PRECISION MEDICINE in COMMUNITY ONCOLOGY: A BLUEPRINT

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CASE

- 60-year-old male with a 3 cm left hilar mass and multiple liver lesions. c/o abd pain, abnormal LFTs. FNA of liver- adenocarcinoma. PET scan–no other disease. Patient presents to you.

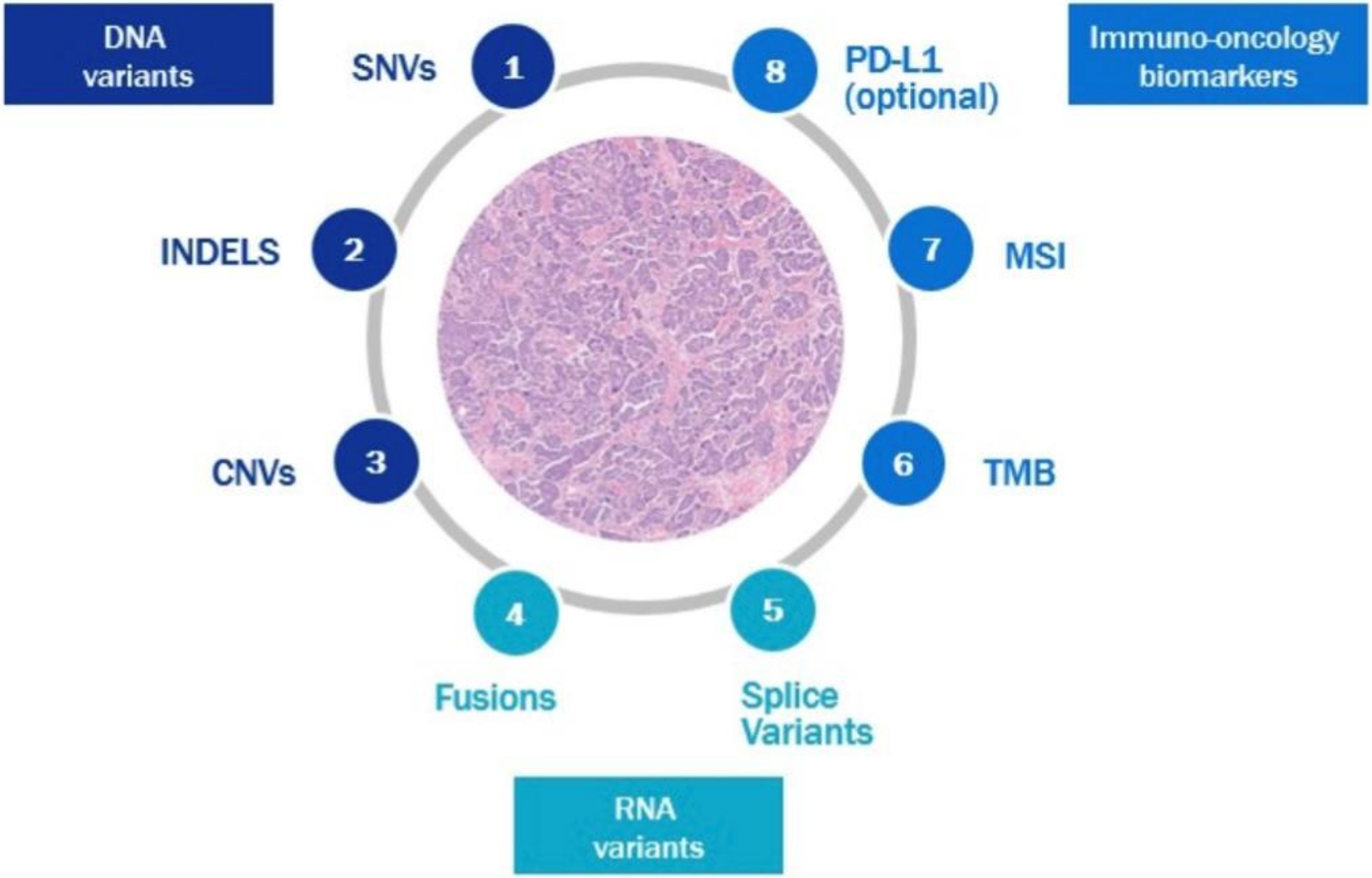
- Do you initiate therapy right away?
- Check biomarkers?
- What test do you order
- Who orders- you/pathologist
- Which vendor
- Tissue versus liquid

