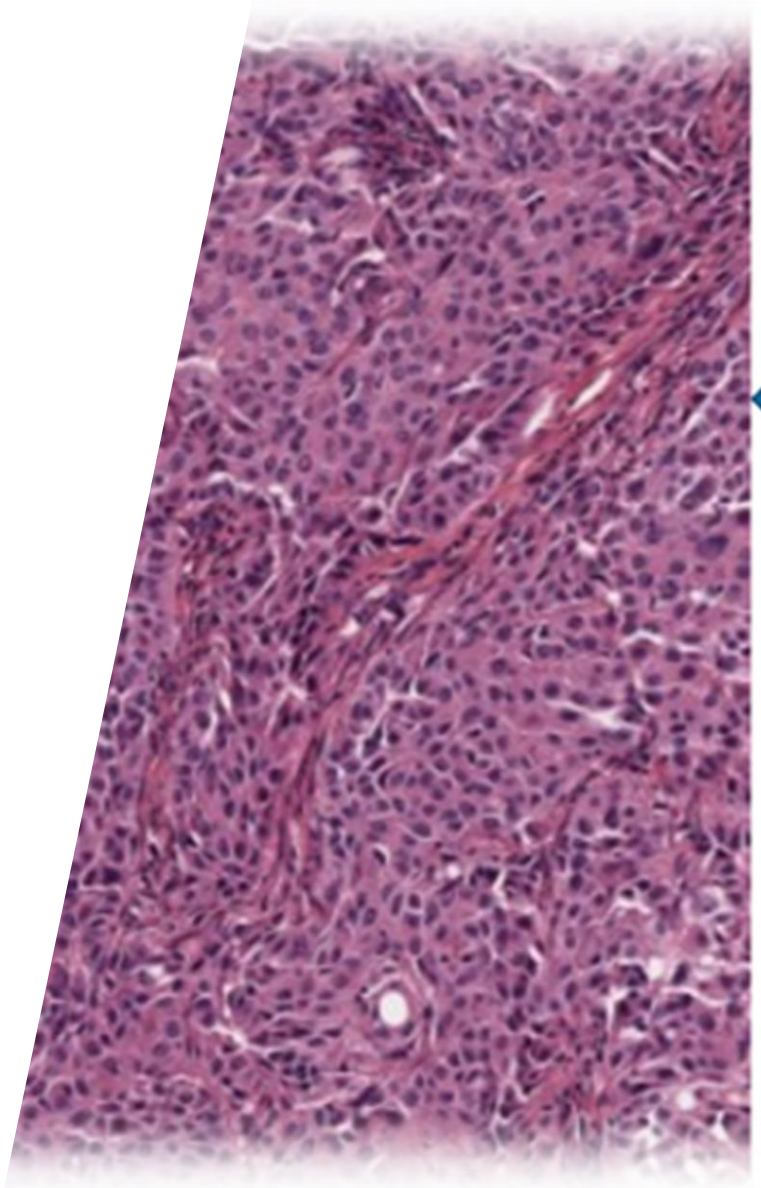
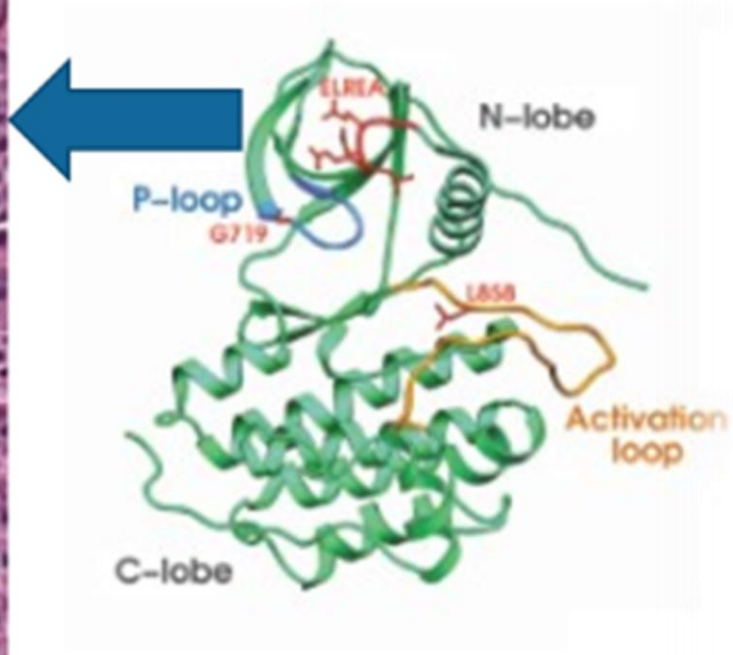
Welcome!

Before we begin…

Today's session will be recorded

Please add your name and organization in the chat





EGFR Mutation

Wednesday, March 6, 2024 • 4:00 – 5:00 PM EST

Lung Cancer Biomarker Testing ECHO Year 3

Session 3: Choice of Panel, Interpretation of Results and Next Steps

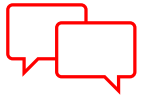
Welcome to Session 3 of the

Lung Cancer Biomarker Testing ECHO Year 3

Each ECHO session will be recorded and will be posted to a publicly-facing website

You will be muted with your video turned off when you join the call. Use the buttons in the *black* menu bar to unmute your line and to turn on your video. **If you do not wish to have your image recorded, please turn OFF the video option**.

Today's materials will be made available on our ACS ECHO website, https://echo.cancer.org.



Please type your full name, the full name of your organization, and e-mail in the chat box

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Questions about Zoom? Type in the chat box @Mindi Odom

The Biomarker ECHO series is made possible with funding provided by:

Additional thanks to Foundation Medicine and founding sponsor, Amgen

Have a question? Don't wait to ask! Feel free to enter in the **Chat** at any time.

Today's Agenda

1 **Housekeeping, Agenda Preview, and Introductions**
15 minutes

2 **Didactic Lecture: Choice of Panel, Interpretation of Results and Next Steps**
Ignacio Wistuba, MD
10 minutes

3 **Didactic Q/A**
5 minutes

4 **Case Presentation: Deaconess Health System**
Angela Stroud, MSN, RN, CMSRN, NE-BC
5 minutes

5 **Case Presentation Recommendations and Discussion**
15 minutes

6 **Post Session Poll & Wrap Up**
5 minutes

Your ECHO Support Team

Korey Hofmann, MPH
ECHO Lead
Program Manager, National Lung Cancer Roundtable

Mindi Odom
Director, Project ECHO
Your ECHO Co-Lead

Beth Graham, MPH, CHES
Program Manager, Project ECHO

Jennifer McBride, PhD
Senior Data & Evaluation Manager

Donoria Evans, PhD, MPH
Director, Data and Evaluation,
National Roundtables and Coalitions

Introductions

Meet Our Lung Cancer Biomarker Testing ECHO HUB Subject Matter Experts (SMEs)

Millie Das, MD
Chief, Oncology
VA Palo Alto Health Care System
Clinical Associate Professor
Stanford University

Aakash Desai, MBBS, MPH
Assistant Professor of Medicine
O'Neal Cancer Center
University of Alabama, Birmingham

Grace Dy, MD
Professor of Oncology
Roswell Park Comprehensive Cancer Center

DuyKhanh Pham "Mimi" Ceppa, MD, FACS
Associate Professor of Thoracic Surgery
Indiana University School of Medicine

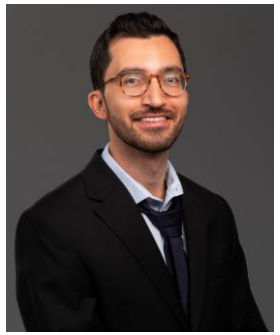
Matthew Facktor, MD
System Chief, Thoracic Surgery
Geisinger Health

Adam Fox, MD
Assistant Professor
Medical University of South Carolina

Jason Merker, MD, PhD
Associate Professor, Department of Pathology and Laboratory Medicine & Genetics
University of North Carolina Lineberger Comprehensive Cancer Center

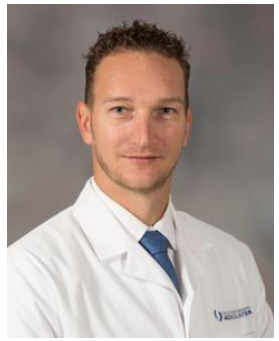
Introductions

Meet Our Lung Cancer Biomarker Testing ECHO HUB Subject Matter Experts (SMEs)



Koosha Paydary, MD, MPH, MSc
Assistant Professor, Department of Internal Medicine
Rush University

Catherine R. Sears, MD
Associate Professor of Medicine, Division of Pulmonary, Critical Care, Sleep and Occupational Medicine
Indiana University School of Medicine
Simon Comprehensive Cancer Center



Michal Senitko, MD
Assistant Professor
The University of Mississippi Medical Center

Gerard Silvestri, MD, MS
Hillenbrand Professor of Thoracic Oncology
Medical University of South Carolina

Heather Wakelee, MD (Ad Hoc)
Professor of Medicine and Chief of the Division of Oncology,
Stanford University School of Medicine
Deputy Director, **Stanford Cancer Institute**

Ignacio Wistuba, MD
Professor and Chair, Department of Translational Pathology
The University of Texas MD Anderson Cancer Center

Welcome to our Participant Learning Sites

ALABAMA

- Mobile Infirmary
- O'Neal Comprehensive Cancer Center at the University of Alabama at Birmingham
- University of South Alabama Health, Mitchell Cancer Institute

CALIFORNIA

- Comprehensive Cancer Center at Desert Regional Medical Center
- Fresno VA Medical Center
- Harbor UCLA
- Providence St. Joseph Health
- Sharp Healthcare

INDIANA

- Ascension St. Vincent Indianapolis
- Deaconess Hospital, Inc.
- Franciscan Alliance Burrell Cancer Center Crown Point
- Methodist Hospitals

