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What is the clinical impact of TumorNext-*HRD*?

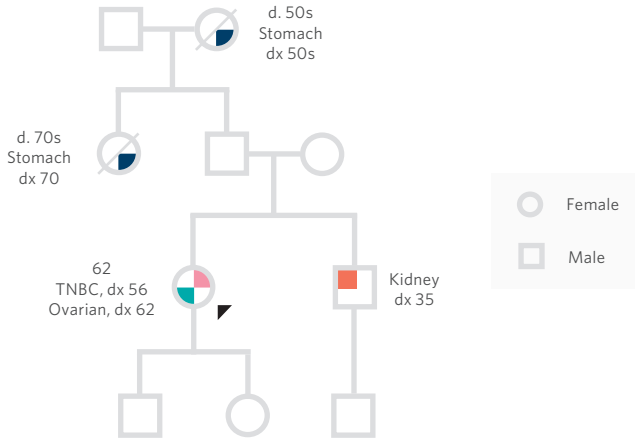
CASE EXAMPLE

Who is the Patient?

- 62 year old female
- Personal history of triple negative breast cancer (TNBC) diagnosed at age 56
- Personal history of ovarian cancer diagnosed at age 62
- No previous genetic testing

What is the Family History?

- Brother diagnosed with kidney cancer at age 35
- Paternal aunt diagnosed with stomach cancer at age 70
- Paternal grandmother diagnosed with stomach cancer in her 50s



What Happened with Genetic Testing?

- Provider ordered Ambry's TumorNext-*HRD*
  - TumorNext-*HRD* is a paired tumor/germline analysis of *BRCA1/BRCA2* plus 9 additional genes* in the homologous recombination repair pathway that are also known to be associated with hereditary cancer, and also includes *BRCA1* and *RAD51C* methylation analysis.

    * Additional genes on TumorNext-*HRD: ATM, BARD1, BRIP1, CHEK2, MRE11A, NBN, PALB2, RAD51C, RAD51D*

Genetic Testing Criteria:

- Patient meets NCCN® Testing Criteria for *BRCA1/2* genetic testing
- Criteria are met because of personal history of ovarian cancer[1,2] and her personal history of TNBC diagnosed less than age 60[1]

Genetic Test Results:

- Positive finding on TumorNext-*HRD*
  - Germline *PALB2* pathogenic (disease causing) mutation
  - Somatic *BRCA1* pathogenic mutation

How did genetic testing impact the patient and family?

PALB2 GERMLINE MUTATION

INCREASED LIFETIME CANCER RISKS

- Breast
- Ovarian
- Pancreatic
- Male breast & prostate (male relatives)

PERSONALIZED SCREENING AND PREVENTION OPTIONS

- Recommended breast MRI (starting at age 30) alternating with mammogram
- Consider prophylactic mastectomy based on family history

IMPACT FOR THE PATIENT'S FAMILY

- Siblings and children have a 50% chance of having the familial mutation.
- Parents can be tested to determine which side of the family is at-risk, so other relatives can be tested.

BRCA1 SOMATIC MUTATION

THERAPEUTIC OPTIONS

- Individuals who carry somatic mutations in the *BRCA1/BRCA2* genes may be eligible for FDA-approved PARP inhibitor(s)
- Alterations in *BRCA1/BRCA2* may predict sensitivity to DNA-damaging drugs, such as platinum therapies, and PARP inhibitors[3-5]

IMPACT FOR THE PATIENT'S FAMILY

- Somatic mutations are not passed down through families, so family members are not at-risk to carry this *BRCA1* mutation and do not need to undergo *BRCA1/2* genetic testing, unless otherwise indicated.

What's the difference between germline and somatic?

	WHAT IS TESTED?	INHERITANCE	RISKS
INHERITED (GERMLINE)	Blood or saliva Genes that are identical in all cells of your patient's body	Can be inherited and passed on to family members	Linked to an increased risk for other cancer(s) Can impact your patient's treatment
TUMOR (SOMATIC)	Your patient's tumor tissue for cancer-specific changes	Not inherited and only present in your patient's tumor cells. Cannot be passed to family members	Does not increase your patient's risk for other cancers Can impact your patient's treatment

POINTS FOR YOUR PRACTICE

- Germline only testing would have missed a somatic mutation which impacts PARP inhibitor eligibility.
- A tumor only test could have missed a germline *PALB2* mutation, which has a significant impact for this patient's family.
- Paired germline and tumor testing allows you to get more complete information to guide healthcare decisions for your patients.

References

1. National Comprehensive Cancer Network®. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Genetic/Familial High-Risk Assessment: Breast and Ovarian. Version 2.2017
2. Society of Gynecologic Oncology Clinical Practice Statement, October 2014
3. Banerjee S & Kaye S. Curr Oncol Rep. 2011 Dec;13(6):442-9
4. Burgess M & Puhalla S. Front Oncol. 2014 Feb 27;4:19
5. Yamamoto KN *et al.* PLoS One. 2014 Aug 26;9(8):e105724).

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