History of Precision Oncology

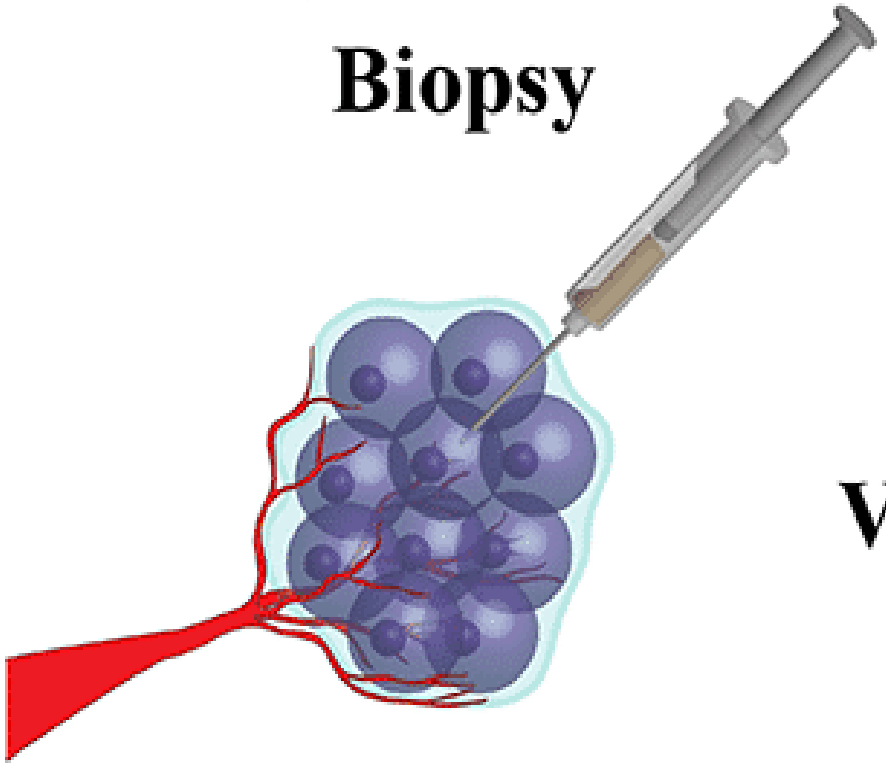
- Right treatment/ right patient/right dose/right time
- 1958- ER identified in breast cancer[5]
- 1998- BCR-ABL rearrangement in CML
- 2003- First draft sequence of the human genome[1]
- NGS - Sequencing technology and costs improved rapidly during the early 2000s- massive parallel sequencing allows determination of alterations in a large number of genes through a timely, cost-effective process.

PATHOGENESIS of CANCER

- Precision oncology= somatic mutations as the foundation of cancer[2]
- Mutations in oncogenes - driver mutations –progression
- Mutations in tumor suppressor genes- cause cancer progression
- Vast number of choices of technologies, commercial entities offering testing, and sometimes conflicting results have overwhelmed clinicians[3]
- Ideally: test=actionable mutation=response (HER2)

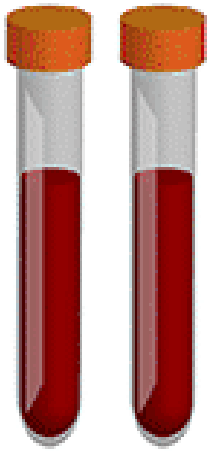

DNA variants
SNVs
1
INDELS
2
CNVs
3
4
Fusions
5
Splice Variants
RNA variants
8
PD-L1 (optional)
7
MSI
6
TMB
Immuno-oncology biomarkers

Standard Biopsy



VS.

Liquid Biopsy



Time-Intensive Procedure
Localized Sampling of Tissue
Not Easily Obtained
Some Pain/Risk
Invasive

Quick
Comprehensive Tissue Profile
Easily Obtained
Minimal Pain/Risk
Minimally Invasive

LIQUID Bx = Somatic

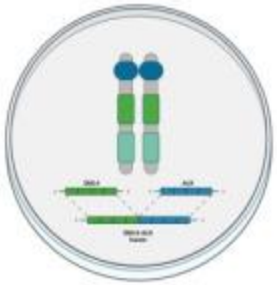
- *Luis E. Raez et al- Liquid Biopsy Versus Tissue Biopsy to Determine Front Line Therapy in Metastatic Non-Small Cell Lung Cancer (NSCLC), Clinical Lung Cancer, 2023*
- Liquid bx NGS - faster than tissue; higher testing success.
- Liquid biopsy was 94.8% to 100% concordant with tissue.
- Liquid-first approach identified guideline-rec biomarkers in 76.5% of pts vs 54.9% in tissue-first approach.
- No significant difference in TTT or survival outcomes (OS, PFS) based on liquid versus tissue biopsy
- Conclusion- Liquid biopsy can be used either as a first-line test or concordantly with tissue biopsy to guide treatment decisions in NSCLC.

