Thank you for joining us.
The program will commence momentarily.

Virtual Molecular Tumor Board: Role of Genomic Profiling for Patients with Solid Tumors and the Optimal Application of Available Testing Platforms

Friday, July 31, 2020

9:00 AM – 10:00 AM ET

Faculty

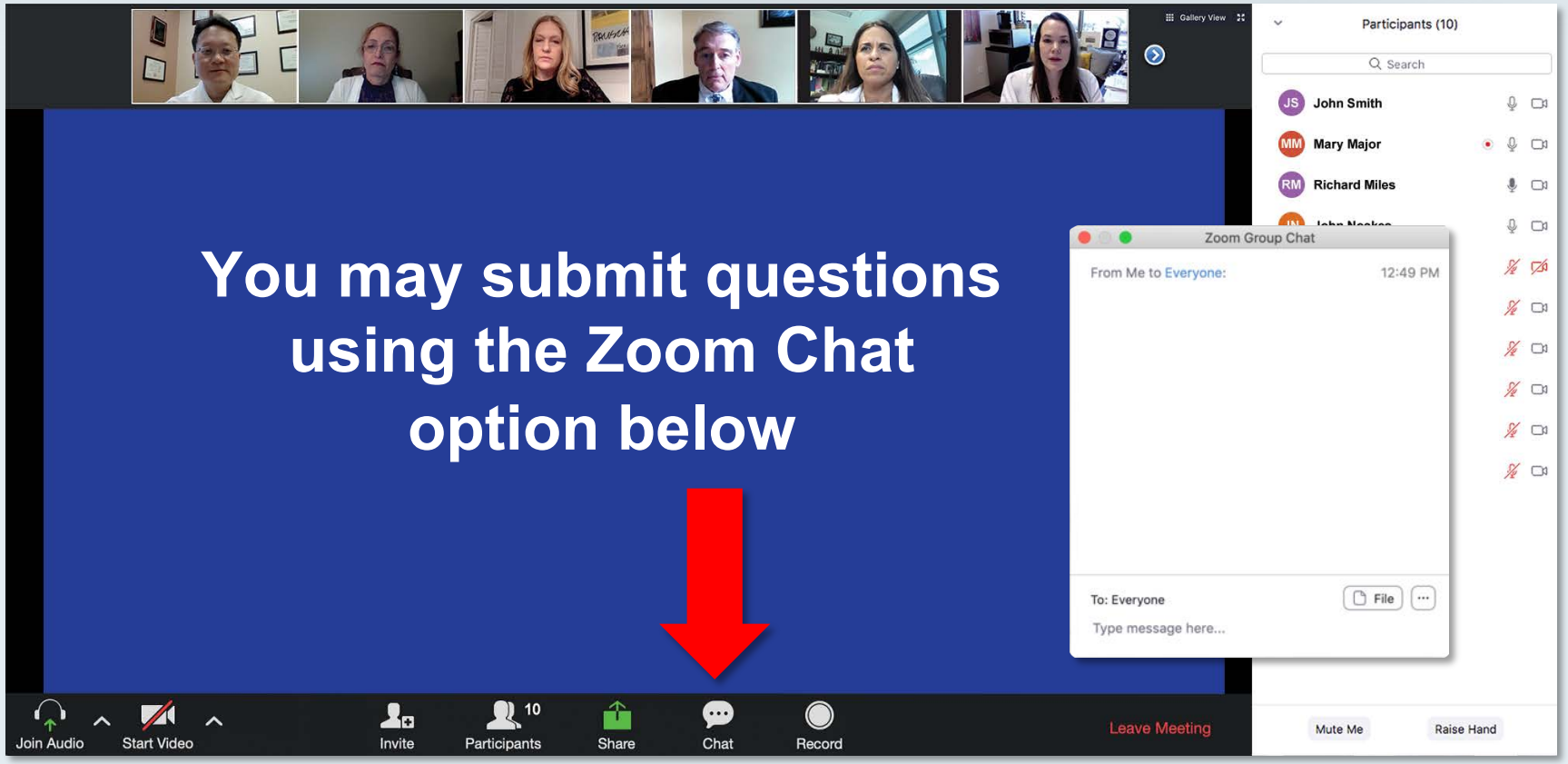
Andrew McKenzie, PhD
Bryan P Schneider, MD
Milan Radovich, PhD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Dr Love and Faculty Encourage You to Ask Questions



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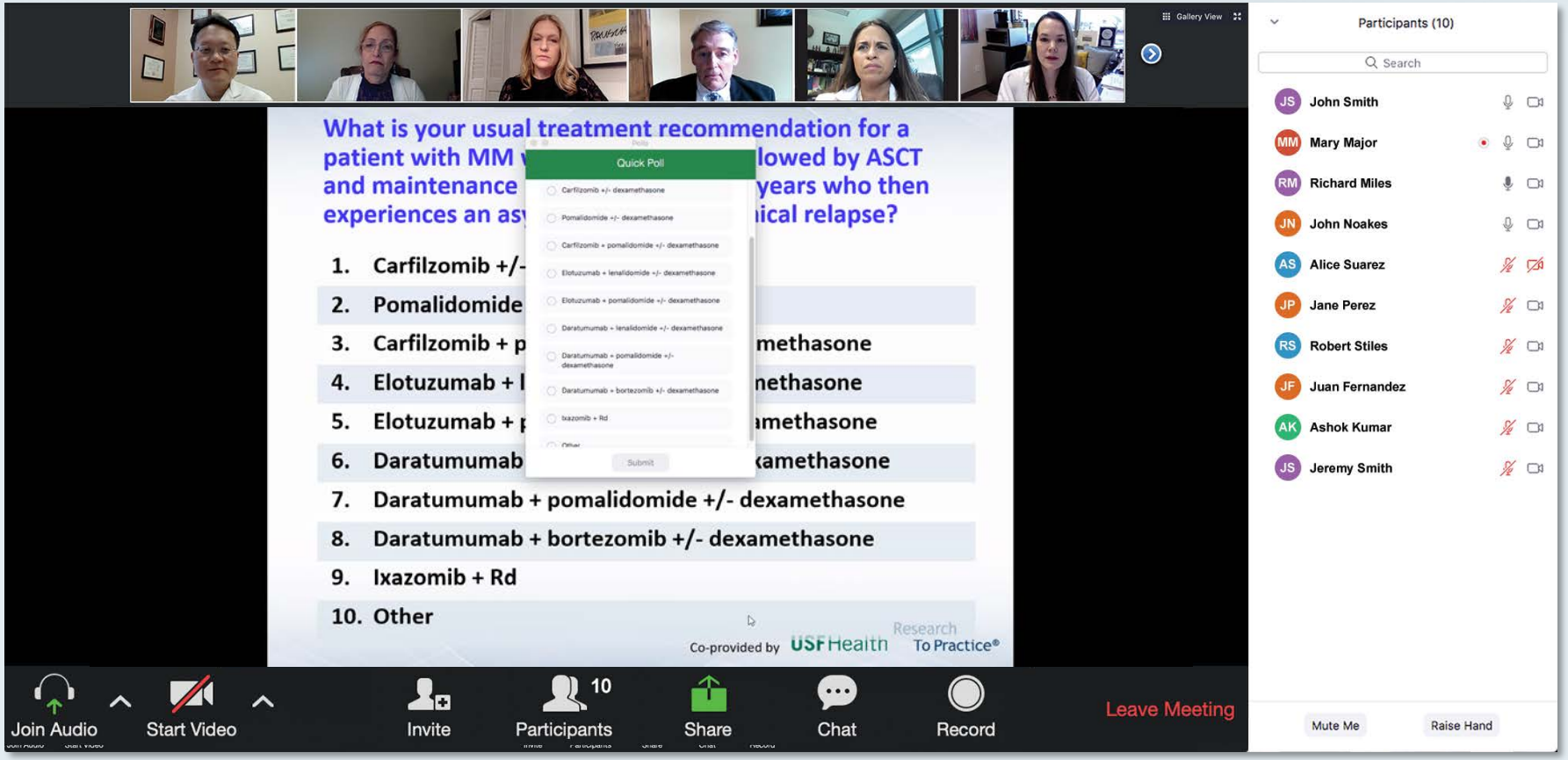
Familiarizing yourself with the Zoom interface
How to answer poll questions



When a poll question pops up, click your answer choice from the available options. Results will be shown after everyone has answered.

Commercial Support

This activity is supported by an educational grant from Lilly.

Dr Love — Disclosures

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Dr McKenzie — Disclosures

No relevant conflicts of interest to disclose

Dr Schneider — Disclosures

No relevant conflicts of interest to disclose

Dr Radovich — Disclosures

Contracted Research	Boston Biomedical Inc, Lilly
Ownership Interest	Immunomedics Inc, LifeOmic Health LLC, Tyme Inc

Virtual Molecular Tumor Board: Optimizing Biomarker-Based Decision-Making for Patients with Solid Tumors

Identification of New and Emerging Genomic Alterations in Metastatic Non-Small Cell Lung Cancer

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9:00 AM – 10:00 AM ET

Alexander E Drilon, MD

Recognition and Management of Targetable Tumor Mutations in Less Common Cancer Types

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Marcia S Brose, MD, PhD

All sessions moderated by Neil Love, MD and featuring Bryan Schneider, MD and Milan Radovich, PhD of the Indiana University Health Precision Genomics Program

Upcoming Live Webinars

Monday, August 3, 2020
5:00 PM – 6:00 PM ET

Recent Advances in Medical Oncology: Urothelial Bladder Carcinoma

Faculty
Arjun Balar, MD
Thomas Powles, MBBS, MRCP, MD
Arlene Siefker-Radtke, MD

Moderator
Neil Love, MD

Tuesday, August 4, 2020
1:00 PM – 2:00 PM ET

Clinical Investigator Perspectives on the Current and Future Management of Multiple Myeloma

Faculty
Shaji K Kumar, MD

Moderator
Neil Love, MD

Upcoming Live Webinars

Wednesday, August 5, 2020
5:00 PM – 6:30 PM ET

Recent Advances in Medical Oncology: Immunotherapy and Other Nontargeted Approaches for Lung Cancer

Faculty
Edward B Garon, MD, MS
Stephen V Liu, MD
David R Spigel, MD

Moderator
Neil Love, MD

Thursday, August 6, 2020
12:00 PM – 1:00 PM ET

Current Questions and Controversies in the Management of Lung Cancer

Faculty
John V Heymach, MD, PhD

Moderator
Neil Love, MD

Upcoming Live Webinars

Monday, August 10, 2020
5:00 PM – 6:00 PM ET

Recent Advances in Medical Oncology: Hodgkin and Non-Hodgkin Lymphomas

Faculty
Jeremy Abramson, MD
Christopher R Flowers, MD, MS

Moderator
Neil Love, MD

Wednesday, August 12, 2020
5:00 PM – 6:30 PM ET

Recent Advances in Medical Oncology: Hepatocellular Carcinoma and Pancreatic Cancer

