FOR PATIENTS WITH METASTATIC AND NONMETASTATIC INVASIVE BREAST CANCER (BC)

Germline *BRCA1* and *BRCA2* Mutation Testing Can Help Guide Management

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Germline *BRCA* Mutation May Indicate Elevated Risks and May Inform Treatment Approaches

Predictive insights

BRCA1/2 mutation status can be used to develop a comprehensive treatment plan[1-4]

- **Informs** treatment decisions[4]
- **Informs** risk-reducing surgery, such as mastectomy or oophorectomy[1,5]

Prognostic insights

BRCA1/2 mutation status may provide insights on the course of disease[6]

- **Higher rates** of brain metastases vs noncarriers[7]
- **Increased risk** of developing additional primary cancers and **elevated risk** of contralateral and ipsilateral BC recurrence[8-10]

Hereditary risk insights

Germline mutations in *BRCA1/2* aid in the assessment of familial risks of cancer[1-3,6]

- **45%-66% cumulative risk** for developing BC by age 70 years[2]
- **Increased risk** for the development of TNBC (*BRCA1*), ER+ BC, and HER2– BC (*BRCA2*), however, all BC subtypes can occur in association with germline *BRCA1/2* mutations[1]

Test appropriate patients for germline *BRCA* mutations to help inform your clinical approach

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Recommendations for *BRCA* Gene Testing for Clinical Management of Patients With Metastatic and Nonmetastatic Invasive BC

Why Test?

- To aid in systemic treatment decisions[11,12]

What to Test?

- Germline *BRCA1* and *BRCA2* mutations[11,12,a,b]

Whom to Test?

- **Nonmetastatic invasive:** All patients with TNBC and certain patients of any age with HR+/HER2– invasive nonmetastatic BC[12]
- **Metastatic:** All patients with recurrent or metastatic BC[12]

When to Test?

- **Nonmetastatic invasive:** Upon diagnostic workup[12]
- **Metastatic:** At initial workup or upon recurrence[12,13]

The American Society of Breast Surgeons: Guidelines for Genetic Testing in BC

Why Test?

- May impact recommendations for surgery, radiation, and systemic therapy[14]

What to Test?

- Germline *BRCA1* and *BRCA2* mutations[14]

Whom to Test?

- **All patients** with newly diagnosed or a personal history of BC[14]

When to Test?

- Upon diagnosis[14,15]

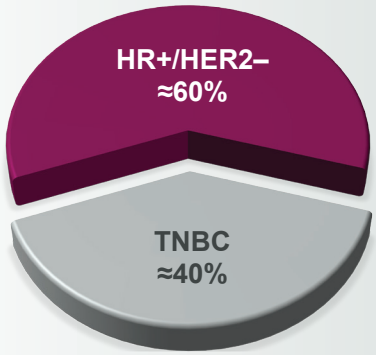
[a]Recommends testing for somatic *BRCA1/2* and germline *PALB2* mutations for metastatic invasive BC (NCCN category of evidence 2B).[12]
[b]Test for other high-penetrance breast cancer susceptibility genes as clinically indicated (*CDH1, PALB2, PTEN*, and *TP53*) for risk assessment and counseling.[11]
Additional recommendations for germline *BRCA1/2* testing may be found in the NCCN Guidelines® for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.[11]

Test appropriate patients with BC rather than testing specific populations[16]

Patients With Varying BC Molecular Subtypes May Be Clinically Indicated for Germline *BRCA* Mutation Testing

≈1 in 10 patients with HER2– BC has a **germline *BRCA* mutation**[17-20,a]

While germline *BRCA* mutations are more prevalent in TNBC, the HR+/HER2– subtype is ≈6x more common than TNBC and accounts for the majority of patients with germline *BRCA* mutation[17,21]



Know germline *BRCA* mutation status for both your patients with TNBC and your patients with HR+/HER2– BC

[a]This image is for illustrative purposes only and may not reflect the incidence of germline *BRCA* mutation in the HER2– BC population.

