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

IDENTITY

Citation

· Burstein HJ, Prestrud AA, Seidenfeld J, Anderson H, Buchholz TA, Davidson NE, Gelmon KE, Giordano SH, Hudis CA, Malin J, Mamounas EP, Rowden D, Solky AJ, Sowers MR, Stearns V, Winer EP, Somerfield MR, Griggs JJ, American Society of Clinical Oncology. American Society of Clinical Oncology clinical practice guideline: update on adjuvant endocrine therapy for women with hormone receptor-positive breast cancer. J Clin Oncol 2010 Aug 10;28(23):3784-96. [124 references]

Date Released

· August 2010

GEM Cut History

GEM Cut Version: 1

GEM Cut Author:

GEM Cut Date October 2012

DEVELOPER

Developer Name

· American Society of Clinical Oncology

Conflict Of Interest Policy

Conflict Of Interest Disclosure

PURPOSE

Objective

INTENDED AUDIENCE

Intended Users

Care Setting

METHOD OF DEVELOPMENT

Rating Scheme

Evidence Quality Rating Scheme

Recommendation Strength Rating Scheme

Qualifying Statement

Patient And Public Involvement

TARGET POPULATION
Inclusion Criterion
· postmenopausal women with hormone receptor–positive breast cancer
Exclusion Criterion

KNOWLEDGE COMPONENTS

DEFINITIONS

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. {Rec_1:Cond_ 15 }

Decision Variable: postmenopausal
Value: true
Decision Variable: adjuvant treatment
Value: true
Decision Variable: tamoxifen use
Value: 2-3 years
Action: Consider taking an AI
Description: Duration of AI therapy should not exceed 5 years
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
Reason: Breast cancer events such as locoregional recurrence, contralateral breast cancer, and early distant metastatic recurrence are clinically important to patients. For this reason, the Update Committee recommended consideration of AI therapy at some time during adjuvant endocrine therapy even though few trials demonstrated statistically significant differences in overall survival.
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. {Rec_1:Cond_ 14 }

Decision Variable: postmenopausal
Value: true
Decision Variable: adjuvant treatment
Value: true
Decision Variable: tamoxifen use
Value: false
Action: consider taking an AI
Description: Duration of AI therapy should not exceed 5 years.
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
Reason: Breast cancer events such as locoregional recurrence, contralateral breast cancer, and early distant metastatic recurrence are clinically important to patients. For this reason, the Update Committee recommended consideration of AI therapy at some time during adjuvant endocrine therapy even though few trials demonstrated statistically significant differences in overall survival.
Logic:

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

Notes: SCENARIO 4

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. {Rec_4:Cond_ 7 }

Decision Variable: AI
Value: true
Decision Variable: tamoxifen
Value: false
Action: consider tamoxifen for a duration of (5 years minus AI duration) years
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.
Reason: Data from randomized, controlled trials demonstrate that women who receive primary AI therapy should be treated for a total of 5 years.
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. {Rec_4:Cond_ 9 }

Decision Variable: in the primary setting
Value: true
Decision Variable: in the extended adjuvant setting
Value: true
Decision Variable: in a AI clinical trial
Value: false
Decision Variable: AI use
Decision Variable: tamoxifen use
Value: 2-3 years
Action: discontinue AI after 5 years total endocrine therapy
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

Notes: SCENARIO 4

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. {Rec_1:Cond_ 1 }

Decision Variable: not menopausal

Description: at the time of diagnosis

Decision Variable: treatment-induced amenorrhea

Action: treat with 5 years of tamoxifen as primary adjuvant endocrine therapy

Description: The Update Committee recommends that clinicians use caution in evaluating menopausal status of patients who were pre- or perimenopausal at diagnosis. Unequivocal determination of menopausal status may be challenging to prove.Even among women who have not experienced menses for more than1 year, laboratory testing is inadequate because patients may recoverovarian function. This particularly applies to those patients who experiencechemotherapy- or tamoxifen-induced amenorrhea.

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

Notes: SCENARIO 3

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 {Rec_6:Cond_ 12 }

Decision Variable: adverse effects are intolerable
Decision Variable: persistently noncompliant with therapy
Action: clinicians may recommend that patients change treatment

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. {Rec_6:Cond_ 16 }

Decision Variable: recommending adjuvant endocrine therapy
Action: consider adverse effects
Action: consider patient preferences
Action: consider pre-existing conditions

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. {Rec_6:Cond_ 17 }

Decision Variable: Recommending adjuvant endocrine therapy
Action: counsel about adverse effect profiles of tamoxifen and AI
Logic:

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

Notes: SCENARIO 4

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. {Rec_7:Cond_ 13 }

Decision Variable: postmenopausal
Decision Variable: intolerant of one AI
Decision Variable: still candidate for adjuvant endocrine therapy
Action: may be advised to consider tamoxifen
Action: may be advised to consider a different AI
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.
Reason: Previous results were limited to reports for principal use of a single AI in each of the clinical settings of primary, sequential, or extended adjuvant therapy. There are stillnodata from head-to-head comparisons of AIs. However, there are

data from randomized trials for each of the commercially available thirdgeneration AIs for all of the adjuvant treatment strategies (primary,sequential, and extended). The Update Committee interprets the existing data comparing the AIs with tamoxifen as qualitatively similar with respect to efficacy and tolerability. Toxicity reports have not suggested obvious clinical advantages of one AI over another with respect to compliance, constitutional or menopausal symptoms, bone health, cardiovascular disease, or quality of life. Anecdotal experience suggests that patients maytolerate one AI better than another, but patterns are neither predictable nor consistent. Two trials—MA.27 and Femara versus Anastrozole Clinical Evaluation (FACE)—are directly comparing one AIagainst another as primary adjuvant therapy. However, data are not yet available from either trial.

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

Notes: SCENARIO 4

ALGORITHM: