

MA-17 Extended Adjuvant Breast Cancer Trial Fact Sheet

Overview

MA-17 is a landmark, breast cancer research study that has brought international attention to the ongoing risk of early breast cancer recurrence. It has changed how many women are treated for the disease.

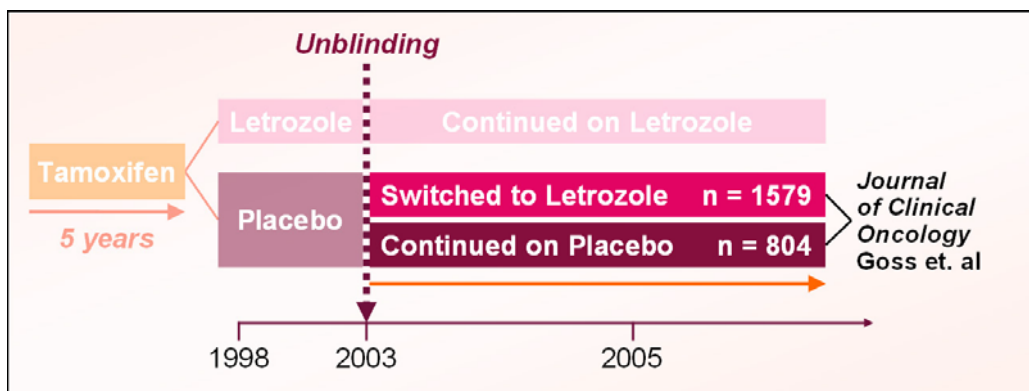
As the first well-controlled trial to clearly demonstrate the efficacy of an aromatase inhibitor as extended adjuvant therapy, the results led to the approval of Femara® (letrozole tablets) for use in women who have completed five years of tamoxifen. Launched in 1998, the trial continues to reveal new information about the clinical relevance of Femara for postmenopausal women once they have finished tamoxifen.

In 2003, compelling results of an interim analysis showed that Femara reduced the risk of breast cancer coming back by 38% compared with placebo, which prompted an independent Data Safety Monitoring Board to recommend unblinding the study results. At that time, the 2,383 women in the placebo arm were offered to begin treatment with Femara. Of those women, 1,579 chose to switch to Femara. All patients from the trial continue to be followed.

Description

- Phase III international, double-blind, randomized, multi-center study of Femara vs. placebo in postmenopausal women with hormone-sensitive primary breast cancer completing 4.5-6 years of adjuvant tamoxifen
- 5,187 patients enrolled

Design



Endpoints:

- Primary: Disease-free survival (recurrence)
- Secondary: Distant disease-free survival (distant spread), overall survival, long-term safety

Key findings

Results based on 28 months:

- Extended adjuvant treatment with Femara reduced the risk of breast cancer recurrence by 38%.
- Femara reduced the chance of breast cancer spreading to other parts of the body by 39%.

Post-unblinding period

- MA-17 was unblinded in 2003, at which time the 2,383 women in the placebo arm were offered to start Femara; 1,579 chose to begin treatment with Femara.
- Women who chose to start Femara several years after completing the recommended five years of tamoxifen therapy reduced the risk of breast cancer coming back by 63% and their risk of it spreading to other areas of the body by 61% compared to those women who chose not to start Femara.
- More than five years after the start of the trial, the significant benefit of Femara vs. placebo in reducing the risk of recurrence observed at the 28 month analysis has been maintained in the group of women originally assigned to receive Femara, even after the more than 60% of women initially taking placebo chose to switch to Femara.
- Researchers analyzed the overall incidence of recurrence after one, two, three and four years of treatment in women taking either Femara or a placebo following five years of tamoxifen. Hazard ratio for disease-free survival (Femara vs. placebo) progressively decreased over four years, from 0.52 at one year to 0.19 at four years.

