American Society of Clinical Oncology Clinical Practice Guideline: Update on Adjuvant Endocrine Therapy for Women With Hormone Receptor–Positive Breast Cancer

TARGET POPULATION	Decidable (Y or N)
Eligibility	
Inclusion Criterion	
· postmenopausal women with hormone receptor–positive breast cancer	
Exclusion Criterion	

RECOMMENDATIONS

Recommendation
1

Conditional: The Update Committee recommends, on the basis of data from randomized, controlled trials, that most postmenopausal women consider taking an AI during the course of adjuvant treatment to lower recurrence risk, either as primary therapy or after 2 to 3 years of tamoxifen—strategies that yield equivalent outcomes in prospective studies. Duration of AI therapy should not exceed 5 years.

IF	Decidable	Vocab
postmenopausal		
Value: true		
adjuvant treatment		
Value: true		
tamoxifen use		
Value: 2-3 years		
THEN	**Executable**	**Vocab**
Consider taking an AI		

Evidence Quality:

Strength of Recommendation:

Reason: In comparison to 5 years of tamoxifen alone, use of an AI in either primary, sequential, or extended treatment improves disease-free survival and reduces the risk of breast cancer events, including distant recurrence, locoregional recurrence, and contralateral breast cancer

Logic:
If
postmenopausal is [true]
AND
adjuvant treatment is [true]
AND
tamoxifen use is [2-3 years]
Then
Consider taking an AI

Conditional: The Update Committee recommends, on the basis of data from randomized, controlled trials, that most postmenopausal women consider taking an AI during the course of adjuvant treatment to lower recurrence risk, either as primary therapy or after 2 to 3 years of tamoxifen—strategies that yield equivalent outcomes in prospective studies. Duration of AI therapy should not exceed 5 years.

IF

Decidable	Vocab
postmenopausal	
Value: true	
adjuvant treatment	
Value: true	
tamoxifen use	
Value: false	

THEN

Executable	Vocab
consider taking an AI	

Evidence Quality:

Strength of Recommendation:

Reason: In comparison to 5 years of tamoxifen alone, use of an AI in either primary, sequential, or extended treatment improves disease-free survival and reduces the risk of breast cancer events, including distant recurrence, locoregional recurrence, and contralateral breast cancer

Logic:
If
postmenopausal is [true]
AND
adjuvant treatment is [true]
AND
tamoxifen use is [false]
Then
consider taking an AI

Recommendation 2

Conditional: The Update Committee recommends that patients who are initially treated with an AI but discontinue treatment before 5 years oftherapy consider taking tamoxifen for a total of 5 years of adjuvant endocrine therapy.

IF	**Decidable**	**Vocab**
AI **Value:** true		
tamoxifen **Value:** false		
THEN	**Executable**	**Vocab**
consider tamoxifen for a duration of (5 years minus AI duration) years		

Evidence Quality:

Strength of Recommendation:

Reason: The treatment regimen for patients in the sequencing trials spanned 5 years. No data support clinical benefits for durations of AIs longer than 2 or 3 years in a sequencing strategy.

Logic:
If
AI is [true]

AND
tamoxifen is [false]
Then
consider tamoxifen for a duration of (5 years minus AI duration) years

Conditional: Therapy with an AI should not extend beyond 5 years in either the primary or extended adjuvant settings outside the clinical trials setting.

IF	**Decidable**	**Vocab**
in the primary setting		
Value: true		
in the extended adjuvant setting		
Value: true		
in a AI clinical trial		
Value: false		
AI use		
tamoxifen use		
Value: 2-3 years		

THEN	**Executable**	**Vocab**
discontinue AI after 5 years total endocrine therapy		

Evidence Quality:

Strength of Recommendation:

Reason: Safety and efficacy data from the primary trials support up to 5 years of AI therapy as a primary adjuvant strategy, a duration used in two trials of extended therapy after 5 years of tamoxifen.

