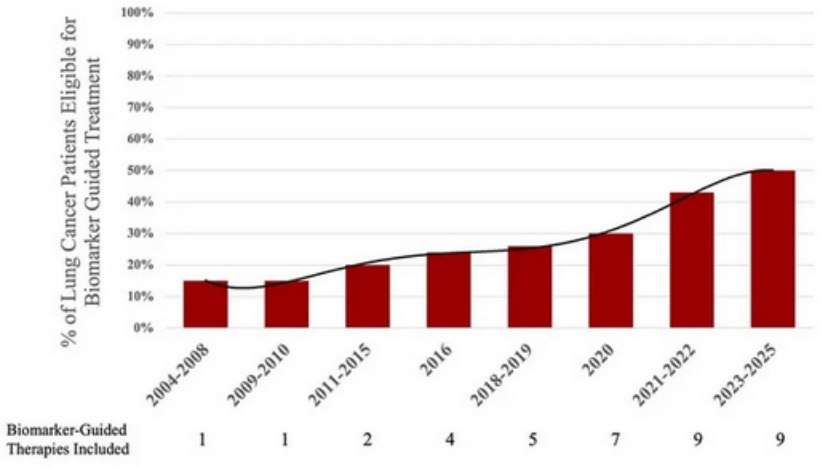


Figure 1: *Eligibility of Lung Cancer Patients for Biomarker-Guided Therapy*

Note: Percentage of all lung cancer patients estimated to be eligible for biomarker-guided treatment. Data is based on cohort studies done at or around the time of FDA approval and/ or increased usage for new biomarker targeted therapies, which results in a range in year for some data points. 2004 –2008 (Michelotti et al., 2022); 2009 –2010 (Gandhi et al., 2018); 2011–2015 (Kazandjian et al., 2014); 2016 (Food and Drug Administration, 2016); 2018–2019 (Michelotti et al., 2022); 2020 (Mathieu et al., 2022); 2021–2022 (Herrera-Juárez et al., 2023); 2023–2025 (Attili et al., 2024)

In the last few years, we seem to have plateaued in the percentage of patients with targetable tumors. This data is difficult to precisely capture as not all patients are tested and only about 20% of lung cancer patients undergo comprehensive genomic profiling (NGS) for large panels (>300) of biomarkers (Wallenta Law et al., 2024). Current estimates for patients that are eligible for biomarker-guided treatment range from 40–50% for therapies other than immunotherapy (Attili et al., 2024). As such, for at least half of all lung cancer patients, we are not yet able guide their treatment based on their tumor's genetic makeup. (Wallenta Law et al., 2024)(Attili et al., 2024)

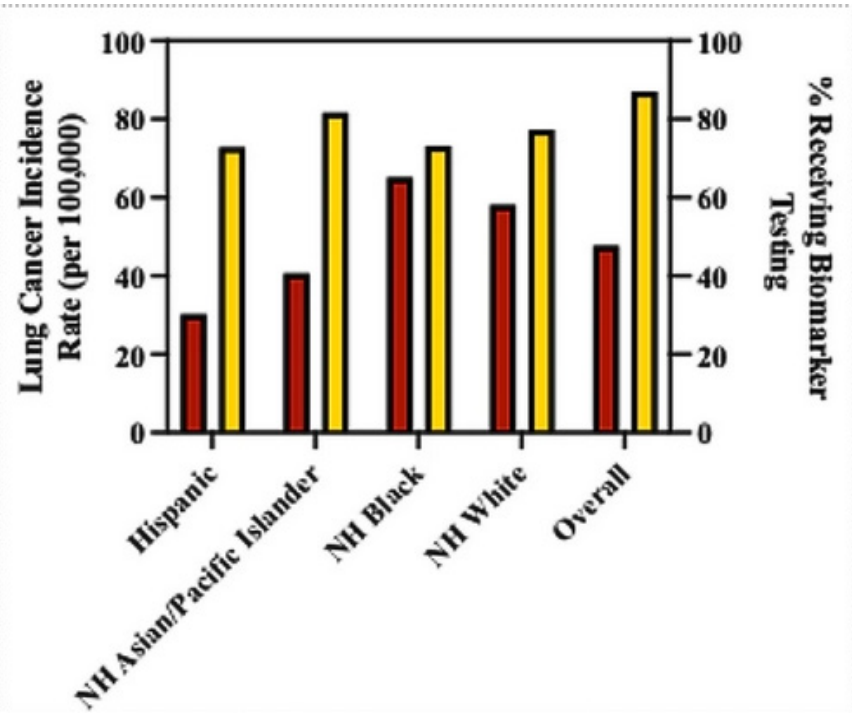
Although men and women are approximately equal in newly diagnosed cases and approximately equal in adoption of molecular testing, women are almost twice as likely to have mutations that are treatable with the current repertoire of medications (Mosleh et al., 2025). Even though testing is being applied equally, biomarker-guided therapy is not possible equally for both sexes, which suggests further research is needed into the sex-related differences in the presence of these mutations.