NORTH CAROLINA

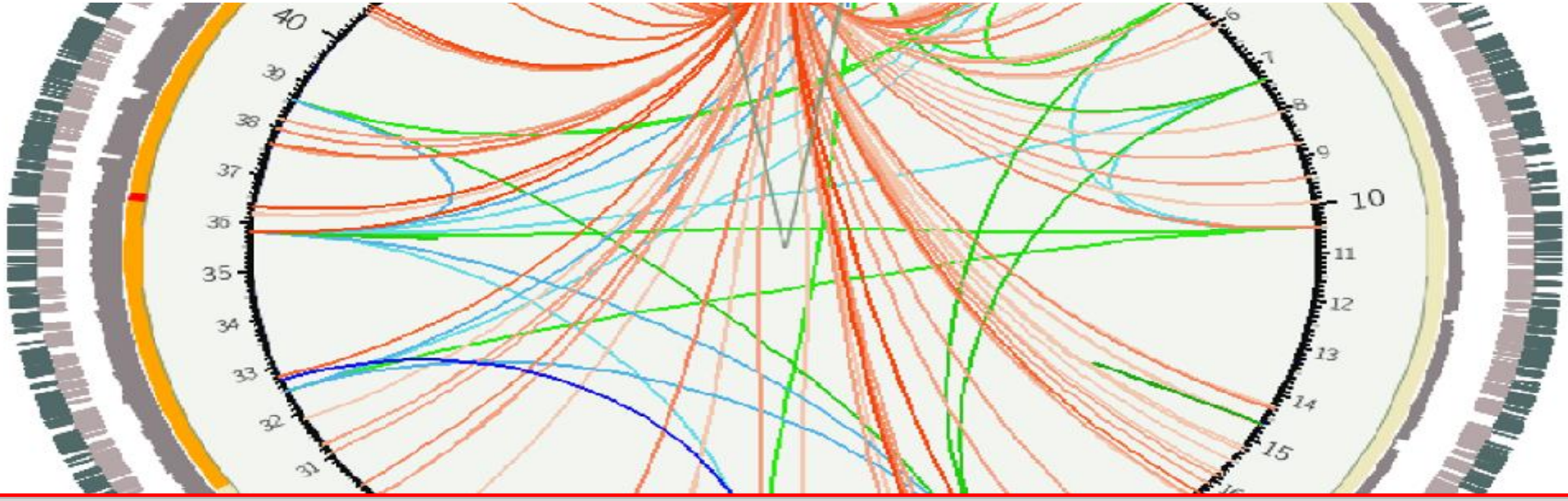
- Cone Health Medical Group/Cone Health Cancer Center
- Novant New Hanover Regional Medical Center
- UNC Caldwell McCreary

Timothy Mullett, MD, MBA, FACS
Medical Director, Markey Cancer Center Network Development

Lung Cancer Biomarker Testing ECHO FACILITATOR

Ignacio Wistuba, MD
Professor and Chair, Department of Translational Pathology
The University of Texas MD Anderson Cancer Center

Session 3 Didactic: Choice of Panel, Interpretation of Results and Next Steps



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Choice of Panel, Interpretation of Results, and Next Steps

ACS Lung Cancer Biomarker ECHO Session
March 6th, 2024

Ignacio I. Wistuba, M.D
Professor and Chair, Department of Translational Molecular Pathology
The University of Texas MD Anderson Cancer Center, Houston, TX

Disclosures

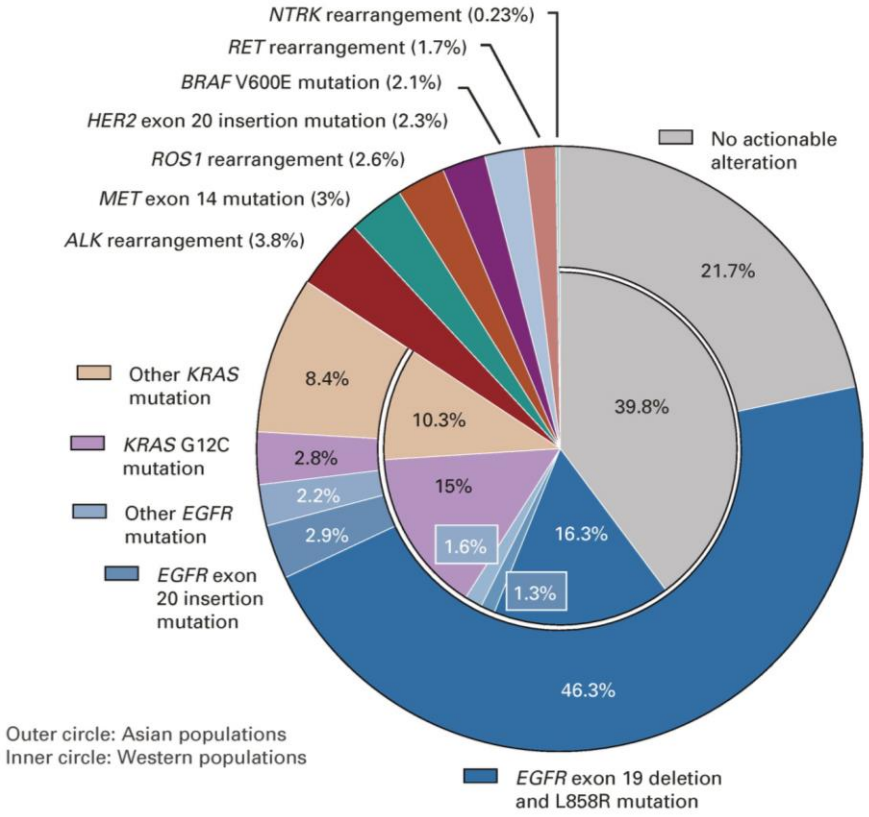
- **Advisory Board:** Genentech/Roche, Bayer, Bristol-Myers Squibb, Astra Zeneca, Pfizer, Merck, Guardant Health, Flame, Novartis, Sanofi, Daiichi Sankyo, Amgen, Jansen, Merus, G1 Therapeutics, Abbvie, Catalyst Therapeutics, Regeneron, and Oncocyte.
- **Speaker:** Medscape, Genentech/Roche, Platform Health, Pfizer, Merus, AstraZeneca, Merck.
- **Research support:** Genentech, Merck, Bristol-Myers Squibb, Medimmune, Adaptive, Adaptimmune, EMD Serono, Pfizer, Takeda, Amgen, Karus, Johnson & Johnson, Bayer, Iovance, 4D, Novartis, and Akoya.

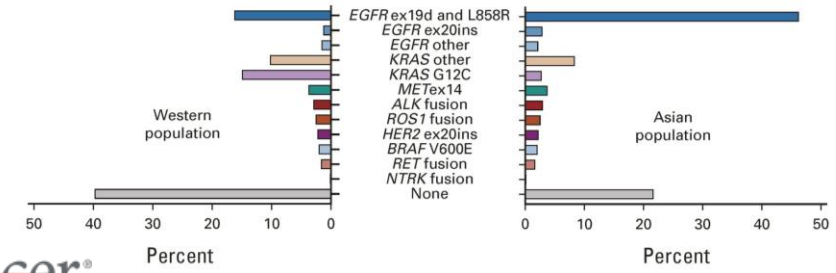
Choice of Panel, Interpretation of Results, and Next Steps

Session Objectives:

- Provide guidance and recommendations regarding the appropriate biomarker testing modalities: next-generation sequencing (NGS), fluorescence in situ hybridization (FISH), and blood testing
- Provide guidance regarding how to interpret the current NGS reports and the appropriate next steps, e.g., recommendations for FDA approved treatments or cancer clinical trials (if no FDA approved treatment exists, etc.)
- Showcase why delayed interpretation of results can lead to the initiation of conventional therapies that may limit the ability of patients to fully benefit from biomarker testing
- Provide practical tips for EHR Workflow strategies

Genomic Abnormalities in Lung Adenocarcinoma



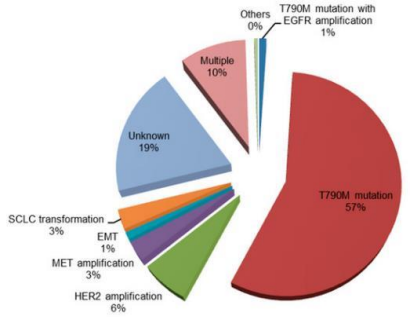


A. Tan, J Clin Oncol, 2022

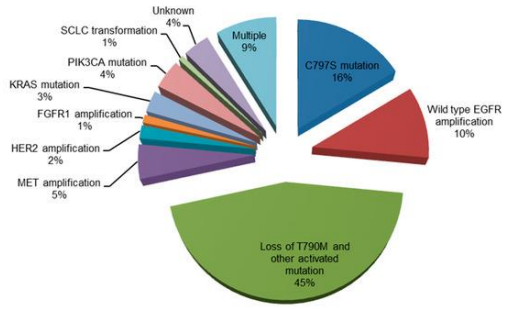
Mechanisms of Resistance

EGFR

First Generation TKIs

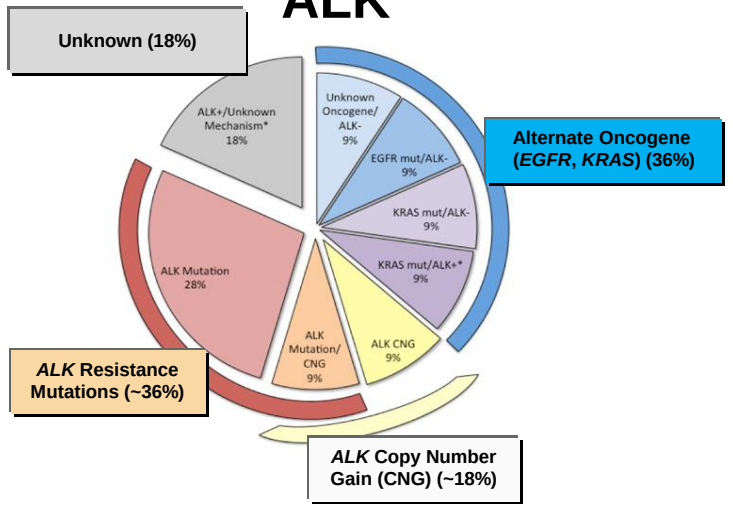


Second Generation TKIs



Nagano T, et al. Cells. 2018;7:212.

ALK



Doebele RC, et al. Clin Cancer Res. 2012;18:1472

Evolution and Expanding List of Guideline Recommendations for Genomic Testing in Advanced Stage NSCLC

"The NCCN NSCLC Guidelines Panel strongly endorses **broader molecular profiling** with the goal of identifying rare driver mutations for which effective drugs may already be available, or to appropriately counsel patients regarding the availability of clinical trials. **Broad molecular profiling** is a key component of the improvement of care of patients with NSCLC)."

