GENE EXPRESSION 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 and Treatment Implications
21-gene (Oncotype Dx) (for pN0 or node negative)	Yes	Yes	Preferred	1	BINV-N (2 of 4)
21-gene (Oncotype Dx) (for pN+ or node positive)	N/A* *awaiting results of RxPONDER study	Yes	Other	2A	BINV-N (2 of 4)
70-gene (MammaPrint) (for node negative and 1–3 positive nodes)	Not determined	Yes	Other	1	BINV-N (3 of 4)
50-gene (PAM 50) (for node negative and 1–3 positive nodes)	Not determined	Yes	Other	2A	BINV-N (3 of 4)
12-gene (EndoPredict) (node negative and 1–3 nodes)	Not determined	Yes	Other	2A	BINV-N (3 of 4)
Breast Cancer Index (BCI)	Not determined	Yes	Other	2A	BINV-N (3 of 4)

[a] Gene expression assays provide prognostic and therapy-predictive information that complements T,N,M and biomarker information. Use of these assays is not required for staging. The 21-gene assay (Oncotype Dx) is preferred by the NCCN Breast Cancer Panel for node-negative breast cancer. Other prognostic gene expression assays can provide additional prognostic information in patients with 1–3 positive lymph nodes but are unknown if predictive of chemotherapy benefit in 1–3 positive lymph nodes.

[b] See Special Consideration for Breast Cancer in Men (BINV-J).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

References

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

Assay	Recurrence Risk	Treatment Implications
70-gene (MammaPrint) (for node negative and 1–3 positive nodes)	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 vs. 95.6 (95% CI, 92.7–97.4) in those who did not receive adjuvant chemotherapy.[10] 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)	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.[11]
	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 the TransATAC study in a similar group.[12]
	Node positive: High (41–100)	
12-gene (EndoPredict) (node negative and 1–3 nodes)	Low (<3.33)	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] The risk score is predictive of chemo-benefit based on a prospective analysis of 3,746 archived, HR-positive, HER2-negative, T1–T3 tumors from chemo-endocrine and endocrine-only cohorts, that included women with lymph node-negative and lymph node-positive disease.[13]
	High (>3.33)	
Breast Cancer Index (BCI)	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. Results of a secondary analysis of the aTTom trial demonstrated that in patients with hormone-receptor positive, node-positive breast cancer, patients with a high BCI (HOXB13/IL17BR) (H/I) derived significant benefit from extending tamoxifen therapy to 10 years vs. 5 years. In contrast, BCI (H/I) low patients derived no benefit from extended adjuvant therapy.[14]
	High risk of late occurrence (5.1–10)	

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References