Biomarker testing is not adopted evenly across lung cancer patients of different demographics.

There is continued disparity in access to extensive biomarker screening across all lung cancer patients. For NGS testing, white patients were about 10% more likely to have this test done than black patients, although more new cancer cases are diagnosed in African Americans, particularly men (Bruno et al., 2022). When analyzed by any type of biomarker testing done, the trend in testing frequency remained the same (Figure 2). The group most affected by lung cancer is not the one getting biomarker testing done the most often.

Perhaps the most striking data point in the disparity of biomarker testing is with respect to insurance status. For any biomarker testing, Medicaid patients are significantly less likely to receive biomarker testing of any variety, including NGS, compared to commercially insured lung cancer patients (Lin et al., 2025). In a 2023 survey by the American Cancer Care Centers, Medicaid patients were less likely to undergo biomarker testing to guide treatment and were at a higher risk of mortality (Comprehensive Cancer Care: The Role of Biomaker Testing, 2023). With approximately 1 in 4 lung cancer patients covered by Medicaid, a large proportion of affected individuals experience accessibility obstacles to the most effective treatment. This disparity in accessibility also correlates with socioeconomic status, facility type, and geographic location.

Figure 2: *Racial Disparity in Application of Biomarker Testing*



Note: Red bars show the age-adjusted incidence rate per 100,000 individuals for lung cancer. Yellow bars show the percentage of individuals diagnosed receiving biomarker screening of any kind within 90 days of initial diagnosis. NH = Non-Hispanic. Adapted from (Baron et al., 2024).

Comprehensive biomarker screening should become the standard of care for lung cancer patients.

Many researchers believe that the eligibility of patients for biomarker-guided treatments, combined with the obstacles to accessibility, has plateaued. Policy change is necessary to ensure continued improvement of lung cancer patient care and prognosis.

The maximum proportion of lung cancer patients estimated to be eligible for biomarker guided therapy is 50%, which means half of lung cancer patients cannot be treated with current strategies. The lung cancer patients contributing to this estimation do not represent an even sampling across the demographics of individuals affected by the disease, which may mean potential therapeutic targets have not been identified.

As of 2025, 15 states, including Indiana, mandated insurance reimbursement for biomarker testing with 13 additional states introducing legislation in 2026 to do the same. While this is certainly a step in the right direction, additional regulation will be required to ensure that all forms of biomarker

testing, including NGS, are reimbursable, and that Medicaid recipients are also guaranteed equal access to testing. Patients receiving NGS-guided therapy demonstrate better responsiveness and overall rates (Jordan et al., 2017)(Jordan et al., 2017) . Simply assuring reimbursement for NGS testing will not be sufficient, however. Targeted therapeutics can only be of benefit if patients have access to the indicated treatments, which should also be a goal of mandating insurance reimbursements.

Biomarker testing is still largely in a forward manner, testing for genetic signatures that indicate eligibility for specific treatment. To identify additional targets for drug development, NGS biomarker assessment can provide an enormous amount of data to better understand the relationship between tumor genotype and response to treatment. Our initial research has demonstrated that mutations in genes such as Tp53, which are not currently a target for biomarker guided therapy, can affect efficacy of treatment with traditional chemotherapeutics. Correlating a more complete genomic profile to responsiveness to treatment, whether targeting specific mutations, immunotherapy, or chemotherapy, will allow for even greater personalization of individual care but also better guidance for future patients.

The urgent need for this deep dive into the mountains of data that will be generated also requires funding considerations. Many lung cancer patient samples have already been screened using NGS and their treatment regimens documented. However, these data remain largely decentralized. Allocating monies for organization and maintenance of available NGS data along with treatment responsiveness should be a priority in the big picture of lung cancer research funding.

Increasing equality of access to biomarker testing improves prognosis for current lung cancer patients and shapes future treatment.

Eliminating obstacles to access to NGS profiling will ensure that this benefit of personalized lung cancer treatment can be distributed evenly across more patients affected by lung cancer. Data from 2019 to the present is yet not available in Indiana, but a significant increase in screening occurred from 2023–2024 that likely will increase the number of early diagnoses (American Lung Association, 2024). Early detection will only serve to improve parameters like five-year survival rates for lung cancer patients, and biomarker data from patients diagnosed at earlier stages can be used to build an even more comprehensive picture of changes over the course of disease progression, potentially allowing identification of not just treatable biomarkers but also diagnostic ones. Early diagnosis is the single most important contributing factor in treatment, with lung cancer patients diagnosed at Stage I having a 60–80% five-year survival rate and less than 7% for patients diagnosed at Stage IV.

Utilizing the power of the data being gathered as patients are treated with increasingly personalized approaches will only further enhance treatment options. Despite early screenings and legislation to discourage risk behaviors like smoking, Indiana continues to have one of the highest rates of new lung cancer cases nationally. The increased accessibility for patients to state-of-the-art genetic screening and increased data collection to drive new drug discoveries will be paramount in improving the prognosis for lung cancer patients.

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