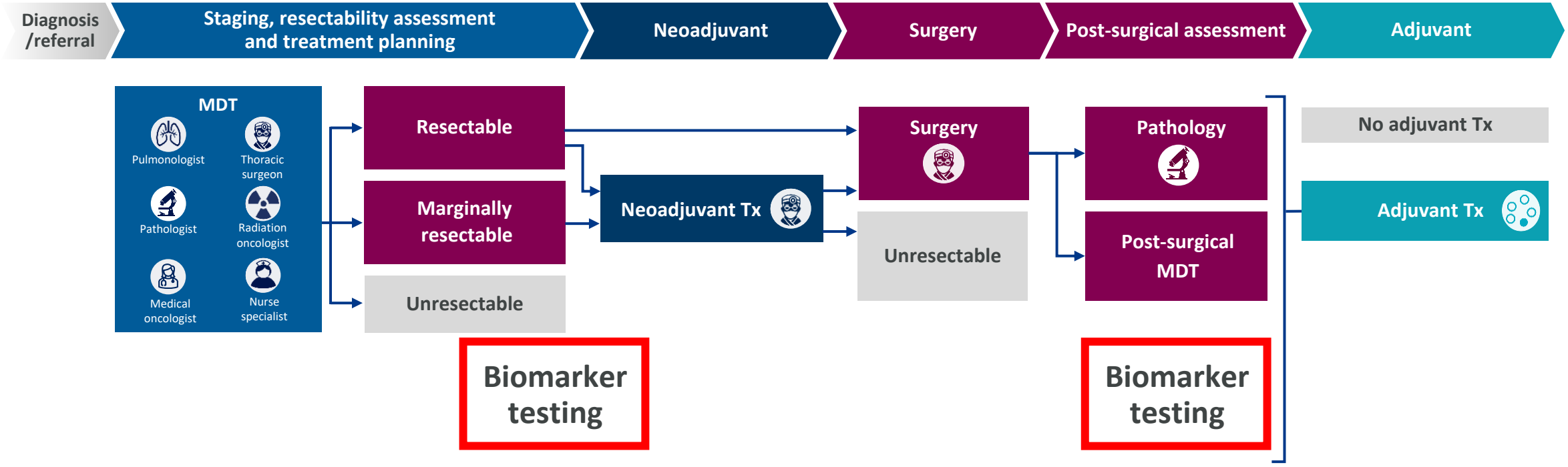
Genomic alteration (i.e., driver event)	Available targeted agents with activity against driver event in lung cancer
***EGFR* mutations**	Osimertinib, erlotinib, gefitinib, afatinib, dacomitinib
***ALK* rearrangements**	Alectinib, brigatinib, ceritinib, crizotinib, lorlatinib
***ROS1* rearrangements**	Crizotinib, ceritinib, entrectinib
***BRAF* V600E mutations**	Dabrafenib + trametinib, vemurafenib
***HER2* mutations**	Ado-trastuzumab emtansine, afatinib, trastuzumab deruxtecan
***MET* amplification/mutation**	Crizotinib, capmatinib
***RET* rearrangements**	Cabozantinib, vandetanib, selpercatinib, pralsetinib
***NTRK* rearrangements**	Entrectinib, larotrectinib,
EGFR Ex20ins	***Amivantamab***
KRAS G12C	***Sotorasib***

Cancer

NCCN Clinical Practice Guidelines. NSCLC. Version 5.2022.

Slide Courtesy of Dr. David Gandara

Biomarker Testing for Resectable NSCLC Helps to Inform Treatment Decisions



To guide neoadjuvant treatment decisions biomarker testing will need to be performed on the diagnostic biopsy sample

MDT, multidisciplinary team; NSCLC, non-small cell lung cancer; Tx, treatment

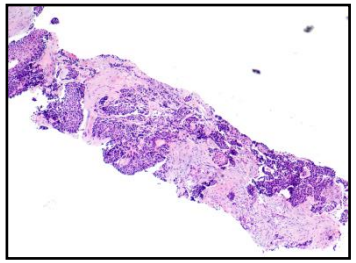
Remon J, et al. Ann Oncol 2021;32:1637–42

Cancer

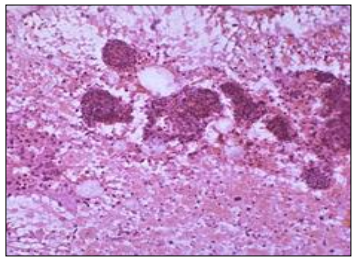
Diagnostic Algorithm for Lung Cancer Diagnosis 2024

cfDNA Testing
(Liquid Biopsy)

Blood

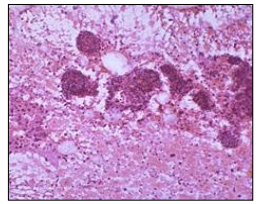


Biopsy



Cytology

Cytology: FNA, EBUS

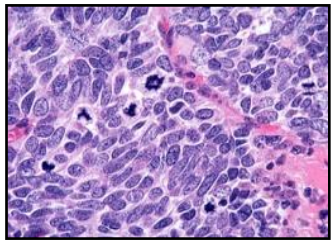


Smears

Cell Block

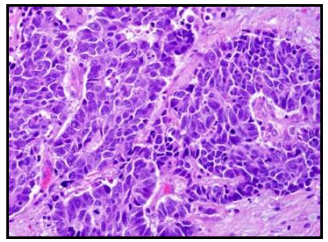
NSCLC

SCLC



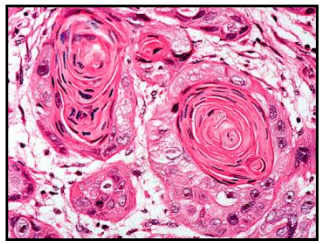
Morphology

LCNEC



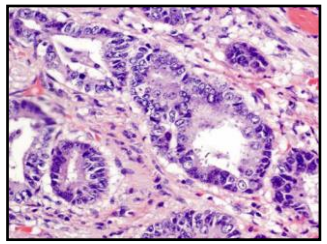
Morphology
IHC NE (+)

Squamous



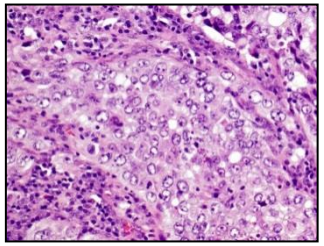
Morphology
IHC p63/p40 (+)

Adenoca



Morphology
IHC TTF1 (+)

NSCLC-NOS



Morphology
IHC (-)

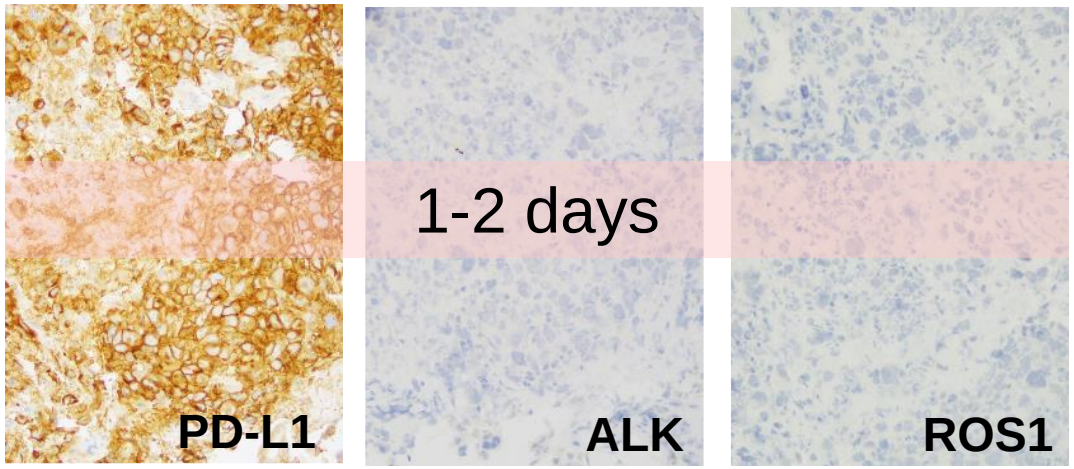
EGFR (incl. Exon 20), BRAF, KRASG12C, **and**
HER2 mutations; MET ex14 **splicing mutations;**
ALK, ROS1, NTRK, RET **and** ***NRG1*** **fusions**

PD-L1 IHC

Cancer

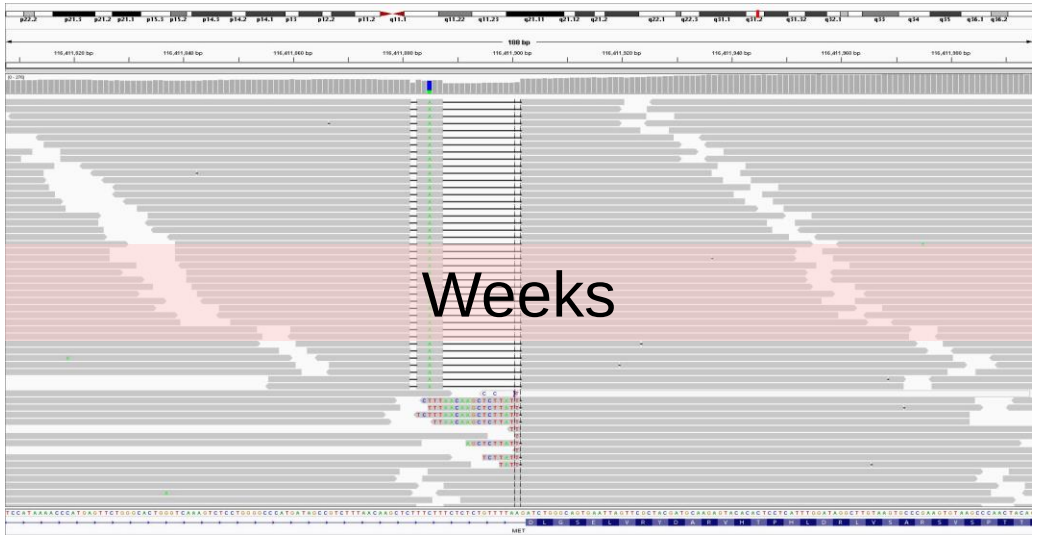
NSCLC Biomarker Testing → Tricky Timing

Immunohistochemistry



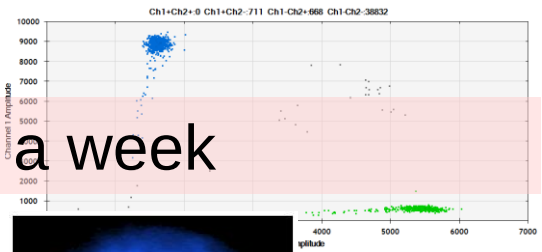
1-2 days

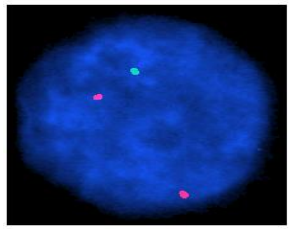
Next Generation of Sequencing (NGS)



Weeks

PCR-based Assay and FISH





Days to a week

Ion Proton
(Thermo Fisher)

Next-Seq
(Illumina)

Cancer

Slide (modified) Courtesy of Lynette Sholl, MD, Harvard Medical School and Brigham And Women's Hospital

