rates of drug-related withdrawal were very low in both the neoadjuvant and the first-line setting.
The ongoing phase III study CONFIRM will provide further clarification of the role of fulvestrant HD in postmenopausal patients with recurrent and metastatic breast cancer.
Sponsored by AstraZeneca. Fulvestrant HD and Fulvestrant for neo-adjuvant treatment are non-approved regimens.

5081 POSTER

Triple combination of 3-weekly trastuzumab (T) plus oral vinorelbine (VNR) and capecitabine (CAP) as first-line treatment in HER2-positive metastatic breast cancer (MBC): an active and well-tolerated regimen that allows patient compliance

R. Palumbo[1], A. Bernardo[1], M.R. Strada[2], G. Poggi[1], C. Teragni[1], A. Amatu[1], M. Frascaroli[2], B. Montagna[1], F. Sottotetti[1], G. Bernardo[1].
[1]Clinica del lavoro Fondazione Salvatore Maugeri, Medical Oncology II, Pavia, Italy; [2]Clinica del lavoro Fondazione Salvatore Maugeri, Rehabilitative Oncology, Pavia, Italy

Background: Both VNR and CAP are known to be active agents combined with T in HER2+ MBC. The possibility of an *all-oral* formulation makes VNR/CAP an attractive new regimen to be combined with T. Based on our previous extended experience with weekly T and oral VNR in this patient population (*EJC Suppl. 2008, vol 6, nº7, abstr.418*), we designed a phase II trial to verify the activity and tolerability of a triple combination of T/VNR*os*/CAP, aiming to further improve clinical outcome and patient compliance.
Patients and Methods: Thirty-four consecutive chemo-naïve patients (pts) with measurable HER2+ (defined as IHC 3+ or FISH+) MBC were enrolled in a prospective phase II trial: median age 52 years (range 41−69); ECOG PS was 0 in 26 pts and 1 in 6; prior neo/adjuvant chemotherapy in 70%; visceral involvement in 82%, 12 pts had bone metastases combined with liver/lung lesions; >2 metastatic sites in 10 pts (29%). Patients received T on day 1 at loading dose of 8 mg/Kg as a 90-minute infusion, then 6 mg/Kg every 3 weeks, combined with VNR at a fixed dose of 60 mg/m^2 *per os* on days 1[amp;]8 and CAP at 1000 mg/m^2 bid days 1->14, every 3 weeks. Treatment was continued until progression or unacceptable toxicity.
Results: Median number of cycles per patient was 9 (range 4−12); median relative dose-intensity was 98% for T, 88% for VNR and 80% for CAP. Worst toxicity was haematological, with WHO 3−4 neutropenia in 36%-12% of pts; no patient developed febrile neutropenia; diarrhoea, mucositis and nausea/vomiting did not exceed gr.2; asymptomatic grade 2 LVEF decline was documented in 2 pts, at the 4th and 6th cycle; asthenia, hand&foot syndrome and constipation were transient and quickly reversible. The overall response rate (RR) was 88% (95% CI: 22−54) with 7 complete (20%, 4 in the liver, 3 in lymph nodes), and 22 partial (65%) responses; 3 pts had stable disease >6 months and 2 pts progressed, for an overall disease control of 94%. Median PFS was 12 months, median overall survival has not been reached.
Conclusions: The tested schedule appeared to be highly active and well tolerated as first-line treatment for HER2+ MBC, also improving patient compliance by allowing a more convenient once every three weeks hospital admission.

5082 POSTER

Lapatinib (L) plus capecitabine (C) in HER2+ metastatic breast cancer (MBC): exploratory analyses by prior therapy

J. Crown[1], M.A. Casey[2], D. Cameron[3], B. Newstat[2], S.H. Stein[2].
[1]Irish Oncology Research Group, Clinical Oncology, Dublin, Ireland; [2]GlaxoSmithKline, Oncology Medicine Development Center, Collegeville, USA; [3]University of Leeds, Oncology and Clinical Research, Leeds, United Kingdom

