Adjuvant Endocrine Therapy for Women with Hormone Receptor-Positive Breast Cancer

Clinical Tools and Resources

Clinical Practice Guideline Update
Introduction

• ASCO initially published its guidance (technology assessment) for the use of endocrine therapy in the adjuvant setting for women with hormone receptor-positive breast cancer in 2002

• ASCO guidelines are updated at intervals by an Update Committee of the original Expert Panel; the last update was in 2010

• Due to new results on the duration of adjuvant tamoxifen, an Update Committee convened for a focused update of this guideline

• For the current update, the Update Committee reviewed literature published since January 2009
Guideline Methodology: Systematic Review

- The Update Committee completed a systematic review and analysis of the medical literature January 2009 through May 2013
  - Medline
  - San Antonio Breast Cancer conference proceedings (2011-2012)
  - ASCO conference proceedings (2011-2013)
  - 3 historical trials
Clinical Questions

(1) Which adjuvant endocrine treatments should be offered to women with hormone receptor–positive breast cancer?

(2) What is the appropriate duration of adjuvant endocrine therapy?

(3) What is the appropriate sequence of adjuvant endocrine therapy?
Recommendations

Women who are pre- or perimenopausal

Options:

IA. Tamoxifen for an initial duration of 5 years.

IB. After 5 years, women should receive additional therapy based on menopausal status.

IB1. If women are pre- or perimenopausal, or if menopausal status is unknown or cannot be determined, they should be offered continued tamoxifen for a total duration of 10 years. (Type: Evidence-Based, Evidence Quality: High, Strength of Recommendation: Strong)
Recommendations

pre- or perimenopausal, continued

IB2. If women have become definitively postmenopausal, they should be offered continued tamoxifen for a total duration of 10 years or switching to up to 5 years of an aromatase inhibitor (AI) for a total duration of up to 10 years of adjuvant endocrine therapy. (Type: Evidence-Based, Evidence Quality for tamoxifen: High, Evidence Quality for AI: High; Strength of Recommendation: Strong)
Recommendations

Women who are postmenopausal - options

IIA. Tamoxifen for a duration of 10 years. (Type: Evidence-Based, Evidence Quality: High, Strength of Recommendation: Strong); or

IIB. An AI for a duration of 5 years. There are insufficient data currently to recommend an AI for a duration of greater than 5 years. (Type: Evidence-Based, Evidence Quality: High, Strength of Recommendation: Strong); or
Recommendations

postmenopausal - options, continued

Options:

IIC. Tamoxifen for an initial duration of 5 years, then switching to an AI for up to 5 years, for a total duration of up to 10 years of adjuvant endocrine therapy. (Type: Evidence-Based, Evidence Quality: High, Strength of recommendation: Strong); or

IID. Tamoxifen for a duration of 2 to 3 years and switching to an AI for up to 5 years, for a total duration of up to 7 to 8 years of adjuvant endocrine therapy. (Type: Evidence-Based, Evidence Quality: High, Strength of Recommendation: Strong)
Recommendations

Women who are postmenopausal and are intolerant of either tamoxifen or an AI:

IIIA. If women have received an AI, but discontinued treatment at less than 5 years, they may be offered tamoxifen for a total of 5 years. (Type: Informal consensus, Evidence Quality: Low, Strength of Recommendation: Weak)

IIIB. If women have received tamoxifen for 2 to 3 years, they should be offered switching to an AI for up to 5 years, for a total duration of up to 7 to 8 years of adjuvant endocrine therapy. (Type: Evidence-Based, Evidence Quality: High, Strength of Recommendation: Strong)
Recommendations

IV. Women who have received 5 years of tamoxifen as adjuvant endocrine therapy should be offered additional adjuvant endocrine treatment.

IVA. If women are postmenopausal, they should be offered continued tamoxifen for a total duration of 10 years or switching to up to 5 years of an AI for a total duration of up to 10 years of adjuvant endocrine therapy. (Type: Evidence-Based, Evidence Quality: High, Strength of Recommendation: Strong)

IVB. If women are pre- or perimenopausal or menopausal status cannot be ascertained, they should be offered five additional years of tamoxifen for a total duration of 10 years of adjuvant endocrine therapy. (Type: Evidence-Based, Evidence Quality: High, Strength of Recommendation: Strong)
Qualifying Statements

There are no specific patient populations or subgroups, except for menopausal status, that derive differing degrees of benefit from an AI versus tamoxifen or for the durations discussed above. Clinicians and patients should discuss a patient’s individual risk/benefit profiles.
Adherence and Communication

- Compliance to, and persistence with, adjuvant endocrine therapy for breast cancer is a clinical challenge
- 20-50% non-persistence rates (early discontinuation of medications)
- 74-84% compliance rates (conformity to prescribed dosing)
Adherence and Communication

• Contributing factors:
  • Treatment side effects
  • Personal health preferences
  • Out-of-pocket costs
  • Age
  • Follow-up by primary care vs. oncology
Adherence and Communication

• Potentially modifiable factors
  • Address side effects
  • Address inadequate social support
  • Share knowledge of recurrence statistics/probabilities

• Suggestions for clinicians
  • Inquire diligently about compliance and side effects
  • Address patient beliefs about medication
  • Discuss rationale for treatment
  • Provide follow-up
Health Disparities

• Low representation of people of color and/or low socio-economic status in clinical trials of adjuvant endocrine therapy

• Low evidence of differences in benefit between black and white women (in clinical trials)

• Awareness of disparities in quality of care should be considered
Limitations and Future Directions

• Differing amounts of median follow-up
• Studies performed in different eras
• Study populations included those with:
  • hormone-receptor positive breast cancer and/or
  • unknown hormone-receptor status
• Few new data on adverse events (studies provided insufficient data on side effects)
• Lack of reporting on health-related quality of life
• Lack of analysis by menopausal status
• Few data on extended durations of aromatase inhibitors
The Bottom Line

• **Intervention**
  – 10 year duration of adjuvant endocrine therapy

• **Target Population**
  – Women with stage I-III hormone receptor-positive breast cancer

• **Target Audience**
  – Medical, surgical, and radiation oncologists; oncology nurses and physician assistants; obstetrician/gynecologists; general practitioners; and women with Stage I-III hormone receptor-positive breast cancer

• **Methods**
  – Systematic review and analysis of the medical literature

• **Additional Information**
  – Recommendations and summary of the literature and analysis in guideline
  – Data Supplements and Clinical Tools and Resources at [http://www.asco.org/endocrinebreast](http://www.asco.org/endocrinebreast)
  – Patient information is available at [http://www.cancer.net](http://www.cancer.net)

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care, and that all patients should have the opportunity to participate
Additional Resources

• The guideline is available at [http://jco.ascopubs.org](http://jco.ascopubs.org)

• The guideline, data supplements, a patient guide, and other resources are available at [www.asco.org/guidelines/endocrinebreast](http://www.asco.org/guidelines/endocrinebreast)

• The patient guide is also available at [http://www.cancer.net](http://www.cancer.net)
# Update Committee Members

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