TISSUE AGNOSTIC APPROVALS

- 2017: Pembrolizumab – dMMR or high MSI
- 2018: Larotrectinib - NTRK fusions-positive tumors
- 2019: Entrectinib- NTRK fusions-positive tumors
- 2020: Pembrolizumab – high TMB
- 2021: Dostarlimab- dMMR
- 2022: dabrafenib + trametinib - BRAF V600E
- 2022: Selpercatinib in RET fusion + tumors[4]

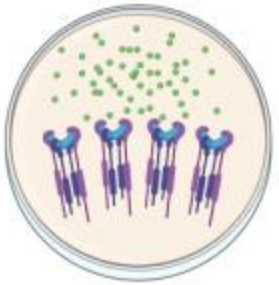
Tissue agnostic targets

Looking under the molecular microscope to identify targets



ALK

HER2



NRG1

FGFR

RET

Challenges of Testing

- National testing rate 50%[6]
- Tests - reliable but slow
- Insurance Coverage-single gene vs NGS
- SB989
- Knowledgeable health care providers- what tests/ when/ how to utilize the results
- Treatment guidelines-outdated before updated
- Appropriate testing infrastructure- efficient and sufficient collection/ handling of tissue
- EMR - manage testing results and assist health care providers in clinical decision making[7]

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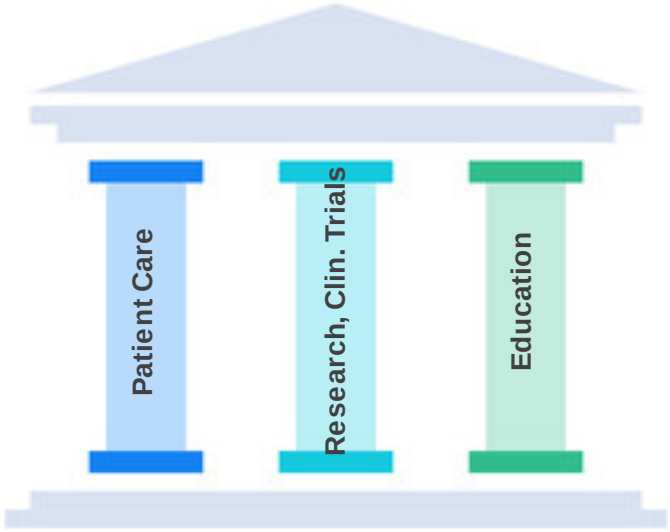
Texas Oncology
Precision Medicine Program

Summary of TxO PM Program



- Expand treatment options
- Enroll more patients in clinical trials patients Selecting treatment options
- Clinician education/shared learning

- **Scalable**
- **Equitable**
- **Easy to Use**
- **Consider the Patient's Journey**

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Increase NGS test orders

	Annual Orders
2015	1,074
2017	3,000
2019	4,495*
2022	14,702*

*** Solid tumor disease only**

Implementation of Trapelo, a Clinical Decision Support Tool

Clinical Qualifications	Panel Selection	Lab Selection
3 OAEs	Small vs. Large	Tempus
Tumor type	Add on biomarkers	Caris
Stage of Disease	Liquid vs. Solid	NeoGenomics
Pathology Block ID		Foundation Medicine
		Agenda
		Genomic Health
		Myriad
		Biotheranostics