Faculty
Tanios Bekaii-Saab, MD
Eileen M O'Reilly, MD
Philip A Philip, MD, PhD, FRCP
Alan P Venook, MD

Moderator
Neil Love, MD

Upcoming Live Webinars

Monday, August 17, 2020
5:00 PM – 6:00 PM ET

Recent Advances in Medical Oncology: ER-Positive Breast Cancer

Faculty
Virginia Kaklamani, MD, DSc
Sara M Tolaney, MD, MPH

Moderator
Neil Love, MD

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Bryan P Schneider, MD
The Vera Bradley Professor of Oncology
Director of the IU Health Precision Genomics Program
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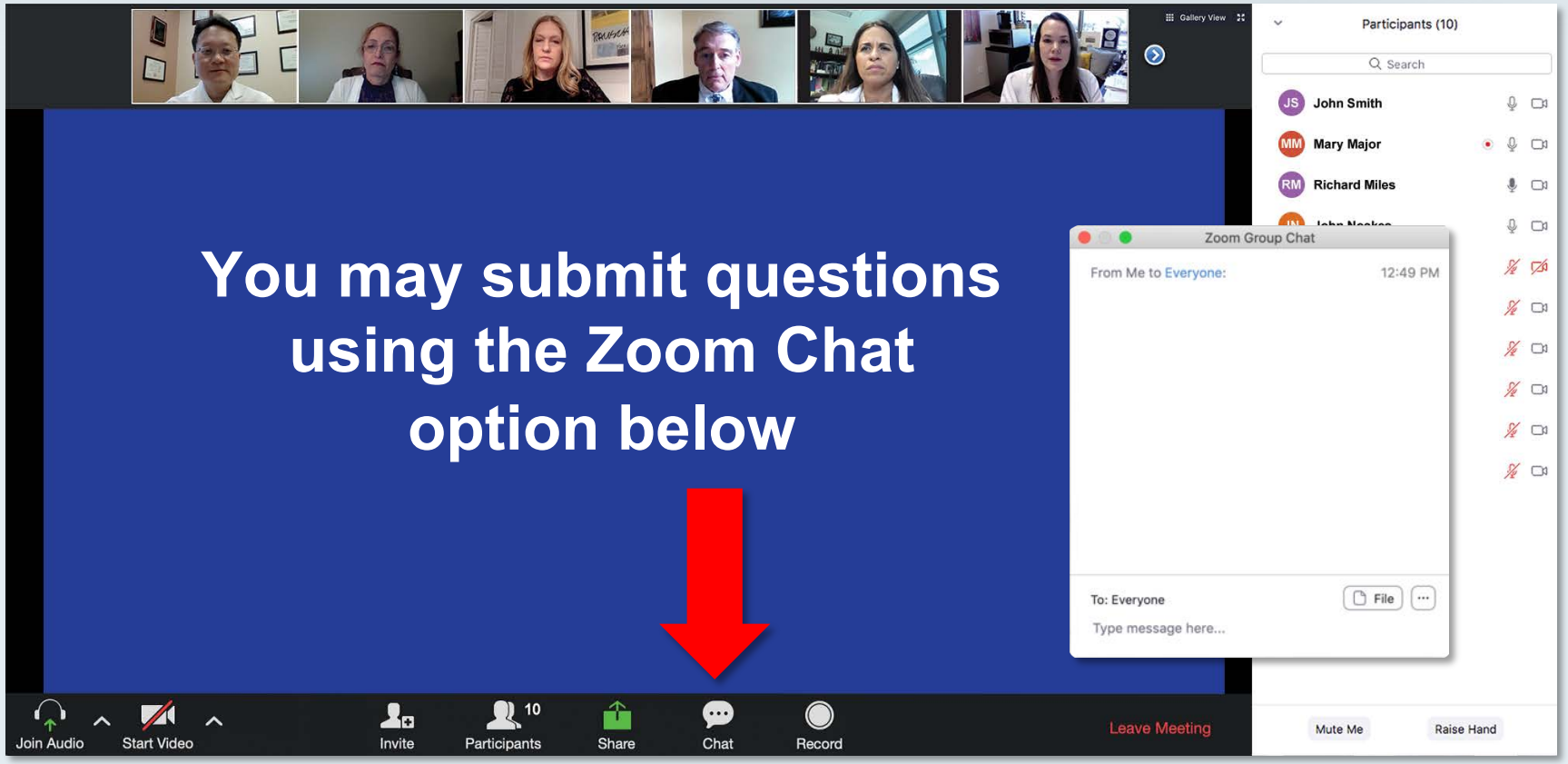

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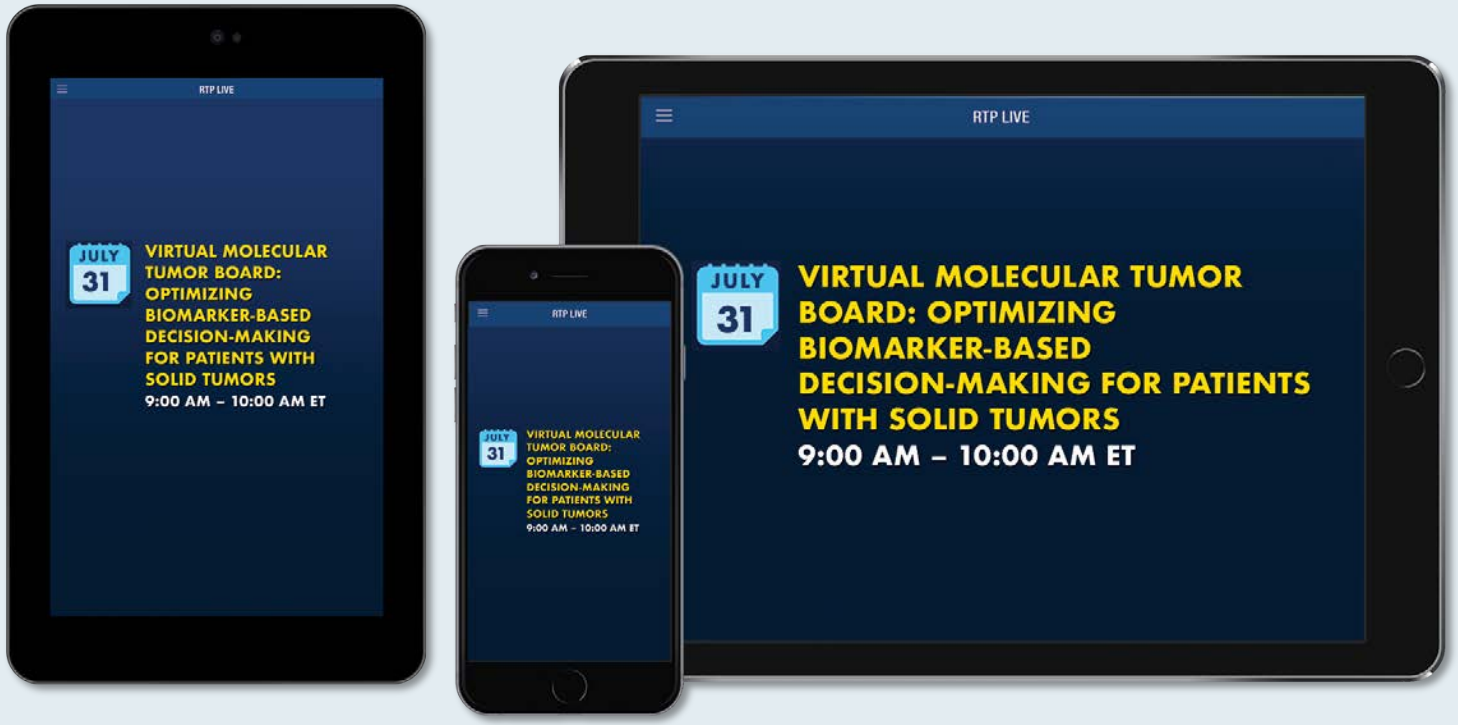

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Case 1: 76-year-old man with prostate cancer

- **HISTORY OF PRESENT ILLNESS:** 76-year-old man with advanced prostate cancer. The patient's history includes having been diagnosed with prostate cancer in 2004. He received 1 month of androgen deprivation therapy and then underwent a prostatectomy where he had a Gleason 8 prostate adenocarcinoma with ductal features. He had salvage radiation therapy due to a biochemical relapse where he completed only 10/32 planned doses due to substantial colitis. He subsequently had biochemical relapse and oligometastatic bone met in 2016 and was started on leuprolide. He did not tolerate the side effects of leuprolide and was switched to degarelix and had radiation therapy to his oligometastatic site in the left acetabulum. He has had substantial toxicity associated with the degarelix including substantial hot flashes, chills, just feeling generally poorly, and has stopped these at this time. His most recent imaging showed no disease outside the bone but new left inferior pubic ramus metastasis and increased disease in the left acetabulum and pubic bone. He is currently off all therapy and here now to discuss genomic sequencing to help guide future targeted therapy.
- **PAST MEDICAL HISTORY:** prostatectomy, cholecystectomy, spinal fusion s/p MVA, appendectomy.
- **FHx:** Brother with colon cancer in his 60s

Courtesy of Bryan P Schneider, MD and Milan Radovich, PhD

Diagnosis: **Prostate cancer**

TUMOR GENOMIC ALTERATIONS[1]				
AKT1 CTNNB1 ERCC5				
GENOMIC TARGETS	FDA-APPROVED DRUGS -for patient's cancer	FDA-APPROVED DRUGS -for another cancer	DRUGS PREDICTED NON-BENEFICIAL	POTENTIAL CLINICAL TRIALS
3	0	2	0	Yes
AKT1 (E17K)		everolimus, temsirolimus		Yes
CTNNB1 (S45P)				Yes
ERCC5 (K904fs)				Yes
TUMOR MUTATION BURDEN (TMB)				
LOW (1 mut/Mb)				No
MICROSATELLITE STATUS (MSI)				
STABLE				No

Courtesy of Bryan P Schneider, MD and Milan Radovich, PhD

Case 2: 80-year-old woman with metastatic endometrial cancer

80-year-old frail woman who was diagnosed with stage III endometrial cancer and had a hysterectomy and radiation therapy. Unable to tolerate adjuvant chemotherapy. Develops metastatic disease about a year later. Refuses chemotherapy. NGS shows AKT2 amplification. See attached NGS. Treated with off label Temsirolimus with disease control and objective response for 2 years and dies later of unrelated causes

Question:

Also has ERRB2 amplification. If you were treating her today could you use Trastuzumab Deruxtecan instead of chemo plus trastuzumab as was recently reported for metastatic uterine cancer?