Practical Points for Lung Cancer Biomarker Testing

- **Type of sample**: tissue, cytology (FNA), blood
- **Stage of the disease**
- **Molecular testing assays**:
  - IHC: PDL-1 and ALK/ROS1 (surrogates)
  - FISH: *ALK*, *ROS1*, and *NTRK* fusions
  - NGS or d/qPCR panels: *EGFR*, *MET ex14*, and *BRAF mutations, pluse ALK*, *ROS1*, and *NTRK* fusions.
- **Tissue turn around times** (TATs):
  - TAT1: Biopsy collection to pathology diagnosis (~2 days)
  - TAT2: Pathology diagnosis to molecular diagnostic lab (~1 – 7 days)
  - TAT3: Molecular diagnostic lab to molecular report (NGS panels, 10 days)
- **Blood TATs**:
  - TAT1: Blood collection to molecular diagnostic lab (~1 – 2 days)
  - TAT2: Molecular diagnostic lab to molecular report (NGS panels, 10 days)

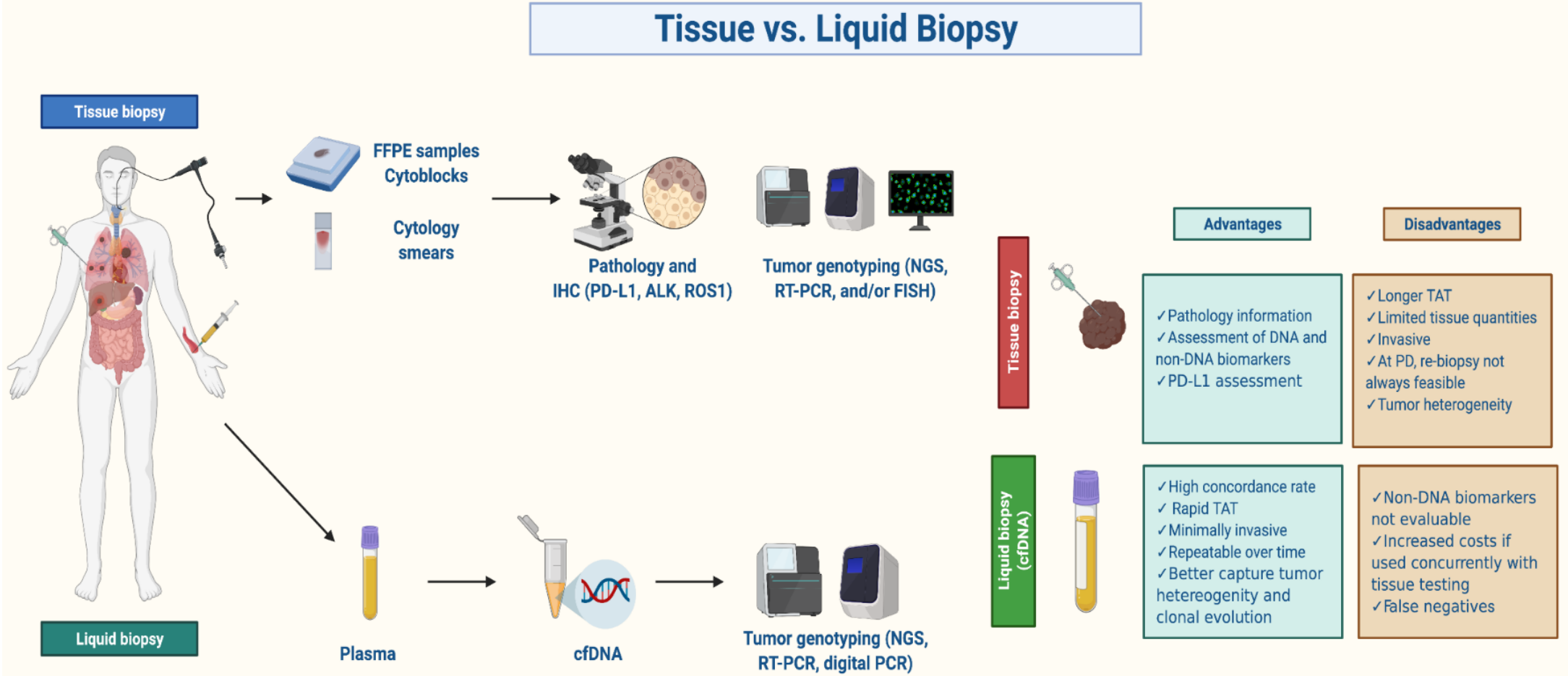
Key Quality Metrics to Guide Quality Improvement on NSCLC Biomarker Testing

Proposed Quality Metric	90% Compliance Goal
Pathology diagnostic TAT (i.e., time from specimen received in pathology to final pathologic diagnosis)	≤ 3 working days
Biomarker Test Order TAT (i.e., time from final pathologic diagnosis to biomarker test ordered)	≤ 2 working days
Pathology biomarker TAT (i.e., time from final pathologic diagnosis and/or biomarker test ordered to specimen sent to molecular lab) for eligible patients	≤ 3 working days
Molecular biomarker TAT (i.e., time from specimen received in molecular testing laboratory to reporting of all biomarker results) for eligible patients	≤ 10 working days
Overall biomarker TAT (i.e., time from final pathologic diagnosis rendered to reporting of all biomarker results) for eligible patients	≤ 14 working days

Cancer®

S. Roy-Chowdhuri, Cancer, in press

Tissue vs. Liquid Biopsy for Molecular Profiling



Cancer

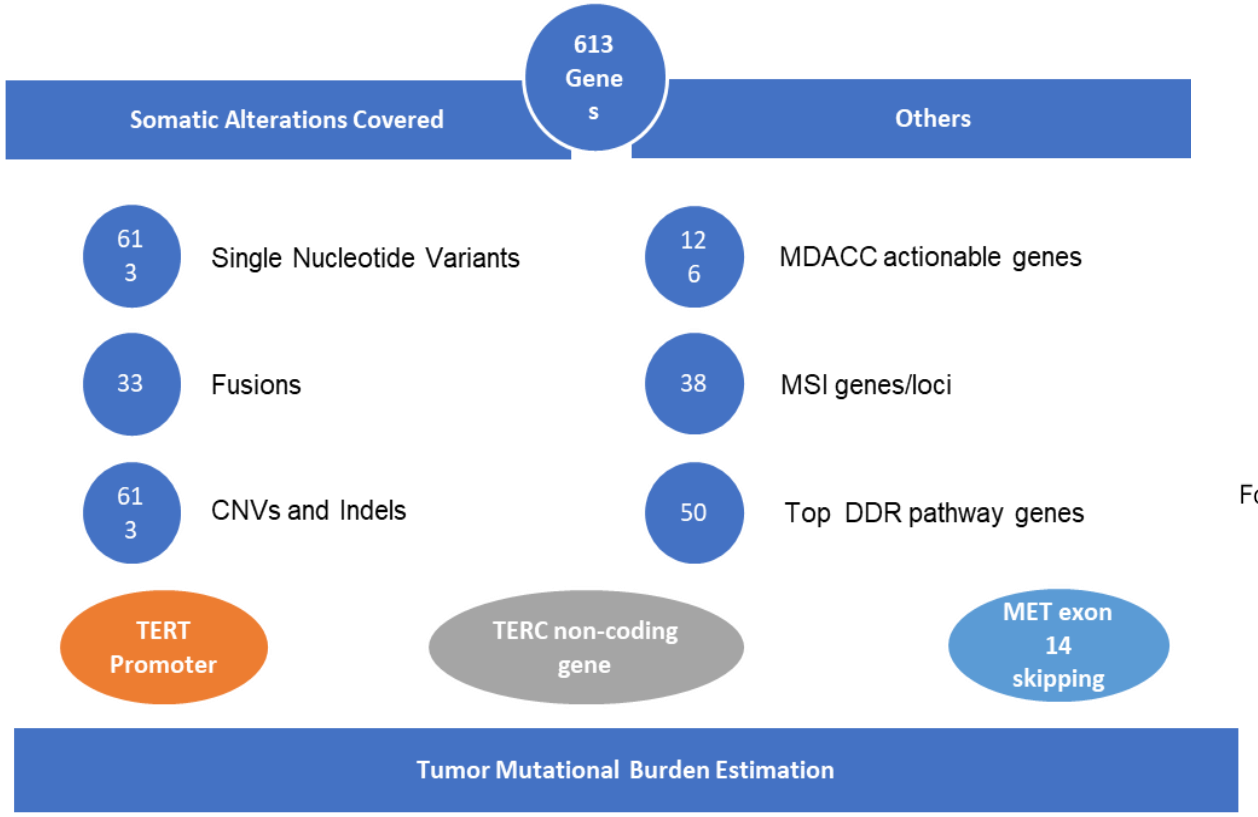
C. Rolfo et al, J Thorac Oncol, 2021

Next-Generation Sequencing (NGS) Panel Major Benefits

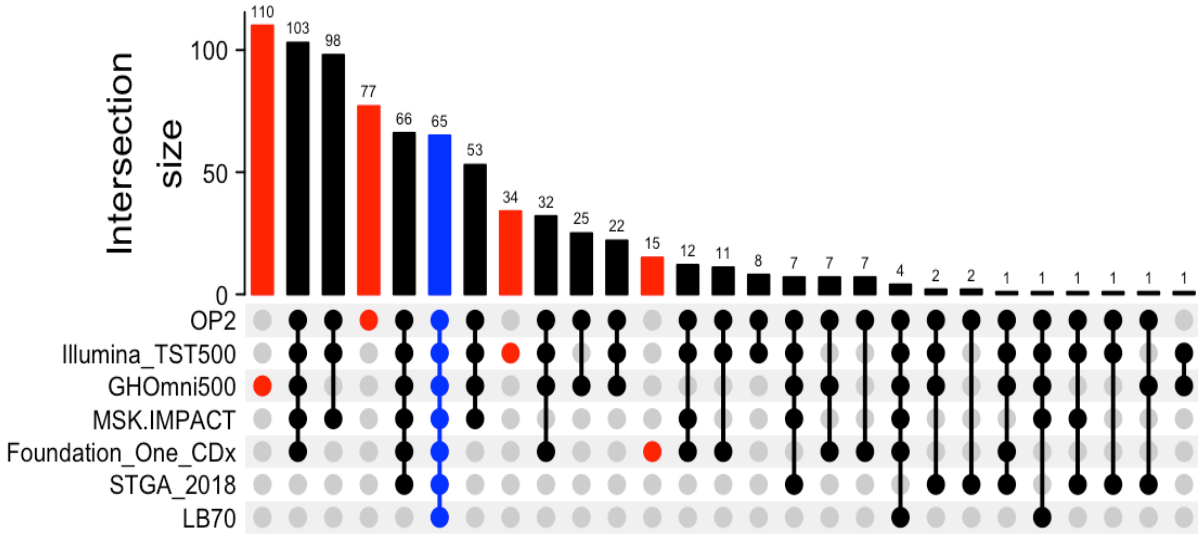
- Provide information in multiple targetable gene abnormalities.
- Data on mutation, copy number variations, indels and translocations
- Can be performed in routine small FFPE tissue samples and liquid biopsy (cfDNA, CTCs, exosome DNA).
- Turn around time acceptable for clinical management and costs being significantly reduced.
- Clinically, it offers to patients more options to get off-label treatment and enter in genomic-based clinical trials.
- May provide information on tumor mutational burden (TMB), and immune-suppressive genotypes (e.g., *LKB1* mutations)

