Breakout session

LIVING BEYOND
BREAST CANCER®

Hosted in partnership with Project Life

From information to empowerment

Understanding pathology reports and scans in metastatic breast cancer

Facilitator: Abigail M. Johnston, JD

Panelists: Amy Beumer, PhD, and Amy Russell-Parliman, MHA

Pathology Reports & Biomarkers

- Biomarker: a molecule, eg. DNA or protein, in the body that can tell us about health or disease
  - Receptors: ER, PR, HER2 → Pathology report
  - Mutations such as ESR1, PIK3CA → Separate DNA sequencing report
- Knowing biomarkers → more targeted treatment → better outcomes
- Why, what, and when of procedures & testing
- Reading pathology reports
- Genomic testing for acquired mutations
- Genetic testing for inherited mutations

Procedure	**Tissue / Tumor Biopsy** Including cancer cells from pleural effusion, ascites, cerebrospinal fluid	**Blood Draw / Liquid Biopsy** Circulating tumor DNA (ctDNA)	**Blood Draw or Saliva** Genetic Testing for Inherited Mutations
Why?	• Help determine treatment • Help determine prognosis & risk of certain metastases	• Help determine treatment • Change treatment with increasing ESR1 mutations	• Help determine treatment • Help determine risk for cancers for you and blood relatives
What?	• Histologic type (ductal, lobular or rarer types)→ **pathology report for primary breast tumor** • Receptor status (proteins): ER, PR, HER2 → **pathology reports** • Other protein testing, eg. PD-L1→ **pathology reports** • **Genomic** testing for acquired/somatic tumor mutations and/or other changes in DNA → **separate reports**	• **Genomic** testing for **acquired** tumor mutations, aka **somatic** mutations, and/or other changes in DNA • Mutations only in tumor/cancer cells • Cannot pass to biological children	• **Genetic** testing for **inherited mutations** • Born with these mutations and can pass to biological children • All cells in your body have these mutations
When?	• Diagnosis & progression • Can change over time	• Diagnosis & progression • Results can change over time	• Once or if a long time has passed • Speak with genetic counselor and/or oncologist

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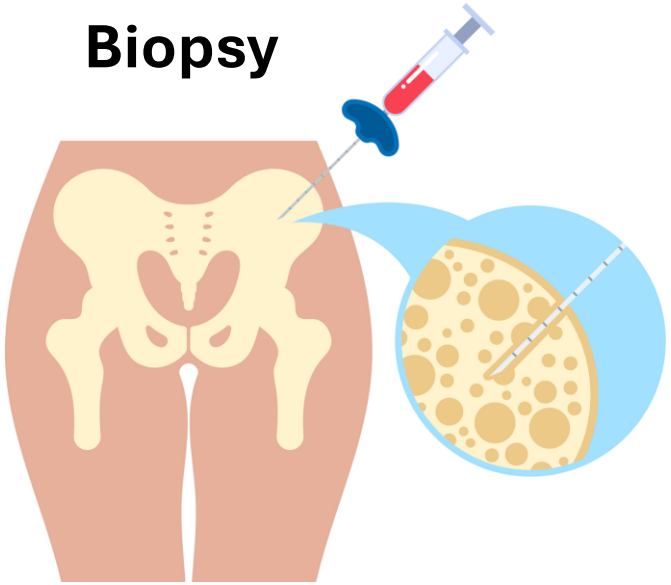
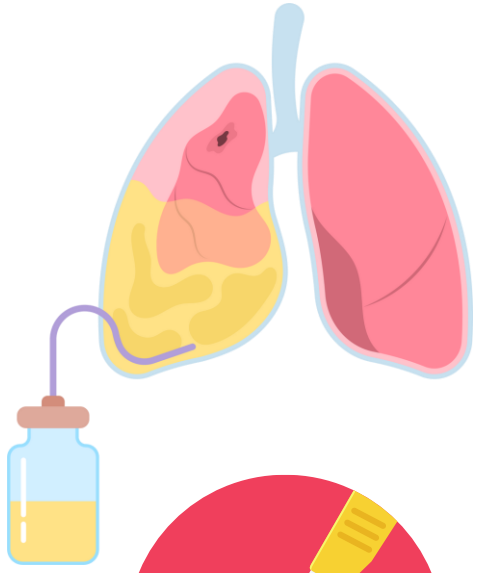
Biopsy