Courtesy of Sulfi Ibrahim, MD

Case 2: NGS Report

OTHER ALTERATIONS & BIOMARKERS IDENTIFIED

Results reported in this section are not prescriptive or conclusive for labeled use of any specific therapeutic product. See *professional services* section for additional information.

Microsatellite status MS-Stable §
Tumor Mutational Burden 3 Muts/Mb §
AKT2 amplification §
CCNE1 amplification §
ERBB2 amplification §
ERBB3 amplification §
KRAS G12V
PIK3R1 K567E
TP53 R175H

§ Refer to appendix for limitation statements related to detection of any copy number alterations, gene rearrangements, MSI or TMB result in this section.

Please refer to appendix for Explanation of Clinical Significance Classification and for variants of unknown significance (VUS).

Courtesy of Sulfi Ibrahim, MD

Case 3: 58-year-old man with salivary gland cancer

- 58yr Male
- Diagnosed 2/2018 with salivary gland HNSCC
- Initiated cisplatin 3/2018
- Switched to carboplatin + paclitaxel 3/2018 – 9/2019 until progression
  - Testing 5/2019 revealed NTRK3-ETV6 fusion
- Larotrectinib initiated 10/2019 – present

SARAH CANNON

Courtesy of Andrew McKenzie, PhD

Case 3: 58-year-old man with salivary gland cancer (cont)

Interpretive content on this page and subsequent pages is provided as a professional service, and is not reviewed or approved by the FDA.

PATIENT

DISEASE Salivary gland myoepithelial carcinoma
NAME
DATE OF BIRTH
SEX Male
MEDICAL RECORD

PHYSICIAN

ORDERING PHYSICIAN
MEDICAL FACILITY
ADDITIONAL RECIPIENT None
MEDICAL FACILITY ID
PATHOLOGIST Not Provided

SPECIMEN

SPECIMEN SITE Lung
SPECIMEN ID
SPECIMEN TYPE Block
DATE OF COLLECTION 11 March 2019
SPECIMEN RECEIVED 27 March 2019

Biomarker Findings

Microsatellite status - MS-Stable
Tumor Mutational Burden - TMB-Low (0 Muts/Mb)

Genomic Findings

For a complete list of the genes assayed, please refer to the Appendix.

NTRK3 ETV6-NTRK3 fusion
ARID1A H203fs*197
CDKN2A/B loss
TERT promoter -146C>T

1 Therapies with Clinical Benefit
0 Therapies with Lack of Response
13 Clinical Trials

Courtesy of Andrew McKenzie, PhD

SARAH CANNON

Case 4: 80-year-old man with UBC

- **HISTORY OF PRESENT ILLNESS:** 80-year-old man with metastatic cancer either of urothelial or salivary gland origin. He was diagnosed with a superficial bladder cancer in 2016, for which he underwent transurethral resection and had a T1 lesion with no muscle invasion. He received BCG and did well until July 2018 when he developed a right anterior neck mass. Biopsy of this was consistent with metastatic urothelial carcinoma, and he subsequently started on pembrolizumab in September 2018. He had a mixed response to therapy, and pembrolizumab was held in January 2019. He then developed another right-sided neck mass, for which he underwent a right neck dissection on January 22, 2019, showing this time metastatic adenocarcinoma in 4 of 8 lymph nodes which were AR positive, GATA3 positive, CK7 positive, and mammaglobin positive. These findings were felt to be most consistent with a salivary gland cancer. Postoperatively, he underwent radiation therapy from March through May 2019. He also had 2 cycles of adjuvant pembrolizumab. More recently, he had progression of disease in September 2019 with increasing bone involvement and restarted pembrolizumab in September 2019. His most recent imaging in June 2020 showed progressive bone metastases with lung and bone involvement. He has recently started gemcitabine and carboplatin. He is status post 1 dose of that and tolerating well.
- **PAST MEDICAL HISTORY:** HTN
- **FHx:** Father lung cancer at 90

Courtesy of Bryan P Schneider, MD and Milan Radovich, PhD

Case 4: 80-year-old man with UBC (cont)

OTHER ALTERATIONS & BIOMARKERS IDENTIFIED

Results reported in this section are not prescriptive or conclusive for labeled use of any specific therapeutic product. See *professional services* section for additional information.

Microsatellite status MS-Stable §
Tumor Mutational Burden 67 Muts/Mb §
ASXL1 E635fs*15
ERBB2 R103Q
ERBB3 T355P
FBXW7 C453fs*43
MAP3K1 splice site 1965+1G>T
NOTCH3 R9fs*16
PALB2 S475*
PARK2 M1I
STAG2 splice site 1117-1G>T
TERT promoter -124C>T
TP53 E180K
TP53 E285V
TSC2 S625*
TSC2 splice site 1717-1G>C

§ Refer to appendix for limitation statements related to detection of any copy number alterations, gene rearrangements, BRCA1/2 alterations, LOH, MSI, or TMB results in this section.

Please refer to appendix for Explanation of Clinical Significance Classification and for variants of unknown significance (VUS).

Courtesy of Bryan P Schneider, MD and Milan Radovich, PhD

Case 5: 68-year-old with UBC

68-year-old with muscle invasive bladder cancer treated with neoadjuvant dose dense MVAC. Unable to tolerate and is stopped. Has a cystectomy. Found to have significant residual disease including metastatic disease to a pelvic lymph node.

Question:

- Would you give carboplatin-based adjuvant therapy or immunotherapy based on this NGS report?

Courtesy of Sulfi Ibrahim, MD

Case 5: NGS Report

OTHER ALTERATIONS & BIOMARKERS IDENTIFIED

Results reported in this section are not prescriptive or conclusive for labeled use of any specific therapeutic product. See *professional services* section for additional information.

Microsatellite status MS-Stable §

Tumor Mutational Burden 16 Muts/Mb §

CASP8 splice site 1356-1G>A

MCL1 amplification §

MLL2 E3081*

NOTCH3 BRD4(NM_014299)-NOTCH3(NM_000435) fusion (B9*; N1*) §

PIK3CA E545K

RAD21 Q214*

RET amplification §

TERT promoter -124C>T

TP53 R273C

§ Refer to appendix for limitation statements related to detection of any copy number alterations, gene rearrangements, BRCA1/2 alterations, LOH, MSI, or TMB results in this section.

Please refer to appendix for Explanation of Clinical Significance Classification and for variants of unknown significance (VUS).

Courtesy of Sulfi Ibrahim, MD

Case 6: 62-year-old man with cholangiocarcinoma

- 62yr Male
- Diagnosed 2/2015 with cholangiocarcinoma
  - Testing revealed FGFR2 rearrangement intron 17
- Adjuvant with capecitabine and irradiation and finished that in March of 2016
- Metastatic disease in the lungs 1/2018
- Cisplatin and gemcitabine 1/2018 – 10/2018
- Treatment break until 4/2019 then FOLFOX initiated until progression 7/2020
  - Test re-run on original 2015 sample confirming FGFR2 rearrangement
- Initiated erdafitinib 7/2020

SARAH CANNON

Courtesy of Andrew McKenzie, PhD

Case 6: 62-year-old man with cholangiocarcinoma (cont)

SPEC #: **S15-281**	STATUS: **SOUT**	PERFORMED AT:
RECEIVED: 02/02/15 1243	TOTAL TIME IN FORMALIN:12:30	
COLLECTED: 02/02/15	COLD ISCHEMIC TIME:0:00	

Addendum

The results of the test are received and yield the following:

Tumor Type: **Unknown Primary Carcinoma (NOS)**

Genomic Alterations Identified
FGFR2 rearrangement intron 17
BAP1 A359fs*39

Additional Findings
Microsatellite status MS-Stable
Tumor Mutation Burden TMB-low; 1 Muts/Mb

Please refer to the Laboratory/Scanned Reports in the patient's EMR for the scanned copy of the original complete report. PJD/dd - 3/8/2018

Date of Birth		Medical Facility			
Sex	Male	Ordering Physician		Specimen Received	12 February 2018
FMI Case #		Additional Recipient	Not Given	Specimen Site	Liver
Medical Record #		Medical Facility ID #		Date of Collection	02 February 2015
Specimen ID		Pathologist		Specimen Type	Block

ABOUT THE TEST:
FoundationOne™ is a next-generation sequencing (NGS) based assay that identifies genomic alterations within hundreds of cancer-related genes.

PATIENT RESULTS

- 4 genomic findings
- 2 therapies associated with potential clinical benefit
- 0 therapies associated with lack of response
- 5 clinical trials

TUMOR TYPE: UNKNOWN PRIMARY CARCINOMA (NOS)

Genomic Alterations Identified†
FGFR2 rearrangement intron 17
BAP1 A359fs*39

Additional Findings†
Microsatellite status MS-Stable
Tumor Mutation Burden TMB-Low; 1 Muts/Mb

† See a complete list of the genes assayed and performance specifications

While new test confirms FGFR2 rearrangement, a new biopsy should be taken to confirm active clone

SARAH CANNON

Courtesy of Andrew McKenzie, PhD

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FDA-approved/guideline-endorsed platforms for genomic testing; advantages and limitations of available assays

FDA Cleared/Approved Nucleic Acid Based Tests

Disease/Use	Trade Name	Submission
Tumor Profiling	MSK-IMPACT (Integrated Mutation Profiling Of Actionable Cancer Targets):A Hybridization-Capture Based Next Generation Sequencing Assay	DEN170058
	FoundationOne CDx	P170019
Tumor Profiling	Myriad myChoice CDx	P190014
Tumor Profiling	Omics Core	K190661
Tumor Profiling	PGDx elio tissue complete	K192063

"This is a list of nucleic acid-based tests that have been cleared or approved by the Center for Devices and Radiological Health. These tests analyze variations in the sequence, structure, or expression of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) in order to diagnose disease or medical conditions, infection with an identifiable pathogen, or determine genetic carrier status."

https://www.fda.gov/medical-devices/vitro-diagnostics/nucleic-acid-based-tests

Factors That Influence NGS Utility

- Analyte (DNA, RNA, Protein)
- Biopsy Type (Blood, Plasma, Urine, Saliva)
- Gene List (FDA approved genes, expanded gene panels)
- Tissue Requirement (Slides, FFPE block, input (ng of DNA/RNA))
- Turnaround Time (3 day (Paradigm) to 10-14 day (typical))
- FDA Approval

