resistance to aromatase inhibitor (AI) treatment in hormone receptor (HR) positive metastatic breast cancer (MBC).
Patients and Methods: Postmenopausal women with HR positive MBC received daily letrozole (2.5 mg orally) plus lapatinib (1,500 mg orally). Two cohorts of patients (pts) were studied: pts with primary resistant tumour who had a progressive disease as best response, or pts with secondary resistant tumour who had disease control followed by progression while they were receiving AI. The primary end point was objective rate response (ORR) at week 12. Secondary objectives included time to response, duration of response (DR), clinical benefit (CB), time to progression (TTP), overall survival (OS) and safety. Study was planned to enrol 110 pts in a 2 steps design. Accrual was closed prematurely at the time of planned interim analysis due to low recruitment.
Results: From January 2006 to December 2008, 28pts were enrolled. One patient was not evaluated due to consent withdrawn before treatment's initiation. Median age was 67.2 year old (range 34−93). All tumours were ER positive, 24 tumours were HER2 negative and the 3 HER2 positive are not included in the present analysis. A total of 7 pts reported a metastatic relapse under adjuvant treatment by AI, 18 (72%) pts had aprogressive disease under the first line of hormone therapy by AI for MBC. All cases analyzed were included in cohort 1 defined by secondary resistance to AI. The ORR at 12 weeks was 4% (95% CI: 0.7−20) (1complete response). Stable and progression disease were reported in 25% (95% CI 12−45) and 71% (95% CI 51−85) of cases respectively. At 24 weeks the ORR increased to 8% (95% CI 2−23). CB (responsive or stable disease >6 months) was 21% (95% CI 9−40). At a median follow up of 27 months, TTP and OS were 3.4 (95% CI 2.8−5.4) and 49.2 (95% CI 21.3- notreached) months, respectively.
The most common grade 1 or 2 (81% of pts)drug-related adverse events were diarrhea (41%), asthenia (30%), rash (26%), nausea and vomiting (22%), and mucositis (22%). Grade 3 or 4 drug-related adverse events were diarrhea (7%), rash(4%) and anorexia (4%). No cardiac toxicity was observed. Lapatinib was decreased at 1000 mg in 7% of pts and discontinuedin 7% of pts due to severe diarrhea.
Conclusion: This trial was prematured closed in November 2009 at the time of interim analysis. Interestingly, these preliminary results suggest that the addition of lapatinib to letrozole may be able to overcome tumoural resistance to AI in some pts with HER2 negative tumours.

5070 POSTER

Evaluation of Clinical Efficacy and Safety of Fulvestrant at a Dose of 500 mg in Patients With Metastatic Breast Cancer (MBC)

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Background: The CONFIRM study has shown that fulvestrant (Faslodex®, F), an estrogen receptor (ER) antagonist, at a dose of 500 mg/monthly (mo) is more effective than the 250 mg-dose. Following this study results, the 500 mg/mo-dose was approved in Spain. This study collected real life data on F use at a dose of 500 mg/mo in Spanish patients (pts).
Objective: To evaluate Clinical Benefit Rate (CBR) of F in postmenopausal pts with hormone receptor-positive MBC previously treated.
Material and Methods: We retrospectively evaluated 44 pts with MBC treated with F at a regime of: 500 mg intramuscularly on day 0, then 500 mg on days 14 and 28 and every 28 days thereafter; F 500 mg/mo). Median age was 60 (34−89). Hormonal receptor status recorded in 40 of 44 pts (40/44): 37 pts (92.5%) ER+/PgR+, 3 pts (7.5%) ER+/PgR−. HER2+ (40/44) 11 pts (27.50%). P53 (34/44) is positive in 6 pts (17.65%), high Ki67 (33/44) in 8 pts (24.24%). No visceral metastases in 36/44 pts (81.8%) and visceral metastasis in 8/44 pts (18.2%). Median number of previous treatment regimens: 3 (1−8).
Results: Average of F500 doses administered was 16 (2−42). CBR (37/44) was 84.1%: 6/44 pts (13.6%) with complete response, 17/44 pts (38.6%) with partial response and 14 /44 pts (31.8%) with stable disease.
There was a significant trend of higher CBR in pts without visceral metastases compared to pts with visceral metastases (94.4% vs. 37.5% $p < 0.0001$). CBR was significantly higher in pts with a reduced Ki67 expression compared with pts with high Ki67 expression (100% vs 62.5% $p = 0.0103$). No significant differences in the CBR was observed between HER2 over expressed group and HER2 negative group (100% vs 75.86% $p = 0.1592$). The median time to progression (TTP) was 16.2 months (8.9, 23.1), in pts with clinical benefits was 20.3 months vs 4.1 months in pts without CB ($p < 0.0001$). Median overall survival has not been reached yet. Toxicities occurred in 15 pts (34.1%), more frequent toxicities were: local injection site pain in 6 pts, hot flushes in 6 pts and less frequent were gastrointestinal disorders and fatigue. Three pts (6.8%) died because of disease progression.
Conclusions: F500 shows a remarkable clinical benefit and acceptable TTP even in pts with previously treated MBC with a suitable toxicity profile.