MD Anderson NGS Precision Panel (MAPP)

MAPP Content



MAPP vs. Other NGS Panels



- The MDA-MAPP panel includes common cancer genes seen on most commercial panels (2022):
  - ~77 genes unique to MDA-MAPP panel
  - Covers all genes present in STGA 2018, LB70
  - ~95% overlap with Foundation _One and TSO500

Cancer

MD Anderson NGS MAPP Report

MDA-MAPP Mutation Analysis Report

SNVs/Indels	CNVs	Fusions	TMB	MSI
EGFR *TP53*	*ERBB2* *MET*	*EML4/ALK*	6 mut/Mb	Stable (MSS)

Somatic Mutations (SNVs/Indels)

Gene	DNA	Protein	Location	VAF	Type
EGFR	c.2369C>T	p.T790M	Exon 20	16%	SNV - Missense
EGFR	c.2389T>A	p.C797S	Exon 20	15%	SNV - Missense
EGFR	c.2573T>G	p.L858R	Exon 21	24%	SNV - Missense
TP53	c.524G>A	p.R175H	Exon 5	16%	SNV - Missense

Copy Number Variations (CNVs)

Gene	Finding	Genomic Position	Cytoband
ERBB2	Amplification	chr17:37855812-37884297	17q12
MET	Amplification	chr7:116339138-116436178	7q31.2

Gene Fusions

Upstream Gene	Downstream Gene	Fusion Details
EML4	*ALK*	EML4-ALK.E13A20

GUIDE TO STANDARDIZED NOMENCLATURE AND EXPLANATION OF CHANGES:

Variants identified are described using an implementation of a standardized nomenclature developed by the Human Genome Variation Society (HGVS, http://www.hgvs.org/varnomen/).

The normative Genbank gene reference sequence identifier and gene symbol in parentheses are provided, followed by the coding DNA sequence change (e.g., "c. 200A>G", which would mean that the position 200 adenine is changed to guanine), and then the inferred protein change (e.g., "p. V35C", which would mean that the amino acid at codon 35 is changed from valine to cysteine).

Additional explanations for the DNA and protein changes seen in the current specimen are shown in the following tables:

Explanation of DNA variant/mutation types seen in this specimen

DNA Change	
SNV	A single nucleotide difference (point mutation) has been identified in the patient sample relative to the reference wild-type gene sequence

Explanation of protein variant/mutation types seen in this specimen

Protein Change	
Missense	A single amino acid residue change in the patient sample relative to the reference wild-type protein sequence

Additional information on genes/variants with findings identified on this assay:

- The primary purpose of this panel is to detect somatic mutations in genes involved in oncogenesis of this patient's tumor. The test or the results thereof should not be used to detect germline variants for hereditary cancer syndromes. If a hereditary cancer syndrome is suspected, separate testing of a germline sample should be performed using an appropriate assay.
- Variants detected below Limits of Detection (LoD) not deemed to be confirmable by independent, orthogonal methods and/or in significant discordance with the tumor cellularity in the tested sample may be excluded as the clinical significance and reliability of such low-level mutation calls is not clear.
- Variant allelic frequency (VAF) is included for reported sequence variants and reflects the percentage of mutant reads compared to all reads present at the variant position. This number reflects a complex mixture of factors including tumor cellularity, potential CNVs and loss of heterozygosity, and potential subclonality. In addition, strand or allelic bias can significantly impact the measurement of specific variants in any sequencing platform. The clinical utility or meaning of this number in general is not considered established. Linearity of measurement should not be assumed.
- Copy number assessment by next generation sequencing can be affected by tumor cellularity, amplitude of gene amplification, enrichment of tumor during pre-analytical phase, library preparation methods and analysis algorithms. False negative results can be obtained in cases with low tumor percentage, low amplicon coverage and/or borderline copy number gains. Correlation with traditional methods of copy number assessment such as fluorescent in situ hybridization (FISH) is recommended as applicable.
- False negative fusion results can occur in cases with low fusion DNA molecules, low tumor cellularity, fusions occurring in highly repetitive intronic sequence contexts or fusions where the genomic breakpoint does not span within targeted introns covered by the panel (See Appendix Table 2). The assay requires a minimum of 20% tumor sample cellularity to reduce the potential for false negative results. Correlation with traditional methods of fusion detection such as fluorescent in situ hybridization (FISH) is recommended as applicable.
- Tumor mutational burden (TMB) is determined by measuring the number of somatic mutations occurring in sequenced genes and specified as a rate (mutations per megabase [mut/Mb]). TMB is calculated for all samples and includes the sum of all somatic synonymous and non-synonymous variants present in the sample at a VAF near LoD and above the noise-level of the assay (after filtering). The number of mutations per megabase may be reported as a nominal number rounded to the closest integer. TMB in cases with low sequence quality cannot be established and may be reported as "Not Reportable".
- The microsatellite instability high (MSI-H) and microsatellite stable (MSS) reported by MDA MAPP is based on the analysis of 40+ informative microsatellite loci. The total number of sites evaluated is dependent on coverage metrics over candidate MSI regions in the paired tumor and normal samples. Microsatellite instability is reported as "Undetermined" if the sample does not meet the required thresholds to make a MSI-H or MSS call. The thresholds for designating these calls were established by analytical concordance to comparator assays (PCR, IHC and NGS) using a wide selection of tumor tissue types including colorectal and endometrial cancers. Confirmatory testing of microsatellite instability (MSI-PCR, *MLH1* promoter methylation) and DNA mismatch repair gene assessment (MMR deficiency) is recommended as applicable for complete evaluation.
- Correlation with clinicopathologic features and prevalent clinical practice guidelines is recommended for complete evaluation and integration of genomic findings in patient care decisions.

Sequencing coverage of the genes: The following table describes the extent and adequacy of coverage for ordered genes only. Covered genes/exons/codons are defined as those having total coverage depth of greater than or equal to 100 UMI-error-corrected, collapsed reads (minimum 100x coverage). Mutations in ordered genes outside the optimally covered regions listed below may be detected with diminished sensitivity and cannot be ruled out. Coverage information for non-ordered genes for this sample is complex and lengthy, but may be requested from the laboratory if required for clinical care or correlative purposes.

Coverage for ordered genes and codon(s) tested with a minimum of 100x coverage

Gene	Exons (codons) tested

APPENDIX:

