Prior (neo)adjuvant CT is permitted if completed ⩾6 months before randomisation (⩾12 months for taxane-containing therapy). Pts receive either Bev+X (21 d cycles: X 1000 mg/m^2 bid d1−14 + Bev 15 mg/kg d1) or Bev+Pac (28 d cycles: Pac 90 mg/m^2 d1, 8, 15 + Bev 10 mg/kg d1, 15). In both arms, treatment is continued until progressive disease (PD), unacceptable toxicity or withdrawal of consent. If one agent is discontinued before PD, the other is continued. The primary objective is to demonstrate non-inferior overall survival with Bev+X versus Bev+Pac (upper limit ⩽1.33 for the 2-sided confidence interval for hazard ratio). Secondary objectives include comparison of overall response rate (RECIST), PFS, time to response, duration of response, time to treatment failure, safety (CTCAE v3) and QoL (EORTC QLQ-30). The recruitment target is 560 pts within 18 months. Assuming 12.5% dropout, a sample size of 490 eligible pts provides 80% power to reject the null-hypothesis of inferiority, assuming 24-month median overall survival with Bev+Pac.

Results: By 31st March 2009, 84 pts from 8 countries had been randomised.

	Bev+X (n = 45)	Bev+Pac (n = 39)
Median age, years (range)	61 (35−77)	60 (36−84)
Post menopausal, n (%)	39 (87)	31 (79)
ECOG PS, n (%)		
0	33 (73)	31 (79)
1	12 (27)	5 (13)
2	0	3 (8)
Stage, n (%)		
I	6 (13)	3 (8)
II	19 (42)	9 (23)
III	11 (25)	11 (28)
IV	9 (20)	13 (33)
n/a	0	3 (8)
ER negative, n (%)	14 (31)	9 (23)
PgR negative, n (%)	15 (33)	13 (33)
Metastatic sites, n (%)		
Liver	16 (36)	15 (38)
Lung	25 (56)	16 (41)
Lymph nodes	24 (53)	21 (54)
Bone	20 (44)	16 (41)
Endocrine therapy, n (%)		
Adjuvant only	18 (40)	15 (38)
LR/MBC only	5 (11)	4 (10)
Both	2 (4)	3 (8)
Adjuvant CT, n (%)	27 (60)	22 (56)
Anthracycline and taxane	6 (13)	4 (10)
Anthracycline, no taxane	18 (40)	14 (36)
Taxane, no anthracycline	0	2 (5)
Other	3 (7)	2 (5)
Mean DFI, months*	59	56

*Excluding 22 pts with primary metastatic disease.

Conclusions: This is the first trial designed to compare two different Bev-containing regimens in LR/MBC. A planned interim safety analysis will be performed when 150 eligible pts have completed 2 cycles of therapy. Updated information will be presented. Trial NCT00600340 is sponsored by CECOG.

5059 POSTER

Epoetin beta therapy in anaemic breast cancer patients receiving chemotherapy: results of a subgroup from a large prospective cohort study

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Background: Anaemia is the most frequent haematological complication in cancer patients (Pts) receiving chemotherapy (CT). Epoetin beta (E) is an Erythropoiesis Stimulating Agent (ESA) approved for the treatment of symptomatic anaemia in adult Pts with non-myeloid malignancies receiving CT. This study is addressing the daily practice of E in anaemic cancer Pts receiving CT and was conducted to assess E use, efficacy, safety and impact on quality of life (QoL).

Material and Methods: This is an analysis of a subgroup (breast cancer Pts) from a large (n = 3265) prospective, multicentric, observational French study in oncology. Eligible Pts were 18 yrs or older, received CT for a solid tumour or a non myeloid haematological malignancy, and treated with E for anaemia. Pts were enrolled between Dec. 2004 and Mar. 2006. Planned follow-up was 4 months. Response to E (i.e. Hb increase of ⩾2 g/dl and/or an achievement of Hb level ⩾12 g/dl without any blood transfusion after E treatment initiation) was the primary endpoint. Data on treatment administration, QoL (FACT-F subscale), transfusions, safety were collected.

