There was a reduction (mean 9.2%) in analgetic use for all patients during ibandronate treatment.
Conclusions: The study shows that in clinical practice intravenous as well as oral ibandronate is a valuable and well-tolerated treatment option for breast cancer patients with metastatic bone disease.

5027 POSTER DISCUSSION

A randomized, phase III trial exploring the effects of neoadjuvant sequential treatment with steroidal (exemestane) and non-steroidal (anastrozole) aromatase inhibitors on biomarkers in post-menopausal women with hormone receptor positive locally advanced breast cancer (LABC)

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Background: Despite many large randomised trials assessing adjuvant aromatase inhibitor (AI) treatment for postmenopausal breast cancer patients, optimal endocrine strategy remains unknown. Neoadjuvant endocrine studies provide the opportunity to model appropriate study design in a more expeditious manner. Several adjuvant trials are exploring sequential AI strategies. This study compared the effect of two sequences of AI use [steroidal (exemestane, *E*) and non-steroidal (anastrozole, *A*)] on serological and pathological biomarkers, when given in the neoadjuvant setting to patients with LABC.
Methods: 30 postmenopausal women with ER and/or PR positive disease were randomised to receive either *E* followed by *A*, or *A* followed by *E*. Each drug was given for 8 weeks. Serum estrone sulphate, and estradiol levels, as well as intra-tumoural Ki67 were evaluated at baseline, 8 weeks, and 16 weeks. Clinical response, patient preference, & quality of life were also assessed.
Results: Despite rapid falls in sex steroid levels with AI use, there was no difference in estradiol, estrone sulphate or Ki67 levels between groups. There was no significant difference in toxicities, or in quality of life scores. Overall clinical response rate was 68% & clinical benefit was 93%. There was a trend towards improved clinical response in the *A* followed by *E* group. The majority of patients expressed a preference of treatment.
Conclusions: Neither sequence of steroidal or non-steroidal AI appears to offer a significant advantage over the other. A trend towards improved clinical response in patients treated with *A* followed by *E* is hypothesis generating and needs confirmation in larger trials.

5028 POSTER DISCUSSION

Neoadjuvant concomitant radio-endocrine therapy for locally-advanced receptor positive elderly breast cancer: an Indian experience

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Background: Locally-advanced breast cancer patients – commonest presentation in developing countries – are conventionally addressed with neoadjuvant chemotherapy, irrespective of hormonal status. Cost and toxicity of chemotherapy often leads to non-compliance. Objective of this study was to evaluate a less expensive, better tolerated neoadjuvant strategy, by combined Radio-hormonal manipulation, to achieve down staging, adequate enough for MRM or even to allow conservative surgery (BCS) in ER+ postmenopausal patients.
Primary end point of the study is overall response of tumor and axillary node(s) to neoadjuvant treatment. Secondary endpoint is the feasibility of BCS.
Materials and Methods: Between June 2007 and October 2008, a total of 221 patients aged >60 years with core biopsy confirmed, receptor positive, invasive adenocarcinoma of breast, who are not amenable to BCS (T_2-T_4, N_1-N_2, M_0) were placed on daily Tamoxifen 20 mg (n = 156) or if HER 2 positive, Letrozole 2.5 mg, (n = 65). Concomitant Radiotherapy (50 Gy in 25 F over 5 weeks) with individualised CT-based planning was started after 3 months of hormone therapy in 217/221 patients. 4 patients were excluded, as they developed systemic metastasis. After completion of radiotherapy, hormonal agent was continued until disease progression. 2–4 weeks after radiotherapy i.e. around 20–24 weeks from the initiation of hormone treatment, patients were assessed for tumor response by clinical examination, mammography and also metastatic work up once again for feasibility of surgery. Surgery consisted of tumerectomy with level II axilla dissection or MRM depending on residual tumor: breast ratio and patient's choice.
Results: All patients completed treatment. Tumor response was evaluated as per RECIST criteria by monthly clinical examination. More than 50% tumor shrinkage was noted prior to radiotherapy in 48/156 (31%) patients on Tamoxifen and 28/65 (43%) on Letrozole. 2–4 weeks after radiotherapy complete and partial remission were achieved in 71/217 and 130/217 patients respectively – stable disease in 16/217 patients. Surgery was possible in 201/217 (92%) patients – BCS in 126/217 (58%) patients, MRM in 75/217 (35%). Pathological CR was noted in 65/217 (30%) patients. No patients had more than RTOG Grade 2 skin toxicity.
Conclusions: Judicious integration of systemic and local therapy is the key to success in breast cancer management. In this single institute study neoadjuvant radio-hormone therapy proved to be an effective, non-toxic, well-tolerated, inexpensive, patient-compliant treatment option, which, till date remains nearly untrodden ground in world literature.

