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NCCN Clinical Practice Guidelines in Oncology
(NCCN Guidelines®)

Breast Cancer

NCCN National Comprehensive Cancer Network®

MULTIGENE ASSAYS FOR CONSIDERATION OF ADDITION OF ADJUVANT SYSTEMIC CHEMOTHERAPY TO ADJUVANT ENDOCRINE THERAPY[a,b]

Assay	Predictive	Prognostic	NCCN Category of Preference	NCCN Category of Evidence and Consensus	Recurrence Risk	Treatment Implications (references on next page)
21-gene (Oncotype Dx) (for pN0 or node negative)	Yes	Yes	Preferred	1	<26	Patients with T1b/c and T2, hormone receptor-positive, HER2-negative and lymph node-negative tumors, with risk scores (RS) between 0-10 have a risk of distant recurrence of less than 4% and those with RS 11-25, derived no benefit from the addition of chemotherapy to endocrine therapy in the prospective TAILORx study.[1] In women 50 years of age or younger, with RS 16-25 addition of chemotherapy to endocrine therapy was associated with a lower rate of distance recurrence compared with endocrine monotherapy. Consideration should be given for the addition of chemotherapy to endocrine therapy in this group.[1]
					26-30	In patients with T1 and T2, hormone receptor-positive, HER2-negative and lymph node-negative tumors and an RS of 26-30, the omission of chemotherapy has not been studied prospectively. Clinicians should consider additional clinical and pathologic factors with regard to the addition of chemotherapy to endocrine therapy in decision-making.[2]
					≥31	For patients with T1b/c and T2, hormone receptor-positive, HER2-negative, and lymph node-negative tumor RS ≥31, the addition of chemotherapy to endocrine therapy is recommended.[2]
21-gene (Oncotype Dx) (for pN+ or node positive)	N/A* *awaiting results of RxPONDER study	Yes	Other	2A	Low (<18)	The RS is prognostic in women with hormone receptor-positive, lymph node-positive tumors receiving endocrine monotherapy.[3-10] A secondary analysis of a prospective registry of women with hormone receptor-positive, HER2-negative, lymph node-positive tumors demonstrated a 5-year risk of distant recurrence of 2.7% in patients with an RS of <18 treated with endocrine monotherapy.[9] In the West German Plan B study, 110 women with hormone receptor-positive, HER2-negative, lymph node-positive tumors and an RS of <11, showed a 5-year disease-free survival of 94.4% when treated with endocrine monotherapy.[6] For hormone receptor-positive, HER2-negative, lymph node-positive tumors, clinicians should be aware that the optimal RS cut-off (< 11 vs. < 18) is still unknown both for prognosis (risk of recurrence) as well as prediction of chemotherapy benefit.
					Intermediate (18-30) or High (≥31)	In a secondary analysis of the SWOG 8814 trial of women with hormone receptor-positive, lymph node-positive tumors, high RS (≥31) was predictive of chemotherapy benefit. Because of a higher risk of distant recurrence, patients with hormone receptor-positive, 1-3 positive lymph nodes and RS of ≥18 should be considered for adjuvant chemotherapy in addition to endocrine therapy.[3]
70-gene (MammaPrint) (for node negative and 1-3 positive nodes)	Not determined	Yes	Other	1	Low	With a median follow-up of 5 years, among patients at high clinical risk and low genomic risk, the rate of survival without distant metastasis in this group was 94.7% (95% CI, 92.5%–96.2%) among those who did not receive adjuvant chemotherapy. Among patients with 1-3 positive nodes, the rates of survival without distant metastases were 96.3% (95% CI, 93.1–98.1) in those who received adjuvant chemotherapy versus 95.6 (95% CI, 92.7–97.4) in those who did not receive adjuvant chemotherapy.[11] Therefore, the additional benefit of adjuvant chemotherapy may be small in this group.
					High	
50-gene (PAM 50) (for node negative and 1-3 positive nodes)	Not determined	Yes	Other	2A	Node negative: Low (0-40)	For patients with T1 and T2 hormone receptor-positive, HER2- negative, lymph node-negative tumors, a risk of recurrence score in the low range, regardless of T size, places the tumor into the same prognostic category as T1a–T1b, N0, M0.[12]
					Node negative: Intermediate (41-60)	
					Node negative: High (61-100)	
					Node positive: Low (0-40)	In patients with hormone receptor-positive, HER2-negative, 1-3 positive lymph nodes with low risk of recurrence score, treated with endocrine therapy alone, the distant recurrence risk was less than 3.5% at 10 years [12] and no distant recurrence was seen at 10 years in TransATAC study in a similar group.[13]
					Node positive: High (41-100)	
12-gene (EndoPredict) (node negative and 1-3 nodes)	Not determined	Yes	Other	2A	Low (<3.3287)	For patients with T1 and T2 hormone receptor-positive, HER2-negative, and lymph node-negative tumors, a 12-gene low-risk score, regardless of T size, places the tumor into the same prognostic category as T1a–T1b, N0, M0.[13] In ABCSG 6/8, patients in the low-risk group had risk of distant recurrence of 4% at 10 years and in the TransATAC study, patients with 1-3 positive nodes in the low-risk group had a 5.6% risk of distant recurrence at 10 years.[13]
					High (>3.3287)	
Breast Cancer Index (BCI)	Not determined	Yes	Other	2A	Low risk of late occurrence (0-5)	For patients with T1 and T2 hormone receptor-positive, HER2-negative, and lymph node-negative tumors, a BCI in the low-risk range, regardless of T size, places the tumor into the same prognostic category as T1a-T1b, N0, M0. There are limited data as to the role of BCI in hormone receptor-positive, HER2-negative, and lymph node-positive breast cancer.[13]
					High risk of late occurrence (5.1-10)	

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