Commercial NGS Tests in Oncology Care

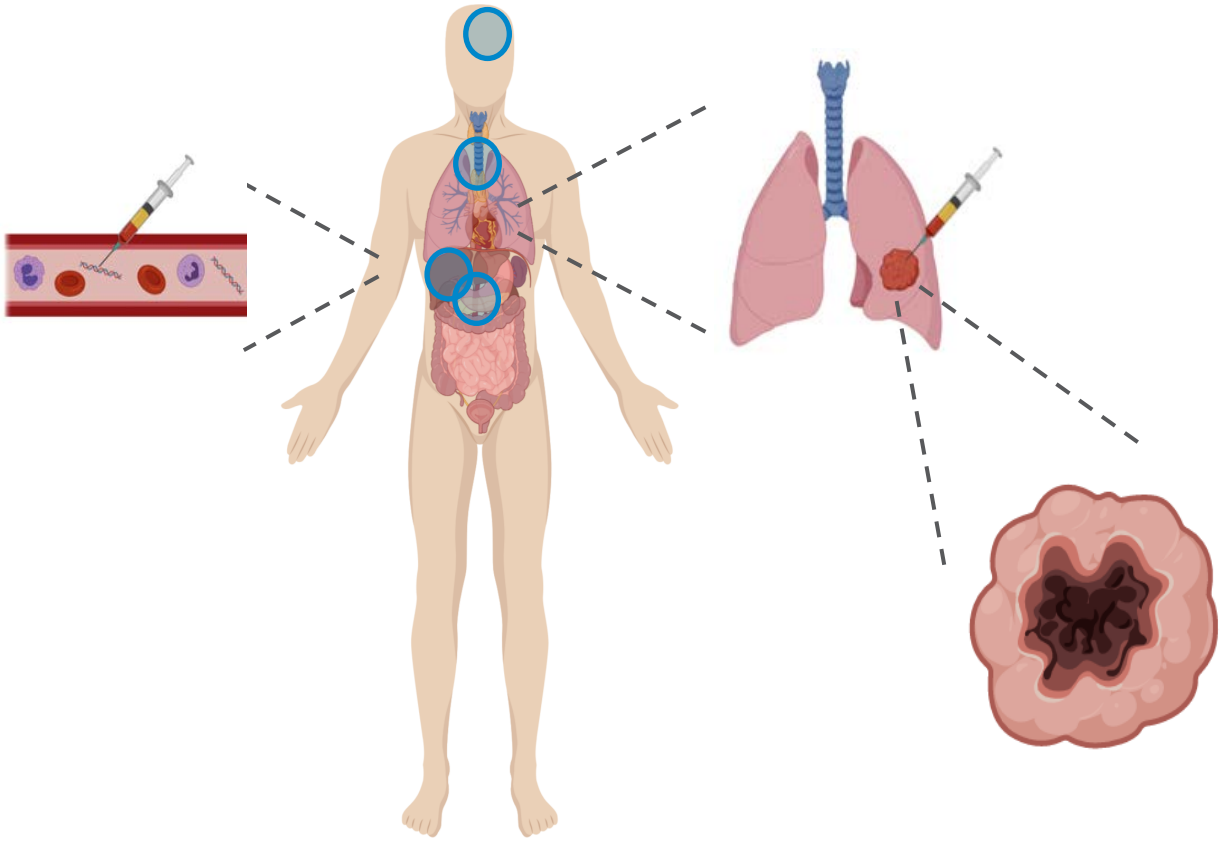
Test Name	Biopsy Type	Analyte	Tumor/Normal	No. of genes on panel	TMB	MSI	FDA approval	Reference
FoundationOne CDx	Tissue	DNA	No	324	Yes	Yes	Yes	https://assets.ctfassets.net/vhribv12lmne/4ZHUEfEiI8iOCk2Q6saGcU/11dd3b532e30c34f56cb8e9b4a896783/F1CDx_TechSpecs_10-
FoundationOne Liquid	Plasma	DNA	No	70	No	Yes	No	https://assets.ctfassets.net/vhribv12lmne/3SPYAcbGdqAeMsOqMyKUog/4e0d771e88afc920dc1a6f0515e2ff83/F1L_TechnicalInfor
FoundationOne Heme	Whole blood, bone marrow aspirate, or tissue	DNA/RNA	No	426	Yes	Yes	No	https://assets.ctfassets.net/vhribv12lmne/zBxaQC12cScqgsEk8seMO/c32a7d1adf083cb0f5d0c0b2439fdb87/F1H_Technical_Inform
MSK-IMPACT	Tissue	DNA	Yes	468	Yes	Yes	Yes	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5461196/
Caris Molecular Intelligence	Tissue	DNA/RNA/Protein*	No	442	Yes	Yes	No	https://www.carismolecularintelligence.com/wp-content/uploads/2017/05/TN0276-v7_Profile-Menu-Brochure.pdf
Guardant 360	Plasma	DNA	No	74	No	Yes	No	http://www.guardant360.com/?utm_source=AdWords&utm_term=Guardant360
PCDx	Tissue	DNA/RNA/Protein*	No	234	Yes	Yes	No	https://www.paradigmdx.com/wp-content/uploads/2018/11/technical-document-181109.pdf
Tempus|xT	Tissue	DNA/RNA/Protein*	Yes	648	Yes	Yes	No	https://www.tempus.com/genomic-sequencing/
Tempus|xF	Plasma	DNA	No	105	No	No	No	https://www.tempus.com/genomic-sequencing/
OncomineDx Target Test	Tissue	DNA/RNA	No	23	No	No	Yes	https://www.thermofisher.com/order/catalog/product/A32451
OmniSeq Advance	Tissue	DNA/RNA/Protein*	No	144	Yes	Yes	No	https://www.omniseq.com/omniseq-advance-assay/
OmniSeq Comprehensive	Tissue	DNA/RNA/Protein*	No	144	No	No	No	https://www.omniseq.com/comprehensive/
SmartGenomics	Tissue	DNA/RNA/Protein*	No	160	Yes	Yes	No	http://www.pathgroup.com/oncology/smartgenomics/
NeoType Discovery		DNA/RNA/Protein	No	323	Yes	Yes	No	https://neogenomics.com/test-menu/neotype-discovery-profile-solid-tumors
Trusight Oncology 500	Tissue	DNA/RNA	No	523	Yes	Yes	No	https://www.illumina.com/products/by-type/clinical-research-products/trusight-oncology-500.html

*Protein is assayed using IHC; vendors vary in the proteins assayed

SARAH CANNON

Utility of liquid biopsy; sensitivity, specificity and concordance with tissue-based testing

Tissue vs. Liquid Specimens



- Tissue
  - Who?
    - Metastatic cancers especially with access to clinical trials
    - Patients with recent biopsies with adequate tumor purity
    - Patients who can tolerate additional lines of therapy
  - Why?
    - DNA/RNA/Protein can all be analyzed
    - Complex fusions are more reliably detected
  - Drawbacks
    - Testing tumor heterogeneity is limited
    - Monitoring response over time is invasive (multiple biopsies)
- Liquid
  - Who?
    - Patients with bone-only or difficult to biopsy disease
    - Low tumor purity on tissue sample
    - No access to fresh biopsy
  - Why?
    - Ease of sample collection
    - Most actionable mutations are easily detected
    - Resistance / tumor heterogeneity monitoring
  - Drawbacks
    - Limited fusion detection
    - No RNA or protein analysis
    - Lower sensitivities

Tissue vs. Liquid Specimens – Same Patient, Different Results

Patient Name [redacted]

Final Report Date 12/2/2019

Non-Small Cell Lung Cancer (NSCLC)

Paradigm Cancer Diagnostic (PCDx)

Case/Specimen ID: [redacted]
Collection Site: Lung
Collection Date: 11/12/2019
Received for testing: 11/25/2019
Turnaround: 3 business days
Tumor cells: 20%
Specimen size: 8 mm²
Requirement met: Minimal

2 actionable genomic findings

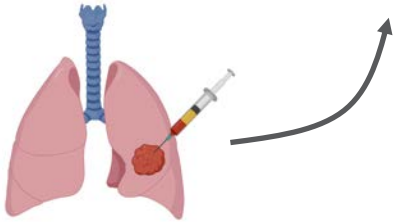
KRAS G12A
TP53 c.560-1G>T

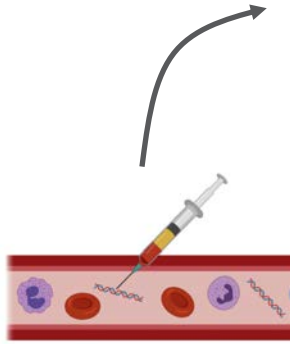
0 IHC

ALK QNS
PDL1:Tumor QNS
ROS1 QNS
hENT1 QNS
PDL1:TILs QNS
PTEN QNS
TRKpan QNS

Additional Findings: ALK Wildtype, BRAF Wildtype, EGFR Wildtype, ERBB2 Wildtype, MET Not Amplified, MYC Not Amplified

Immunotherapy TMB: Low (4muts/mb) MSI: Stable PD-L1: QNS





[redacted]
Patient MRN: [redacted] | DOB: FEB-28-1938 | Gender: Female
Diagnosis: Lung adenocarcinoma | Test Number 1

REPORTING
Report Date: DEC-03-2019
Receipt Date: NOV-26-2019
Collection Date: NOV-25-2019
Specimen: Blood
Status: FINAL

PHYSICIAN

Complete Tumor Response Map on page 2

Summary of Somatic Alterations & Associated Treatment Options

KEY Approved in indication | Approved in other indication | Lack of response

Alteration	% cfDNA or Amplification	Associated FDA-approved therapies	Clinical trial availability (see page 3)
EGFR R222C	0.1%	Afatinib, Dacomitinib, Erlotinib, Gefitinib, Neratinib, Osimertinib	Yes
TP53 V143M	1.7%	None	Yes
TP53 R248G	0.6%	None	Yes
TP53 I195F	0.3%	None	Yes

Variants of Uncertain Significance
MAPK3 Q266E (0.2%), *RIT1* R120* (0.2%)
The functional consequences and clinical significance of alterations are unknown. Relevance of therapies targeting these alterations is uncertain.

Synonymous Alterations
FGFR2 A314A (0.2%)
This sequence change does not alter the amino acid at this position and is unlikely to be a therapeutic target. Clinical correlation is advised.

Comments
Microsatellite status: MSI-High NOT DETECTED

SARAH CANNON

Different Results Are Somewhat Expected

Comparative Study > JAMA Oncol. 2017 Jul 1;3(7):996-998. doi: 10.1001/jamaoncol.2016.4983.