Table 1: Genes of interest for SNVs, INDELs and CNVs

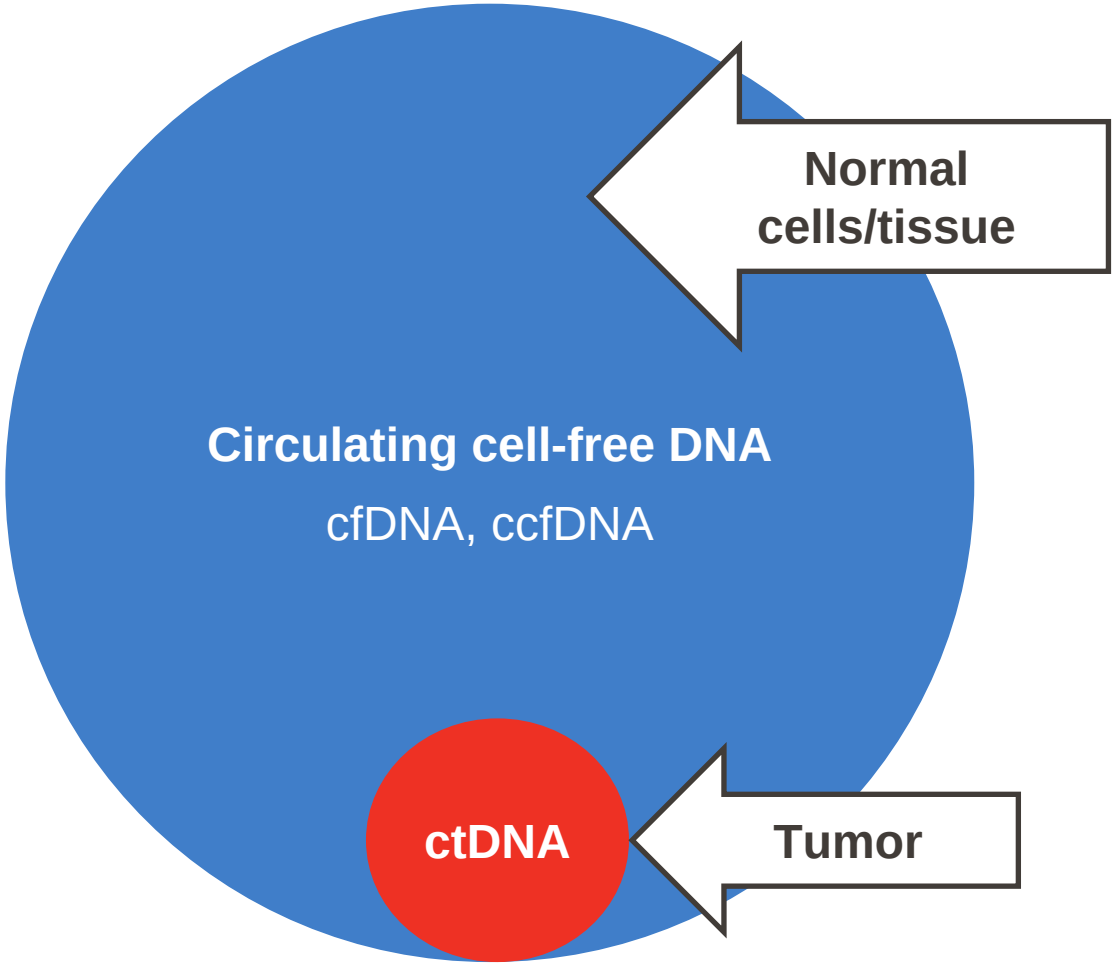
ABL1	*BRCA1*	*CTNNA1*	*ETV4*	*GNA13*	*IRF2*	*MGMT*	*PAXX*	*PTPN11*	*SDHC*	*TEK*
ABL2	*BRCA2*	*CTNNB1*	*ETV5*	*GNAQ*	*IRF4*	*MITF*	*PBRM1*	*PTPRB*	*SDHD*	*TENT5C*
ABRAXAS1	*BRD4*	*CUL3*	*ETV6*	*GNAS*	*IRS1*	*MLH1*	*PCNA*	*PTPRD*	*SESN1*	*TERC*+*
ACVR1	*BRIP1*	*CUL4A*	*EWSR1*	*GPS2*	*IRS2*	*MLH3*	*PDCD1*	*PTPRS*	*SETBP1*	*TERT^*
ACVR1B	*BTG1**	*CUL4B*	*EXO1*	*GRIN2A*	*JAK1*	*MPL*	*PDCD1LG2*	*PTPRT*	*SETD2*	*TET1*
ACVR2A	*BTG2**	*CUX1*	*EZH2*	*GRM3*	*JAK2*	*MRE11*	*PDGFB*	*QKI*	*SF3B1*	*TET2*
ADGRA2	*BTK*	*CXCR4*	*FADD*	*GSK3B*	*JAK3*	*MSH2*	*PDGFRA*	*RAB35*	*SGK1*	*TFE3*
AJUBA	*BUB1*	*CYLD*	*FANCA*	*H1-2**	*JUN*	*MSH3*	*PDGFRB*	*RAC1*	*SH2B3*	*TGFB1*
AKT1	*CALR*	*CYP2C19*	*FANCC*	*H2AX**	*KAT6A*	*MSH6*	*PDK1*	*RAD21*	*SH2D1A*	*TGFBR1*
AKT2	*CARD11*	*DAXX*	*FANCD2*	*H2BC5**	*KDM5A*	*MST1*	*PER1*	*RAD50*	*SHLD1*	*TGFBR2*
AKT3	*CASP8*	*DCLRE1C*	*FANCE*	*H3-3A**	*KDM5C*	*MST1R*	*PGD*	*RAD51*	*SHLD2*	*TMEM127*
AKTIP	*CBFB*	*DCUN1D1*	*FANCF*	*H3-3B**	*KDM6A*	*MTAP*	*PGR*	*RAD51AP1*	*SHPRH*	*TMPRSS2*
ALK	*CBL*	*DDB1*	*FANCG*	*H3-4**	*KDR*	*MTOR*	*PHF6*	*RAD51B*	*SHQ1*	*TNF*
ALOX12B	*CCN6*	*DDR1*	*FANCI*	*H3-5**	*KEAP1*	*MUTYH*	*PHOX2B*	*RAD51C*	*SLC34A2*	*TNFAIP3*
AMER1	*CCNA2*	*DDR2*	*FANCL*	*H3C1**	*KEL*	*MXD4*	*PIK3C2B*	*RAD51D*	*SLIT2*	*TNFRSF14*
ANKRD11	*CCND1*	*DDX3X*	*FANCM*	*H3C10**	*KIT*	*MYB*	*PIK3C2G*	*RAD52*	*SLX4*	*TOP1*
APC	*CCND2*	*DICER1*	*FAS*	*H3C11**	*KLF4*	*MYC*	*PIK3C3*	*RAD54L*	*SMAD2*	*TOP2A*
AR	*CCND3*	*DIS3*	*FAT1*	*H3C12**	*KLHL6*	*MYCL*	*PIK3CA*	*RAF1*	*SMAD3*	*TOP3A*
ARAF	*CCNE1*	*DLL3*	*FBXW7*	*H3C13**	*KMT2A*	*MYCN*	*PIK3CB*	*RARA*	*SMAD4*	*TOPBP1*
ARFRP1	*CD274*	*DNA2*	*FGF10*	*H3C2**	*KMT2B*	*MYD88*	*PIK3CD*	*RASA1*	*SMARCA2*	*TP53*
ARID1A	*CD276*	*DNAJB1*	*FGF14*	*H3C3**	*KMT2C*	*MYOD1*	*PIK3CG*	*RB1*	*SMARCA4*	*TP53BP1*
ARID1B	*CD74*	*DNMT1*	*FGF19*	*H3C4**	*KMT2D*	*NBN*	*PIK3R1*	*RBM10*	*SMARCAD1*	*TP53I3*
ARID2	*CD79A*	*DNMT3A*	*FGF23*	*H3C6**	*KNSTRN*	*NCOA3*	*PIK3R2*	*RECQL4*	*SMARCB1*	*TP63*
ARID5B	*CD79B*	*DNMT3B*	*FGF3*	*H3C7**	*KRAS*	*NCOR1*	*PIK3R3*	*REL*	*SMARCD1*	*TRAF2*
ASCC3	*CDBA*	*DOT1L*	*FGF4*	*H3C8**	*LATS1*	*NEGR1*	*PIM1*	*RET*	*SMC1A*	*TRAF7*
ASPM	*CDC20*	*E2F3*	*FGF5*	*HDAC2*	*LATS2*	*NF1*	*PLCG1*	*REV3L*	*SMC3*	*TRAPPC13*
ASXL1	*CDC27*	*EED*	*FGF6*	*HDAC9*	*LCK*	*NF2*	*PLCG2*	*RFC1*	*SMC5*	*TSC1*
ASXL2	*CDC6*	*EGFL7*	*FGF9*	*HELQ*	*LIG4*	*NFE2L2*	*PLK2*	*RFC2*	*SMC6*	*TSC2*
ATM	*CDC73*	*EGFR*	*FGFR1*	*HERC2*	*LMO1*	*NFKBIA*	*PMAIP1**	*RFC3*	*SMO*	*TSHR*
ATR	*CDH1*	*EIF1AX*	*FGFR2*	*HFM1*	*LRP1B*	*NHEJ1*	*PML*	*RFC4*	*SNCAIP*	*TTK*
ATRX	*CDK12*	*EIF4A2*	*FGFR3*	*HGF*	*LYN*	*NKX2-1*	*PMS1*	*RFC5*	*SOCS1*	*TYRO3*
AURKA	*CDK2*	*EIF4E*	*FGFR4*	*HLA-A*	*MAD2L2*	*NKX3-1*	*PMS2*	*RHEB*	*SOS1*	*U2AF1*
AURKB	*CDK4*	*ELF3*	*FH*	*HNF1A*	*MAGOH*	*NOTCH1*	*PNKP*	*RHOA*	*SOX10*	*VEGFA*
AURKC	*CDK6*	*ELOC*	*FLCN*	*HOXB13*	*MALT1*	*NOTCH2*	*PNRC1*	*RICTOR*	*SOX17*	*VHL*
AXIN1	*CDK8*	*EMSY*	*FLT1*	*HRAS*	*MAP2K1*	*NOTCH3*	*POLA1*	*RIF1*	*SOX2*	*VTCN1*
AXIN2	*CDKN1A*	*ENO1*	*FLT3*	*HSD3B1*	*MAP2K2*	*NOTCH4*	*POLD1*	*RIT1*	*SOX9*	*WRN*
AXL	*CDKN1B*	*EP300*	*FLT4*	*HSP90AA1*	*MAP2K4*	*NPM1*	*POLE*	*RMI1*	*SPEN*	*WT1*
B2M	*CDKN2A*	*EPCAM*	*FOXA1*	*HSP90AB1*	*MAP2K7*	*NRAS*	*POLQ*	*RMI2**	*SPOP*	*XIAP*
BAP1	*CDKN2B*	*EPHA2*	*FOXL2*	*ICOSLG*	*MAP3K1*	*NSD1*	*PPARG*	*RNF43*	*SRC*	*XPO1*
BARD1	*CDKN2C**	*EPHA3*	*FOXO1*	*ID3**	*MAP3K13*	*NSD3*	*PPM1D*	*ROS1*	*SRSF2*	*XRCC2*
BBC3	*CEBPA*	*EPHA5*	*FOXP1*	*IDH1*	*MAP3K14*	*NT5C2*	*PPP1R3A*	*RPA1*	*SSBP1*	*XRCC3*
BCL10	*CENPA*	*EPHA7*	*FRS2*	*IDH2*	*MAP3K4*	*NTRK1*	*PPP2R1A*	*RPA2*	*STAG2*	*XRCC4*
BCL11A	*CENPE*	*EPHB1*	*FTO*	*IFNGR1*	*MAPK1*	*NTRK2*	*PPP2R2A*	*RPA3**	*STAT3*	*XRCC5*
BCL2	*CHAF1A*	*ERBB2*	*FUBP1*	*IGF1*	*MAPK3*	*NTRK3*	*PPP4R4*	*RPA4*	*STAT4*	*XRCC6*
BCL2L1	*CHEK1*	*ERBB3*	*FYN*	*IGF1R*	*MAPK8*	*NUP93*	*PPP6C*	*RPS6KA4*	*STAT5A*	*YAP1*
BCL2L11	*CHEK2*	*ERBB4*	*GABRA6*	*IGF2*	*MAX*	*NUTM1*	*PRC1*	*RPS6KB1*	*STAT5B*	*YES1*
*BCL2L2**	*CIC*	*ERCC1*	*GADD45A*	*IKBKE*	*MCL1*	*PAK1*	*PRDM1*	*RPS6KB2*	*STK11*	*ZFHX3*
BCL6	*COL2A1*	*ERCC2*	*GATA1*	*IKZF1*	*MDC1*	*PAK3*	*PREX2*	*RPTOR*	*STK19*	*ZNF217*
BCOR	*COP1*	*ERCC3*	*GATA2*	*IL10*	*MDM2*	*PAK5*	*PRG4*	*RSPO1*	*STK40*	*ZNF703*
BCORL1	*CREBBP*	*ERCC4*	*GATA3*	*IL7R*	*MDM4*	*PALB2*	*PRKAR1A*	*RSPO2*	*SUFU*	*ZRSR2*
BCR	*CRKL*	*ERCC5*	*GATA4*	*INHA*	*MED12*	*PARP1*	*PRKCI*	*RUNX1*	*SUZ12*	
BIRC2	*CRLF2*	*ERCC6*	*GATA6*	*INHBA*	*MEF2B*	*PARP2*	*PRKDC*	*RUNX1T1*	*SYK*	
BIRC3	*CSF1R*	*ERG*	*GEN1*	*INO80*	*MEN1*	*PARP3*	*PRKN*	*RYBP*	*TBC1D4*	
BLM	*CSF3R*	*ERRFI1*	*GID4*	*INPP4A*	*MERTK*	*PARP4*	*PTCH1*	*SDHA*	*TBX3*	
BMPR1A	*CTCF*	*ESR1*	*GLI1*	*INPP4B*	*MET*	*PARP8P*	*PTEN*	*SDHAF2*	*TCF3*	
BRAF	*CTLA4*	*ETV1*	*GNA11*	*INSR*	*MGA*	*PAX5*	*PTK2*	*SDHB*	*TCF7L2*	

