(95% CI: 23−37) and 61 (95% CI: 44−77) weeks (wks), respectively. The ORR for 1st line treatment was 51% compared with 35% for 2nd and 3rd line treatment (p = 0.03). There was no significant difference between 1st and 2nd/3rd line treatment for duration of response (41 vs 55 wks; p = 0.8), TTP (31 vs 21; p = 0.4) or OS (74 vs 52 wks; p = 0.1). No significant difference was seen between pts receiving the full planned dose versus reduced dose for ORR (48% vs 42%; p = 0.9), OS (72 vs 62 wks; p ⩾ 0.9), TTP (27 vs 30 wks; p = 0.5) or duration of response (43 vs 44 wks; p = 0.3). The median OS was 93 (95% CI: 66–120) wks for soft tissue and/or bone metastases vs 49 (95% CI: 39−58) wks for visceral disease (p = 0.03). No significant difference in ORR, TTP or duration of response was seen between these 2 groups. Cap was generally well tolerated, although 35% had treatment delays and 57% required dose reductions. Grade 3−4 hand-foot syndrome toxicity occurred in 11%, lethargy 9% and diarrhoea 2%. No grade 3−4 haematological toxicity was seen except in 5 pts with bone marrow infiltration.

Conclusion: Capecitabine is an effective and well tolerated drug in elderly pts with LA or MBC including for 1st line treatment. Dose reduction is frequently required but does not appear to affect outcome.

472 Poster

A phase II trial of oral combination chemotherapy with capecitabine and cyclophosphamide (XC) in metastatic breast cancer

M. Hirata[1], S. Takao[2], Y. Okamoto[3], S. Yamashita[4], Y. Kawaguchi[5], M. Takami[6], H. Furusawa[7], C. Abe[8], J. Sakamoto[9], M. Yoshimoto[10]. *[1]JR Tokyo General Hospital, Breast Surgery, Tokyo, Japan; [2]Hyogo Cancer Center, Breast Oncology, Tokyo, Japan; [3]Toho University Ohashi Medical Center, Breast Surgery, Tokyo, Japan; [4]Fukaya Red Cross Hospital, Breast Surgery, Saitama, Japan; [5]Gifu University Hospital, Breast Surgery, Gifu, Japan; [6]Tokyo Metropolitan Fuchu Hospital, Breast Surgery, Tokyo, Japan; [7]Breastopia Namba Hospital, Breast Surgery, Miyazaki, Japan; [8]Non profit organization Epidemiological and Clinical Research information Network, Epidemiology, Kyoto, Japan; [9]Nagoya University Graduate School of Medicine, Epidemiology, Aichi, Japan; [10]International University of Health and Welfare Mita Hospital, Breast Surgery, Tokyo, Japan*

Background: A phase II multicenter trial in patients with metastatic breast cancer (MBC) was conducted to evaluate oral combination chemotherapy (XC) comprising capecitabine (X) and cyclophosphamide (C). We report the results from this trial.

Material and Methods: Patients received XC therapy as follows: 1657 mg/m^2/day (X) plus 65 mg/m^2/day (C), days 1−14, q3w. Patients must have received none or one prior chemotherapy regimen for MBC. The primary endpoint was response rate, secondary endpoints were progression-free survival (PFS) and incidence of adverse events (AEs).

Results: A total of 51 patients (median age 61 years; range 32−82) were enrolled between May 2007 and April 2009. An interim efficacy analysis in 35 patients, showed tumor response to therapy in 16 patients (complete response [CR] in four patients, partial response [PR] in 12 patients), an additional 12 patients achieved stable disease. Progression of disease (PD) was seen in six patients and one patient was non-evaluable (NE). The response rate (RR) was 45.7% with a 54.2% clinical benefit rate (CR + PR + SD ⩾24 weeks). The median PFS was 373 days (range 178–474). A subset analysis suggests that XC therapy is effective even for triple-negative or luminal A (ER+ & HER2−) type breast cancers. An interim safety analysis was conducted in 49 patients. The number of patients who experienced AEs ⩾ grade 3 was: leukocytopenia, 11 patients (22.4%); neutropenia, five patients (10.2%); hemoglobin reduction, one patient (2.0%) and ALP reduction, one patient (2.0%). Grade 2 Hand-foot syndrome (HFS) was reported in 7 patients (14.3%), no grade 3 HFS was reported.