Comparison of 2 Commercially Available Next-Generation Sequencing Platforms in Oncology

Nicole M Kuderer [1], Kimberly A Burton [1], Sibel Blau [2], Andrea L Rose [2], Stephanie Parker [2], Gary H Lyman [3], C Anthony Blau [4]

Affiliations + expand

PMID: 27978570 PMCID: PMC5824236 DOI: 10.1001/jamaoncol.2016.4983

Abstract

This study compares reports from 2 next-generation sequencing tests to determine the level of concordance between platforms.

Patient No./Sex	Tumor Type	Stage	Time Difference, mo	F1 or G360, No.	Both, No. (%)
1/F	Breast cancer	IV	0.5	13	7 (54)
2/F	Pancreatic cancer	IV	1	16	4 (25)
3/F	Breast cancer	IV	15	8	5 (63)
4/F	Thymic carcinoma	I	0.5	0	0
5/F	Breast cancer	IV	0	9	5 (56)
6/F	Breast cancer	IV	0.5	19	4 (21)
7/M	Lung cancer	IV	1	18	7 (39)
8/M	Salivary gland cancer	IV	2.5	10	2 (20)
9/F	Breast cancer	III	0	19	11 (58)
Total				112	45 (40)

Abbreviations: F1, FoundationOne; G360, Guardant360.

*"Both the F1 and G360 tests have **high specificities (>99%)** and somewhat lower sensitivities."*

SARAH CANNON

Different Vendors Offer Different Gene Panels

Current Gene List[2]

Genes with full coding exonic regions included in FoundationOne®CDx for the detection of substitutions, insertion-deletions (indels), and copy-number alterations (CNAs).

ABL1	ACVR1B	AKT1	AKT2	AKT3	ALK	ALOX12B	AMER1 (FAM123B)	APC
AR	ARAF	ARFRP1	ARID1A	ASXL1	ATM	ATR	ATRX	AURKA
AURKB	AXIN1	AXL	BAP1	BARD1	BCL2	BCL2L1	BCL2L2	BCL6
BCOR	BCORL1	BRAF	BRCA1	BRCA2	BRD4	BRIP1	BTG1	BTG2
BTK	C11orf30 (EMSY)	CALR	CARD11	CASP8	CBFB	CBL	CCND1	CCND2
CCND3	CCNE1	CD22	CD274 (PD-L1)	CD70	CD79A	CD79B	CDC73	CDH1
CDK12	CDK4	CDK6	CDK8	CDKN1A	CDKN1B	CDKN2A	CDKN2B	CDKN2C
CEBPA	CHEK1	CHEK2	CIC	CREBBP	CRKL	CSF1R	CSF3R	CTCF
CTNNA1	CTNNB1	CUL3	CUL4A	CXCR4	CYP17A1	DAXX	DDR1	DDR2
DIS3	DNMT3A	DOT1L	EED	EGFR	EP300	EPHA3	EPHB1	EPHB4
ERBB2	ERBB3	ERBB4	ERCC4	ERG	ERRFI1	ESR1	EZH2	FAM46C
FANCA	FANCC	FANCG	FANCL	FAS	FBXW7	FGF10	FGF12	FGF14
FGF19	FGF23	FGF3	FGF4	FGF6	FGFR1	FGFR2	FGFR3	FGFR4
FH	FLCN	FLT1	FLT3	FOXL2	FUBP1	GABRA6	GATA3	GATA4
GATA6	GID4 (C17orf39)	GNA11	GNA13	GNAQ	GNAS	GRM3	GSK3B	H3F3A
HDAC1	HGF	HNF1A	HRAS	HSD3B1	ID3	IDH1	IDH2	IGF1R
IKBKE	IKZF1	INPP4B	IRF2	IRF4	IRS2	JAK1	JAK2	JAK3
JUN	KDM5A	KDM5C	KDM6A	KDR	KEAP1	KEL	KIT	KLHL6
KMT2A (MLL)	KMT2D (MLL2)	KRAS	LTK	LYN	MAF	MAP2K1 (MEK1)	MAP2K2 (MEK2)	MAP2K4
MAP3K1	MAP3K13	MAPK1	MCL1	MDM2	MDM4	MED12	MEF2B	MEN1
MERTK	MET	MITF	MKNK1	MLH1	MPL	MRE11A	MSH2	MSH3
MSH6	MST1R	MTAP	MTOR	MUTYH	MYC	MYCL (MYCL1)	MYCN	MYD88
NBN	NF1	NF2	NFE2L2	NFKBIA	NKX2-1	NOTCH1	NOTCH2	NOTCH3
NPM1	NRAS	NT5C2	NTRK1	NTRK2	NTRK3	P2RY8	PALB2	PARK2
PARP1	PARP2	PARP3	PAX5	PBRM1	PDCD1 (PD-1)	PDCD1LG2 (PD-L2)		PDGFRA
PDGFRB	PDK1	PIK3C2B	PIK3C2G	PIK3CA	PIK3CB	PIK3R1	PIM1	PMS2
POLD1	POLE	PPARG	PPP2R1A	PPP2R2A	PRDM1	PRKAR1A	PRKCI	PTCH1
PTEN	PTPN11	PTPRO	QKI	RAC1	RAD21	RAD51	RAD51B	RAD51C
RAD51D	RAD52	RAD54L	RAF1	RARA	RB1	RBM10	REL	RET
RICTOR	RNF43	ROS1	RPTOR	SDHA	SDHB	SDHC	SDHD	SETD2
SF3B1	SGK1	SMAD2	SMAD4	SMARCA4	SMARCB1	SMO	SNCAIP	SOCS1
SOX2	SOX9	SPEN	SPOP	SRC	STAG2	STAT3	STK11	SUFU
SYK	TBX3	TEK	TET2	TGFBR2	TIPARP	TNFAIP3	TNFRSF14	TP53
TSC1	TSC2	TYRO3	U2AF1	VEGFA	VHL	WHSC1 (MMSET)	WHSC1L1	WT1
XPO1	XRCC2	ZNF217	ZNF703					

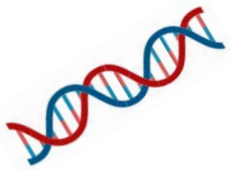
315 genes

Point Mutations (SNVs) and Deletion Variants (Indels) (74 Genes)						Amplifications (18 Genes)		Fusions (6 Genes)
AKT1	**ALK**	APC	AR	ARAF	ARID1A	AR	BRAF	**ALK**
ATM	**BRAF**	BRCA1	BRCA2	CCND1	CCND2	CCND1	CCND2	FGFR2
CCNE1	CDH1	CDK4	CDK6	CDK12	CDKN2A	CCNE1	CDK4	FGFR3
CTNNB1	DDR2	**EGFR**	**ERBB2**	ESR1	EZH2	CDK6	EGFR	**NTRK1**
FBXW7	FGFR1	FGFR2	FGFR3	GATA3	GNA11	ERBB2	FGFR1	**RET**
GNAQ	GNAS	HNF1A	HRAS	IDH1	IDH2	FGFR2	KIT	**ROS1**
JAK2	JAK3	KIT	KRAS	MAP2K1	MAP2K2	KRAS	**MET**	
MAPK1	MAPK3	**MET**	MLH1	MPL	MTOR	MYC	PDGFRA	
MYC	NF1	NFE2L2	NOTCH1	NPM1	NRAS	PIK3CA	RAF1	
NTRK1	NTRK3	PDGFRA	PIK3CA	PTEN	PTPN11			
RAF1	RB1	**RET**	RHEB	RHOA	RIT1			
ROS1	SMAD4	SMO	STK11	TERT†	TP53			
TSC1	VHL							

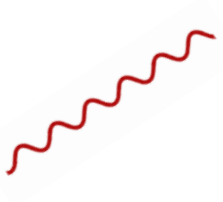
70 genes

SARAH CANNON

Different NGS Vendors Probe Different Analytes

DNA 

- FOUNDATIONONE®
- GUARDANT360
- Paradigm
- TEMPUS
- CARIS LIFE SCIENCES

RNA 

- TEMPUS
- CARIS LIFE SCIENCES

Protein 

- Paradigm
- TEMPUS
- CARIS LIFE SCIENCES

Capacity of testing methods to accurately identify various genomic abnormalities (eg, germline mutations, gene fusions, amplifications)

Molecular Profiling Technologies

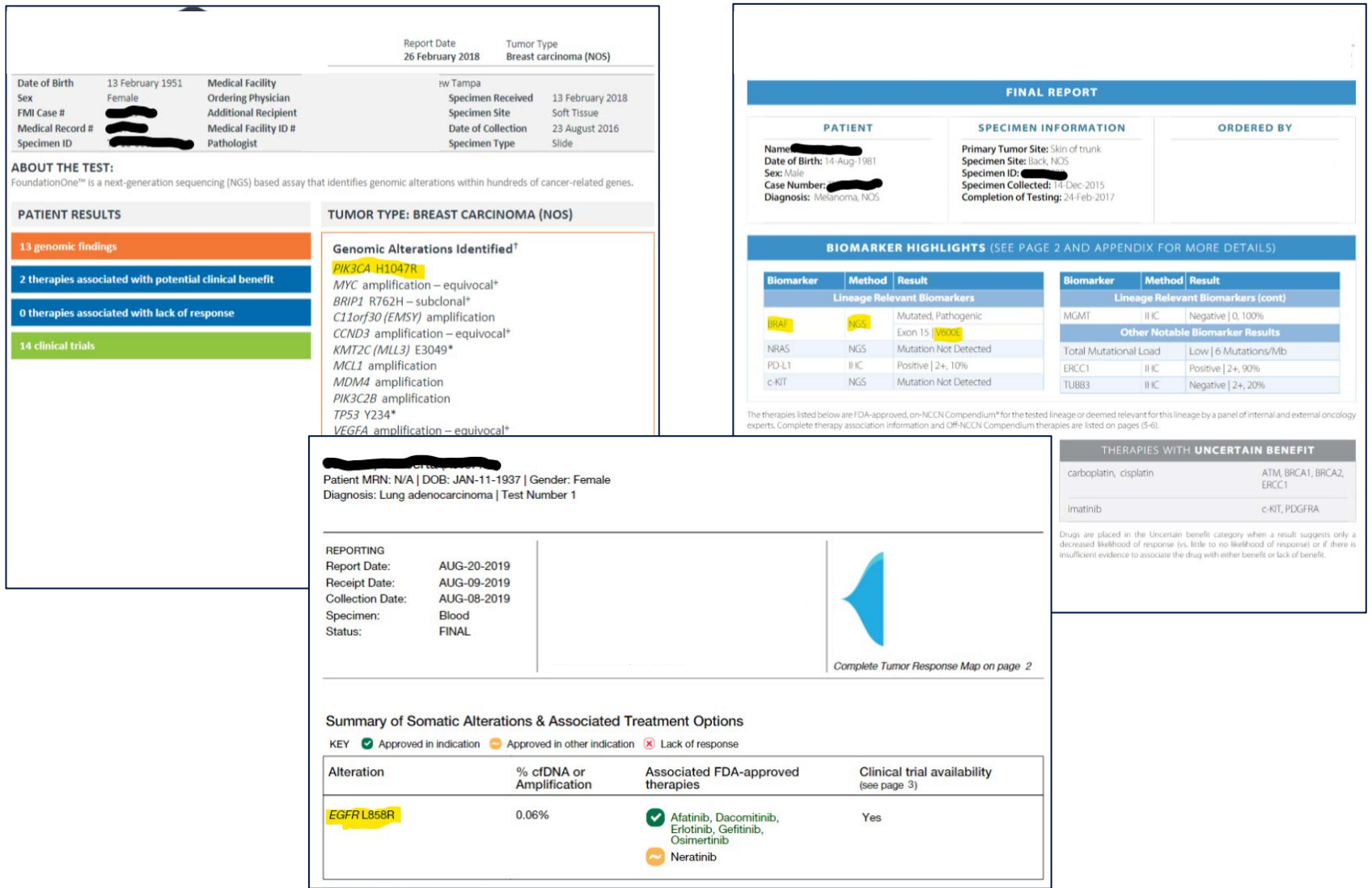
Detect the presence or absence of a specific protein
- Immunohistochemistry (IHC)
- Proteomics