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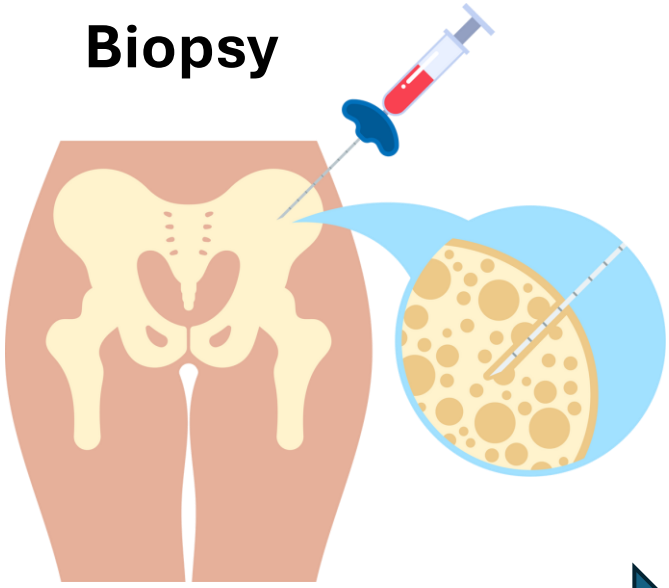
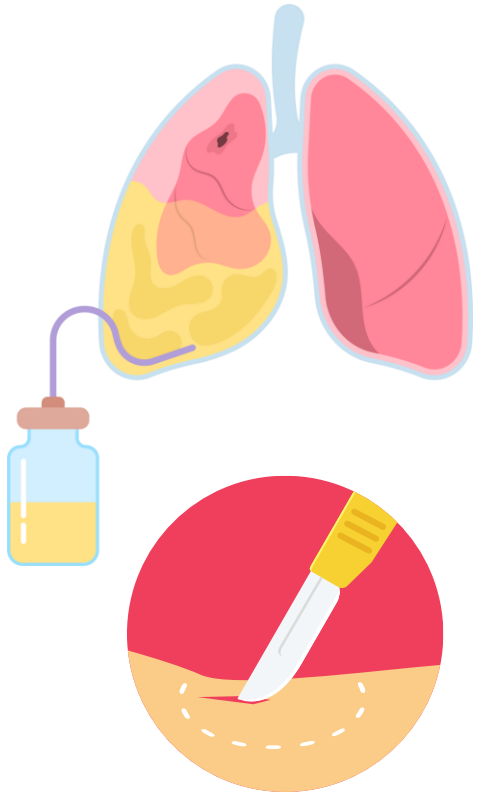
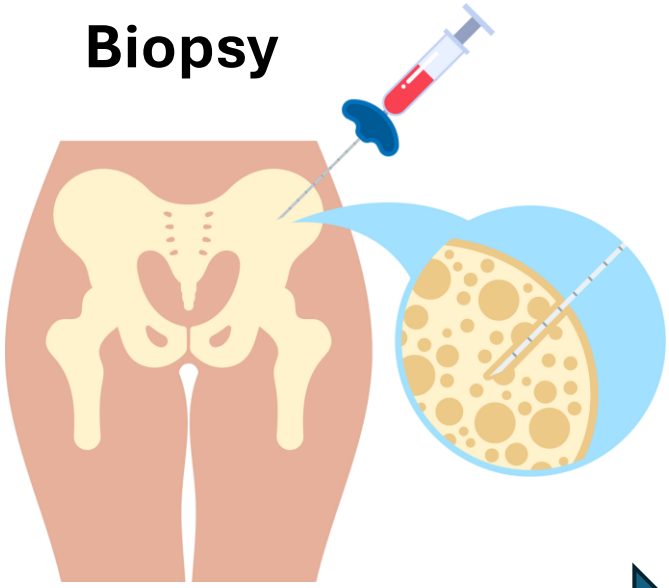