5071 POSTER

Oral Vinorelbine in Combination With Capecitabine as a First Line Treatment in Patients (pts) With Metastatic Breast Cancer (MBC) Previously Treated With Anthracyclines ± Taxanes − Preliminary Results of a Multicentric Phase II Trial in Egypt

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Background: Oral chemotherapy (CT) represents a step forward in the management of MBC with a growing use in this setting. In parallel to pts' preferences for oral drugs, Oral Vinorelbine (V) with Capecitabine (C) is an active full oral combination used for the treatment of Her2 negative MBC with response rates ranging from 48 to 70% in published phase II data. We are reporting preliminary results of a study evaluating efficacy and safety of Oral (V) +(C) as a first line treatment for MBC.
Methods: 37 pts were enrolled in 6 centers in Egypt between July 2009 and July 2010. Eligible pts were female⩾18 years with Her2 negative MBC (84%) or with extensive local recurrence (16%). All pts had measurable disease relapsing after (neo) adjuvant anthracycline ± taxane based treatment, WHO PS⩽2, adequate bone marrow, hepatic and renal functions and no adjuvant CT within the last 6 months.
Pts were treated with Oral (V) 60 mg/m^2 D1, D8 for the first cycle and thereafter 80 mg/m^2 D1, D8 in combination with(C) 825 mg/m^2 twice daily from D1 to D14, every 21 days for 6 cycles. Continuing treatment beyond 6 cycles was possible for pts not having progressive disease. Primary endpoint (EP) was TTP;secondary EPs were RR, OS and safety.
Results: Median age was 55 years [range 34−74];median WHO PS 1 [0−2]. Thirty pts (81%) were post-menopausal, with previous (neo)adjuvant anthracycline-based therapy in 77% and anthracyclines+taxane based in 19%. Median disease-free interval from end of previous CT was 2 years. 25(82%) pts had 2 or more metastatic sites; bone (46%),liver (35%) and lung (32%) being the most frequent sites.
A median of 6 [3−9] CT cycles were given with a total number of 205 cycles delivered. 27 (73%) of pts completed the 6 cycles of treatment. Objective tumour response was achieved in 20 pts (54%), including 6 complete (16%) and 14 partial responses (38%), 10 pts (27%) had stable disease.
Median TTP and median OS are not yet reached.
No WHO G4 toxicities were noted.1 pt (3%) developed G3 nausea-vomiting. G2 neutropenia was reported in 3(8%) of pts and G2 hand foot-syndrome in 5(13%) of pts.5 (14%) and 12 (32%) of pts developed G2 neuropathy and G2 diarrhea respectively.
Conclusions: Preliminary results show that oral (V) + (C) combination is effective and well tolerated in first line MBC pts previously treated with anthracyclines ± taxanes. Results achieved in this study are comparable to data reported in literature. Oral CT appears to be a valid alternative to I.V treatment.