*Gene not included for CNV reporting
^ Includes promoter region
+ ncRNA Gene

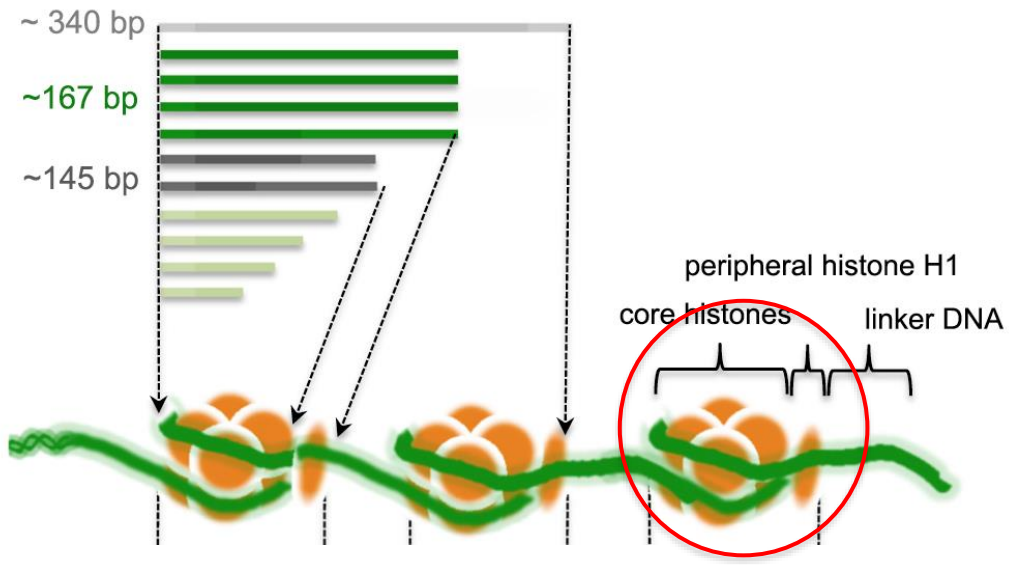
Table 2. Genes with select intronic regions for the detection of DNA-based gene rearrangements

ALK introns: 18-19	*BRCA2* introns: 2	*ETV4* introns: 5-6	*EZR* introns: 9-11	*KIT* introns: 16	*MYB* introns: 14	*NTRK2* introns: 12	*RARA* introns: 2	*SDC4* introns: 2

Characteristics and Terminology for Circulating Tumor DNA (ctDNA)



167 bp fragments of DNA, a nucleosome



The linker DNA between nucleosomes is cleaved leaving 167 bp cell-free DNA fragments (145 bp plus a ~20 bp segment wrapping histone H1). Originally described by Wyllie in 1980.

Cancer

Chandrananda et al. 2015 BMC Medical Genomics.
Wyllie 1980 Nature.; Slide from Rick Lanman

cfDNA Genotyping Analysis

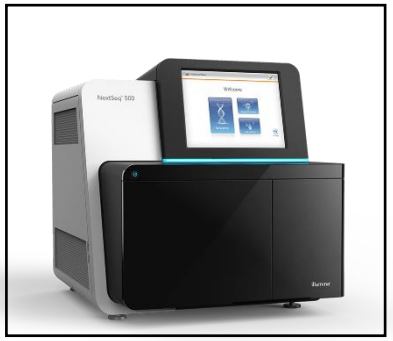
Pre-analytical Issues

Plasma

- Amount of blood/plasma
- Type of tubes
- Time for processing

Next Generation of Sequencing (NGS)

Ion Proton (Thermo Fisher)



Next-Seq (Illumina)

Large/ Intermediate Panels

- **1% VAF: ~100** tumor genomic equivalents (typical detection limit of most ctDNA assays)
- **0.01% VAF: ~1** tumor genomic equivalent

VAF = variant allele frequency

PCR-base Methods

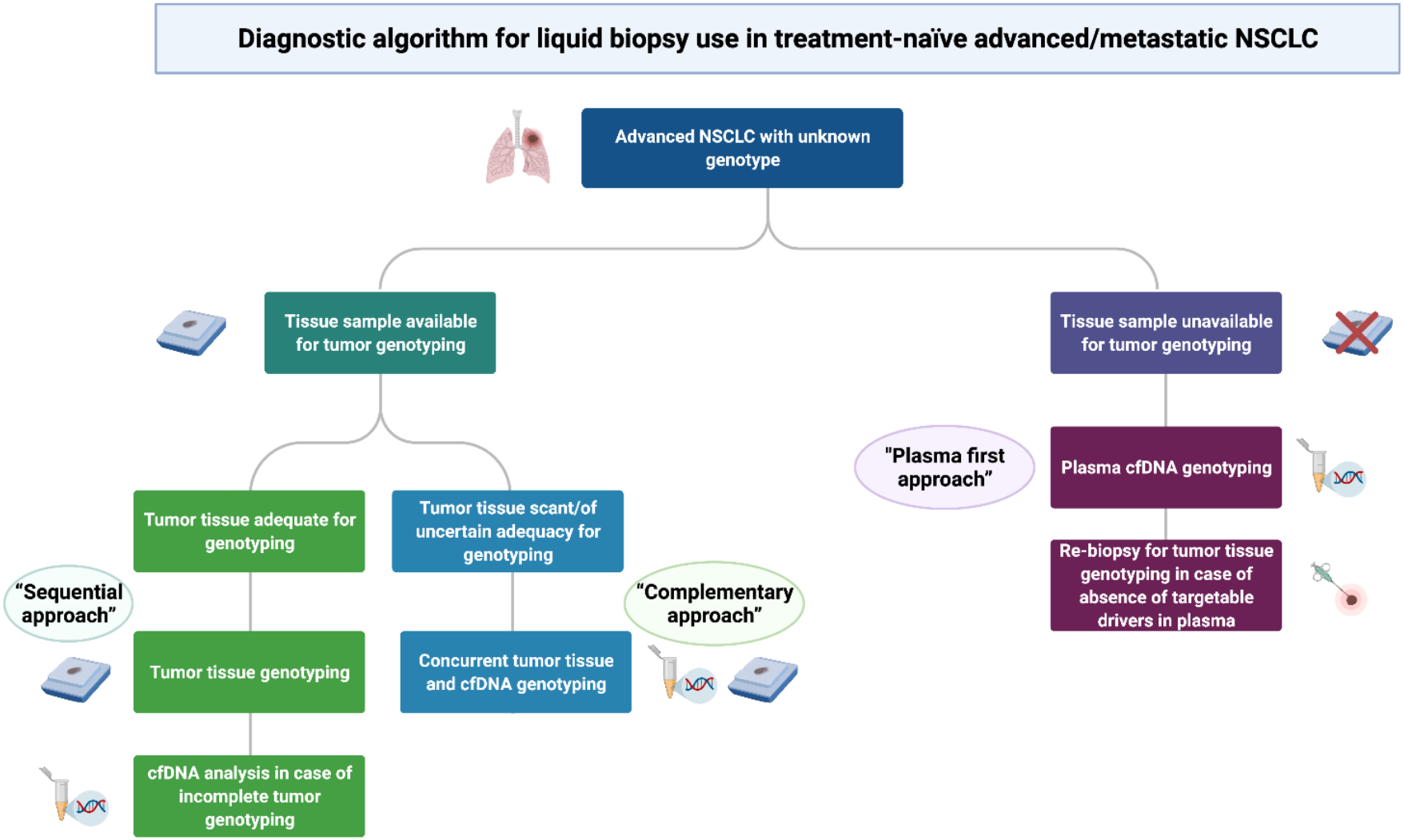
Didigal Droplet (dd)PCR (Biorad)

qPCR (Cobas)

Small Panels/ Single Genes

Cancer

Tissue vs. Liquid Biopsy for Molecular Profiling



Cancer

C. Rolfo et al, J Thorac Oncol, 2021

Thank You

Open Discussion: Questions & Answers

Angela Stroud, MSN, RN, CMSRN, NE-BC
Oncology Service Line Manager
Deaconess Health System

Session 3
Case Presentation

Session 3 Case Study

Provided by: Angela Stroud, MSN, RN, CMSRN, NE-BC
Deaconess Hospital, Evansville, Indiana
Focus: System-Level

Cancer Services: Locations

Henderson Hospital (KY)
- Medical Oncology
- Infusion

Gibson Hospital (IN)
- Medical Oncology
- Infusion

Memorial Hospital (IN)
- Medical Oncology
- Infusion
- Radiation Oncology

Chancellor Center for Oncology (IN)
- Medical Oncology
- Infusion
- Radiation Oncology

The Women's Hospital (IN)
- GYN/Breast Oncology
- High Risk Breast Clinic

JV: Baptist Health Deaconess (KY)
- Medical Oncology
- Infusion
- Radiation Oncology

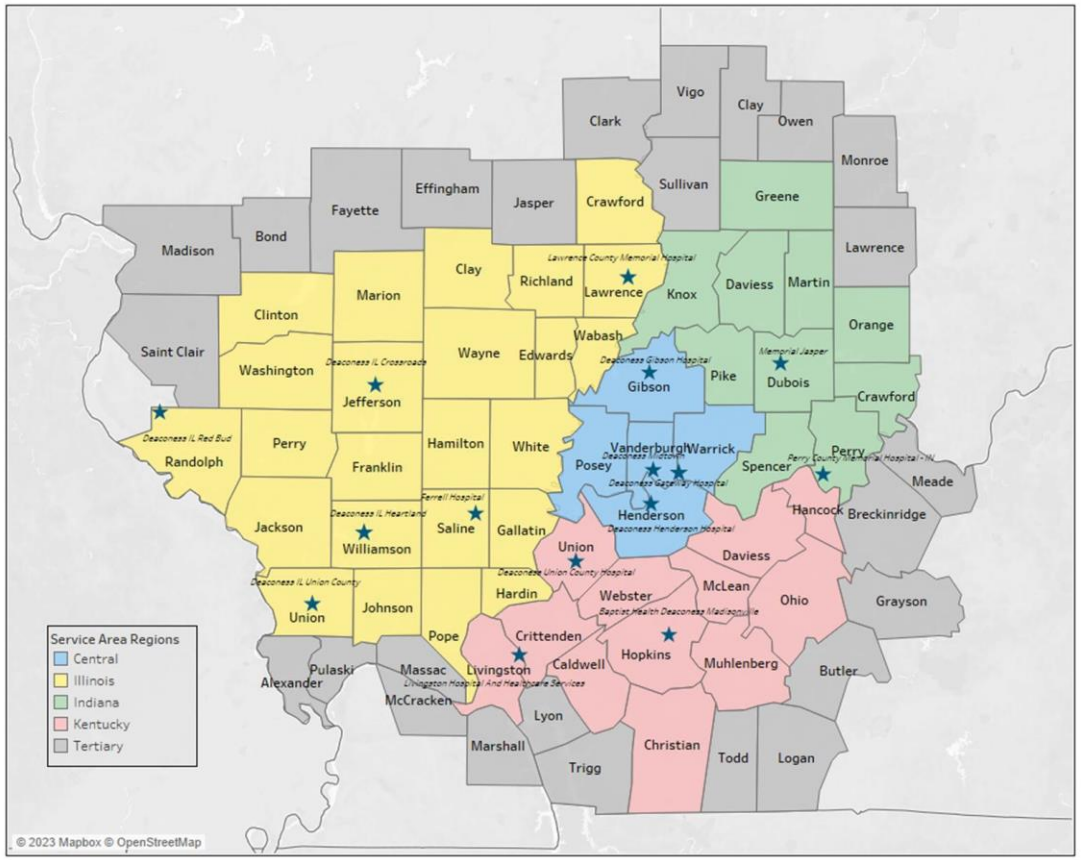
Heartland Hospital et al. (IL)
- *No current Oncology Program*
- *Non-chemo infusions*
- *1 PT Hematology provider*

