BIOMARKER TESTING IN **BREAST CANCER**

Knowledge Check 2

1 **True or False:** NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend verifying negative liquid biopsy results with tumor tissue testing.

a True
b False

2 The collaboration of and clear communication within the entire team taking care of patients with metastatic breast cancer are paramount. Which of the following HCPs are part of the multidisciplinary team and are essential to obtaining a molecular diagnosis for metastatic breast cancer patients?

a Oncologist
b Nurse navigator
c Pathologist
d Interventionalist/surgeon
e Laboratory staff
f All of the above

3 Which of the following institutions provide important guidelines on the clinical utility of valid biomarker tests, as well as recommendations on testing standardization in order to improve testing consistency.

a ASCO-CAP
b NCCN Guidelines®
c International Ki-67 Working Group
d All of the above
e None of the above
f A and B only

4 **True or False:** FISH is recommended for most biomarkers.

a True
b False

5 Match the testing modality with the appropriate statement from the right column.

a Sanger sequencing	i. May require a pre-amplification step in situations with low target DNA sample input
b Pyrosequencing	ii. Can potentially detect SNVs, indels, CNAs, and fusions
c NGS	iii. Has low sensitivity (LOD >20% VAF)
d RT-PCR	iv. Read length capacity is low (~100 bases)
e dPCR	v. Detects known mutations with a variable sensitivity (LOD ~5% VAF)

ANSWERS

Precision Medicine

1 **True.** NCCN Guidelines recommend reflex testing to tissue biopsy in case of a negative result with liquid biopsy.[1] (page 17)

2 **F. All of the above.** The oncologist, interventionalist/breast cancer surgeon, nurse navigator, pathologist, and laboratory staff all play an important role in molecular diagnostics and breast cancer care.[2,3] (page 8)

3 **D. All of the above.** ASCO-CAP, NCCN Guidelines, and the International Ki-67 Working Group have all released guidelines that have information pertinent to biomarker testing in breast cancer.[4-9] (pages 7,14)

4 **False.** FISH is recommended for HER2 testing only.[4,10-16] (page 11)

5

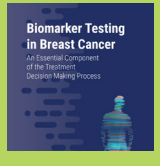
A.iii. Sanger sequencing has a low sensitivity (>20% VAF)[17]

B.iv. Pyrosequencing has read lengths of ~100 bases.[18]

C.ii. NGS can potentially detect SNVs, indels, CNAs, and fusions, dependent on assay design.[19]

D.v. RT-PCR detects known mutations with a variable sensitivity (LOD ~5% VAF).[17,20,21]

E.i. dPCR may require a pre-amplification step in situations with low target DNA sample input[22,23] (page 10)



This knowledge check is connected to the chapter "Biomarker Testing in Breast Cancer: An Essential Component of the Treatment Decision Making Process." To get a copy of this and other chapters, please visit: **https://www.hcp.novartis.com/precision-medicine**

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ASCO, American Society of Clinical Oncology; CAP, College of American Pathologists; CNA, copy number alteration; DNA, deoxyribonucleic acid; dPCR; digital polymerase chain reaction; FISH, fluorescence in situ hybridization; HCP, healthcare professional; HER2, human epidermal growth factor receptor 2; LOD; limit of detection; NGS; next generation sequencing; RT-PCR, real time-polymerase chain reaction; SNV, single nucleotide variant; VAF, variant allele frequency.
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References: **1**. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.4.2022. ©National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed June 30, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **2**. De Las Casas LE, Hicks DG. *Am J Clin Pathol*. 2021;155(6):781-792. **3**. Saini KS et al. *Ann Oncol*. 2012;23(4):853-859. **4**. Wolff AC et al. *J Clin Oncol*. 2018;36(20):2105-2122. **5**. Allison KH et al. *J Clin Oncol*. 2020;38(12):1346-1366. **6**. Referenced with permission from the National Comprehensive Cancer Network, Inc. ©National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed February 8, 2022. To view the most recent and complete version of the recommendations, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **7**. Wolff AC et al. *J Clin Oncol*. 2007;25(1):118-145. **8**. Hammond MEH et al. *Arch Pathol Lab Med*. 2010;134(7):e48-e72. **9**. Nielsen TO et al. *J Natl Cancer Inst*. 2021;113(7):808-819. **10**. Cheang MCU et al. *Oncologist*. 2015;20(5):474-482. **11**. Schick J et al. *Breast Cancer (Auckl)*. 2021;15:1178223421995854. **12**. Nielsen TO et al. *J Natl Cancer Inst*. 2021;113(7):808-819; **13**. Toland AE et al. *NPJ Genom Med*. 2018;3:7. doi: 10.1038/s41525-018-0046-7; **14**. Preobrazhenskaya EV et al. *Breast Cancer Res Treat*. 2017;165(3):765-770; **15**. Matikas A et al. *Clin Cancer Res*. 2019;25(18):5717-5726; **16**. Mosele F et al. *Ann Oncol*. 2020;31(3):377-386; **17**. MacConaill LE *J Clin Oncol*. 2013;31(15):1815-1824. **18**. Metzker ML et al. *Genome Res*. 2005;15(12):1767-1776. **19**. Jennings LJ et al. *J Mol Diagn*. 2017;19(3):341-365. **20**. Pennell NA et al. *Am Soc Clin Oncol Educ Book*. 2019;39:531-542. **21**. Alvarez-Garcia V et al. *Sci Rep*. 2018;8(1):4290. **22**. ThermoFisher. Real-Time vs. Digital PCR vs. Traditional PCR. https://www.thermofisher.com/us/en/home/life-science/pcr/real-time-pcr/real-time-pcr-learning-center/real-time-pcr-basics/real-time-vs-digital-vs-traditional-pcrl. Accessed November 10, 2021. **23**. Sigma Aldrich. Digital PCR. https://www.sigmaaldrich.com/technical-documents/articles/biology/digital-pcr.html. Accessed November 10, 2021.

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