ASCO Guidelines

ASTRO
AMERICAN SOCIETY FOR RADIATION ONCOLOGY

SSO
SOCIETY OF SURGICAL ONCOLOGY

MANAGEMENT OF HEREDITARY BREAST CANCER: ASCO-ASTRO-SSO GUIDELINE		
Clinical Question	**Recommendation**	**Evidence Rating**
What is the appropriate surgical management of the index malignancy for women with newly diagnosed non-metastatic breast cancer who have a *BRCA1/2* mutation?	Germline *BRCA* status should not preclude a patient with newly diagnosed breast cancer otherwise eligible for breast conserving therapy (BCT) from receiving BCT.	Type: Formal consensus Evidence quality: Intermediate Strength of recommendation: Moderate
	Surgical management of the index malignancy (BCT vs. ipsilateral therapeutic and contralateral risk-reducing mastectomy) in *BRCA1/2* mutation carriers should be discussed considering the increased risk of contralateral breast cancer and possible increased risk of an ipsilateral new primary breast cancer compared to non-carriers.	Type: Formal consensus Evidence quality: Intermediate Strength of recommendation: Strong
	The following factors should be considered for assessing risk of contralateral breast cancer (CBC) and role of risk-reducing mastectomy in *BRCA1/2* mutation carriers: age of diagnosis (the strongest predictor of future contralateral breast cancer; see Table 1), family history of breast cancer, overall prognosis from this or other cancers (e.g., ovarian), ability of patient to undergo appropriate breast surveillance (MRI), comorbidities, and life expectancy.	Type: Formal consensus Evidence quality: Intermediate Strength of recommendation: Moderate
	BRCA1/2 mutation carriers who do not have bilateral mastectomy should undergo high-risk breast screening of remaining breast tissue with annual mammogram and MRI.	Type: Formal consensus Evidence quality: Intermediate Strength of recommendation: Moderate
What is the appropriate surgical management of the index malignancy for women with newly diagnosed non-metastatic breast	For women with newly diagnosed breast cancer who have a mutation in a moderate-penetrance breast cancer susceptibility gene, mutation status alone should not determine local therapy decisions for the index tumor or contralateral risk-reducing mastectomy.	Type: Formal consensus Evidence quality: Low Strength of recommendation: Moderate

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cancer who have a selected moderate-penetrance mutation?	In breast cancer patients with a mutation in a moderate-penetrance breast cancer susceptibility gene, breast conserving therapy (BCT) should be offered to patients for whom BCT is an appropriate treatment option. There is a lack of data regarding ipsilateral breast cancer events after BCT among patients with moderate-risk mutations.	Type: Formal consensus Evidence quality: Low Strength of recommendation: Moderate
	The evidence regarding contralateral breast cancer risk is limited for mutations in moderate-penetrance breast cancer genes, aside from some data for *CHEK2 1100delC*. Information about the specific gene and what is known about the risk of contralateral breast cancer should be discussed in the context of shared decision-making.	Type: Formal consensus Evidence quality: Low Strength of recommendation: Moderate
	Patients with mutations in moderate-penetrance genes who do not have bilateral mastectomy should undergo high-risk breast screening of remaining breast tissue with annual mammogram and MRI.	Type: Formal consensus Evidence quality: Low Strength of recommendation: Moderate
Among women with breast cancer who have a *BRCA1/2* germline mutation or selected moderate-penetrance, non-*BRCA1/2* germline mutations who are undergoing therapeutic mastectomy, what is the role of nipple-sparing mastectomy?	For women with newly diagnosed breast cancer undergoing mastectomy who have a deleterious mutation in *BRCA 1* or *2*, nipple-sparing mastectomy is a reasonable oncologic approach to consider in appropriately selected patients.	Type: Formal consensus Evidence quality: Intermediate Strength of recommendation: Moderate
	For women with newly diagnosed breast cancer undergoing mastectomy who have a deleterious mutation in moderate-penetrance genes, nipple-sparing mastectomy is a reasonable oncologic approach to consider in appropriately selected patients.	Type: Formal consensus Evidence quality: Low Strength of recommendation: Moderate