5072 POSTER

First-Line Bevacizumab (Bev) Combined With Paclitaxel (pac) in Older Patients (pts) Treated for HER2-Negative Metastatic Breast Cancer (mBC) in a Routine Oncology Practice Study

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Background: First-line Bev combined with weekly pac significantly improves progression-free survival (PFS) and response rate (RR) vs pac alone in HER2-negative mBC, as shown in E2100. The benefit of Bev

combined with other chemotherapy (CT) agents was demonstrated in AVADO and RIBBON-1. Subgroup analyses of all 3 trials suggest similar benefit with Bev in pts aged ⩾65 y. Data from the ATHENA study give insight into the tolerability of Bev with standard first-line CT in pts ⩾70 y. To understand better the safety and efficacy of first-line Bev–pac in older pts treated in routine oncology practice, we analysed data in pts ⩾65 y in a German non-interventional study.

Materials and Methods: Pts who had received no prior CT for their mBC received Bev–pac per the European label. Efficacy and safety were documented for up to 1 y (or until progression, death or Bev discontinuation if earlier) with additional long-term follow-up.

Results: By Jan 2011, data were available for 818 pts, of whom 262 (32%) were aged ⩾65 y and 133 (16%) were ⩾70 y. Among those aged ⩾65 y, 16% had mBC at diagnosis, 15% had triple-negative mBC, 29% had ⩾3 metastatic sites, 45% had liver metastases and 36% had lung metastases. Prior therapy included (neo)adjuvant CT in 55% and endocrine therapy for mBC in 26%. ECOG performance status was ⩾2 in 10% of pts. The overall RR in pts ⩾65 y was 57% (complete response in 10%); only 9% had progressive disease as best response. The RR in pts aged ⩾70 y was 57%. Median PFS was 9.2 and 9.3 months in pts aged ⩾65 and ⩾70 y, respectively. Key grade ⩾3 adverse events in pts ⩾65 y were: hypertension in 7% of pts (1% grade 4); cardiac toxicity in 1%, arterial thromboembolic events (ATEs) considered Bev related in 1% and GI perforation in <1%. Further CT lines were reported in at least 37% of pts.

Conclusion: The efficacy and safety of Bev–pac in pts ⩾65 y treated in routine practice is consistent with subgroup analyses of E2100, AVADO, RIBBON-1 and ATHENA. ATEs and cardiac toxicity were infrequent; hypertension was manageable and rarely grade 4. Efficacy data are similar to those reported in the whole population. First-line Bev–pac offers an active, well-tolerated therapy, even in elderly pts who may not be candidates for combination CT. ML21165, sponsored by Roche, is fully accrued.

5073 POSTER

Bevacizumab (Bev) Combined With Paclitaxel (Pac) as First-line Therapy for Metastatic Triple-negative Breast Cancer (TNBC) − Analysis of 147 Patients (pts) Treated in Routine Oncology Practice in Germany

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Background: Both progression-free survival (PFS) and response rate (RR) are significantly improved when Bev is combined with 1st-line chemotherapy for metastatic breast cancer (mBC), as shown in three randomised phase III trials (E2100, AVADO, RIBBON-1). Subpopulation analyses suggest meaningful benefit in pts with TNBC (median PFS 10.6 months with Bev–Pac vs 5.3 months with Pac in E2100; hazard ratio 0.49). To further evaluate the efficacy of first-line Bev–Pac in this setting, we analysed efficacy in the subgroup of pts with TNBC treated in a large German observational study of Bev–Pac in routine oncology practice.

Materials and Methods: Pts with HER2-negative mBC received first-line Bev–Pac according to the European label. Safety and efficacy data were collected for up to 1 year (or until progression, death, or Bev discontinuation if earlier). Study endpoints were safety and efficacy. We conducted an exploratory analysis in the subset of pts with TNBC.