Conclusions: Interim results from this trial demonstrated efficacy of XC oral combination chemotherapy in MBC. In addition, high efficacy of XC was suggested in luminal A type breast cancers and also in triple-negative breast cancers. Adverse drug reactions with XC were mild and the regimen is convenient for patients. Final efficacy and safety results of the trial will be reported at EBCC based on the full follow-up data.

473 Poster

Quality of life in women with metastatic breast cancer during nine months after randomization in the TEX trial (epirubicin and paclitaxel w/o capecitabine)

H. Svensson[1], Z. Einbeigi[1], H. Johansson[2], T. Hatschek[2], Y. Brandberg[2]. *[1]Sahlgrenska University Hospital, Oncology, Gothenburg, Sweden; [2]Karolinska University Hospital, Oncology-Pathology, Stockholm, Sweden*

Background: Women with metastatic breast cancer have a relatively short expected survival. Therefore, the impact of treatment on quality of life is an important factor to consider. In the TEX trial, two first line treatment regimens were compared in patients with metastatic breast cancer.

The aim of this paper is to compare the effects of two treatment regimens in the TEX trial on HRQOL at two assessment points (2 and 9 months after random assignment).

Material and Methods: A total of 287 patients at ten Swedish hospitals were randomized to treatment with either epirubicin plus paclitaxel (ET, 143 patients) or epirubicin, paclitaxel and capecitabine (TEX, 144 patients). Treatment was given in 3-week cycles.

Health related quality of life (HRQOL) was assessed by the EORTC-QLQ C30 and EORTC QLQ-BR23 questionnaire at 3 points during nine months from randomization.

Results: 163 patients (70%) completed the questionnaire at baseline, and 2 and 9 months after random assignment. There were no statistical significant differences between the TEX group and the ET group on any of the subscales two months after randomization. Small clinical differences (5 to 10 points difference) were found for Global quality of life, Role functioning, Social functioning and Insomnia, favouring patients treated with ET. This group also scored lower on Fatigue, Dyspnoea, and Diarrhoea than patients who received TEX, although the differences were small. At the nine months assessment, the TEX group scored statistically significantly higher on Global quality of life and Physical functioning. No other statistically significant differences were found for any of the subscales analyzed. In contrast to the findings at the two months assessment, small clinically significant differences were found for Global health related quality of life, Physical functioning, Role functioning, Emotional functioning, Dyspnoea, and Insomnia, all in favor of the TEX group.

Conclusions: At the time when side-effects of chemotherapy were present, patients treated with the combination TEX appeared to fare a bit worse than those receiving ET. However, after nine months, when the patients had adapted to treatment, the TEX group seemed to have a slightly better quality of life.

474 Poster

First results of an international, retrospective observational study of metastatic breast cancer patients treated with oral vinorelbine based-chemotherapy

A. Garcia Palomo[1], H. Sommer[2], N. Malamos[3], I. Glogowska[4], E. Kilar[5], J. Lopez Vega[6], L. Torrecillas[7], J. Finek[8], S. Paepke[9], T. Delozier[10]. *[1]Hospital de León, Medical Oncology Unit, León, Spain; [2]Klinikum der Universitaet, Klinik und Poliklinik für Frauenheilkunde und Geburtshilfe, Munich, Germany; [3]Elena Venizelou Hospital, Medical Oncology Unit, Athens, Greece; [4]Oncology Center Institute, Medical Oncology, Warsaw, Poland; [5]Regional Hospital Latawiec, Medical Oncology, Swidnica, Poland; [6]Hospital Universitario Marques de Valdecilla, Medical Oncology Unit, Santander, Spain; [7]Centro Medico 20 de Noviembre, Oncology, Mexico D.F., Mexico; [8]University Hospital Pilsen, Oncology Department, Pilsen, Czech Republic; [9]Klinikum rechts der Isar, Frauenklinik und Poliklinik, Munich, Germany; [10]Centre Francois Baclesse, Department of Medical Oncology, Caen, France*