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What is the role of contralateral prophylactic mastectomy for women with breast cancer who have a *BRCA1/2* mutation or a select moderate-penetrance gene mutation?	For women with breast cancer who have a *BRCA1/2* mutation and who have been treated or are being treated with unilateral mastectomy, contralateral risk-reducing mastectomy (CRRM) should be offered. CRRM is associated with a decreased risk of contralateral breast cancer; there is insufficient evidence for improved survival. The following factors should be considered for assessing risk of contralateral breast cancer (CBC) and role of risk-reducing mastectomy: age of diagnosis (the strongest predictor of future contralateral breast cancer), family history of breast cancer, overall prognosis from this or other cancers (e.g., ovarian), ability of patient to undergo appropriate breast surveillance (MRI), comorbidities, and life expectancy.	Type: Formal consensus Evidence quality: Intermediate Strength of recommendation: Moderate
	For women with breast cancer who have a mutation in a moderate-penetrance breast cancer predisposition gene and who have been treated or are being treated with unilateral mastectomy, the decision regarding contralateral risk-reducing mastectomy (CRRM) should not be based predominantly on the mutation status. Additional factors that predict CBC such as age at diagnosis and family history should be considered, as they are in all cases. The impact of CRRM on decreasing risk of contralateral breast cancer (CBC) is dependent on the risk of CBC for each individual gene. Data regarding the risk of CBC due to moderate-penetrance genes are limited.	Type: Formal consensus Evidence quality: Low Strength of recommendation: Moderate
Among women with breast cancer who have a *BRCA1/2* germline mutation or selected moderate-penetrance mutations who are	For breast cancer patients with a deleterious germline *BRCA1/2* mutation interested in a contralateral risk-reducing mastectomy, physicians should discuss the option of nipple-sparing mastectomy as a reasonable oncologic option.	Type: Formal consensus Evidence quality: Intermediate Strength of recommendation: Strong

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undergoing contralateral risk-reducing mastectomy, what is the role of nipple-sparing mastectomy?	For breast cancer patients with a mutation in a moderate-penetrance gene who are interested in a contralateral risk-reducing mastectomy, physicians should discuss the option of nipple sparing mastectomy as a reasonable oncologic option.	Type: Formal consensus Evidence quality: Low Strength of recommendation: Moderate
What is the role of radiation therapy in women with breast cancer who have a *BRCA1/2* germline mutation or selected moderate-penetrance, non-*BRCA1/2* germline mutations?	For women with breast cancer who are treated with BCT or with mastectomy for whom post-mastectomy radiotherapy is considered, radiation therapy should not be withheld due to mutation status, except for mutations in *TP53* (see below). There is no evidence of a significant increase in toxicity or contralateral breast cancers (CBC) related to radiation exposure among patients with a mutation in a *BRCA1/2* or a moderate-penetrance gene.	Type: Formal consensus Evidence quality: Intermediate Strength of recommendation: Strong
	For women with breast cancer who are carriers of an ATM mutation, radiation therapy should be offered when clinically indicated. Data regarding rates of toxicity between ATM mutation carriers and non-carriers are limited and inconsistent. Potential absolute risks appear to be small; however, more research is needed. Discussion with ATM carriers interested in BCT is encouraged.	Type: Formal consensus Evidence quality: Low Strength of recommendation: Moderate
	For women with breast cancer who are carriers of a germline *TP53* mutation, radiotherapy of the intact breast is contraindicated. Mastectomy is the recommended therapeutic option. Postmastectomy radiation therapy should only be considered in patients with significant risk of local regional recurrence.	Type: Formal consensus Evidence quality: Low Strength of recommendation: Moderate

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What is the role of platinum chemotherapy in women who have a *BRCA1/2* mutation or selected moderate-penetrance germline mutations and advanced breast cancer?	When offering chemotherapy for germline *BRCA* mutation carriers with metastatic breast cancer, platinum chemotherapy is preferred to taxane therapy for patients who have not previously received platinum. There are no data to address platinum efficacy in other germline mutation carriers.	Type: Evidence based Evidence quality: Intermediate Strength of recommendation: Moderate
What is the role of (neo)adjuvant platinum chemotherapy in women who have a *BRCA1/2* mutation or selected moderate-penetrance germline mutations and breast cancer?	For germline *BRCA* mutation carriers with breast cancer treated with (neo)adjuvant therapy, data do not support the routine addition of platinum to anthracycline and taxane-based chemotherapy. While single-agent platinum has demonstrated activity in the neoadjuvant setting, there are no data yet comparing it to standard chemotherapy. There are no data to address platinum efficacy in other germline mutation carriers.	Type: Evidence based Evidence quality: Intermediate Strength of recommendation: Moderate
What is the role of Poly (ADP-ribose) polymerase (PARP) inhibitors in women who have a *BRCA1/2* mutation or selected moderate-penetrance germline mutations and advanced breast cancer?	For *BRCA*1/2 mutation carriers with metastatic HER2-negative breast cancer, olaparib or talazoparib should be offered as an alternative to chemotherapy in the 1st-3rd line setting. For *BRCA1/2* mutation carriers with metastatic HER2-negative breast cancer, there are no data directly comparing efficacy of PARP inhibitor to platinum chemotherapy.	Type: Evidence based Evidence quality: High Strength of recommendation: Strong
	For breast cancer patients with mutations in moderate-penetrance genes, there are currently no robust data to support the use of PARP inhibitors.	Type: Informal consensus Evidence quality: Insufficient Strength of recommendation: Moderate
What is the role of PARP inhibitors in women who have a *BRCA1/2* mutation or selected moderate-penetrance mutations and non-metastatic breast cancer?	For germline *BRCA* mutation carriers, there is insufficient data at this time to recommend a PARP inhibitor for patients with non-metastatic breast cancer.	Type: Evidence based Evidence quality: Intermediate Strength of recommendation: Moderate