Detect the amplification or loss of a specific gene
- In Situ Hybridization (ISH)
- DNA sequencing
- RNA sequencing

Detect large gene rearrangements or fusions
- In Situ Hybridization (ISH)
- DNA sequencing
  - PCR
  - NGS
- RNA sequencing

Detect gene mutations
- DNA sequencing
  - PCR
  - NGS

Driver Mutations Across Tumor Types



Challenges in the interpretation and applicability of NGS results; current clinical validity of genetic alterations in various solid tumors and potential role of emerging tumor drivers

SARAH CANNON

Challenges – Complexity of Biomarkers

As new data and technologies emerge, clinicians are required to interpret and act upon increasingly complex information

An increasing number of standard of care treatment options and clinical trials require the knowledge of a molecular alteration

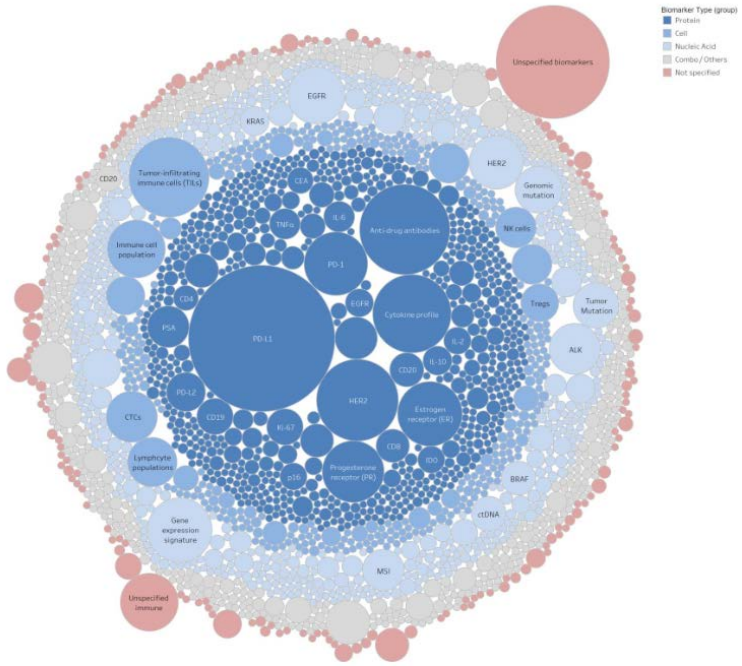
Molecular reports do not present information in an easily clinically actionable format

DNA Gene List: Entire Coding Sequence for the Detection of Base Substitutions, Insertion/Deletions, and Copy Number Alterations

ABL1	*ABL2*	*ACVR1B*	*AKT1*	*AKT2*	*AKT3*	*ALK*	*AMER1 (FAM123B)*	*APC*	*AR*
ARAF	*ARFRP1*	*ARID1A*	*ARID1B*	*ARID2*	*ASXL1*	*ATM*	*ATR*	*ATRX*	*AURKA*
AURKB	*AXIN1*	*AXL*	*BAP1*	*BARD1*	*BCL2*	*BCL2L1*	*BCL2L2*	*BCL6*	*BCOR*
BCORL1	*BLM*	*BRAF*	*BRCA1*	*BRCA2*	*BRD4*	*BRIP1*	*BTG1*	*BTK*	*C11orf30 (EMSY)*
CARD11	*CBFB*	*CBL*	*CCND1*	*CCND2*	*CCND3*	*CCNE1*	*CD274*	*CD79A*	*CD79B*
CDC73	*CDH1*	*CDK12*	*CDK4*	*CDK6*	*CDK8*	*CDKN1A*	*CDKN1B*	*CDKN2A*	*CDKN2B*
CDKN2C	*CEBPA*	*CHD2*	*CHD4*	*CHEK1*	*CHEK2*	*CIC*	*CREBBP*	*CRKL*	*CRLF2*
CSF1R	*CTCF*	*CTNNA1*	*CTNNB1*	*CUL3*	*CYLD*	*DAXX*	*DDR2*	*DICER1*	*DNMT3A*
DOT1L	*EGFR*	*EP300*	*EPHA3*	*EPHA5*	*EPHA7*	*EPHB1*	*ERBB2*	*ERBB3*	*ERBB4*
ERG	*ERRFI1*	*ESR1*	*EZH2*	*FAM46C*	*FANCA*	*FANCC*	*FANCD2*	*FANCE*	*FANCF*
FANCG	*FANCL*	*FAS*	*FAT1*	*FBXW7*	*FGF10*	*FGF14*	*FGF19*	*FGF23*	*FGF3*
FGF4	*FGF6*	*FGFR1*	*FGFR2*	*FGFR3*	*FGFR4*	*FH*	*FLCN*	*FLT1*	*FLT3*
FLT4	*FOXL2*	*FOXP1*	*FRS2*	*FUBP1*	*GABRA6*	*GATA1*	*GATA2*	*GATA3*	*GATA4*
GATA6	*GID4 (C17orf39)*	*GLI1*	*GNA11*	*GNA13*	*GNAQ*	*GNAS*	*GPR124*	*GRIN2A*	*GRM3*
GSK3B	*H3F3A*	*HGF*	*HNF1A*	*HRAS*	*HSD3B1*	*HSP90AA1*	*IDH1*	*IDH2*	*IGF1R*
IGF2	*IKBKE*	*IKZF1*	*IL7R*	*INHBA*	*INPP4B*	*IRF2*	*IRF4*	*IRS2*	*JAK1*
JAK2	*JAK3*	*JUN*	*KAT6A (MYST3)*	*KDM5A*	*KDM5C*	*KDM6A*	*KDR*	*KEAP1*	*KEL*
KIT	*KLHL6*	*KMT2A (MLL)*	*KMT2C (MLL3)*	*KMT2D (MLL2)*	*KRAS*	*LMO1*	*LRP1B*	*LYN*	*LZTR1*
MAGI2	*MAP2K1*	*MAP2K2*	*MAP2K4*	*MAP3K1*	*MCL1*	*MDM2*	*MDM4*	*MED12*	*MEF2B*
MEN1	*MET*	*MITF*	*MLH1*	*MPL*	*MRE11A*	*MSH2*	*MSH6*	*MTOR*	*MUTYH*
MYC	*MYCL1 (MYCL1)*	*MYCN*	*MYD88*	*NF1*	*NF2*	*NFE2L2*	*NFKBIA*	*NKX2-1*	*NOTCH1*
NOTCH2	*NOTCH3*	*NPM1*	*NRAS*	*NSD1*	*NTRK1*	*NTRK2*	*NTRK3*	*NUP93*	*PAK3*
PALB2	*PARK2*	*PAX5*	*PBRM1*	*PDCD1LG2*	*PDGFRA*	*PDGFRB*	*PDK1*	*PIK3C2B*	*PIK3CA*
PIK3CB	*PIK3CG*	*PIK3R1*	*PIK3R2*	*PLCG2*	*PMS2*	*POLD1*	*POLE*	*PPP2R1A*	*PRDM1*
PREX2	*PRKAR1A*	*PRKCI*	*PRKDC*	*PRSS8*	*PTCH1*	*PTEN*	*PTPN11*	*QKI*	*RAC1*
RAD50	*RAD51*	*RAF1*	*RANBP2*	*RARA*	*RB1*	*RBM10*	*RET*	*RICTOR*	*RNF43*
ROS1	*RPTOR*	*RUNX1*	*RUNX1T1*	*SDHA*	*SDHB*	*SDHC*	*SDHD*	*SETD2*	*SF3B1*
SLIT2	*SMAD2*	*SMAD3*	*SMAD4*	*SMARCA4*	*SMARCB1*	*SMO*	*SNCAIP*	*SOCS1*	*SOX10*
SOX2	*SOX9*	*SPEN*	*SPOP*	*SPTA1*	*SRC*	*STAG2*	*STAT3*	*STAT4*	*STK11*
SUFU	*SYK*	*TAF1*	*TBX3*	*TERC*	*TERT (promoter only)*	*TET2*	*TGFBR2*	*TNFAIP3*	*TNFRSF14*
TOP1	*TOP2A*	*TP53*	*TSC1*	*TSC2*	*TSHR*	*U2AF1*	*VEGFA*	*VHL*	*WISP3*
WT1	*XPO1*	*ZBTB2*	*ZNF217*	*ZNF703*					

DNA Gene List: For the Detection of Select Rearrangements

ALK	*BCL2*	*BCR*	*BRAF*	*BRCA1*	*BRCA2*	*BRD4*	*EGFR*	*ETV1*	*ETV4*
ETV5	*ETV6*	*FGFR1*	*FGFR2*	*FGFR3*	*KIT*	*MSH2*	*MYB*	*MYC*	*NOTCH2*
NTRK1	*NTRK2*	*PDGFRA*	*RAF1*	*RARA*	*RET*	*ROS1*	*TMPRSS2*		



TUMOR TYPE: STOMACH ADENOCARCINOMA (NOS)

Genomic Alterations Identified†

CDC73 V230fs*28
CIC P1116fs*45
DICER1 C1354fs*1
MLL2 R4904*
MSH2 Q183fs*31
PPP2R1A R183W
RUNX1T1 R458C
SOX9 Q505fs*72

Additional Findings†

Microsatellite status MSI-High
Tumor Mutational Burden TMB-High; 32 Muts/Mb

Additional Disease-relevant Genes with No Reportable Alterations Identified†

ERBB2

SARAH CANNON

Challenges – Different tests reveal different results

Comparative Study > JAMA Oncol. 2017 Jul 1;3(7):996-998. doi: 10.1001/jamaoncol.2016.4983.

