11 Proffered Paper Oral

Internation breast cancer intervention study I: updated side effects analysis

I. Sestak[1], R. Kealy[1], R. Edwards[1], A. Howell[2], J. Forbes[3], J. Cuzick[1]. [1]*Cancer Research UK, Wolfson Institute of Preventive Medicine, London, United Kingdom;* [2]*Cancer Research UK, Christie Hospital NHS Trust, Manchester, United Kingdom;* [3]*Department of Surgical Oncology, University of Newcastle, Newcastle, Australia*

Background: Tamoxifen is an effective drug, both for preventing and treating breast cancer, but its role in prevention is limited by its side effect profile, particularly related to endometrial problems and thrombotic events. In the IBIS-I study, 7154 women at increased risk of breast cancer were either randomised to tamoxifen 20 mg/day or placebo for 5 years.

Methods: Women in the IBIS-I study gave detailed information of specific side effects at each 6 monthly follow-up visit. Gynaecological, vasomotor symptoms and other factors were evaluated according to follow-up time, severity and use of hormone replacement therapy. In addition, non-breast related cancer deaths have been updated. Here, we will present updated results on side effects and deaths incorporating four additional years of follow-up.

Results: After a median of 84 months follow-up, 95.4% of women had completed their active treatment. Very large numbers of side effects were reported by participants in both treatment arms. However, the only major categories that showed significant differences were vasomotor and gynaecological side effects which were about 12% higher in the tamoxifen group than the placebo group. There were higher proportions of hot flushes, irregular bleeding, vaginal discharge, and vaginal thrush in the tamoxifen group whereas breast complaints reports were about 27% lower in the tamoxifen group than in the placebo group (607 vs. 830, $P < 0.0001$). In particular, breast diseases such as cysts (99 vs. 221, $P < 0.0001$) and breast pain (162 vs. 242, $P < 0.0001$) were reduced in the tamoxifen group. The occurrence of nail changes, particularly brittle nails, were higher in the tamoxifen group (171 vs. 111, $P = 0.0003$). To date, no significant differences had been found for osteoporotic, non-osteoporotic fractures, cataracts or any other eye problems between the two treatment groups. All cause mortality was non-significantly higher in the tamoxifen group (54 vs. 44, $P = 0.24$). The relative excess is smaller since our first report (25 vs. 11).

Conclusions: The updated IBIS-I side effects analysis shows no new adverse events and no increased death rate is found with tamoxifen. Although very large numbers of side effects were reported, tamoxifen was well tolerated and no new safety concerns were identified.

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Zoledronic acid in the prevention of cancer treatment-induced bone loss in postmenopausal women receiving letrozole as adjuvant therapy for early breast cancer (ZO-FAST study)

N. Bundred[1], I. Campbell[2], R. Coleman[3], R. DeBoer[4], H. Eidtmann[5], A. Frassolati[6], A. Llombart[7], A. Monnier[8], P. Neven[9], R. Dias[10]. [1]*South Manchester University Hospital, Academic Surgery, Education and Research Centre, Manchester, United Kingdom;* [2]*Waikato Hospital, Breast Care Centre, Hamilton, New Zealand;* [3]*Weston Park Hospital, Sheffield, United Kingdom;* [4]*Royal Melbourne Hospital, Victoria, Australia;* [5]*Frauenklinik, Kiel, Germany;* [6]*Azienda Policlinco Hospital, Modena, Italy;* [7]*Institute Oncologia, Valencia, Spain;* [8]*Centre Hospitalier Belfort-Montbeliard, Medical Oncology, Montbeliard Cedex, France;* [9]*Hospital Gasthuisberg, Leuven, Belgium;* [10]*Dias, Rosh, Florham Park, USA*

Rationale: Letrozole has been demonstrated to be safe and effective in the treatment of early receptor positive breast cancer in post-menopausal women, reducing the risk of recurrences by 19% as early adjuvant therapy, and by 42% in the extended adjuvant setting. Like other aromatase inhibitors (AIs), long-term letrozole is associated with loss of bone mineral density (BMD). Defining the role of bisphosphonates is becoming more important with the increased use of AIs as adjuvant therapy for 3 to 5 years or longer. Zoledronic acid, a potent bisphosphonate, has been shown to prevent BMD loss in premenopausal patients on adjuvant estrogen-suppression therapy. ZO-FAST was designed to investigate the optimum timing of zoledronic acid with adjuvant letrozole (2.5 mg/d for 5 yrs) in postmenopausal women.