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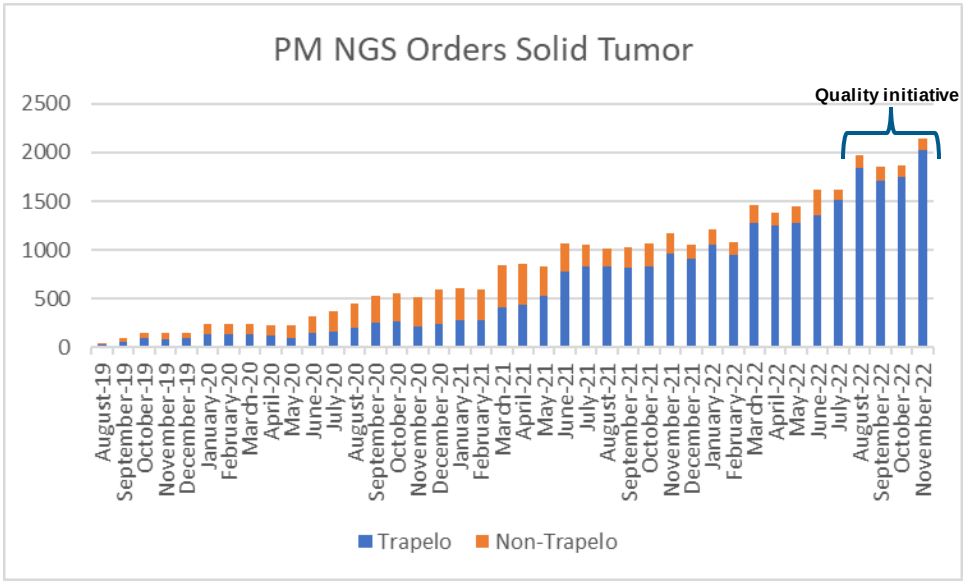
PMQI[9]

"It is strongly recommended that all medical oncologists order appropriate biomarker testing (NGS/mutational analysis/multi-gene panel) on all patients with advanced (stage IV) solid tumors. Such testing should be ordered via Trapelo (which can be accessed via a hyperlink found in G2 and will guide stage- appropriate testing) or a chart message can be sent to the Precision Medicine team with the testing requisition. The vendors offering testing are listed in Trapelo and can be chosen as per physician preference. If such testing is ordered by outside entity/pathologist etc.–the medical oncologist should ensure that appropriate testing is ordered. If there is paucity of tissue, a liquid biopsy can be substituted. If neither is feasible, the reason for not ordering the test should be stated in the chart. Before any systemic therapy is initiated on the patient, Pharmacy will check/ensure that such testing has been ordered (or resulted). Any exceptions should be submitted to the appropriate Exceptions approver. This initiative will serve as a pilot for the first year, closely monitored, data collected and analyzed, and appropriate reforms made. Due to the rapidly changing science in Precision Medicine, the choice of biomarkers/stage appropriateness/choice of companies will be regularly updated in Trapelo. Educational opportunities for ordering physicians will be available through various forums offered by Texas Oncology.

Quality Initiative: Pharmacy Collaboration

NGS Solid Tumor Orders



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Virtual Molecular Tumor Board

Clinical Decision Support enables more personalized, virtual care
Molecular Tumor Board facilitates cross-specialty education

- Increase trial enrollment and awareness by identifying clinical trial opportunities based on an individual patient's condition, genomic alterations and institution's postal code.
- Discover and search for patient-specific medical literature and gain access to the latest data to support treatment decisions.
- Easily review the latest guidelines and record patient diagnostic and treatment paths

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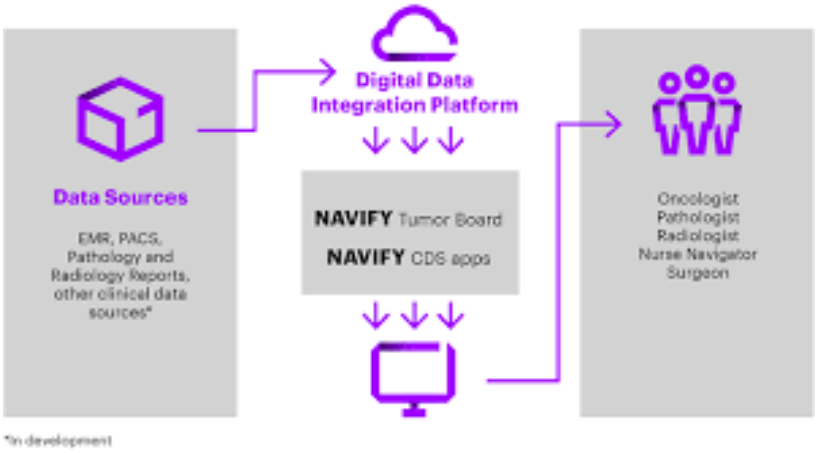
Roche Navify®



- Facilitates virtual patient discussion and collaboration between clinical care teams
- Enables standardization and secure collaboration
- Allows asynchronous case discussions from any place and time