Differences in 28 month and post-unblinding analysis

	Analysis based on 28 months	Post-unblinding analysis
Number of women	5187	1579 of 2383 women originally assigned to placebo elected to start Femara
Time off tamoxifen	Maximum of 3 months	Median: 2.8 years
Median follow-up from initial randomization	2.4 years	5.3 years
Analysis	Protocol-specified	Exploratory, retrospective

MA-17 publication directory

Post-unblinding analysis

- Goss PE, Ingle JN, Pater JL, et al. Late extended adjuvant treatment with letrozole improves outcome in women with early-stage breast cancer completing 5 years of tamoxifen. J Clin Oncol. 2008
- Ingle JN, Tu D, Pater JL, et al. Intent-to-treat analysis of the placebo-controlled trial of letrozole for extended adjuvant therapy in early breast cancer: NCIC CTG MA.17. Annals of Oncology. 2008

Receptor analysis

- Goss PE, Ingle JN, Martino S et al. National Cancer Institute of Canada Clinical Trials Group MA.17: efficacy of letrozole extended adjuvant therapy according to estrogen receptor and progesterone receptor status of the primary tumor. J Clin Oncol 2007; 25: 2006–2013.

28-month publication

- Goss PE, Ingle JN, Martino S et al. Randomized trial of letrozole following Tamoxifen as extended adjuvant therapy in receptor-positive breast cancer: updated findings from NCIC CTG MA.17. J Natl Cancer Inst 2005; 97:1262–1271.

Initial study report

- Goss PE, Ingle JN, Martino S et al. A randomized trial of letrozole in postmenopausal women after five years of tamoxifen therapy for early-stage breast cancer. N Engl J Med 2003; 349: 1793–1802.

About Femara

Femara[®] (letrozole tablets) is approved for the adjuvant (following surgery) treatment of postmenopausal women with hormone receptor-positive early stage breast cancer. The benefits of Femara in clinical trials are based on 24 months of treatment. Further follow-up will be needed to determine long-term results, safety and efficacy.

Femara is also approved for the extended adjuvant treatment of early stage breast cancer in postmenopausal women who are within three months of completion of five years of tamoxifen therapy. The benefits of Femara in clinical trial are based on 24 months of treatment. Further follow-up will be needed to determine long-term results, including side effects.

In addition, Femara is approved for the treatment of postmenopausal women with estrogen receptor-positive or estrogen receptor-unknown breast cancer that has spread to another part of the body (metastatic cancer).

Important Safety Information

You should not take Femara if you are premenopausal. Your doctor should discuss the need for adequate birth control if you have the potential to become pregnant, if you are not sure of your postmenopausal status, or if you recently became postmenopausal. Femara is only indicated in postmenopausal women. Talk to your doctor if you're allergic to Femara or any of its ingredients. You should not take Femara if you are pregnant as it may cause fetal harm. Some women reported fatigue and dizziness with Femara. Until you know how it affects you, use caution before driving or operating machinery. Some patients taking Femara had an increase in cholesterol. Additional follow-up is needed to determine the risk of bone fracture associated with long-term use of Femara.

In the adjuvant setting, commonly reported side effects are generally mild to moderate. The most common side effects seen with Femara include hot flashes, joint pain, night sweats, weight gain, nausea, tiredness, other heart-related events and bone fractures. Other less commonly reported side effects include vaginal bleeding, blood clots, other cancers, osteoporosis, stroke, heart attack and endometrial cancer.

In the extended adjuvant setting, commonly reported side effects are generally mild to moderate. Commonly reported side effects for Femara include hot flashes, fatigue, joint pain, headache, increase in sweating, swelling due to fluid retention, increase in cholesterol, dizziness,

constipation, nausea, cardiovascular ischemic events, muscle pain, osteoporosis, arthritis and bone fracture.

In the metastatic cancer setting, commonly reported side effects are generally mild to moderate and may include bone pain, hot flashes, back pain, nausea, joint pain, shortness of breath, tiredness, coughing, constipation, limb pain, chest pain and headache.

Femara is a once-daily convenient prescription tablet.

For additional safety information, please see prescribing information.

For more information about Femara visit online at www.femara.com or call toll-free 1-866-44-FEMARA (1-866-443-3627).