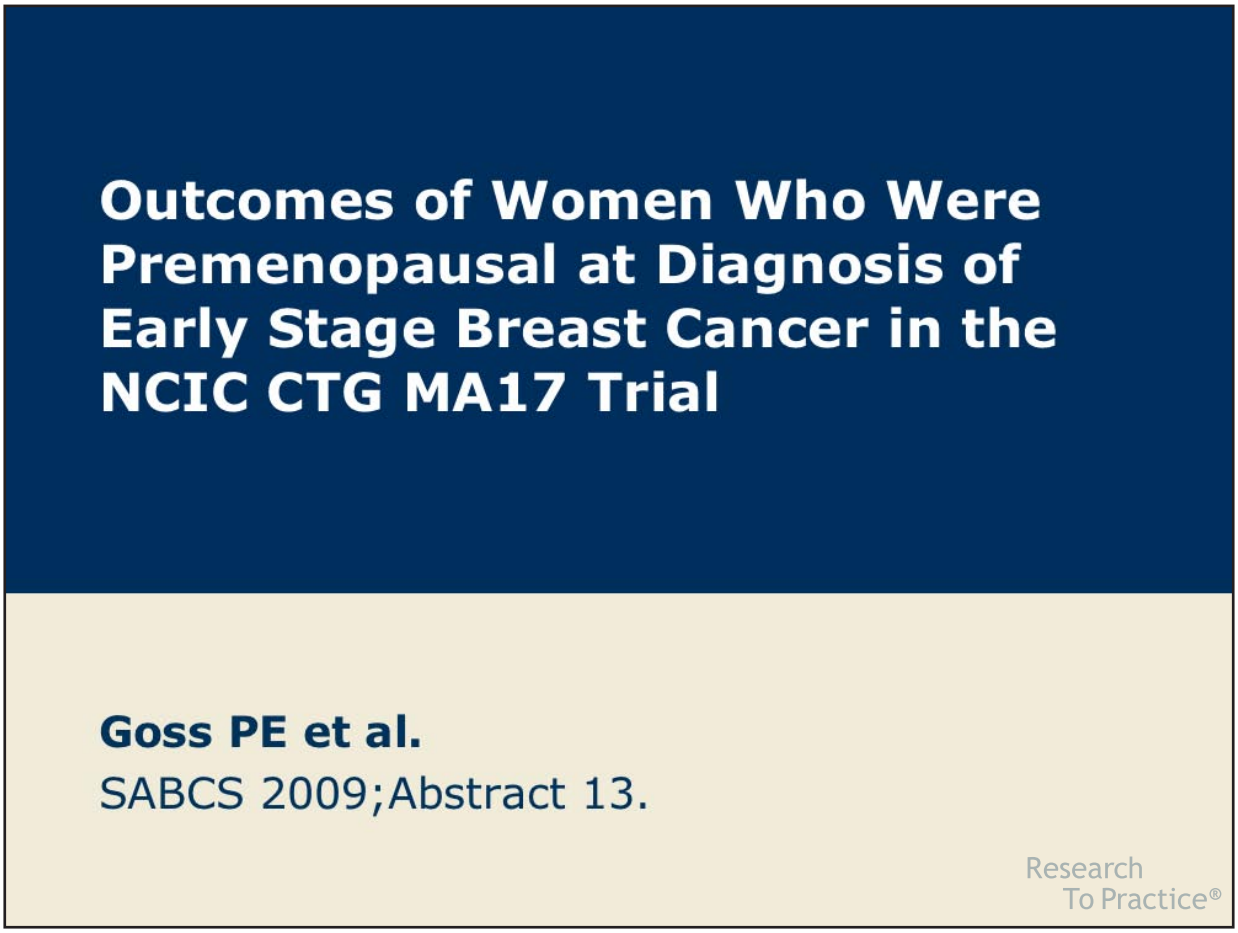
Outcomes of Women Who Were Premenopausal at Diagnosis in the MA17 Trial of Extended Letrozole After Five Years of Tamoxifen

Presentation discussed in this issue:

Goss PE et al. **Outcomes of women who were premenopausal at diagnosis of early stage breast cancer in the NCIC CTG MA17 trial.** San Antonio Breast Cancer Symposium 2009;**Abstract 13**.