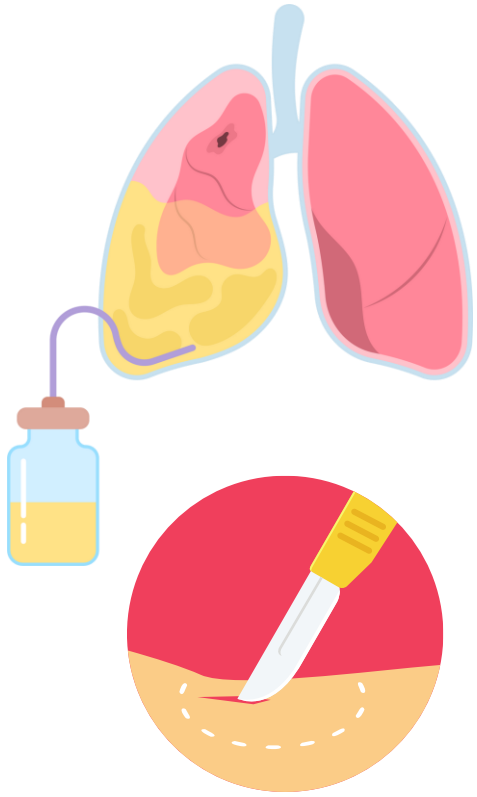


Cells/tissue on Microscope Slide

Stain for Receptors (ER, PR, HER2) & other *biomarkers* using immunohistochemistry (IHC)

Biopsy





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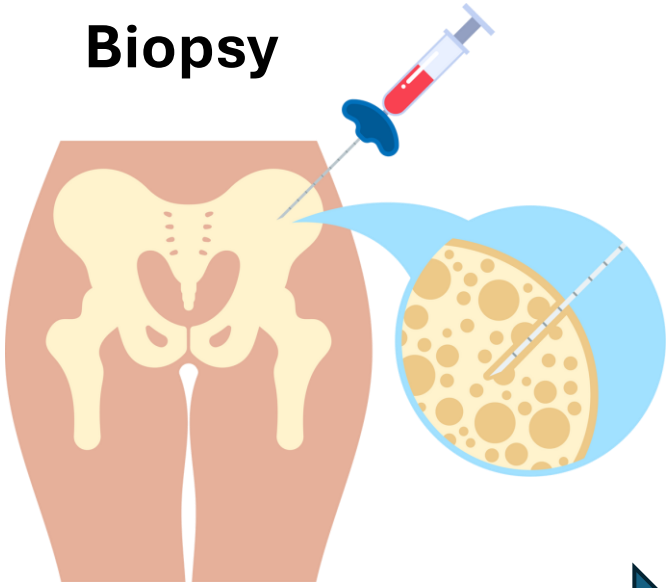
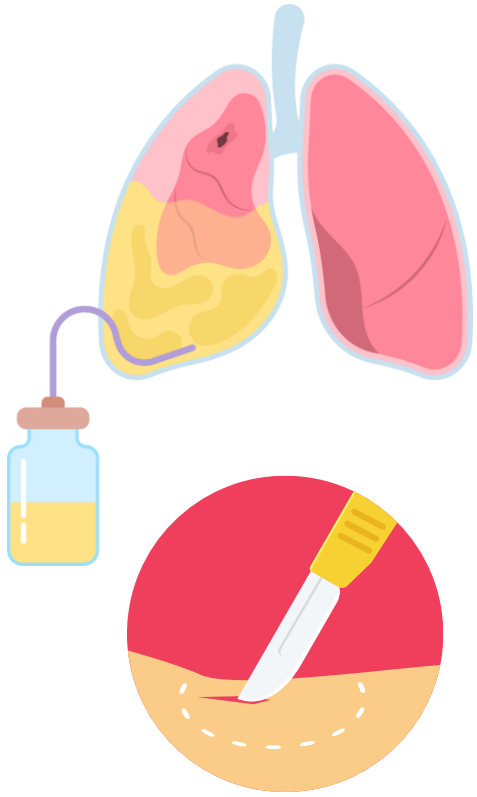
Stain for Receptors (ER, PR, HER2) & other *biomarkers* using immunohistochemistry (IHC)

Examine Under Microscope

Biopsy





Cells/tissue on Microscope Slide

Stain for Receptors (ER, PR, HER2) & other *biomarkers* using immunohistochemistry (IHC)

Examine Under Microscope

Estrogen Receptor (ER) → Percent & Positive, Negative, or Low
Progesterone Receptor (PR) → Percent & Positive or Negative
HER2 → 0, 1+, 2+, 3+ and if 2+ ISH results Positive or Negative

HER2 Negative, Low, UltraLow, or Positive?

IHC Score 0

HER2 Negative/Null

IHC Score 3+

HER2 Positive

HER2 Negative, Low, UltraLow or Positive?