5029 POSTER DISCUSSION

Motesanib (AMG 706) in combination with paclitaxel or docetaxel: phase 1b study in patients with locally recurrent, unresectable or metastatic breast cancer

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Background: Motesanib, an oral inhibitor of angiogenesis, selectively targets VEGF receptors 1, 2, and 3; PDGF and Kit receptors. This ongoing phase 1b open-label dose-finding study determines the maximum-tolerated dose (MTD), safety, pharmacokinetics (PK), and efficacy of motesanib plus paclitaxel (P) or docetaxel (D) in patients (pts) with advanced breast cancer (ClinicalTrials.gov ID NCT00322400; sponsor: Amgen Inc.).
Methods: Pts with ECOG 0/1 and $\leqslant$1 prior chemotherapy regimen for metastatic breast cancer are eligible. Pts were treated with (until toxicity or disease progression) motesanib (50 or 125 mg) QD orally continuously from cycle 1 day 3 plus either P (Arm A) 90 mg/m^2 on days 1, 8, and 15 of each 28-day cycle; or D (Arm B) at either 100 mg/m^2 on day 1 of every 21-day cycle; or at 75 mg/m^2 with motesanib at MTD (125 mg). Objective response (OR) per RECIST was assessed every 8 (Arm A) or 6 wks (Arm B).
Results: 33 pts (Arm A, n = 10; Arm B, n = 23) have received $\geqslant$1 dose of motesanib. Median age is 51 (range 28–66) yrs. 5 dose-limiting toxicities (all grade [gr] 3) occurred in 4 pts: abnormal liver function test and deep vein thrombosis (Arm A, 125 mg), fatigue (Arm A, 125 mg), gallbladder enlargement (Arm B, 125 mg+D 75 mg/m^2), and migraine (Arm B, 125 mg). The motesanib MTD has not been reached; the target dose is 125 mg QD. 28 (85%) pts had motesanib-related adverse events (AEs). The most common (highest gr) AEs were: diarrhea, Arm A/B 60%/61% (gr 3, 0%/13%); fatigue, 30%/26% (gr 3, 10%/4%); hypertension, 20%/22% (gr 3, 10%/4%); and nausea, 10%/26% (no gr 3). No related AE $\geqslant$gr 4 was reported. 2 deaths occurred on study (Arm B; 50 and 125 mg, n = 1 each); neither was considered to be motesanib-related. Motesanib PK parameters were generally within the range described for single-agent motesanib treatment. PK profiles of P and D showed high interpatient variability; AUC was higher in some pts after motesanib coadministration. Efficacy at data cutoff in pts with measurable disease at baseline is shown (Table).

	Best OR, n (%)	
	Arm A (n = 7)	Arm B (n = 18)
Partial response	2 (29)	5 (28)
Stable disease (SD)	2 (29)	9 (50)
SD $\geqslant$24 wks	0	3 (17)
Duration of response, median days (range)	169 (58+, 169)	198 (96, 337+)

Conclusions: Motesanib in combination with P or D appears to be tolerable and shows evidence of antitumor activity in pts with advanced breast cancer. Coadministration with either P or D had no major effect on motesanib PK.