Slides from a presentation at SABCS 2009



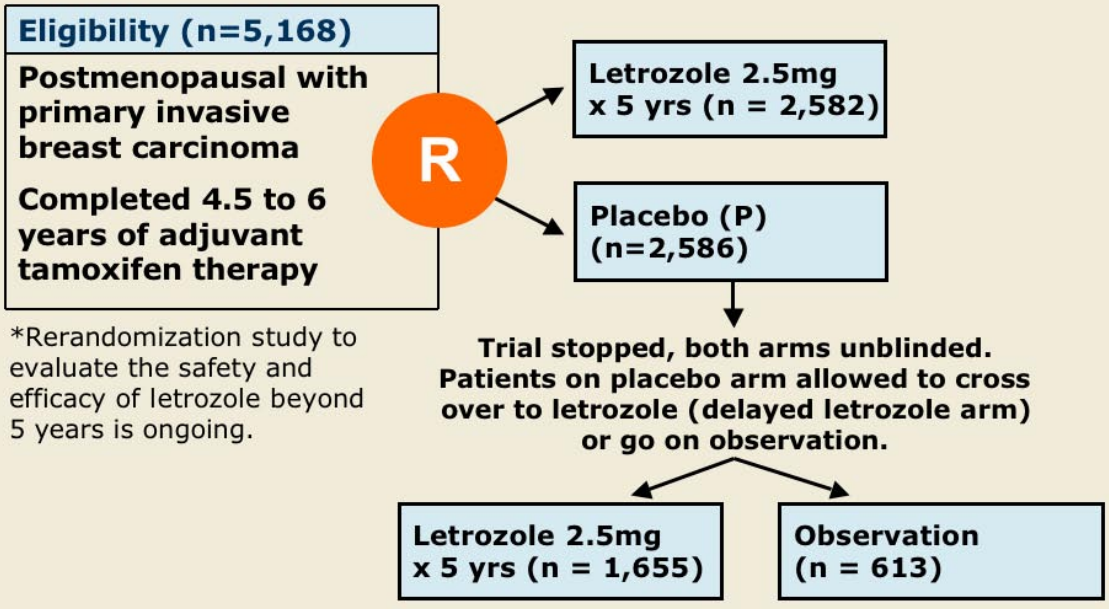
Introduction

- Extended aromatase inhibitor (AI) therapy is a standard of care for postmenopausal women with hormone receptor-positive (HR+) breast cancer who have received 5 years of tamoxifen (*NEJM* 2003;349:1793, *JCO* 2008;26:1965).
- Five years of tamoxifen therapy remains a common standard adjuvant hormonal therapy in premenopausal patients.
- A substantial proportion of premenopausal patients with estrogen receptor-positive breast cancer recur after 5 years of tamoxifen therapy (SABCS 2007;Abstract P-1).
- **Current study objective**:
  - Assess the benefit of extended aromatase inhibitor therapy after five years of tamoxifen in women who are premenopausal at the time of diagnosis and become postmenopausal during tamoxifen.

Goss PE et al. SABCS 2009;Abstract 13.

Research To Practice®

NCIC CTG MA17: Trial Schema*



*Rerandomization study to evaluate the safety and efficacy of letrozole beyond 5 years is ongoing.

Goss PE et al. SABCS 2009;Abstract 13.

Research To Practice®

MA17: Patient Menopausal Status at Primary Diagnosis

- **Premenopausal (n=889)**
  - < 50 years of age with menses, but underwent subsequent bilateral oophorectomy when tamoxifen therapy started.
  - < 50 years of age with menses, but became amenorrheic during adjuvant chemotherapy or on tamoxifen.
- **Postmenopausal (n=4,277)**
  - ≥ 50 years of age without menses at diagnosis.
  - < 50 years of age without menses and considered postmenopausal at diagnosis.
  - Considered postmenopausal in terms of menopausal LH/FSH levels.

Goss PE et al. SABCS 2009;Abstract 13.

Research To Practice®

Premenopausal Patients Have a Worse Prognosis

Patient Characteristic	Premenopausal (n=889)	Postmenopausal (n=4,227)	*p*-value
Median age at diagnosis	~45 yrs	~60 yrs	<0.0001
Node-positive	56%	44%	<0.001
Both ER- and PR-positive	77%	74%	0.02
Chemotherapy	80%	38%	<0.0001
Mastectomy	55%	50%	0.003
Letrozole treatment	48%	51%	0.14

Goss PE et al. SABCS 2009;Abstract 13.

Research To Practice®

Absolute Differences in Four-Year Disease-Free Survival Rates (Letrozole versus Placebo)

	Premenopausal (n=889)	Postmenopausal (n=4,277)
All patients	10.1% HR=0.25; $p<0.0001$	3.3% HR=0.69; $p=0.0008$

In years 0 through 4 post completion of tamoxifen, premenopausal patients had a greater treatment benefit from letrozole than postmenopausal patients.