Background: Full oral Chemotherapy (CT) is an active and convenient therapeutic option for metastatic breast cancer (MBC) patients (pts). In this retrospective analysis, we reviewed the characteristics and the outcome of pts treated by oral vinorelbine either as a single-agent or in combination with capecitabine as a first or second line chemotherapy in the metastatic setting.

Materials and Methods: We analysed 216 MBC pts who started treatment with a full oral CT in 13 centres and 7 countries between 2006 and 2008. To be eligible, pts must have received either as a 1st (56%) or 2nd (44%) line oral vinorelbine as a single agent (54%) or in combination with capecitabine (46%).

Results: Main pts characteristics in the full population (n = 216): median age (range): 61 years (32−87); categories of age: <50: 18%, 50−65: 44%, ⩾65: 38%; hormone receptor positive: 63%; ⩾2 metastatic sites: 58%; visceral metastases: 49%; prior CT: 86%; prior CT for MBC: 44%; prior anthracycline: 69%; prior taxane: 43%; prior anthracycline + taxane: 38%; prior hormone therapy: 63%. Median number of cycles: 6 (range:1−54); 52% of pts received more than 6 cycles. G3/4 toxicities: neutropenia 8%, anaemia 2%, thrombocytopenia 1%, febrile neutropenia/neutropenic infection 2%, nausea 6%, vomiting 4%, diarrhoea 6%, fatigue 6%, hand-foot syndrome 14% (combination with capecitabine), neuropathy 1%, alopecia (grade 2) 1%. Efficacy: disease control rate 77% (95% CI [71−83]), 74% as single-agent, 81% in combination, 82% in 1st line, 71% in 2nd line. Median progression-free survival was 9.7 months (95% CI [8.2–12.6]) in 1st line and 6.6 months (95% CI [5.5−8.5]) in 2nd line. With a median follow up of 17.5 months (1st line) and 14.5 months (2nd line), 128 patients were alive, 34 pts were lost to follow-up and 54 pts were dead at the time of

the analysis. 21 pts were still under treatment. Caregivers described these oral regimens as convenient (81%), well tolerated (84%) and with a good compliance by pts (76%).

Detailed analysis of the results by regimen (single-agent or combination) and line of treatment (1st or 2nd) will be presented during the meeting.

Conclusion: These data from every-day practice confirm, as shown in different clinical trials, that oral vinorelbine is an active and well tolerated chemotherapy for MBC, either as a first or second line in pts pretreated by anthracyclines and/or taxanes. The convenience of its oral administration associated with its good tolerance profile allows continuation of treatment until disease progression without a pre-planned maximum of cycles.

475 Poster

Consistent progression-free survival benefit of capecitabine-bevacizumab in all prespecified subgroups of the RIBBON-1 study in patients with metastatic breast cancer (MBC)

J. O'Shaughnessy[1], V. Dieras[2], S. Chan[3]. [1]*Baylor-Sammons Cancer Center, Texas Oncology, Dallas Texas, USA;* [2]*Institut Curie, Département d'Oncologie Médicale, Paris, France;* [3]*Nottingham University Hospitals NHS Trust, Oncology, Nottingham, United Kingdom*

Background: RIBBON-1 was a randomised, placebo-controlled, phase III study of bevacizumab (A) or placebo (p) in two independently powered cohorts, receiving capecitabine (X) or taxane/anthracycline. Progression-free survival (PFS), the primary endpoint, was significantly greater with A combined with chemotherapy in both cohorts. Here, we report PFS sub-analyses based on prespecified subgroups of the X cohort.