Outreach Locations:
- Good Samaritan Hospital (IN)
- Ferrell Hospital (IL)
- *VA Hospital (IN)**
- *Wabash General (IL)**

**independent contracted facility*

ALL FOR YOU

Cancer Services: Service Area Map

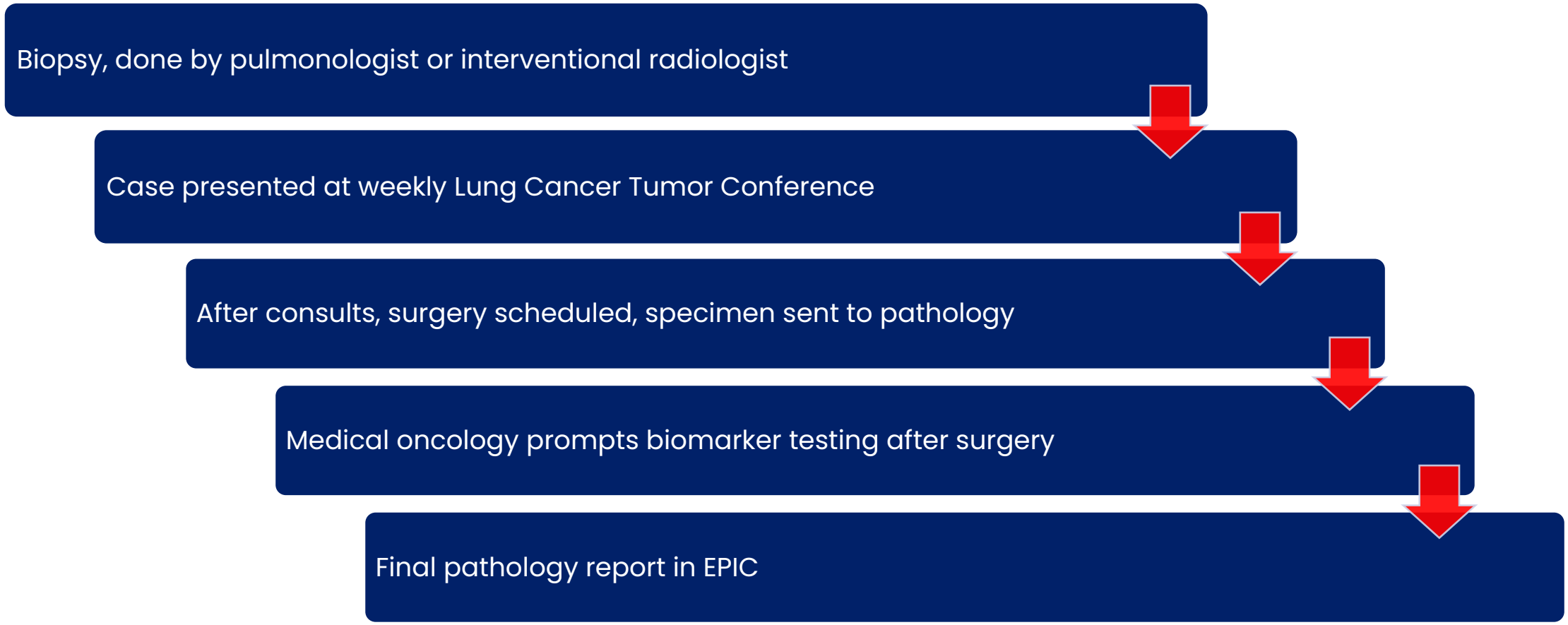


- Deaconess Health System is a multi-hospital system in 3 states (Indiana, Kentucky, and Illinois)
- Current service area includes 51-counties
- 4 separate CoC accredited programs within our system.
- Total analytic caseload for 2022 (IN locations only) 2655 with **267 Non-Small Cell Lung Cancer (NSCLC)**

Session 3 Case Study

Provided by: Angela Stroud, MSN, RN, CMSRN, NE-BC
Deaconess Hospital, Evansville, Indiana
Focus: System-Level

Current Workflow



Session 3 Case Study

Provided by: Angela Stroud, MSN, RN, NE-BC, CMSRN
Deaconess Hospital, Evansville, Indiana
Focus: System-Level

Challenges/Barriers

- No clearly defined system process for biomarker testing
- Health system and pathology/lab dept use different electronic health records
  - Health System uses EPIC
  - Pathology uses SunQuest
- No in-house biomarker testing options
- Pathologists are non-employed by the hospital but are contracted physicians, they don't do anything in Epic
- Pathologists do not make recommendations for specific further testing

Challenges/Barriers

- Biomarker testing isn't being ordered until the patient is seen by medical oncologists
- It could be requested/ordered through any number of reference labs depending on who medical oncologists prefers or who the pathologists send to
- High support staff turnover in pathology dept. delays specimens being sent out

Session 3 Case Study

Provided by: Deaconess Hospital
Focus: System

What are we trying to improve?

- Standardized process for where the specimen gets sent for testing
- Surveyed physicians on most used reference labs; identified top two companies
- We brought in top 2 (Foundation One and Neo-genomics) to pitch platforms
- Working on EPIC/Sunquest interface with vendors for ease of reporting and finding test results

Ideal State

- Defined system process for ordering the biomarker testing earlier in the process by having
- Pathology initiate the ordering and getting the specimens sent out sooner for testing
- Fully interfaced reporting between the reference lab and hospital system for ease of locating results report

Recent changes & impact

- Physician survey to narrow lab options from 5-6 to 2 preferred reference labs
- Working with pathology dept. leadership to track TAT for initial pathology reports and specimens sent out for testing
  - Timeline for each step in the process
- Current timing for in-house initial pathology results is 2-6 days

Session 3 Case Study

Provided by: Deaconess Hospital

Focus: System

Discussion & Questions

- Current best practice models/processes for getting the biomarker testing initiated?
- What others are doing to improve processes?

Key points

- Pathologists and laboratory department not part of hospital (contract) and uses SunQuest (hospital uses EPIC)
- No in-house biomarker testing options
- Medical oncologists currently order biomarker testing; recently identified two reference lab companies used most often

Case Summary

- Total analytic caseload for 2022 (IN locations only) 2655 - **267 (NSCLC) cases**
- 53 patients diagnosed with Stage IVA - 21 cases receiving biomarker testing
- 19 patients diagnosed with Stage IVB - 16 cases receiving biomarker testing
- Working to create standardized process for biomarker testing; narrowed to two reference lab companies
- Ideally new process will have pathology initiating ordering and sending specimens for testing earlier
- Creating EPIC/SunQuest interfaces with vendors to improve reporting/results

Open Discussion: Questions & Answers

Session Reminders

Session 3 Slides, Recordings, & Resources will be made available within one week. All resources will be available on the **ACS ECHO Website.**

Register Today for Session 4

March 27, 2024

4:00 – 5:00 PM EST

Topic: Improving Turnaround Time
Didactic Presenter: Jason Merker, MD, PhD, Associate Professor, Department of Pathology and Laboratory Medicine & Genetics
University of North Carolina
Lineberger Comprehensive Cancer Center
Case Presenter:

Session #	Month	Date	Time (ET)	Didactic Topic	Didactic Presenter	Facilitator
~~0~~	~~December~~	~~Weds. 12/13~~	~~4:00 -5:00pm~~	~~Series Kick-Off: Introduction to ECHO and Biomarker Testing Guideline Overview:~~	~~Mimi Ceppa, MD, Aakash Desai, MBBS, MPH, Hilary Goeckner~~	~~Bruce E. Johnson, MD, FASCO~~
~~1~~	~~January~~	~~Weds. 1/17~~	~~4:00 -5:00pm~~	~~Understanding the Barriers and Pathways to Lung Cancer Biomarker Testing~~	~~Millie Das, MD~~	~~Timothy Mullett, MD, MBA, FACS~~
~~2~~	~~February~~	~~Fri. 2/9~~	~~4:00 -5:00pm~~	~~Adequate Tissue for Sampling~~	~~Nichole Tanner, MD, MSCR~~	~~Bruce E. Johnson, MD, FASCO~~
~~3~~	~~March~~	~~Weds. 3/6~~	~~4:00 -5:00pm~~	~~Choice of Panel, Interpretation of Results and Next Steps~~	~~Ignacio Wistuba, MD~~	~~Timothy Mullett, MD, MBA, FACS~~
4	March	Weds. 3/27	4:00 -5:00pm	Improving Turnaround Time	Jason Merker, MD, PhD	Bruce E. Johnson, MD, FASCO
5	April	Weds. 4/24	2:00 - 3:00pm	Navigating Insurance Complexities	Hilary Goeckner & Cori Chandler	Bruce E. Johnson, MD, FASCO
6	May	Fri. 5/24	12:00 - 1:00pm	Series Wrap Up and Next Steps	Patient speaker	Timothy Mullett, MD, MBA, FACS

A Few Reminders

Next ECHO Session: March 27, 2024, 4:00-5:00 PM ET Topic: Improving Turnaround Time

Please *register now* for **Session 4** by using the QR code or the link in the chat.

Slides, Recordings, & Resources will be made available within one week. All resources will be available on the **ACS ECHO Website.**

Case Presentations: Ready to schedule your presentation?
Contact Korey.Hofmann@cancer.org

Please send us a high-definition logo for your system.

Contact Korey if you haven't received calendar invitations for **Sessions 4 -6**.

Questions? Korey Hofmann | korey.hofmann@cancer.org or Mindi Odom | mindi.odom@cancer.org

Questions?

American Cancer Society | NATIONAL LUNG CANCER ROUNDTABLE | Project ECHO

Thank You