

MEDIA RELEASE • COMMUNIQUE AUX MEDIA • MEDIENMITTEILUNG**Compelling disease-free survival results in breast cancer trial prompt independent researchers to offer patients the opportunity to switch to Femara[®], as reported in New England Journal of Medicine**

Interim results from first study to explore post-tamoxifen use of Femara[®] (letrozole) in postmenopausal women with early breast cancer showed dramatically reduced risk of recurrence (43%) and significantly improved disease-free survival

Basel, Switzerland, 9 October 2003—Postmenopausal women with early breast cancer who completed five years of post-surgical hormonal therapy with tamoxifen benefited significantly from extended adjuvant treatment with Femara[®] (letrozole), according to interim results of a study published for early online release in today's *New England Journal of Medicine*. The data prompted an Independent Data Monitoring Committee to unblind the study so that patients in the control arm could consider switching from placebo to Femara, according to an announcement at a press conference held today in Toronto, Canada. This international study was coordinated by the National Cancer Institute of Canada Clinical Trials Group, Kingston, Ontario.

“Historically, there has been no proven post-tamoxifen therapy to address the significant ongoing risk of recurrent breast cancer,” said Paul Goss, MD, director of Breast Cancer Prevention and Research, Princess Margaret Hospital, Toronto, Canada. “The data announced today provide the first clinical evidence that extended adjuvant drug therapy with Femara, following five years of treatment with tamoxifen, may have a substantial impact on the overall treatment outcome for postmenopausal breast cancer patients.” Dr. Goss conceived of, and was international chair of, the clinical trial.

Study Highlights

The international breast cancer trial of nearly 5 200 women, called MA-17, is the first study to examine the effectiveness of an aromatase inhibitor, Femara, in the extended adjuvant setting, the period following five years post-surgery tamoxifen treatment. During this period, women do not typically receive drug therapy, despite the ongoing risk of breast cancer recurrence.

At a median follow-up of 2.4 years, the data in the Femara group showed a 43% reduction in risk of overall recurrence compared with placebo (P=0.00008) as well as a significant reduction (46%) in spreading contralateral disease, cancer occurring in the other breast. The estimated absolute improvement in disease-free survival at four years was 6% for postmenopausal patients taking Femara compared with placebo (93% Femara vs. 87% placebo). Disease-free survival is defined as the time from randomization to the time of first recurrence of the primary disease in the breast (including contralateral breast), chest wall, nodal or metastatic sites.

According to data from the Early Breast Cancer Trialists' Group, Oxford, UK, more than 50% of breast cancer recurrence happens in women later than five years after initial diagnosis. Tamoxifen, which reduces the risk of breast cancer recurrence during the first five years of post-surgical therapy, has been shown not to be beneficial beyond five years of treatment. Approximately one million postmenopausal women worldwide currently receive tamoxifen therapy for reduction of breast cancer recurrence. Tamoxifen is currently considered the gold standard hormonal therapy during the first five years of treatment in this population.

“With this trial, significant progress is being made towards addressing a critical challenge faced by post-menopausal women who have completed early adjuvant treatment for breast cancer – the need to protect against the ongoing risk of recurrence following tamoxifen therapy,” said Diane Young, MD, vice president, global head, Clinical Development, Novartis Oncology. “Femara has continuously demonstrated remarkable results, and we look forward to data from our ongoing clinical program.”

Study Details

The MA-17 study is a Phase III, global, double-blind, randomized, multi-center trial. The primary objective of the study is to compare the disease-free survival of postmenopausal women taking Femara vs. placebo after approximately five years of tamoxifen therapy. Ninety-eight percent of the participants have known receptor positive tumors. The remaining patients have tumors that are estrogen receptor unknown. Women were randomized to the two arms of the study and, prior to the change in protocol, were to have received five years' daily treatment with either 2.5 mg of Femara or placebo (oral). Those who switch from placebo to the Femara arm of the study will be now eligible to receive treatment with Femara.

Secondary objectives of the MA-17 study include comparison of overall survival, incidence of contralateral breast cancer, long-term safety of Femara and quality of life. In addition, subsets of the study are exploring the effect of Femara on lipid metabolism and bone mineral density. According to the interim analysis, no difference in cholesterol levels has, so far, been seen between study arms, nor have there been any differences in patient-reported cardiovascular events to date.