Logic:
If
(in the primary setting is [true]
OR
in the extended adjuvant setting is [true])
AND
in the clinical trials setting is [false]
AND
(AI use
OR

tamoxifen use is [2-3 years])
Then
discontinue AI after 5 years total endocrine therapy

Recommendation
3

Conditional: The Update Committee recommends thatwomen who are pre- or perimenopausal at the time of breast cancer diagnosis be treated with 5 years of tamoxifen.

IF

Decidable	Vocab
not menopausal	
treatment-induced amenorrhea	

THEN

Executable	Vocab
treat with 5 years of tamoxifen as primary adjuvant endocrine therapy	

Evidence Quality:

Strength of Recommendation:

Reason: AI therapy has been shown tobe effective only in postmenopausal women and is contraindicated in patients with residual ovarian function. Patients accrued to ABCSG-12, the only trial to include premenopausal women, were all treatedwith gonadotropin-releasing hormone agonist therapy to achieve apostmenopausal state. Eligible patients had favorable prognosis and low-grade breast cancer, and none received adjuvant chemotherapy, though 5% did receive neoadjuvant chemotherapy. These patients are not necessarily representative of younger women with early-stage breast cancer. ABCSG-12 demonstrated equivalence with respect to time to recurrence, disease-free survival, and overall survival between tamoxifen and AI therapy in premenopausal women given ovarian suppression. Because of tamoxifen equivalence with AI therapy in that setting and the occasional failure to achieve menopausal status with ovarian uppression, the Update Committee strongly recommends tamoxifen as primary adjuvant endocrine therapy for all pre- or perimenopausal women and women with treatment-induced amenorrhea.

Logic: If
not menopausal
OR

treatment-induced amenorrhea
Then
treat with 5 years of tamoxifen as primary adjuvant endocrine therapy

Recommendation
4

Conditional: The Update Committee suggests that clinicians consider recommending that patients change treatment if adverse effects are intolerable or if patients are persistently noncompliant with therapy

IF

Decidable	Vocab
adverse effects are intolerable	
persistently noncompliant with therapy	

THEN

Executable	Vocab
clinicians may recommend that patients change treatment	

Evidence Quality:

Strength of Recommendation:

Reason:

Logic:
If
adverse effects are intolerable
OR
persistently noncompliant with therapy
Then
clinicians may recommend that patients change treatment

Conditional: The Update Committee recommends that clinicians consider adverse effect profiles, patient preferences, and pre-existing conditions when recommending an adjuvant endocrine strategy for postmenopausal women.

IF

Decidable	Vocab

recommending adjuvant endocrine therapy

THEN

Executable	Vocab
consider adverse effects	
consider patient preferences	
consider pre-existing conditions	

Evidence Quality:

Strength of Recommendation:

Reason:

Logic:

If
recommending adjuvant endocrine therapy
Then
consider adverse effects
AND
consider patient preferences
AND
consider pre-existing conditions

Conditional: Clinicians should discuss adverse effect profiles when presenting available treatment options.

IF

Decidable	Vocab
Recommending adjuvant endocrine therapy	

THEN

Executable	Vocab
counsel about adverse effect profiles of tamoxifen and AI	

Evidence Quality:

Strength of Recommendation:

Reason:

Logic:

If
Recommending adjuvant endocrine therapy
Then
counsel about adverse effect profiles of tamoxifen and AI

Recommendation
5

Conditional: In the clinical opinion of the Update Committee (rather than direct evidence from randomized trials), postmenopausal patients intolerant of one AI but who are still candidates for adjuvant endocrine therapy may be advised to consider tamoxifen or a different AI.

IF	**Decidable**	**Vocab**
postmenopausal		
intolerant of one AI		
still candidate for adjuvant endocrine therapy		
THEN	**Executable**	**Vocab**
may be advised to consider tamoxifen		
may be advised to consider a different AI		

Evidence Quality:

Strength of Recommendation:

Reason: In the absence of direct comparisons, the Update Committee interprets available data as suggesting that benefits of AI therapy represent a "class effect." Meaningful clinical differences between the commercially available third-generation AIs have not been demonstrated to date.

Logic:
If
postmenopausal
AND
intolerant of one AI
AND
still candidate for adjuvant endocrine therapy
Then
may be advised to consider tamoxifen
OR
may be advised to consider a different AI