Minimizing Turnaround Time for Molecular Testing Among Patients With NSCLC

<40% of eligible patients receive targeted therapy, with **31%** of this patient loss due to barriers with biomarker test ordering, communication of findings, and subsequent treatment decisions.[1] Examining common barriers and solutions may help standardize molecular biomarker testing and improve patient access to targeted therapies.

Pre-Analytic

Barrier: Limited Sample

Solution: Collect Additional Biopsy Passes[2]

Collect extra biopsy passes to ensure sufficient tissue for diagnosis and downstream molecular testing when suspicion for malignancy is high

Designate "molecular-only" biopsies that will not be processed for IHC or FISH.[2]

Most NGS platforms require a sample size of **≥25 mm²** tumor surface area and **≥20%** tumor content per sample.[3,4]

Tip to improve accuracy of tumor cell count:

Consider manually counting viable tumor cells or enabling an AI solution to assist with tumor cell estimation.[4,5]

Solution: Tissue Tracking[2,6]

Track which tissue blocks are adequate for molecular testing

- Flag in report for tissue navigator and/or lab technician[2]

Solution: Tissue Navigator[7]

- Ensure optimal utilization of limited tissue resources and selection of appropriate tissue blocks
- Facilitate shipment and receipt of tissue for testing
- Minimize delays in test ordering and treatment decisions by liaising between patients, pathologists, and treating physicians

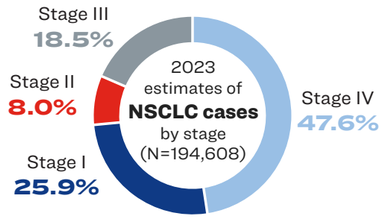
Key Takeaways[2,6]

- Designate and track tissue samples for molecular testing to streamline ordering process
- IHC should be used conservatively

Barrier: Delays in Test Ordering

Solution: Educate on Eligibility

Most NSCLC cases are advanced or metastatic at diagnosis[8]



54% of NSCLC cases progress to Stage IV.[9]

Patients with Stage IV NSCLC should have broad molecular profiling of all actionable biomarkers[10]:

- *ALK, BRAF, EGFR, ERBB2 (HER2), KRAS, MET, NTRK1/2/3, RET,* and *ROS1*

Solution: Reflex or Algorithmic Testing[11-14]

Pathologist-led biomarker testing

Biomarker testing begins immediately after pathological diagnosis instead of waiting until after a patient's first post-biopsy treatment with their oncologist or discussion amongst the care team.[6]

- *Creates a systematic ordering process*
- *Results in more patients being tested*
- *Reduces turnaround time for testing and biomarker-informed treatment decisions*

Key Takeaways[10]

- Patients with Stage IV NSCLC should have comprehensive genomic profiling
- Testing before 1L treatment enables more accurate diagnoses and prognoses and informs clinical trial eligibility

Analytic

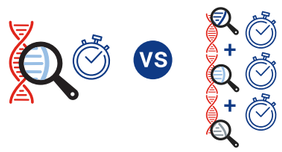
Barrier: Extended Analysis Time

Solution: Consolidate Testing[6]

Collect a liquid biopsy at the time of tissue biopsy, and test both in parallel[6]

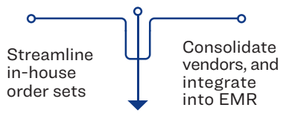
Plasma-based results can be used to screen for positive results when a shorter turnaround time is needed or when tissue is insufficient.[10]

Perform comprehensive NGS instead of sequential SGTs



Although an SGT may have a shorter turnaround time than NGS, NGS is faster than sequential testing with SGTs.[15] Upfront NGS testing in mNSCLC is associated with reduced cost and time-to-results for commercial and CMS payers.[16]

Limit menu of vendors and tests[12]



Key Takeaway[6,10,12]