Additional Femara Adjuvant Clinical Trial

A second Phase III adjuvant study with Femara is being conducted by the Breast International Group (BIG 1-98) in collaboration with Novartis. This study has four treatment arms comparing five years of Femara, five years of tamoxifen, two years of Femara followed by three of tamoxifen, and two years of tamoxifen followed by three years of Femara. Recruitment in the BIG 1-98 trial was recently closed, with more than 8 000 women enrolled.

About Femara

Femara, an aromatase inhibitor, is an oral once-a-day first-line treatment for postmenopausal women with hormone receptor positive or hormone receptor unknown locally advanced or metastatic breast cancer. It is also approved for the treatment of advanced breast cancer in postmenopausal women with disease progression following antiestrogen therapy, and as neo-adjuvant (pre-operative) therapy. Femara is currently available in more than 75 countries worldwide. Not all indications are available in every country.

Femara Contraindications and Adverse Events

In the MA-17 analysis, the most common adverse events were hot flashes, sweating, edema, hypercholesterolemia, headache, arthralgia, myalgia, fatigue, constipation and dizziness, in greater than 10% of patients in either arm of the study. Of these, hot flashes, arthralgia, and myalgia were more common in those receiving Femara than placebo ($P < 0.05$). Vaginal bleeding was more common in those taking placebo ($P < 0.05$).

The number of women reporting a new bone fracture to date is 77/2166 (3.6%) in the Femara group, compared with 63/2157 (2.9%) in the placebo group ($P = 0.24$). The authors noted a trend to more newly diagnosed osteoporosis in women taking Femara (124/2166 [5.7%]) vs. placebo (97/2157 [4.5%]) ($P = 0.07$).

Femara is contraindicated in patients with known hypersensitivity to Femara or any of its excipients. Femara is generally well tolerated. In a first-line registration trial versus the antiestrogen tamoxifen, the most commonly reported adverse events for Femara were bone pain (22% vs. 21%), hot flushes (19% vs. 16%), back pain (18% vs. 19%), nausea (17% vs.

17%), dyspnea or labored breathing (18% vs. 17%), arthralgia (16% vs. 15%), fatigue (13% vs. 13%), coughing (13% vs. 13%), constipation (10% vs. 11%), chest pain (6% vs. 6%) and headache (8% vs. 6%). Femara may cause fetal harm when administered to pregnant women. There is no clinical experience to date on the use of Femara in combination with other anticancer agents. The incidence of peripheral thromboembolic events, cardiovascular events, and cerebrovascular events was 3-4% in each treatment arm.

The foregoing release contains forward-looking statements that can be identified by terminology such as “offer...opportunity”, “could consider,” “may have a substantial impact,” “look forward,” or similar expressions, or by express or implied discussions regarding potential future sales of Femara. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with Femara to be materially different from any future results, performance or achievements expressed or implied by such statements. There are no guarantees that the aforementioned clinical trial will result in Femara reaching any particular sales levels. In particular, management's expectations regarding commercialization of Femara could be affected by, among other things, additional analysis of Femara clinical data; new clinical data; unexpected clinical trial results; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; increased government pricing pressures; and other risks and factors referred to in the Company's current Form 20-F on file with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected.

About Novartis

Novartis AG (NYSE: NVS) is a world leader in pharmaceuticals and consumer health. In 2002, the Group's businesses achieved sales of USD 20.9 billion and a net income of USD 4.7 billion. The Group invested approximately USD 2.8 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 78 200 people and operate in over 140 countries around the world. For further information please consult <http://www.novartis.com>.

For more information on the results of this clinical trial, please visit the Canadian Cancer Society website at www.cancer.ca, or contact the Canadian Cancer Society's information service toll-free in Canada at 1 888 939-3333.

Background material and pictures can be found at:

http://novartis.imagedirector.net/album?album_code=ud0xqs3vkia5

Additional media information can be found at www.novartisoncologyvpo.com.

Patients and physicians interested in more information regarding Femara or Novartis Oncology can contact the websites www.novartis.com, www.femara.com, or www.novartisoncology.com.