Methods: Patients with HER2-negative MBC were randomised to X 1,000 mg/m^2 b.i.d. on Days 1−14 per 3-week cycle plus A or p. Subgroups analysed included: disease-free interval; number of metastatic sites; age; race; ECOG performance status; sites of involvement; disease measurability; size of target lesions; oestrogen receptor (ER) status; hormone receptor status; triple-negative status; prior therapy, and others.

Results: Baseline characteristics in the Xp control (n = 206) and XA (n = 409) arms were similar. Median PFS was 5.7 (Xp) and 8.6 (XA) months (stratified analysis hazard ratio [HR] 0.69, p = 0.0002). The XA combination improved the HR for PFS across all tested subgroups (table). The risk reduction was consistent with the significant benefit seen in the overall X cohort.

Conclusions: The XA combination was effective first-line therapy for HER2-negative MBC. XA provided clinical benefit to all tested patient subgroups.

Baseline risk factor [n]	Median PFS, months		HR [95% CI], unstratified analysis
	Xp	XA	
All patients [615]	5.7	8.6	0.67 [0.55–0.82]
ECOG performance status			
0 [324]	5.9	9.0	0.70 [0.53–0.92]
1 [288]	4.7	8.2	0.64 [0.48–0.84]
Age			
<50 [173]	4.5	8.0	0.51 [0.35–0.73]
⩾50 [442]	5.9	8.9	0.74 [0.59–0.93]
SLD of target lesions, cm			
<median 6.5 [262]	4.4	8.0	0.67 [0.50–0.89]
⩾median [239]	4.4	8.2	0.65 [0.47–0.88]
Hormone receptor			
positive [458]	6.2	9.2	0.69 [0.55–0.87]
negative [143]	4.2	6.1	0.70 [0.48–1.01]
ER/PgR/HER2-negative			
yes [137]	4.2	6.1	0.72 [0.49–1.06]
no [462]	6.1	9.2	0.68 [0.54–0.86]
Metastatic sites			
<3 [345]	6.4	10.2	0.63 [0.49–0.83]
⩾3 [270]	4.2	6.6	0.74 [0.55–0.98]
Visceral disease			
yes [423]	4.4	8.1	0.72 [0.57–0.90]
no [192]	6.2	10.6	0.58 [0.40–0.83]
Liver metastases only			
involved [24]	6.1	11.3	0.34 [0.12–0.93]
not involved [591]	5.5	8.5	0.69 [0.57–0.84]
Prior adjuvant chemotherapy			
yes [444]	4.4	8.3	0.64 [0.51–0.80]
no [171]	6.7	9.2	0.80 [0.54–1.18]
Prior anthracyclines			
yes [390]	4.4	8.3	0.64 [0.51–0.81]
no [225]	6.7	9.7	0.78 [0.55–1.09]
Prior taxanes			
yes [245]	4.2	8.7	0.62 [0.45–0.84]
no [370]	6.1	8.3	0.72 [0.56–0.92]

476 Poster

PFS by patient subgroup for standard chemotherapies in combination with bevacizumab (BV) in the first-line treatment of HER2-negative locally recurrent (LR) or metastatic breast cancer (mBC): results from RIBBON-1

I. Bondarenko[1], J. Glaspy[2], A. Brufsky[3], O. Lipatov[4], E.A. Perez[5], S. Chan[6], X. Zou[7], S.C. Phan[8], N.J. Robert[9], V. Dieras[10]. [1]*Dnepropetrovsk Municipal Clinical Hospital, Oncology, Dnepropetrovsk, Ukraine;* [2]*UCLA David Geffen School of Medicine, Medicine Department of Hematology and Oncology, Los Angeles, USA;* [3]*University of Pittsburgh, Medical Oncology, Pittsburgh, USA;* [4]*Republican Clinical Oncology Dispensary, General Oncology, Ulfa, Russian Federation;* [5]*Mayo Clinic, Hematology/Oncology, Jacksonville FL, USA;* [6]*Nottingham University Hospital, Oncology, Nottingham, United Kingdom;* [7]*Genentech Inc, Biostatistics, South San Francisco, USA;* [8]*Genentech Inc, BioOncology, South San Francisco, USA;* [9]*U.S. Oncology, Fairfax Northern Virginia Hematology Oncology, Fairfax Virginia, USA;* [10]*Institut Curie, Medical Oncology, Paris, France*

