P R E S S R E L E A S E

Breast cancer: Clear improvements in young patients' chances of survival

ABCSG study results attract worldwide attention at US presentation

The Viennese oncologist Prof. Michael Gnant, MD, President of the Austrian Breast & Colorectal Cancer Study Group (ABCSG) presented spectacular study results to the participants of the globally most important cancer conference in Chicago, USA: He demonstrated that treatment with a bisphosphonate crucially improves young breast cancer patients' chances to remain permanently healthy after their cancer operation.

Vienna, June 2, 2008 – The results of several years of investigation in the framework of ABCSG Trial 12 now attracted attention on the occasion of the 44th Annual Meeting of the American Society of Clinical Oncology (ASCO), particularly as 500,000 women, according to the World Health Organization (WHO), die annually due to a breast cancer relapse or metastasis. Furthermore, the incidence rate among young patients has been on the increase for some time.

Before an audience of 20,000, the elite of cancer research from across the globe, Dr. Gnant reported how the bisphosphonate, zoledronate or Zoledronic Acid (ZOL), impacts premenopausal, early breast cancer patients' health. This program included 1,803 women with hormone receptor-positive breast cancer, stage I or II, who had received three years of treatment post-surgery and were followed up for another two years.

The results are truly impressive:

- ZOL reduced the risk of recurrence in women with early-stage breast cancer receiving hormonal treatment. As compared to exclusively endocrine therapy, adding ZOL to the treatment plan improved the rate of recurrence-free survival by 35%.
- The patients' overall prognosis in ABCSG-12 is excellent. Even without adjuvant chemotherapy, more than 98% of these breast cancer patients are still alive after 5 years – this is one of the best results of a clinical trial ever presented.
- In addition, a trend towards improved overall survival was observed in women treated with the bisphosphonate.

"Zoledronic acid counteracts the loss of bone mineral density in breast cancer patients who receive adjuvant endocrine treatment. Having brought to light that we may also reduce the probability of a breast cancer relapse is considered as a decisive step ahead in cancer treatment", said Dr. Gnant. "This trial is the first large-scale investigation worldwide to demonstrate the significant value of this particular bisphosphonate in cancer treatment. It will assist oncologists across the globe in improving the adjuvant treatment standards in premenopausal patients with hormone-responsive breast cancer."

The mode of action

For some time now science has hoped to see, on the basis of experimental research, that ZOL unfolds an antitumor effect and may protect patients from a recurrence or spread of disease prior to its reaching an advanced stage.
The precise mode of action has not yet been fully disclosed. Laboratory investigations demonstrated that ZOL impedes tumor dissemination in various ways: inhibition of small blood vessel growth, stimulation of killer cells, induction of tumor cell apoptosis (programmed cell death), and improvement of the activity of other antitumor treatments.

The agent: Zoledronic acid

ZOL is a bisphosphonate that in various ways affects tumor cells and decisively impedes tumor growth. Many breast cancer patients receive bisphosphonates intravenously, e.g. every four weeks in the presence of metastasis. Infusions are generally well tolerated. In the present clinical study, the spectacular effect was generated with biannual infusions.

These agents have another important effect: Bisphosphonates lead to an increase in bone calcium and thus bone stabilization. For this reason, ZOL is already now widely applied to prevent bone complications. ZOL is also frequently prescribed for patients with breast cancer. In many women, cancer treatment unfortunately brings about osteoporosis.

Bisphosphonates counteract the loss of bone mineral density associated with otherwise successful cancer treatments. ABCSG Trial 12 also confirmed this effect. Overall, measurements of bone mineral density were done after 6 months, 1 year, 3 years and 5 years in 401 patients. Twelve percent of the women receiving endocrine treatment, but no ZOL, experienced a loss of bone after two years. Bone mineral density was completely constant in patients given the bisphosphonate in addition.

Future investigations will focus on optimizing administration and dosage, as well as exploring which patients draw the greatest benefit from treatment with ZOL.

(Anti-)hormonal treatment

Sixty percent of all malignant tumors in premenopausal women and 75% of those in postmenopausal women are endocrine-responsive. This results in increased tumor growth under hormonal influence. The endocrine dependency shown by such cancer cells is the toehold for (anti-)hormonal therapy: The body's hormones, such as the female sex hormone estrogen, are deactivated in an attempt to inhibit tumor dissemination. Endocrine breast cancer treatment is applied in both adjuvant and palliative settings.

Histology tells us whether a tumor is hormone-responsive or not. The extent of endocrine responsiveness is seen today as an important criterion for developing treatment strategies. In this case, hormonal withdrawal or deprivation may possibly stem tumor dissemination. Aromatase inhibitors may stop the estrogen production by inhibiting aromatase, the key enzyme in this process.

Study details

Trial 12 of the *Austrian Breast & Colorectal Cancer Study Group* (ABCSG) is an open-label, multicentric Phase III study having accrued 1,803 premenopausal patients with endocrine-responsive breast cancer, stage I or II, and ten or less involved axillary lymph nodes. Following surgical tumor removal, the patients were brought into the trial to receive goserelin treatment in order to suppress ovarian function. They were randomized into one of four treatment groups: 1. Anastrozole plus ZOL; 2. Anastrozole alone; 3. Tamoxifen plus ZOL; or 4. Tamoxifen alone. This treatment was given for three years, and median follow-up was for another two years.

For further information, please contact: Brigitte Grobbauer, MA, ABCSG-Public Relations, T: (0043) 0664/5440807,
E-Mail: gitti.grobbauer@abcsg.at