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
postmenopausal

Value: true

adjuvant treatment

Value: true
tamoxifen use

Value: 2-3 years

THEN
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
postmenopausal

Value: true
adjuvant treatment

Value: true
tamoxifen use

Value: false
THEN
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 of therapy consider taking tamoxifen for a total of 5 years of adjuvant endocrine therapy.

IF
AI

Value: true
tamoxifen

Value: false
THEN
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 in the primary setting
  Value: true
in the extended adjuvant setting
  Value: true
in a AI clinical trial
  Value: false
AI use
  Value: false
tamoxifen use
  Value: 2-3 years
THEN 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
  Value: [false] )
  OR
  (AI use
  OR
  tamoxifen use
  Value: [true] )
  OR
  (AI use
  OR
  tamoxifen use
  Value: [2-3 years] )
tamoxifen use is [2-3 years]
Then
discontinue AI after 5 years total endocrine therapy

Recommendation
3

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

IF
not menopausal
treatment-induced amenorrhea
THEN
treat with 5 years of tamoxifen as primary adjuvant endocrine therapy

Evidence Quality:

Strength of Recommendation:

Reason: AI therapy has been shown to be 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 treated with gonadotropin-releasing hormone agonist therapy to achieve a postmenopausal 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 suppression, 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
adverse effects are intolerable
persistently noncompliant with therapy
THEN
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
recommending adjuvant endocrine therapy

THEN
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
Recommending adjuvant endocrine therapy
THEN
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.

**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