Background: In two phase III trials (E2100 and AVADO), BV in combination with a taxane (T) as first-line therapy for mBC improved progression-free survival (PFS), compared with T alone. In RIBBON-1, combination of BV with standard first-line chemotherapy regimens also improved PFS in mBC patients (pts).

Methods: Pts were randomised 2:1 to BV plus chemotherapy vs placebo (PL) plus chemotherapy. Investigators could choose capecitabine (Cap) (2000 mg/m^2 x 14 d), T (nab-paclitaxel 260 mg/m^2 or docetaxel 75 or 100 mg/m^2), or anthracycline (Anth) (doxorubicin [A] or epirubicin [E] combinations: AC, EC, FAC or FEC-based chemotherapy, q3w). BV or PL were administered at 15 mg/kg, q3w. Key eligibility criteria were LR or mBC, no prior cytotoxic therapy for mBC, ECOG PS 0−1, HER2-negative disease and no CNS metastases. The primary endpoint was investigator-assessed PFS. The Cap cohort and pooled T/Anth cohorts were independently powered and analysed using a 2-sided stratified log-rank test (Cap: 80% power to detect HR = 0.75; T/Anth: 90% power to detect HR = 0.7).

Results: 1,237 pts (Cap=615; T=307; Anth=315) were enrolled. Combination with BV improved PFS (Cap cohort: PL 5.7 months (mo), BV 8.6 mo; p = 0.0002; T/Anth cohort: PL 8.0 mo, BV 9.2 mo; p < 0.0001). In prespecified subgroups, HRs favoured BV treatment arms.

	HR (95% CI)	
	Cap (n = 615)	T/Anth (n = 622)
All pts	0.67 (0.55–0.82)	0.66 (0.54–0.81)
Age, yr		
<65	0.67 (0.53–0.84)	0.63 (0.50–0.78)
⩾65	0.69 (0.47–1.02)	0.83 (0.52–1.34)
Triple negative		
Yes	0.72 (0.49–1.06)	0.78 (0.53–1.15)
No	0.68 (0.54–0.86)	0.61 (0.48–0.77)
No. of metastatic sites		
<3	0.63 (0.49–0.83)	0.65 (0.49–0.86)
⩾3	0.74 (0.55–0.98)	0.64 (0.48–0.85)
Bone-only disease		
Yes	0.47 (0.26–0.87)	0.39 (0.18–0.88)
No	0.70 (0.57–0.86)	0.72 (0.59–0.89)
Visceral involvement		
Yes	0.72 (0.57–0.90)	0.68 (0.54–0.86)
No	0.58 (0.40–0.83)	0.63 (0.42–0.94)
Disease-free interval		
<12 mo	0.81 (0.54–1.21)	0.62 (0.45–0.85)
⩾12 mo	0.63 (0.51–0.79)	0.69 (0.53–0.89)
Prior adjuvant chemotherapy		
Yes	0.64 (0.51–0.80)	0.67 (0.50–0.90)
No	0.80 (0.54–1.18)	0.64 (0.49–0.85)
Prior adjuvant T		
Yes	0.62 (0.45–0.84)	0.65 (0.39–1.07)
No	0.72 (0.56–0.92)	0.66 (0.53–0.83)

Conclusions: The overall treatment effect of combining BV with Cap, T, or Anth in RIBBON-1 is seen across the prespecified clinically relevant subgroups. Results are consistent with the findings of E2100 and AVADO and suggest that BV plus standard chemotherapies provides benefit to HER2-negative mBC pts with various clinical characteristics and disease histories.