Methods: Patients are randomized between zoledronic (4 mg IV q 6 months) starting at initiation of letrozole versus delayed zoledronic acid (i.e. when T score decreases < −2 SD below normal, or in the case of non-traumatic fracture). Change in lumbar spine BMD is the primary endpoint. Clinically significant bone loss was defined as: 6% reduction in BMD per year, cumulative reduction of 8% over any period of time, BMD < −2.5 SD, and fracture or impending fracture on x-ray.

Results: 1066 patients have been recruited by 112 centers in 28 countries. Patients by stratification factors: prior adjuvant chemo-therapy: yes: 573; no: 493. Baseline BMD T score: > −1 SD: 718; −1 to −2 SD: 348. Median age (range): 58 (37–87) yrs. The most common side effect reported is arthralgia (21.3%). 90 (8%) patients have been withdrawn from the study as of November 2005, with only 42 (4%) patients withdrawing due to adverse events. Safety data trends including summaries by treatment arm will be presented at the meeting. Data lock is planned for January 2006.

First results on safety, 12 Month BMD and the number of patients on the delayed arm who met the criteria for starting Zometa will be available at that time and the data will be presented at the meeting.

Conclusions: ZO-FAST, along with the companion protocol Z-FAST, will offer important insights into the prevention and treatment of aromatase inhibitor related bone loss and help the medical community define the best strategy of addressing this issue by combining the aromatase inhibitor letrozole with zoledronic acid in early breast cancer.

Wednesday, 22 March 2006 14:15–16:00

SCIENTIFIC SESSION

Imaging

13 Invited

PET in the axilla

Abstract not received.

14 Invited

Breast cancer diagnosis – when is MRI indicated?

S.H. Heywang-Köbrunner, A. Artmann, K. Hellerhoff. *Department of Breast Imaging, Radiology, Klinikum rechts der Isar, Technical University Munich, Munich, Germany*

Introduction: Breast MRI has proven to be the most sensitive method for detection of invasive breast cancer and for complementing mammography in the detection of DCIS. Due to its limited specificity, the difficult localisation of lesions visible by MRI alone and its high costs, indications need to be well selected.

Procedure and Results: MR technique is meanwhile well established and appropriate recommendations exist in the literature.

Indications, which are considered for breast MRI include:

- local staging before breast conservation in the difficult-to-assess breast;
- high risk patients;
- search for primary tumor (CUP-syndrome);
- diagnostic problems in patients with silicon implants or in patients with scarring after breast conservation;
- monitoring of therapy;
- very selected diagnostic problems which cannot be solved by conventional imaging.

An overview of the present literature is provided. To date the level of evidence for most indications is "3". Randomized studies and studies concerning long-term outcome are needed.

Conclusion: MRI can provide valuable additional information. In order to minimize unnecessary false alarm and work-up, MRI should be strictly limited to appropriate indications. It should be performed in breast centers where high experience with conventional, interventional and MR breast imaging is available, where an interdisciplinary team is present and where systematic documentation of the results and regular feed-back is guaranteed.

15 Invited

Monitoring response to therapy with imaging

A. Tardivon, C. El Khoury, F. Thibault, L. Ollivier. *Institut Curie, Department of radiology, Paris, France*

Neoadjuvant chemotherapy (NC) has become popular for patients with advanced breast cancer or operable cancers. The advantages of this systemic therapy serves as an in vivo sensitivity test, increases the rate of breast conserving surgery and facilitates the study of cancer biology. In addition, the pathological response of tumours to NC appears to be a surrogate marker for patient outcome. Besides clinical examination, breast imaging is used to evaluate the shrinkage of tumours under treatment and determine responders. Mammography allows detection of malignant microcalcifications that is poorly responsive to NC. The combination of physical examination with either mammography or ultrasound significantly