IHC Score 0

HER2 Negative/Null

IHC Score > 0 < 1+

HER2 UltraLow

IHC Score 1+

HER2 Low

IHC Score 3+

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(F)ISH

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IHC Score 3+

HER2 Positive

MERCYHEALTH

Mercy Health Anderson
7500 State Rd
Cincinnati, OH 45255
Fax 513-624-4891 Ph 513-624-4590

Department of Pathology

FINAL SURGICAL PATHOLOGY REPORT

Patient Name: **BEUMER, AMY** [redacted]
DOB: [redacted]
Age/Sex:
Med Rec No:
Attending Phys:
Perform Phys:

Location: SAWKA
Date Collected: 02/17/2017
Date: Received: 02/18/2017
Date Completed: 02/20/2017

VTS17-1084

FINAL DIAGNOSIS:

Right breast, biopsy:
- **Invasive ductal carcinoma, Nottingham Grade 2 – SEE SYNOPTIC REPORT and Comment.**
- **Associated ductal carcinoma in-situ (DCIS), intermediate nuclear grade.**

SYNOPTIC REPORT – NEEDLE CORE BIOPSIES, BREAST

Invasive carcinoma: Present
Location: Right breast
Number of cores involved/total cores: 1/3 cores/fragments involved by invasive carcinoma
Longest length on slide: 12 mm
Histologic type: Invasive mammary carcinoma of no special type (ductal, not otherwise specified)
Modified Bloom-Richardson (Nottingham) Grade: Grade 2 (total score 6; tubule score 3; nuclear score 2; mitotic score 1)
Lymphatic/Vascular invasion: Not identified
Ductal carcinoma in-situ: Present
Number of cores involved/total cores: 1/3 cores/fragments involved by DCIS
Nuclear grade: Intermediate grade (grade 2)
Necrosis: Absent
Architectural pattern: solid
Tavassoli grade: 2
Microcalcifications: Absent

pTNM: Not possible on needle core biopsies

Breast profile studies: performed on block A1

Antibody: ER
%Tumor staining/Intensity: >95%/Strong
Interpretation: Positive

Antibody: PR
%Tumor staining/Intensity: <1%/Moderate
Interpretation: Negative

[redacted]

Interpretation: Nuclear staining of 1% or more of tumor cells showing weak or greater intensity is interpreted as positive.

HER-2 EXPRESSION (by Immunohistochemistry): Negative (score 1+).

Duration of fixation: 50 hours

Performed by immunohistochemistry with manual quantitation. ER clone is Ventana SP1. PR clone is Ventana clone 1E2. Test is performed on formalin fixed paraffin embedded tissue using Ventana iVIEW DAB detection kit (Biotin streptavidin). Positive and negative control tissue shows appropriate staining.

Her2/neu scoring follows the ASCO/CAP guidelines: 0, 1+, 2+, 3+. Her2/neu "positive" (3+) requires intense membranous signal on greater than 10% of the invasive tumor cells (see: Journal of Clinical Oncology, Vol 31, No. 31 (November 1), 2013: pp. 3997-4013). Select cases, including all 2+/equivocal for Her2/neu on routine IHC staining, will be sent for Her2/neu analysis by FISH, those results to be the subject of a separate report.

Breast Biomarker Reporting Template
Applies To: Metastatic adenocarcinoma involving liver
Test(s) Performed:
Estrogen Receptor (ER) Status: Positive (greater than 10% of cells demonstrate nuclear positivity)
Percentage of Cells with Nuclear Positivity: 11-20%
Average Intensity of Staining: Weak
Test Type: Food and Drug Administration (FDA) cleared (test / vendor) - Confirm ER, Ventana
Primary Antibody: SP1
Progesterone Receptor (PgR) Status: Positive
Percentage of Cells with Nuclear Positivity: 3%
Average Intensity of Staining: Weak
Test Type: Food and Drug Administration (FDA) cleared (test / vendor) - Confirm PR, Ventana
Primary Antibody: 1E2
HER2 by Immunohistochemistry: Negative (Score 0)
Test Type: Food and Drug Administration (FDA) cleared (test / vendor) - Pathway Her2neu, Ventana
Primary Antibody: 4B5
Scoring guidelines comply with the most recent versions of the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines on HER2 and hormone receptor testing.
Cold Ischemia and Fixation Times: Cannot be determined - Formalin times were not recorded

SUPPLEMENTAL REPORT:

PD-L1 IHC
PD-L1 IHC Interpretation
Negative

Methods
Antibody
22C3

Controls
External controls available, expected immunoreactivity
Assay Information
Food and Drug Administration (FDA) cleared test / vendor
LEO NIEMEIER MD
Pathologist
Electronically signed 08/07/2024

SUPPLEMENTAL REPORT:

The HER2/neu immunostain was reviewed again at clinician's request to evaluate for ultra-low expression. The tumor cells show focal membrane staining (involving 3 cells of >1000 tumor cells) and considered HER2 ultra-low expression/negative (score 0 with staining).

