NOVARTIS

Video: Major Independent Trial Demonstrates Significant Anticancer Benefit of Zometa® in Women With Early-Stage Breast Cancer

May 31, 2008

- - Zometa when added to hormone therapy, following surgery, significantly reduced the risk of cancer returning or death by 36% beyond clinical benefits achieved with hormone therapy alone(1)
- - Findings may allow clinicians to improve standard of care for premenopausal women diagnosed with hormone-sensitive, early-stage breast cancer
- - These are the first data from a large clinical program exploring the direct anticancer effect of Zometa in breast, lung and prostate cancer

EAST HANOVER, N.J., May 31 /PRNewswire/ -- New data presented today showed that Zometa® (zoledronic acid) offered a significant anticancer benefit for premenopausal women with hormone-sensitive, early-stage breast cancer. The study found that Zometa when added to hormone therapy, following surgery, significantly reduced the risk of cancer returning or death by 36% beyond clinical benefits achieved with hormone therapy alone.

To view the Multimedia News Release, go to: http://www.prnewswire.com/mnr/novartis/33472/

Investigators from the Austrian Breast & Colorectal Cancer Study Group (ABCSG) announced the findings during a plenary presentation today at the 44th Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago, Illinois, USA.

"This study is the first large-scale trial to demonstrate the significant antitumor benefit of zoledronic acid," said lead investigator Michael Gnant, M.D., of the Medical University of Vienna. "These new findings may allow oncologists to further improve the standard of care for premenopausal women with hormone-sensitive breast cancer."

According to the World Health Organization (WHO), each year approximately 500,000 women die worldwide because their breast cancer has returned or spread(2). Moreover, the incidence of breast cancer has been rising in recent decades(3).

"These results represent a tremendous advance for women hoping to prevent the return of their cancer," said David Epstein, President and CEO of Novartis Oncology. "We continue to explore the anticancer benefit of Zometa in a large clinical program with nearly 20,000 patients in 10 trials worldwide. We anticipate additional results over the next two to three years."

The ABCSG-12 study, in which women were treated for three years and observed for an additional two years, demonstrated that the addition of Zometa to hormone therapy (tamoxifen or anastrozole) significantly prolonged both disease-free survival and recurrence-free survival. With Zometa, the risk of disease-free survival events (which include death from any cause) fell by 36% (P=0.01), compared to hormone therapy alone. Furthermore, the risk of recurrence-free survival events fell by 35% (P=0.015) with Zometa, compared to hormone therapy alone. A positive but non-significant trend toward an overall survival benefit was also seen in patients who received Zometa(1).

Zometa is the world's leading treatment for the prevention or delay of skeletal-related events (SREs) in patients with advanced malignancies involving bone across a broad range of tumors. Laboratory research had suggested that Zometa may also help protect patients from the spread of cancer to other parts of the body (distant metastatic sites) and help keep patients recurrence-free.

Zometa slows the bone-destroying effect that occurs with bone metastases by fighting abnormal activation of osteoclasts, cells that normally break down old bone, and osteoblasts, cells that normally build new bone. Growth factors produced by cancer cells overstimulate osteoclasts and osteoblasts, causing excessive erosion of bone and/or the abnormal buildup of new but unstable bone.

Laboratory research has suggested that Zometa may also have anticancer effects, including helping to protect against the return and spread of cancer before it reaches an advanced stage. A tumor passes through six stages on its path to metastasizing (spreading)(4). In the laboratory, Zometa has been shown to make passage through these stages more difficult by inhibiting angiogenesis (formation of blood vessels that grow and feed cancer cells), stimulating cancer-fighting T-cells, inducing tumor cell apoptosis (programmed cell death) and increasing the activity of anticancer agents that target tumor cell metastases(5).

A growing number of clinical studies are examining the potential anticancer impact of Zometa. One of the largest of these studies, AZURE (Adjuvant Zoledronic acid to redUce REcurrence), has completed enrollment. The study will evaluate the impact of Zometa in reducing risk of cancer recurrence in 3,360 premenopausal and postmenopausal women with Stage II/III breast cancer.

Another study presented at this year's ASCO meeting evaluated the effect of Zometa on bone marrow micrometastases. The study was conducted in 120 premenopausal and postmenopausal women with Stage II/III breast cancer undergoing treatment pre- and post-surgery. For those women who were negative for disseminated cancer cells at baseline, significantly more women who took Zometa in addition to chemotherapy remained negative for disseminated cancer cells over time.

Study Details

The Austrian Breast & Colorectal Cancer Study Group Trial 12 (ABCSG-12) is an open-label, multicenter, Phase III study that enrolled 1,803 premenopausal women with estrogen-receptor-positive Stage I or II breast cancer, with fewer than 10 axillary lymph nodes involved. Patients were recruited for the study after curative surgery and initiation of goserelin treatment for ovarian suppression, and randomly assigned into one of four study groups: (1) anastrozole plus Zometa; (2) anastrozole alone; (3) tamoxifen plus Zometa; (4) tamoxifen alone. The treatment period was three years and the median follow-up period was an additional two years(1).