Results: Of the 786 pts with complete data at the time of analysis, 147 (19%) had TNBC. Baseline characteristics and efficacy are shown in the table.

Conclusions: In this ongoing study, first-line Bev–Pac demonstrated a 50% RR, median PFS of 7.9 months, and median OS of 15.2 months in pts with TNBC. This compares favourably with efficacy reported for chemotherapy and/or investigational agents, suggesting that Bev–Pac is an effective first-line option in this difficult to treat population. ML21165, sponsored by Roche, has completed accrual.

	TNBC (n = 147)	Non-TNBC (n = 639)[a]
Median age, years (range)	53 (26−79)	59 (28−87)
Age <40 years, %	9	5
Metastatic at first diagnosis, %	15	20
Disease-free interval <1 year, %	53	17
Tumour grade, %		
1/2	27	57
3	66	32
Unknown	7	11
Metastatic sites, %		
Bone	35	59
Liver	24	48
Lung	46	32
CNS	3	2
Prior (neo)adjuvant chemotherapy, %	79	62
(Neo)adjuvant taxane	38	21
RR, %	50	65
Complete response	12	10
Partial response	39	54
PFS		
Events, n (%)	113 (77)	416 (65)
Median, months (95% CI)	7.9 (7.2−9.0)	10.0 (9.1–10.8)
6-month PFS rate, % (95% CI)	65 (58−74)	75 (72−79)
Overall survival (OS)		
Events, n (%)	81 (55)	224 (35)
Median, months (95% CI)	15.2 (13.8–18.5)	Immature
1-year OS rate, % (95% CI)	65 (57−75)	75 (71−79)

[a]ER, PgR, and/or HER2 status positive/unknown.

5074 POSTER

Evaluation of Serum Testosterone and Dehydroepiandrosterone (DHEA) in Indian Women With Breast Cancer

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Background: Among the endogenous sex steroid hormones, estrogens have been implicated in breast carcinogenesis. However, there have been reports of positive association between serum testosterone levels and pre-menopausal and postmenopausal breast cancer. The hyperandrogenism is usually of an ovarian origin but dehydroepiandrosterone (DHEA) and its sulfate (DHEAS) are major androgens of adrenal origin. The aim of this study was to determine serum testosterone and dehydroepiandrosterone levels in female breast cancer patients and study their relationship with menstrual status, parity, early menarche, late menopause and body mass index.

Materials & Methods: 40 patients with histologically proven, untreated, invasive breast cancer and 50 age matched normal healthy females (controls) were studied. Women who had either received hormone replacement therapy or were on oral contraceptive pills were excluded. All women were consented and the study was approved by the Institute Ethical committee. Blood samples were collected after an overnight fast between 8.00–9.00 AM. Serum was separated and stored. Estimation of serum testosterone and DHEA was done by I^{125} radioimmunoassay. Early menarche was defined as onset of menarche before 12 years, late menopause was described as onset of menopause at the age of 50 or more. Body mass index was calculated by the formula Weight (in kg)/[Height (in m)]^2.

Results: The mean serum testosterone levels were significantly higher ($p = 0.01$) in breast cancer patients (0.37 ng/ml) as compared to controls (0.28 ng/ml). This difference was seen in both premenopausal and postmenopausal women. Serum DHEA levels were higher only in post-menopausal breast cancer patients. Postmenopausal breast cancer patients had higher serum testosterone and DHEA levels than premenopausal breast cancer patients ($p < 0.05$). There was no statistically significant difference in serum testosterone levels between nulliparous and parous women but the serum DHEA levels were higher in nulliparous women as compared to parous women ($p < 0.05$). There was no relationship between serum testosterone and DHEA levels and early menarche, late menopause and body mass index.

Conclusion: The serum testosterone and DHEA levels in Indian women with breast cancer indicate significant differences from their Caucasian