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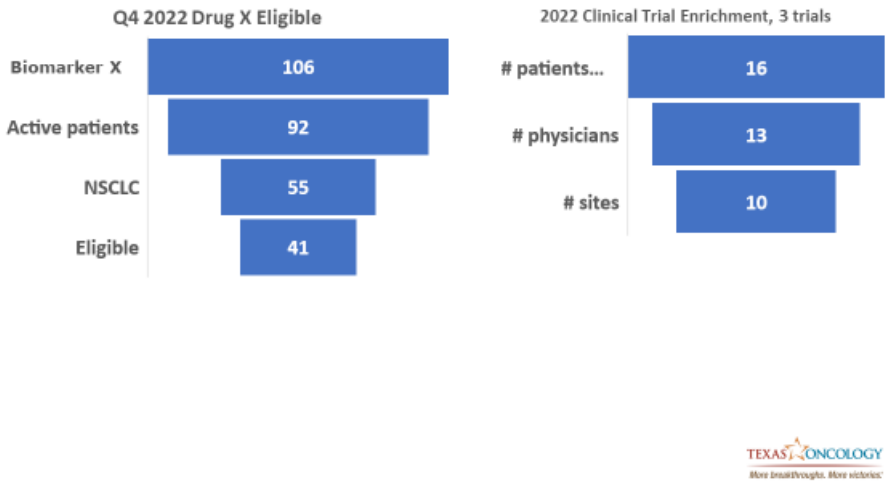
Standard of Care and Clinical Trial Enrichment

Maximizing Therapeutic Opportunities



Innovative Biomarker Testing Initiative in a Community Oncology Setting[8]

Background: *It is well documented that biomarker testing in cancer lags far behind recommended guidelines. To improve testing rates and provide patients access to targeted therapies and clinical trials, a Precision Medicine Quality Initiative (PMQI) was launched across Texas Oncology in July 2022 and is ongoing. The PMQI recommended testing all eligible advanced solid tumor patients utilizing a broad panel next-generation sequencing (NGS) teston somatic tissue or with a liquid biopsy. This study assessed the impact of the initiative on biomarker testing rates and various testing metrics.*

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Innovative Biomarker Testing Initiative in a Community Oncology Setting.

Methods: *This retrospective study analyzed data on biomarker testing during the period of Jan2022 to Mar 2023. The target population included patients from Texas Oncology (largest private community oncology group in the country) with a diagnosis of advanced "solid tumor" (non-hematologic malignancy). Per PMQI, biomarker testing was ordered through Trapelo (online clinical decision support tool) or Precision Medicine Team. The order was tracked through IknowMed (EMR system) and CareEvolve (provider facing, customized database tracking orders/results real-time). This study analyzed data in CareEvolve to assess tests ordered per month, by tumor type, somatic vs liquid biopsy, small gene panel vs broad panel tests, labs utilized and by geographic region.*

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Innovative Biomarker Testing Initiative in a Community Oncology Setting.

Results: *Biomarker testing rates increased by 150% after the launch of the PMQI (from average of 1378 tests/month before, to 2046/month after). Tests more than doubled during study period - 1213 tests in Jan '22 to 2602 in Mar '23. Testing was performed in all tumor types, including breast (14%), lung (22%), colorectal (15%), pancreatic (6%) and others. 79%of total tests were somatic broad panel NGS, 16% were NGS on liquid biopsy, and 5% were single gene/small panel tests. 6442 tests were early-stage cancer prognostics. Caris was the most used lab (35%). After the PMQI, somatic NGS orders increased by 53% (from 800 to1230/month) and liquid biopsies increased by 101% (from 134 to 269/month). The highest increase in testing was in the regions of West Texas (154%) and Gulf Coast (176%).*

Innovative Biomarker Testing Initiative in a Community Oncology Setting.

Conclusions: *This study shows the success of the PMQI-biomarker testing increased across all tumor types, theoretically providing increased access to targeted therapies and clinical trials. Increasingly, broad panel NGS tests were ordered instead of single or small gene panels. Liquid biopsies more than doubled (can be effective in overcoming challenges of testing in community). Testing increased in rural/ underserved regions of the practice, suggesting that such an initiative may reduce disparities in access. Even though this study showed increased overall testing, it was not designed to assess testing rates in all eligible patients. this study confirms that with coordination between providers, PM liaisons, Pharmacy, and Labs, such a complex, large scale and first of its kind initiative can be feasible and effective.*

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