The primary endpoint of the study was disease-free survival for all four study groups. Recurrence-free survival, overall survival, and safety were secondary endpoints. (Disease-free survival was defined as the length of time after randomization during which patients had no local recurrence, contralateral breast cancer, distant metastasis, secondary carcinoma, and/or death from any cause. Recurrence-free survival was defined as the length of time after randomization during which patients had no local recurrence, contralateral breast cancer, distant metastasis, and/or secondary carcinoma.) Exploratory endpoints included bone-metastases-free survival(1).

At the median follow-up of five years, disease-free survival events were reduced by 36% (P=0.01) with Zometa and the risk of recurrence-free survival events fell by 35% (P=0.015) versus hormone therapy alone. Sixteen deaths had occurred among patients who received Zometa with hormone therapy versus 26 deaths in patients who received hormone therapy alone, which resulted in a nonsignificant reduction in the risk of death in patients who received Zometa compared with those who received hormone therapy alone (P=0.103). A similar trend was noted toward a reduction in bone metastases among patients who received Zometa compared with

those who received hormone therapy alone (16 versus 23). Longer follow-up and a larger number of events will be necessary to determine if any significant differences exist between the groups for overall survival and bone-metastases-free survival. Overall, treatment was generally well-tolerated and side effects were consistent with known drug safety profile(1).

About Zometa

Zometa is indicated for patients with multiple myeloma and documented bone metastases from solid tumors in conjunction with standard antineoplastic therapy; prostate cancer should have progressed after treatment with at least one hormonal therapy.

Important Safety Information

Zometa is contraindicated in patients with hypersensitivity to zoledronic acid or other bisphosphonates, or any of the excipients in the formulation of Zometa. Hypersensitivity reactions, including rare cases of urticaria and angioedema and very rare cases of anaphylactic reaction/shock, have been reported.

Due to the risk of clinically significant deterioration in renal function, which may progress to renal failure, single doses of Zometa should not exceed 4 mg, and the duration of infusion should be no less than 15 minutes. Risk factors for the deterioration of renal function include impaired baseline renal function and multiple cycles of bisphosphonate treatment.

Zometa is not recommended in patients with bone metastases with severe renal impairment. In patients with mild to moderate renal impairment at baseline, lower doses of Zometa are recommended based on calculated creatinine clearance. Before each Zometa dose, serum creatinine should be measured and treatment should be withheld for renal deterioration until serum creatinine has returned to within 10% of the baseline value.

Zometa should not be used during pregnancy. Women of childbearing potential should be advised to avoid becoming pregnant. If the patient becomes pregnant while taking this drug, the patient should be apprised of the potential harm to the fetus.

Osteonecrosis of the jaw (ONJ) has been reported predominantly in cancer patients treated with intravenous bisphosphonates, including Zometa. Many of these patients were also receiving chemotherapy and corticosteroids, which may be risk factors for ONJ. Postmarketing experience and the literature suggest a greater frequency of reports of ONJ based on tumor type (advanced breast cancer, multiple myeloma) and dental status (dental extraction, periodontal disease, local trauma, including poorly fitting dentures). Many reports of ONJ involved patients with signs of local infection, including osteomyelitis. Cancer patients should maintain good oral hygiene and should have a dental examination with preventive dentistry prior to treatment with bisphosphonates. While on treatment, these patients should avoid invasive dental procedures, if possible. No data are available as to whether discontinuation of bisphosphonate therapy reduces the risk of ONJ in patients requiring dental procedures. A causal relationship between bisphosphonate use and ONJ has not been established. Clinical judgment of the treating physician should guide the management plan of each patient based on individual benefit/risk assessment.

In postmarketing experience, severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported infrequently in patients taking bisphosphonates.

The most common adverse events (greater than or equal to 15%) in bone metastases clinical trials, regardless of causality, with Zometa 4 mg (n=1031) were as follows: bone pain (55%), nausea (46%), fatigue (39%), anemia (33%), pyrexia (32%), vomiting (32%), constipation (31%), dyspnea (27%), diarrhea (24%), weakness (24%), myalgia (23%), anorexia (22%), cough (22%), arthralgia (21%), lower-limb edema (21%), malignant neoplasm aggravated (20%), headache (19%), dizziness (excluding vertigo) (18%), insomnia (16%),

decreased weight (16%), back pain (15%), and paresthesia (15%).

Caution is advised when bisphosphonates are administered with aminoglycosides, loop diuretics, and potentially nephrotoxic drugs.

