Friday, 23 March 2012 15:00–17:00

KEYNOTE SYMPOSIUM

Key Messages to Take Back to Your Practice on Monday Morning

1LBA Late Breaking Abstract

Intra-operative Ultrasound is Imperative to Obtain Adequate Tumour Margins and Excision Volumes in Breast-conserving Surgery for Palpable Breast Cancer: Results of a Randomised Controlled Trial

N.M.A. Krekel[1], M.H. Haloua[1], A.M.F. Lopes Cardozo[2], A.M. Bosch[3], S. Muller[4], L. de Widt[5], A.H.M. Taets van Amerongen[6], E. Bergers[6], S. Meijer[1], M.P. van den Tol[1]. *[1]VU University Medical Center (VUmc), Surgical Oncology, Amsterdam, The Netherlands; [2]Medical Center Alkmaar (MCA), Surgical Oncology, Alkmaar, The Netherlands; [3]Gelderse Vallei Hospital, Surgical Oncology, Ede, The Netherlands; [4]Red Cross Hospital, Surgical Oncology, Beverwijk, The Netherlands; [5]Waterland Hospital, Surgical Oncology, Purmerend, The Netherlands; [6]VU University Medical Center (VUmc), Radiology, Amsterdam, The Netherlands*

Background: Breast-conserving surgery for palpable breast cancer is worldwide associated with a high rate of tumour-involved margins and excessively large excision volumes. Ultrasound-guided surgery (USS) may resolve both problems, thereby improving surgical accuracy. A randomised controlled trial was initiated to compare USS with the standard palpation-guided surgery (PGS) for palpable breast cancer in terms of margin status and extent of healthy breast tissue resection.

Materials and Methods: A total of 124 eligible patients with palpable T1−T2 invasive breast cancer were randomised to either USS (n = 61) or PGS (n = 63). Specimen margins were analysed for tumour-invasion. A calculated resection ratio (CRR) was determined, indicating the excess of healthy tissue resection, and calculated by using the surgical specimen volumes and the tumour diameters (CRR 2.0 implies volume two times too large).

Results: In the USS-group, 3.3% of margins were involved with invasive carcinoma, compared with 16.4% in the PGS-group ($p < 0.05$). The use of intra-operative US resulted in a significant reduction of re-excisions, mastectomies, and irradiation boosts. Excision volume and CRR were smaller with USS (40 vs 58 cc, and 1.0 vs 1.9, respectively (both, $p < 0.05$)). Tumours larger than 2.0 cm were associated with lower CRR ($p < 0.0001$), but higher positive margin rate ($p = 0.064$).

Conclusions: USS can prevent the unacceptably high rate of tumour-involved resection margins in palpable breast cancer excision, thus avoid subsequent surgery or radiotherapy. In addition, USS largely reduces the amount of unnecessary healthy breast tissue resection to optimal volume resection, thereby contributing to the improvement of cosmetic results.

2LBA Late Breaking Abstract

Fulvestrant Alone or with Concomitant Anastrozole Vs Exemestane Following Progression On Non-steroidal Aromatase Inhibitor − First Results of the SoFEa Trial (CRUKE/03/021 & CRUK/09/007) (ISRCTN44195747)

S. Johnston[1], L.S. Kilburn[2], P. Ellis[3], D. Cameron[4], D. Dodwell[5], A. Howell[6], Y.H. Im[7], G. Coombes[2], M. Dowsett[8], J.M. Bliss[2]. *[1]The Royal Marsden NHS Trust, Department of Medicine, London, United Kingdom; [2]The Institute of Cancer Research, ICR Clinical Trials & Statistics Unit (ICR-CTSU), Sutton, United Kingdom; [3]Guy's and St Thomas's NHS Foundation Trust, Department of Medical Oncology, London, United Kingdom; [4]Western General Hospital, Edinburgh Cancer Research Centre, Edinburgh, United Kingdom; [5]St James's Hospital, St James's Institute of Oncology, Leeds, United Kingdom; [6]The Christie NHS Foundation Trust, Breast Cancer Research and Development, Manchester, United Kingdom; [7]Samsung Medical Center, Department of Internal Medicine, Seoul, South Korea; [8]The Royal Marsden NHS Trust, Department of Academic Biochemistry, London, United Kingdom*

Background: Optimal endocrine treatment (trt) for post-menopausal women with advanced ER+ breast cancer progressing on a non-steroidal (NS) aromatase inhibitor (AI) is unclear. The EFECT study showed no difference in efficacy between the steroidal antiestrogen fulvestrant (F) & steroidal AI exemestane (E) in this setting. Pre-clinical data suggest F may be more effective in a low estrogen environment. Two recent trials of F combined with anastrozole (F+A) compared with A alone in first-line setting gave mixed results. SoFEA investigated F+A in patients (pts) with acquired resistance to previous AI compared with F alone & E, a recognised standard of care.

Methods: In SoFEA, a multi-centre partially blinded randomised phase III study, postmenopausal women were allocated to F 250 mg monthly (IM) with 500 mg loading dose plus A 1 mg daily (F+A n = 243), F plus placebo (n = 231) or E 25 mg daily (n = 249). Pts should have responded to previous NSAI in metastatic setting (>6 months (mo) trt) or received >12 mo NSAI as adjuvant; progressing on NSAI at trial entry. Primary endpoint was progression-free survival (PFS) between F+A vs F & F vs E. Secondary endpoints included objective response rate (ORR), clinical benefit rate (CBR), overall survival (OS) & tolerability. Serum estradiol (E2) levels were measured in a subset of pts at baseline (BL) & 3 mo.