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Current Gene List[2]

Genes with full coding exonic regions included in FoundationOne®CDx for the detection of substitutions, insertion-deletions (indels), and copy-number alterations (CNAs).

ABL1	ACVR1B	AKT1	AKT2	AKT3	ALK	ALOX12B	AMER1 (FAM123B)	APC
AR	ARAF	ARFRP1	ARID1A	ASXL1	ATM	ATR	ATRX	AURKA
AURKB	AXIN1	AXL	BAP1	BARD1	BCL2	BCL2L1	BCL2L2	BCL6
BCOR	BCORL1	BRAF	BRCA1	BRCA2	BRD4	BRIP1	BTG1	BTG2
BTK	C11orf30 (EMSY)	CALR	CARD11	CASP8	CBFB	CBL	CCND1	CCND2
CCND3	CCNE1	CD22	CD274 (PD-L1)	CD70	CD79A	CD79B	CDC73	CDH1
CDK12	CDK4	CDK6	CDK8	CDKN1A	CDKN1B	CDKN2A	CDKN2B	CDKN2C
CEBPA	CHEK1	CHEK2	CIC	CREBBP	CRKL	CSF1R	CSF3R	CTCF
CTNNA1	CTNNB1	CUL3	CUL4A	CXCR4	CYP17A1	DAXX	DDR1	DDR2
DIS3	DNMT3A	DOT1L	EED	EGFR	EP300	EPHA3	EPHB1	EPHB4
ERBB2	ERBB3	ERBB4	ERCC4	ERG	ERRFI1	ESR1	EZH2	FAM46C
FANCA	FANCC	FANCG	FANCL	FAS	FBXW7	FGF10	FGF12	FGF14
FGF19	FGF23	FGF3	FGF4	FGF6	FGFR1	FGFR2	FGFR3	FGFR4
FH	FLCN	FLT1	FLT3	FOXL2	FUBP1	GABRA6	GATA3	GATA4
GATA6	GID4 (C17orf39)	GNA11	GNA13	GNAQ	GNAS	GRM3	GSK3B	H3F3A
HDAC1	HGF	HNF1A	HRAS	HSD3B1	ID3	IDH1	IDH2	IGF1R
IKBKE	IKZF1	INPP4B	IRF2	IRF4	IRS2	JAK1	JAK2	JAK3
JUN	KDM5A	KDM5C	KDM6A	KDR	KEAP1	KEL	KIT	KLHL6
KMT2A (MLL)	KMT2D (MLL2)	KRAS	LTK	LYN	MAF	MAP2K1 (MEK1)	MAP2K2 (MEK2)	MAP2K4
MAP3K1	MAP3K13	MAPK1	MCL1	MDM2	MDM4	MED12	MEF2B	MEN1
MERTK	MET	MITF	MKNK1	MLH1	MPL	MRE11A	MSH2	MSH3
MSH6	MST1R	MTAP	MTOR	MUTYH	MYC	MYCL (MYCL1)	MYCN	MYD88
NBN	NF1	NF2	NFE2L2	NFKBIA	NKX2-1	NOTCH1	NOTCH2	NOTCH3
NPM1	NRAS	NT5C2	NTRK1	NTRK2	NTRK3	P2RY8	PALB2	PARK2
PARP1	PARP2	PARP3	PAX5	PBRM1	PDCD1 (PD-1)	PDCD1LG2 (PD-L2)		PDGFRA
PDGFRB	PDK1	PIK3C2B	PIK3C2G	PIK3CA	PIK3CB	PIK3R1	PIM1	PMS2
POLD1	POLE	PPARG	PPP2R1A	PPP2R2A	PRDM1	PRKAR1A	PRKCI	PTCH1
PTEN	PTPN11	PTPRO	QKI	RAC1	RAD21	RAD51	RAD51B	RAD51C
RAD51D	RAD52	RAD54L	RAF1	RARA	RB1	RBM10	REL	RET
RICTOR	RNF43	ROS1	RPTOR	SDHA	SDHB	SDHC	SDHD	SETD2
SF3B1	SGK1	SMAD2	SMAD4	SMARCA4	SMARCB1	SMO	SNCAIP	SOCS1
SOX2	SOX9	SPEN	SPOP	SRC	STAG2	STAT3	STK11	SUFU
SYK	TBX3	TEK	TET2	TGFBR2	TIPARP	TNFAIP3	TNFRSF14	TP53
TSC1	TSC2	TYRO3	U2AF1	VEGFA	VHL	WHSC1 (MMSET)	WHSC1L1	WT1
XPO1	XRCC2	ZNF217	ZNF703					

315 genes

Point Mutations (SNVs) and Deletion Variants (Indels) (74 Genes)						Amplifications (18 Genes)		Fusions (6 Genes)
AKT1	**ALK**	APC	AR	ARAF	ARID1A	AR	BRAF	**ALK**
ATM	**BRAF**	BRCA1	BRCA2	CCND1	CCND2	CCND1	CCND2	FGFR2
CCNE1	CDH1	CDK4	CDK6	CDK12	CDKN2A	CCNE1	CDK4	FGFR3
CTNNB1	DDR2	**EGFR**	**ERBB2**	ESR1	EZH2	CDK6	EGFR	**NTRK1**
FBXW7	FGFR1	FGFR2	FGFR3	GATA3	GNA11	ERBB2	FGFR1	**RET**
GNAQ	GNAS	HNF1A	HRAS	IDH1	IDH2	FGFR2	KIT	**ROS1**
JAK2	JAK3	KIT	KRAS	MAP2K1	MAP2K2	KRAS	**MET**	
MAPK1	MAPK3	**MET**	MLH1	MPL	MTOR	MYC	PDGFRA	
MYC	NF1	NFE2L2	NOTCH1	NPM1	NRAS	PIK3CA	RAF1	
NTRK1	NTRK3	PDGFRA	PIK3CA	PTEN	PTPN11			
RAF1	RB1	**RET**	RHEB	RHOA	RIT1			
ROS1	SMAD4	SMO	STK11	TERT†	TP53			
TSC1	VHL							

70 genes

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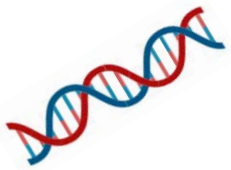
Different Vendors Probe Different Analytes

DNA 

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Agenda

Part 1: Case Discussion

- Case 1 – Drs Radovich, Schneider: A 76-year-old man with prostate cancer (AKT E17k mutation)
- Case 2 – Dr Ibrahim: A frail 80-year-old woman with endometrial cancer (AKT mutation)
- Case 3 – Dr McKenzie: A 58-year-old man with salivary gland HNSCC (NTRK3-ETV6 fusion)
- Case 4 – Drs Radovich, Schneider: An 80-year-old man with bladder cancer (TMB 67 Muts/Mb)
- Case 5 – Dr Ibrahim: A 68-year-old man with muscle-invasive bladder cancer (PIK3CA, RET amplification)
- Case 6 – Dr McKenzie: A 62-year-old man with cholangiocarcinoma (FGFR2 rearrangement)

Part 2: FDA-approved and Guideline-endorsed Platforms For Genomic Testing

- Advantages and limitations of available assays

Part 3: Case Discussion

- Case 7 – Drs Radovich, Schneider: A 64-year-old woman with glioblastoma (FGFR3-TACC3 fusion)
- Case 8 – Dr Ibrahim: An 82-year-old man with cancer of unknown primary (TMPRSS2 ERG)
- Case 9 – Dr McKenzie: A 64-year-old woman with metastatic breast cancer (PIK3CA, ESR1 mutations)
- Case 10 – Drs Radovich, Schneider: A 64-year-old woman with pancreatic cancer (KRAS G12C)
- Case 11 – Dr McKenzie: A 66-year-old woman with metastatic adenocarcinoma of the lung (KRAS G12C)

Case 7: 64-year-old woman with glioblastoma

- **HISTORY OF PRESENT ILLNESS:** 64-year-old right-handed woman with recently diagnosed left frontotemporal brain glioblastoma, MGMT methylated. The patient's pertinent history includes having increasing difficulty with word finding and weakness, and presented with a seizure at work on 01/17/2020. She had a gross total resection of the mass on 02/14/2020, where she had worsening aphasia and worsening weakness in the left arm thereafter. She briefly had improvement in aphasia, but then subsequently again worsened. The patient began temozolomide with concurrent radiation therapy. The temozolomide has been held recently due to platelet count, but she is 2 days away from completing her radiation therapy.
- **PAST MEDICAL HISTORY:** hyperlipidemia, supraventricular tachycardia
- **FHx:** none

Courtesy of Bryan P Schneider, MD and Milan Radovich, PhD

Case 7: 64-year-old woman with glioblastoma (cont)

OTHER ALTERATIONS & BIOMARKERS IDENTIFIED

Results reported in this section are not prescriptive or conclusive for labeled use of any specific therapeutic product. See *professional services* section for additional information.

Microsatellite status MS-Stable §

Tumor Mutational Burden 1 Muts/Mb §

CDK4 amplification §

FGFR3 FGFR3(NM_000142)-TACC3(NM_006342) fusion (F17; T11) §

MDM2 amplification §

TERT promoter -146C>T

§ Refer to appendix for limitation statements related to detection of any copy number alterations, gene rearrangements, BRCA1/2 alterations, LOH, MSI, or TMB results in this section.

Please refer to appendix for Explanation of Clinical Significance Classification and for variants of unknown significance (VUS).

Courtesy of Bryan P Schneider, MD and Milan Radovich, PhD

Case 8: 82-year-old who presents with high-grade neuroendocrine carcinoma

82-year-old presented with left supraclavicular lymph node - biopsy shows high grade neuroendocrine carcinoma with no obvious primary - has retroperitoneal adenopathy as well - treated with Carboplatin and Etoposide and then progression.

NGS done shows TMPRSS2 ERG which is characteristic of prostate cancer - PSA is 10

- Started on Leuprolide and now doing great
- Also has MRE 11A which is marker of response to PARP inhibitor
- NGS changed him from looking like hospice, to now doing great and with several more options upon progression

Courtesy of Sulfi Ibrahim, MD

Case 8: NGS Report

OTHER ALTERATIONS & BIOMARKERS IDENTIFIED

Results reported in this section are not prescriptive or conclusive for labeled use of any specific therapeutic product. See *professional services* section for additional information.