Zometa contains the same active ingredient as found in Reclast® (zoledronic acid). Patients being treated with Zometa should not be treated with Reclast.

Patients should be administered an oral calcium supplement of 500 mg and a multiple vitamin containing 400 IU of vitamin D daily.

Please see full Prescribing Information.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by terminology such as "may", "continue to", "anticipate", "potential", "will", or similar expressions, or by express or implied discussions regarding potential new indications or labelling for Zometa or regarding potential future revenues from Zometa. Such forward-looking statements reflect the current views of the Company regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with Zometa to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Zometa will be submitted or approved for any additional indications or labelling in any market. Nor can there be any guarantee that Zometa will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Zometa could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry and general public pricing pressures, and other risks and factors referred to in Novartis AG'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. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis

Novartis Pharmaceuticals Corporation researches, develops, manufactures and markets leading innovative prescription drugs used to treat a number of diseases and conditions, including those in the cardiovascular, metabolic, cancer, organ transplantation, central nervous system, dermatological, GI and respiratory areas. The company's mission is to improve people's lives by pioneering novel healthcare solutions.

Located in East Hanover, New Jersey, Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG (NYSE: NVS), which provides healthcare solutions that address the evolving needs of patients and societies. Focused solely on growth areas in healthcare, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic pharmaceuticals, preventive vaccines and diagnostic tools, and consumer health products. Novartis is the only company with leading positions in these areas. In 2007, the Group's continuing operations (excluding divestments in 2007) achieved net sales of USD 38.1 billion and net income of USD 6.5 billion. Approximately USD 6.4 billion was invested in R&D activities throughout the Group. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 98,200 full-time associates and operate in over 140 countries around the world. For more information, please visit

http://www.novartis.com/.

For more information

Additional information regarding Zometa and Novartis Oncology can be found on the websites http://www.novartisoncologyvpo.com/, http://www.zometa.com/ and http://www.novartisoncology.com/.

References
1. Gnant, M. et al. Efficacy of Zoledronic Acid in Premenopausal Women With Breast Cancer Receiving Adjuvant Endocrine Therapy - The ABCSG-12 trial. Presented at: the 44th Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago, Ill., 31 May - 2 June, 2008; Abstract LBA4.

2. World Health Organization. http://www.who.int/mediacentre/factsheets/fs297/en/index.html

3. Breastcancer.org: http://www.breastcancer.org/about_us/press_room/press_kit/cancer_facts.jsp

4. Mundy, GR, et al. Metastases to bone: causes, consequences and therapeutic opportunities. Nature Reviews Cancer. 2002; 2:584-593.

5. Aft, R, et al. ABSTRACT 1021: Effect of zoledronic acid on bone marrow micrometastases in women undergoing neoadjuvant chemotherapy for breast cancer.

Contact Information

Media Only:
Megan Humphrey
Novartis Oncology
1-862-778-6725
megan.humphrey@novartis.com
Dana Kahn Cooper
1 -732-239-6664

Investors Only:
Jill Pozarek
Novartis Corporation
1-212-830-2445

Video: http://www.prnewswire.com/mnr/novartis/33472

SOURCE: Novartis

CONTACT: Media, Megan Humphrey, Novartis Oncology, +1-862-778-6725, megan.humphrey@novartis.com, or Dana Kahn Cooper, +1-732-239-6664, for Novartis; Investors, Jill Pozarek, Novartis Corporation, +1-212-830-2445

Web site: http://www.novartis.com/
http://www.novartisoncologyvpo.com/
http://www.zometa.com/
http://www.novartisoncology.com/
http://www.asco.org/ASCO/Meetings/ASCO+Annual+Meeting

Source URL: *https://prod1.novartis.com/us-en/news/media-releases/video-major-independent-trial-demonstrates-significant-anticancer-benefit-zometa-women-early-stage-breast-cancer*

List of links present in page

1. https://prod1.novartis.com/us-en/us-en/news/media-releases/video-major-independent-trial-demonstrates-significant-anticancer-benefit-zometa-women-early-stage-breast-cancer
2. http://www.prnewswire.com/mnr/novartis/33472/
3. http://www.novartis.com/
4. http://www.novartisoncologyvpo.com/
5. http://www.zometa.com/
6. http://www.novartisoncology.com/
7. http://www.who.int/mediacentre/factsheets/fs297/en/index.html
8. http://www.breastcancer.org/about_us/press_room/press_kit/cancer_facts.jsp
9. http://www.prnewswire.com/mnr/novartis/33472
10. mailto:megan.humphrey@novartis.com
11. http://www.novartis.com/
12. http://www.novartisoncologyvpo.com/
13. http://www.zometa.com/
14. http://www.novartisoncology.com/
15. http://www.asco.org/ASCO/Meetings/ASCO+Annual+Meeting