Genomic Testing for Acquired Mutations

- DNA biomarkers from tissue/tumor biopsy or liquid biopsy (ctDNA)
- Also known as genomic testing for somatic mutations or next gen sequencing (NGS)
- Mutations: changes in DNA
  - Examples: ESRI mutations, PIK3CA mutations, Genomic Signatures
  - Large scale changes in DNA
  - Examples: Tumor Mutational Burden (TMB)
- Acquired by cancer cells/tumors over time
- Results often change over time as tumors evolve

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Liquid Biopsy/ctDNA Results (Example)

Summary of Genomic & Epigenetic Biomarkers with Associated Treatment Options

✓ Approved in indication ~ Approved in other indication ⊗ Lack of response

DETECTED ALTERATION(S) / BIOMARKER(S)	ASSOCIATED FDA-APPROVED THERAPIES	CLINICAL TRIALS (SEE PAGE 6)	% CFDNA OR COPY NUMBER
FGFR1 **Amplification**	None	**Yes**	**Medium (++)**
SMAD4 **Splice Site SNV**	None	**No**	**0.4%**
GATA3 **R331Lfs*24**	None	**No**	**12.7%**

Variants of uncertain clinical significance listed on following pages.

Additional Biomarkers

Tumor Mutational Burden (TMB)	Not Evaluable	
MSI-High	NOT DETECTED	
Homologous Recombination Deficiency (HRD)	**Genomic Instability Status**	**HRR mutations**
	Not detected	Not detected
Tumor Fraction[#]	11.4% - Based on 1960 patient-specific biomarkers	

[#] Tumor fraction is defined as the proportion of tumor molecules present in the cfDNA within the submitted specimen and is based on epigenomic signals.

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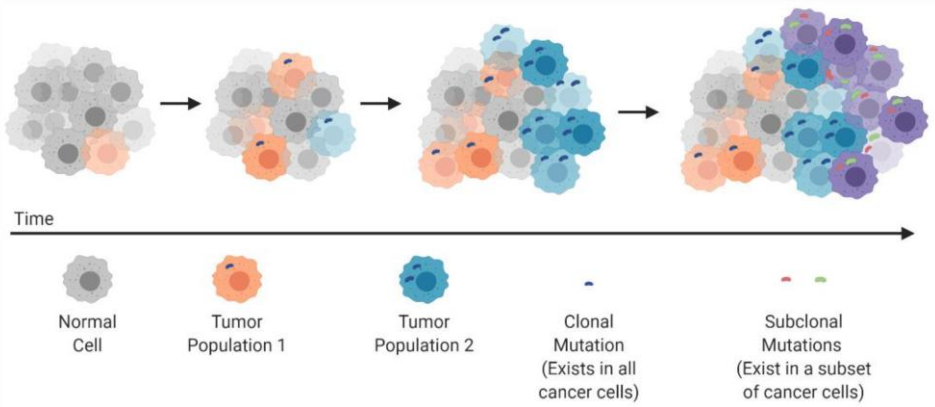

El-Sayes N, Vito A, Mossman K. Tumor Heterogeneity: A Great Barrier in the Age of Cancer Immunotherapy. *Cancers*. 2021; 13(4):806. https://doi.org/10.3390/cancers13040806 (CC BY 4.0)