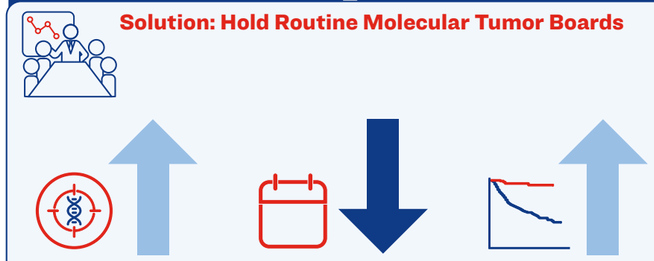
- Consolidate testing and reduce analysis time by running liquid-based and tissue-based tests in parallel, ordering comprehensive NGS, and streamlining testing options

Post-Analytic

Barrier: Lack of Integration of All Multidisciplinary Team Members

Barrier: Delayed Review of Report

Solution: Hold Routine Molecular Tumor Boards



>16% increase in recommended treatment choice[17,18]

~30% decrease in time to treatment initiation[17-19]

~40% absolute increase in overall patient survival rate[20]

Solution: Patient Navigator[21]

Dedicated MTB coordinators and patient navigators can help with:

- Consolidation of reports
- Follow-up of results and communication of findings
- Upload of reports in EMR
- Facilitation of multidisciplinary discussions

Solution: Recordkeeping[2]

Ensure EMR access for all key stakeholders, and keep records of:

- Frequency of and reasons for QNS
- Molecular testing results
- Viable tumor cell count
- Biopsy complications

Effective recordkeeping enables quality and process improvements.

Key Takeaway[17-20]

- MTBs can decrease time to appropriate treatment and increase overall patient survival by integrating multidisciplinary team members

Solution: EMR Technology[22]

- Implement rare biomarker alerts
- Consider integration of therapy and clinical trial matching algorithms and/or lab vendor portals into EMR

Key Takeaway[21,22]

- Patient navigators and EMR technology can help streamline the communication of results and decrease turnaround time

CMS = Centers for Medicare & Medicaid Services; EMR = electronic medical records; FISH = fluorescence *in situ* hybridization; IHC = immunohistochemistry; MTB = molecular tumor board; NGS = next-generation sequencing; NSCLC = non-small cell lung cancer; QNS = quantity not sufficient; SGT = single gene test.

1. Sadik H, et al. *JCO Precis Oncol*. 2022;6:e2200246. 2. Fintelmann FL, et al. *Respir Res*. 2023;24(1):17. 3. Tomlins SA, et al. *JCO Precis Oncol*. 2021;5:1312-1324. 4. Smits AJJ, et al. *Mod Pathol*. 2014;27(2):168-174. 5. Abel J, et al. Abstract presented at: Association for Molecular Pathology Annual Meeting; November 14-18, 2023. 6. Gregg JP, et al. *Transl Lung Cancer Res*. 2019;8(3)286-301. 7. Tavora F, de Sousa JC. *ESMO Open*. 2023;8(5):101827. 8. Non-Small Cell Lung Cancer: Epidemiology Forecast to 2029. New York, NY:GlobalData; June 2023. 9. Karacz CM, et al. *Clin Lung Cancer*. 2020;21(2):127-135.e3. 10. Hendriks LE, et al; ESMO Guidelines Committee. *Ann Oncol*. 2023;34(4):339-357. 11. Zacharias M, et al. *Transl Lung Cancer Res*. 2021;10(11):4221-4234. 12. Dias-Santagata D, et al. *Oncologist*. 2022;27(11):930-939. 13. Miller TE, et al. *J Clin Pathol*. 2018;71(12):1108-1115. 14. Schneider F, et al. *Am J Clin Pathol*. 2015;143(2):193-200. 15. Zheng Y, et al. *Future Oncol*. 2022;18(4):505-518. 16. Pennell NA, et al. *JCO Precis Oncol*. 2019;3:1-9. 17. Friedman EL, et al. *J Multidiscip Healthc*. 2016;9:267-274. 18. Freeman RK, et al. *Eur J Cardiothorac Surg*. 2010;38(1):1-5. 19. Senter J, et al. *Int J Radiat Oncol Biol Phys*. 2016;96(2):S134. 20. Huang B, et al. *JCO Precis Oncol*. 2021;5:1530-1539. 21. Doerfler-Evans RE, et al. *J Thorac Dis*. 2016;8(suppl 6):S498-S500. 22. Williams MS, et al. *Front Genet*. 2019;10:1059.

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