Microsatellite status MS-Stable §

Tumor Mutational Burden 3 Muts/Mb §

FGFR1 amplification §

LYN amplification §

MRE11A E506*

MYC amplification §

NSD3 (WHSC1L1) amplification §

RAD21 amplification §

TMPRSS2 TMPRSS2(NM_005656)-ERG(NM_004449) fusion (T2; E4) §

ZNF703 amplification §

§ Refer to appendix for limitation statements related to detection of any copy number alterations, gene rearrangements, BRCA1/2 alterations, LOH, MSI, or TMB results in this section.

Please refer to appendix for Explanation of Clinical Significance Classification and for variants of unknown significance (VUS).

FoundationOne®CDx (F1CDx) is a next generation sequencing based in vitro diagnostic device for detection of substitutions, insertion and deletion alterations (indels), and copy number alterations (CNAs) in 324 genes and select gene rearrangements, as well as

TABLE 1: COMPANION DIAGNOSTIC INDICATIONS

INDICATION	BIOMARKER	THERAPY
	EGFR exon 19 deletions and *EGFR* exon 21 L858R alterations	Gilotrif® (Afatinib), Iressa® (Gefitinib), Tagrisso® (Osimertinib), or Tarceva® (Erlotinib)

Courtesy of Sulfi Ibrahim, MD

Case 9: 64-year-old woman with metastatic breast cancer

- 64yr Female
- Initially diagnosed in 2004 as stage T1 cN0 grade 2 ER+/HER2- breast cancer
- Metastatic recurrence in 2018
  - BRCA negative
- Initiated palbociclib/anastrozole Dec 2018 – May 2020
  - Jan 2020 tissue-based testing was performed on original 2018 specimen. PIK3CA mutations were found and EGFR nonsense mutation was detected
- Progression in May 2020
  - Liquid-based test due to hard-to-biopsy metastatic disease in the pleural space
  - High concordance with tissue-based test with the addition of ESR1 mutations indicative of resistance to aromatase inhibitors
- Initiated fulvestrant/alpelisib May 2020 – present (potential opportunity for next-gen SERD upon progression)

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Courtesy of Andrew McKenzie, PhD

Case 9: 64-year-old woman with metastatic breast cancer (cont)

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PATIENT

DISEASE Breast carcinoma (NOS)
NAME
DATE OF BIRTH
SEX Female
MEDICAL RECORD #

PHYSICIAN

ORDERING PHYSICIAN
MEDICAL FACILITY
ADDITIONAL RECIPIENT None
MEDICAL FACILITY ID
PATHOLOGIST Provided, Not

SPECIMEN

SPECIMEN SITE Soft Tissue
SPECIMEN ID 18CH-004489 18
SPECIMEN TYPE Block
DATE OF COLLECTION 10 December 2018
SPECIMEN RECEIVED 19 February 2020

Biomarker Findings

Microsatellite status - MS-Stable
Tumor Mutational Burden - 3 Muts/Mb

Genomic Findings

For a complete list of the genes assayed, please refer to the Appendix.

PIK3CA **E545K, H1047R**
EGFR **R1068***
MYC **amplification - equivocal†**
RAD21 **amplification**

3 Disease relevant genes with no reportable alterations: *BRCA1, BRCA2, ERBB2*

† See About the Test in appendix for details.

8 Therapies with Clinical Benefit **23 Clinical Trials**
0 Therapies with Lack of Response

Report Date: 26-Feb-2020
Specimen collected: 10-Dec-2018

Report date: 16-May-2020
Specimen collected: 11-May-2020

Alteration	% cfDNA or Amp	
PIK3CA E545K	1.4%	
PIK3CA H1047R	1.4%	
EGFR R1068*	0.7%	
SMAD4 R87R	0.5%	Synonymous Alteration §
ESR1 Y537S	0.3%	
ESR1 D538G	0.2%	
NTRK1 V658V	0.1%	Synonymous Alteration §

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Courtesy of Andrew McKenzie, PhD

Case 10: 64-year-old woman with pancreatic cancer

- **HISTORY OF PRESENT ILLNESS:** 64-year-old woman with recently diagnosed pancreatic cancer. The patient presented in the late fall of 2019 with persistent abdominal discomfort and weight loss. CT scan of the abdomen and pelvis showed a pancreatic head mass concerning for pancreatic cancer. She underwent an EUS on 11/18/2019 that showed pancreatic mass and FNA was positive for adenocarcinoma consistent with pancreatic cancer. The patient was recommended preoperative FOLFIRINOX, however, deferred this to go directly to surgery. She underwent a Whipple procedure on 12/12/2019 where she was found to have a 1.7 cm adenocarcinoma of the pancreatic head, moderate to poorly differentiated with 1/20 lymph nodes involved, making this a pT1c N1.
- **PAST MEDICAL HISTORY:** arthritis, hypercholesterolemia, rectal prolapse, hypothyroidism secondary to thyroidectomy.
- **FHx:** No cancer

Courtesy of Bryan P Schneider, MD and Milan Radovich, PhD

Diagnosis: **Pancreatic Cancer**

TUMOR GENOMIC ALTERATIONS[1]				
KRAS MAP2K4 TP53				
GENOMIC TARGETS	FDA-APPROVED DRUGS -for patient's cancer	FDA-APPROVED DRUGS -for another cancer	DRUGS PREDICTED NON-BENEFICIAL	POTENTIAL CLINICAL TRIALS
3	0	0	0	Yes
KRAS (G12C)				Yes
MAP2K4 (Q163fs)				Yes
TP53 (V73fs)				Yes
TUMOR MUTATION BURDEN (TMB)				
LOW (2 mut/Mb)				No
MICROSATELLITE STATUS (MSI)				
STABLE				No

Courtesy of Bryan P Schneider, MD and Milan Radovich, PhD

Case 11: 66-year-old woman with metastatic NSCLC

- 66yr Female
- Diagnosed stage IIIa NSCLC adenocarcinoma Jan-2019
  - Adjuvant Carboplatin/Pemetrexed July-2019 – Oct-2019
  - Tissue-based NGS reveals KRAS G12C, AKT3 amp, STK11, CHEK2 splice site, NFKBIa amp, NKX21 amp, MS-stable, TMBI.
- 7-Jan-2020 metastatic diagnosis
  - Carboplatin/pemetrexed/pembrolizumab Jan-2020 – April-2020
- Progression 20-April-2020
- KRAS G12C inhibitor initiated in phase I clinical trial
  - Jun-2020: C3D1 KRAS G12C inhibitor – “first disease eval shows partial response!”
  - Jul-2020: C4D1 KRAS G12C inhibitor – “Feeling stronger and stronger.”

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Courtesy of Andrew McKenzie, PhD

Case 11: 66-year-old woman with metastatic NSCLC (cont)

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PATIENT

DISEASE Lung adenocarcinoma
NAME
DATE OF BIRTH
SEX Female
MEDICAL RECORD #

PHYSICIAN

ORDERING PHYSICIAN
MEDICAL FACILITY
ADDITIONAL RECIPIENT None
MEDICAL FACILITY ID
PATHOLOGIST Provided, Not

SPECIMEN

SPECIMEN SITE Lung
SPECIMEN ID SS-19-0001806 AS
SPECIMEN TYPE Block
DATE OF COLLECTION 09 April 2019
SPECIMEN RECEIVED 28 January 2020

Biomarker Findings

Microsatellite status - MS-Stable
Tumor Mutational Burden - 8 Muts/Mb

Genomic Findings

For a complete list of the genes assayed, please refer to the Appendix.

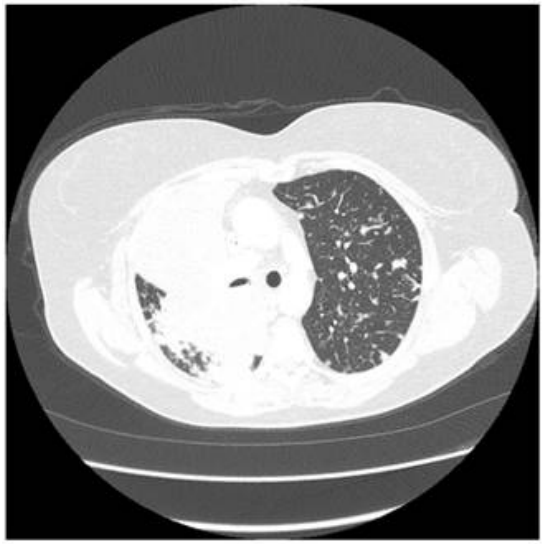
AKT3 **amplification - equivocal†**
STK11 **I322fs*14**
KRAS **G12C**
CHEK2 **splice site 444+1G>A**
NFKBIA **amplification**
NKX2-1 **amplification**

7 Disease relevant genes with no reportable alterations: *EGFR, ALK, BRAF, MET, RET, ERBB2, ROS1*

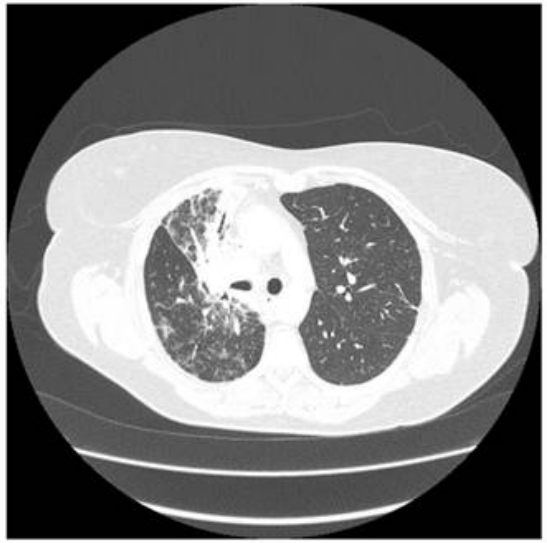
† See About the Test in appendix for details.

2 Therapies with Clinical Benefit
0 Therapies with Lack of Response
22 Clinical Trials

Pre-treatment



Cycle 2 Day 1



PR: -86% reduction in target lesion measurements

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Courtesy of Andrew McKenzie, PhD

Recent Advances in Medical Oncology: Urothelial Bladder Carcinoma

Monday, August 3, 2020

5:00 PM – 6:00 PM ET

Faculty

Arjun Balar, MD
Thomas Powles, MBBS, MRCP, MD
Arlene Siefker-Radtke, MD

Moderator

Neil Love, MD

Co-provided by USF Health RTP RESEARCH TO PRACTICE

Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 days.