- **Premenopausal: 10.1% absolute decrease in disease recurrence (75% risk reduction)**
- **Postmenopausal: 3.3% absolute decrease in disease recurrence (31% risk reduction)**

Goss PE et al. SABCS 2009;Abstract 13.

Research To Practice®

Absolute Differences in Four-Year DFS Rates in Node-Positive BC (Letrozole versus Placebo)

	Premenopausal (n=501)	Postmenopausal (n=1,857)
Node-positive	9.6% HR=0.37; $p=0.008$	7.0% HR=0.68; $p=0.03$

In patients with node-positive disease (years 0 to 4 post completion of tamoxifen), premenopausal patients had a greater treatment benefit from letrozole than postmenopausal patients.

- **Premenopausal: 9.6% absolute decrease in disease recurrence (63% risk reduction)**
- **Postmenopausal: 7.0% absolute decrease in disease recurrence (32% risk reduction)**

Goss PE et al. SABCS 2009;Abstract 13.

Research To Practice®

Absolute Differences in Four-Year DFS Rates in Node-Negative BC (Letrozole versus Placebo)

	Premenopausal (n=375)	Postmenopausal (n=2,192)
Node-negative	11.5% HR=0.00; p=0.005	1.1% HR=0.58; p=0.04

In patients with node-negative disease (years 0 to 4 post completion of tamoxifen), premenopausal patients had a greater treatment benefit from letrozole than postmenopausal patients.

- **Premenopausal: 11.5% absolute decrease in disease recurrence (100% risk reduction)**
- **Postmenopausal: 1.1% absolute decrease in disease recurrence (42% risk reduction)**

Goss PE et al. SABCS 2009;Abstract 13.

Research To Practice®

Absolute Differences in Five-Year DFS Rates (Delayed Letrozole vs Observation)

	Premenopausal (n=425)	Postmenopausal (n=1,957)
DFS	8.2% HR=0.39; p=0.007	3.0% HR=0.36; p=0.0003

In patients who delayed (up to six years post completion of tamoxifen) extended AI therapy, premenopausal patients had a greater treatment benefit from letrozole than postmenopausal patients.

- **Premenopausal: 8.2% absolute decrease in disease recurrence (61% risk reduction)**
- **Postmenopausal: 3.0% absolute decrease in disease recurrence (64% risk reduction)**

Goss PE et al. SABCS 2009;Abstract 13.

Research To Practice®

Absolute Differences in Five-Year Distant DFS Rates (Delayed Letrozole vs Observation)

	Premenopausal (n=425)	Postmenopausal (n=1,957)
Distant DFS	5.9% HR=0.15; *p*=0.02	2.2% HR=0.45; *p*=0.03

In patients who delayed (up to six years post completion of tamoxifen) extended AI therapy, premenopausal patients had a greater treatment benefit from letrozole than postmenopausal patients.

- **Premenopausal: 5.9% absolute decrease in distant disease recurrence (85% risk reduction)**
- **Postmenopausal: 2.2% absolute decrease in distant disease recurrence (55% risk reduction)**

Goss PE et al. SABCS 2009;Abstract 13.

Research To Practice®

Treatment-Related Toxicities

Adverse Event	Premenopausal		*p*-value
	Letrozole (n=424)	Placebo (n=465)	
Arthralgia	24%	16%	0.004
Vaginal bleeding	10%	16%	0.01

Adverse Event	Postmenopausal		*p*-value
	Letrozole (n=2,157)	Placebo (n=2,120)	
Hot flushes	55%	50%	0.001
Arthralgia	25%	21%	0.002
Myalgia	15%	12%	0.007
Alopecia	5%	3%	0.003

Goss PE et al. SABCS 2009;Abstract 13.

Research To Practice®

Conclusions

- Premenopausal patients with ER-positive breast cancer benefit significantly from extended AI (letrozole) therapy after they become postmenopausal.
  - Absolute difference in 4-year % DFS in patients treated with letrozole versus placebo:
    - Premenopausal at diagnosis: 10.1%
    - Postmenopausal at diagnosis: 3.3%
- A similar treatment benefit was observed in patients who delayed letrozole therapy up to 6 years after completion of tamoxifen therapy.
- Reported treatment-related toxicities in premenopausal women were infrequent.

Goss PE et al. SABCS 2009;Abstract 13.

Research To Practice®