How to Test?

- Germline testing can be performed on blood or saliva/buccal swabs[22]
- If a commercial assay is used for testing, check the manufacturer's sample requirements

Coordination Among Members of Multidisciplinary Team Around the Need for Genetic Testing Is Critical[22-25]

A collaborative multidisciplinary team approach can help navigate patients through the diagnostic journey and enable comprehensive care[26]

Breast Surgeon/ Treating Surgeon
- Pre-diagnosis
- Obtain consent from patients for genetic testing

Pathologist
- Diagnosis
- Obtain consent from patients for genetic testing

Phlebotomist/ Lab Technologist
- Blood or saliva sample collection
- Obtain consent from patients for genetic testing

Qualified Laboratory Scientist
- Biomarker testing
- Obtain consent from patients for genetic testing

Medical Oncologist
- Return of test results and post-test counseling
- Obtain consent from patients for genetic testing

Genetic Counseling
- In-person appointments
- Telegenetics, including telephone and video conferencing
- Patient-directed online referral tools

Talk to your multidisciplinary team to establish a standardized germline testing protocol

Select Diagnostic Assays for *BRCA1* and *BRCA2* Mutation Testing

A number of commercial assays are available for germline testing of *BRCA1* and *BRCA2* mutations[a]

LABORATORY	TEST NAME	CONTACT INFORMATION/PORTAL	PATIENT ASSISTANCE PROGRAM
Ambry Genetics	*BRCA1* and *BRCA2*[27,28]	949.900.5500 AmbryPort®[30]	Program application[31]
	CancerNext®[27,29]		
Myriad Genetics	BRACAnalysis CDx®[32-34,b]	800.469.7423 MyriadPro™[38]	Program application[39]
	MyRisk® Hereditary Cancer[35-37]		
GeneDx	*BRCA1/2* Sequencing and Deletion/ Duplication Analysis[40,41]	888.729.1206 GeneDX portal[44]	Financial assistance application[45]
	Comprehensive Common Cancer Panel[42,43]		
Invitae	*BRCA1* and *BRCA2* STAT Panel[46]	800.436.3037 Invitae online portal[49]	Program application[50]
	Common Hereditary Cancers Panel[47,48]		
Natera	Empower™ *BRCA1* and *BRCA2* Panel[51]	650.489.9050[52]	Patient Information[53]
	Empower™ Multi-cancer Panel[51]		
Color Health, Inc.	Hereditary Cancer Genetic Test[54]	844.352.6567 Color[55]	Patient support[56]

[a]The turnaround time for commercial assays is ≈2 weeks.[28,29,33,34,37,40,42,46,47,51,57]

[b]FDA-approved diagnostic.[58]

These QR codes will take you to a third-party website not maintained, sponsored, or reviewed by AstraZeneca. Please use your smartphone's camera to zoom in and scan the desired code

Test select patients with HER2– early BC to help inform clinical decisions[11,17,21,59]

Providers should contact third-party laboratories for information on their patient assistance programs.

Abbreviations

BC, breast cancer; ***BRCA***, breast cancer susceptibility gene; ***BRCA1***, breast cancer susceptibility gene 1; ***BRCA2***, breast cancer susceptibility gene 2; ***BRCA1/2***, breast cancer susceptibility gene 1 and/or 2; ***CDH1***, Cadherin1; **CDx**, companion diagnostic; **ER+**, estrogen receptor–positive; **FDA**, US Food and Drug Administration; **HER2–**, human epidermal growth factor receptor 2–negative; **HR+**, hormone receptor–positive; **NCCN**, National Comprehensive Cancer Network® (NCCN®); ***PALB2***, partner and localizer of *BRCA2*; ***PTEN***, Phosphatase and tensin homolog; **TNBC**, triple-negative breast cancer; ***TP53***, tumor protein 53.

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