Background: EGF100151 demonstrated L+C improved time to progression (TTP) relative to C alone in women with HER2+, trastuzumab-exposed MBC (Geyer, NEJM;355(26):2006). Eligible patients (pts) had prior exposure to anthracyclines, taxane, and trastuzumab. These exploratory analyses evaluated TTP and overall survival (OS) in subgroups based on prior regimens.
Methods: TTP is based on independently reviewed data as of 03 April 2006, when enrollment was halted with 399 pts. OS was based on data as of 01 October 2008 and includes 9 pts who were in the screening process and permitted to enroll to L+C for a total of 408 pts. TTP and OS were evaluated using Kaplan Meier analyses. The three subgroups were defined as follows: (1) pts treated with <3 prior regimens; (2) pts treated with ⩾3 prior regimens, where a regimen was defined as any prior therapy in any setting (neo-adjuvant, adjuvant or metastatic); and (3) pts treated with only 1 prior metastatic trastuzumab regimen, regardless of other regimens received in neo-adjuvant or adjuvant settings. Cox regression with treatment (trt), prior regimens, and an interaction was performed.
Results: Table 1 presents results. Pts with <3 prior regimens on L+C had a 63% reduction in the risk of progression and a 49% reduction in the risk of death. Pts with ⩾3 prior regimens had a 41% reduction in risk of progression with L+C but no significant improvement in OS. TTP cox model indicated a significant trt effect and no effect due to prior regimens or the interaction. OS cox model indicated a significant interaction, however trt and number of regimens were not significant. Pts who received only 1 prior metastatic trastuzumab regimen had a 46% reduction in the risk of progression with L+C and a 37% reduction in the risk of death.

Table 1: Exploratory Analyses by Prior Regimens: TTP and OS

Subgroup	<3 regimens (any)		⩾3 regimens (any)		only 1 prior metastatic trastuzumab (2nd line trmt)	
(pts treated)	L+C	C	L+C	C	L+C	C
TTP						
N treated	29	37	169	164	44	44
Median wks	49.4	19.7	25.4	18.6	26.7	20.7
HR 95% CI, p	0.37 [0.18, 0.77] p = 0.006		0.59 [0.43, 0.82] p = 0.001		0.54 [0.28, 1.03], p = 0.046	
OS						
N treated	31	37	176	164	45	46
Median wks	87.3	55.1	71.4	66.6	94.3	62.6
HR 95% CI, p	0.51 [0.30, 0.86] p = 0.009		0.95 [0.76, 1.21] p = 0.698		0.63 [0.40, 1.00], p = 0.042	

Conclusion: Results from these exploratory analyses suggest there may be benefit in using L+C in pts treated with fewer prior regimens and with only one prior trastuzumab regimen.

5083 POSTER

Interaction between bisphosphonates and taxanes in patients with metastatic bone disease

I. Luis[1], I. Alho[2], J. Ribeiro[1], I. Fernandes[1], M. Semedo[1], T. Rodrigues[1], O. Vicente[3], S. Casimiro[2], L. Costa[1]. *[1]Hospital de Santa Maria, Oncology, Lisboa, Portugal; [2]Instituto de Medicina Molecular, Oncology, Lisboa, Portugal; [3]Hospital de Santa Maria, Pathology, Lisboa, Portugal*

Background: A synergism between bisphosphonates (BP) and taxanes in breast cancer cell line MCF-7 was previously demonstrated *(Jagdev et al, BJC, 2001)*. Taxanes have important antitumor effect by interfering with microtubule structure and have showed to be very active in patients with prostate cancer and bone metastases. Since osteoclasts are rich in microtubules (needed for their polarity) it is possible that taxanes could act also directly on osteoclasts potentiating the action of BP.
The aim of the present study was to analyse the effect of adding taxanes in patients with solid tumors and bone metastases progression already treated with BP and chemotherapy.
Material and Methods: Twenty-six patients (median age 59.5) with bone metastases treated before with BP (zoledronate: 15; pamidronate: 5, pamidronate followed by zoledronate: 6) and previous chemotherapy regimens were included. Fourteen patients (53.8%) had breast cancer, 9 had prostate cancer, 2 had gastric cancer and 1 had lung cancer. The median time between the beginning of BP and the beginning of the taxane (paclitaxel – 9 patients or docetaxel – 17 patients) was 17 months. All patients continued on the same BP regimen at the moment of association of taxane and all patients had bone disease progression.
The bone resorption marker (NTx) was determined before adding taxanes and during the study.
Results: After received both drugs median time to progression in bone was 5.4 months; 34.6% (n = 9) of the patients didn't have any record of progression on bone until death. 13 patients (out of 14 with basal NTx record) had elevated levels of NTx before starting taxanes (median value: 8839 BCE; range: 38904−51.9 BCE (normal value ⩽64 BCE)). NTx determination at 3 or 6 month of therapy with taxanes decreased in all patients except one, but only 4 patients achieved NTx normalization.
Conclusions: Our results suggest a positive clinical impact of BP and taxanes combination therapy in metastatic bone disease.