Results: 723 pts (median age 64 years) were enrolled from 82 UK & 4 South Korean centres (03/2004–04/2010). Prior AI had been given as adjuvant trt to 18% pts for a median of 27.9 mo (18.8-43.1 IQR), and to 82% pts for locally advanced/metastatic disease for a median of 19.3 mo (12.1-31.2 IQR). Trt was well tolerated; serious adverse events were rare. There was no evidence of a difference in PFS: median 4.4 mo (95% CI 3.4-5.4), 4.8 mo (95% CI 3.6-5.5), and 3.4 mo (95% CI 3.0-4.6) for F+A, F, and E, respectively. As expected, longer PFS was positively correlated with duration of prior AI exposure but no interaction with treatment was observed. No differences were observed for ORR, CBR & OS. 85/94 pts (90.4%) had E2 levels <3.0 pmol/l at BL, while 3 mo E2 mean values differed as expected between pts treated with F+A (2.8 pmol/l) and F (15.0 pmol/l), confirming estrogen suppression with F+A.

Conclusion: SoFEA provides no evidence that F+A (with F loading dose) is more effective than F alone or E in pts with acquired resistance to NSAI. Median PFS in SoFEA is similar to EFECT & lack of added benefit for F+A is consistent with FACT.

3LBA Late Breaking Abstract

Everolimus Added to Exemestane Reduced Bone Markers and Disease Progression in Bone in Postmenopausal Women with Advanced Breast Cancer: Updated Results From the BOLERO-2 Trial

M. Gnant[1], G.N. Hortobagyi[2], H. Rugo[3], H.A. Burris[4], S. Noguchi[5], K.I. Pritchard[6], J. Baselga[7], T. Sahmoud[8], H. Bauly[9], M. Piccart[10]. *[1]University of Vienna, Department of Surgery, Vienna, Austria; [2]University of Texas MD Anderson Cancer Center, Department of Breast Medical Oncology, Houston, USA; [3]University of California San Francisco, Helen Diller Family Comprehensive Cancer, San Francisco, USA; [4]Sarah Cannon Research Institute, Drug Development Program, Nashville, USA; [5]Osaka University, Department of Breast and Endocrine Surgery, Osaka, Japan; [6]Sunnybrook Odette Cancer Centre and the University of Toronto, Toronto, Canada; [7]Massachusetts General Hospital, Boston, USA; [8]Novartis Pharmaceuticals Corporation, Florham Park, USA; [9]Novartis Pharma AG, Basel, Switzerland; [10]Jules Bordet Institute, Brussels, Belgium*

Background: BOLERO-2 (NCT00863655), a multinational, double-blind, placebo-controlled, phase 3 study comparing everolimus (EVE) plus exemestane (EXE) versus EXE plus placebo (PBO) in postmenopausal women with estrogen receptor-positive (ER^+) advanced breast cancer refractory to letrozole or anastrozole, demonstrated improved response and progression-free survival (PFS) with EVE plus EXE. Nonsteroidal aromatase inhibitors (NSAIs) are associated with reduced bone mineral density and increased risk of fractures. Thus, it is important to evaluate whether new therapies used with/after NSAIs affect bone turnover. This BOLERO-2 subanalysis evaluated the effect of EVE plus EXE versus EXE plus PBO on bone formation/resorption markers and on disease progression in bone.

Material and Methods: Eligible patients received EXE 25 mg/d and were randomized (2:1) to EVE 10 mg/d or PBO. Primary endpoint was PFS based on 457 events and 12.5 months' median follow-up. Bone turnover markers were exploratory endpoints analyzed at 6 and 12 weeks after treatment initiation and included bone-specific alkaline phosphatase (BSAP), amino-terminal propeptide of type I collagen (P1NP), and C-terminal cross-linking telopeptide of type I collagen (CTX).

Results: 724 patients were randomized to receive EVE (n = 485) or PBO (n = 239). Baseline disease characteristics, including bone metastases (76% EVE vs 77% PBO) were well balanced between treatment arms, but baseline bisphosphonate use was not (44% EVE vs 54% PBO). Median PFS was longer with EVE versus PBO by investigator (7.4 vs 3.2 months; hazard ratio [HR] = 0.44; $P < 1 \times 10^{-16}$) and central (11.0 vs 4.1 months; HR = 0.36; $P < 1 \times 10^{-16}$) assessment. Bone marker levels decreased versus baseline with EVE at 6 weeks (−5.5% BSAP, −20.4% P1NP, −6.3% CTX) and 12 weeks (−3.6% BSAP, −26.8% P1NP, −0.5% CTX), but increased with PBO. The cumulative incidence rate of progression in bone was lower for EVE (3.03%) vs PBO (6.16%) at day 60 in the overall population and in the subgroup of patients with bone metastases at baseline (3.95% EVE vs 8.11% PBO). Similar trends were observed at timepoints beyond 60 days. All reported bone-related adverse events were grade 1/2 and occurred with similar frequency with EVE (2.9%) and PBO (3.8%).

Conclusion: The combination of EVE plus EXE reduced bone turnover markers during the first 12 weeks of therapy and reduced disease progression in bone versus EXE plus PBO, suggesting favorable bone health clinical benefits.