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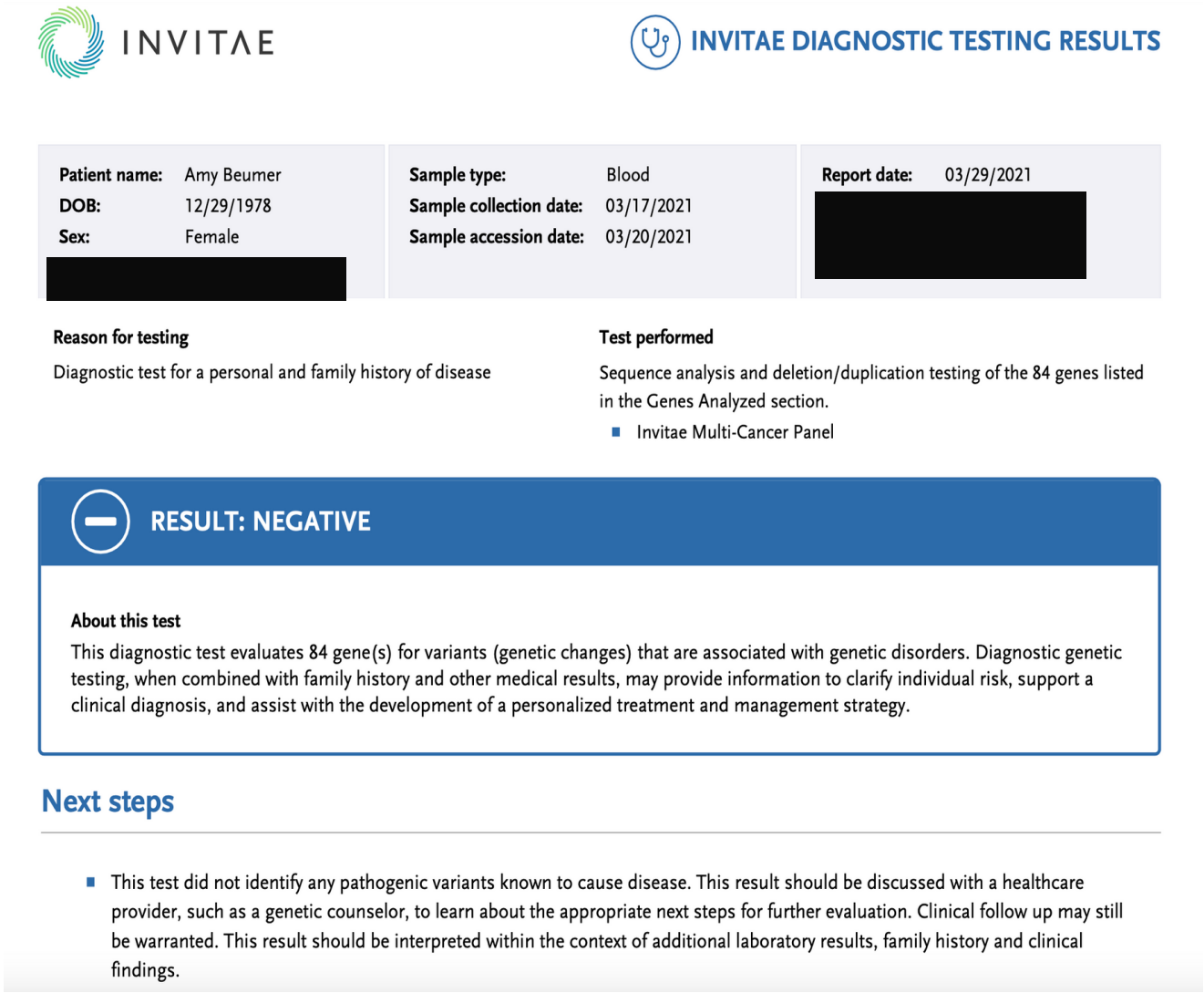

INVITAE

INVITAE DIAGNOSTIC TESTING RESULTS

Patient name:	Amy Beumer	**Sample type:**	Blood	**Report date:**	03/29/2021
DOB:	12/29/1978	**Sample collection date:**	03/17/2021	[redacted]	
Sex:	Female	**Sample accession date:**	03/20/2021		
[redacted]					

Reason for testing

Diagnostic test for a personal and family history of disease

Test performed

Sequence analysis and deletion/duplication testing of the 84 genes listed in the Genes Analyzed section.

- Invitae Multi-Cancer Panel

RESULT: NEGATIVE

About this test

This diagnostic test evaluates 84 gene(s) for variants (genetic changes) that are associated with genetic disorders. Diagnostic genetic testing, when combined with family history and other medical results, may provide information to clarify individual risk, support a clinical diagnosis, and assist with the development of a personalized treatment and management strategy.

Next steps

- This test did not identify any pathogenic variants known to cause disease. This result should be discussed with a healthcare provider, such as a genetic counselor, to learn about the appropriate next steps for further evaluation. Clinical follow up may still be warranted. This result should be interpreted within the context of additional laboratory results, family history and clinical findings.

Next steps…

- Talk to your oncologist.
  - Have I had biomarker testing?
  - If yes, what kind and what were the results?
  - If no, why not? Which biomarker tests do you recommend?
  - Have I had genetic testing for inherited mutations?
- Get copies of your pathology report(s) and any genomic sequencing for acquired mutations (from tissue or ctDNA) or genetic testing for inherited mutations.
- Write down your biomarkers
- For more in depth information: Spinning Science & Resource List