Results: 420 Pts with breast cancer were enrolled. Baseline characteristics in this subgroup (mean±SD): age 57.2±11.9 yrs, weight 64.3±13.8 kg, Hb level 10.2±1.0 g/dl. WHO PS 0 (18%), 1 (50%), ⩾2 (32%). Baseline Hb (g/dl): <9 (13.4%), [9−11[(64.4%), [11−12[(21%), ⩾12 (1.2%). Presenting stages were III-IV in 46% of Pts. Median time from initial diagnosis to inclusion: 22.1 months. Pts received first line (43.4%), second line (20.9%), third line or more (35.7%) CT. PolyCT was administered in 72.4% of the Pts: taxanes (42%), anthracyclins (45.1%), platinum-based CT (8.3%), targeted therapy (13.4%). At inclusion, prior radiotherapy was given in 54.1%, prior ESA in 13.9% and iron supplementation in 42.3% (1.9% intravenously). Almost all Pts (99.5%) were treated on a once weekly E regimen at a median starting dose of 30.000 IU, i.e. about 450 UI/kg. Response rate to E was 63.3% at the end of the study [95%CI: 58.1−68.2]. Mean FACT-F score improved from 27.1±11.3 at inclusion [95%CI: 25.6−28.6] to 33.5±10.5 at the end of study [95%CI: 32.1−34.9]. Only 15.2% of Pts required red blood cell transfusions. Epoetin beta was well tolerated. Thromboembolic events were reported only in 5 pts (1.3%).

Conclusions: This study conducted in routine practice confirms that epoetin beta is effective and well-tolerated to treat CT-induced anaemia in breast cancer Pts.

5060 POSTER

Comparable efficacy of low-dose (1,000 mg/m^2 b.i.d.) capecitabine and standard-dose (1,250 mg/m^2 b.i.d.) capecitabine administered for ⩾6 weeks in older women with advanced breast cancer

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Background: Capecitabine (X) is a tumour activated oral fluoropyrimidine that generates 5-FU preferentially in tumour tissue. In patients with metastatic breast cancer, X has demonstrated consistently high efficacy with a favourable safety profile. This phase II, open-label, single-centre, sequential study (M66106) evaluated the safety and efficacy of X in older women with advanced breast cancer (ABC).

Methods: Patients were aged ⩾65 years, had a confirmed diagnosis of ABC, with measureable or evaluable disease in at least one non-irradiated site, ECOG performance status 0−2, a life expectancy ⩾3 months and adequate bone marrow, renal and hepatic function. Patients were previously untreated or had received ⩽1 prior chemotherapy and/or ⩽2 hormonal regimens for metastatic disease. Previous 5-FU-based chemotherapy was only permitted if completed ⩾1 year before study enrolment. X was initially administered at a standard dose of 1,250 mg/m^2 b.i.d. on days 1−14 every 21 days, with the treatment cycle repeated at least once. Due to the poor tolerability of standard-dose X in this population, the starting dose of X for all patients enrolled after 27 October 2000 was reduced to 1,000 mg/m^2 b.i.d. (low-dose X). The primary study endpoint was tolerability, while secondary endpoints included response rate and time to disease progression (TTP). Tumour assessments (WHO criteria) were made at 6-weekly intervals and at study withdrawal. Safety and efficacy data for the ITT population (all patients who received ⩾1 course of study treatment) have been published previously [Bajetta et al. JCO 2005;23:2155−61]. Here we report efficacy results for the standard population (all patients who received ⩾6 weeks of X at ⩾50% of the planned dose).

	Low-dose X (1,000 mg/m^2 b.i.d.) [n = 38]	Standard-dose X (1,250 mg/m^2 b.i.d.) [n = 24]
Complete response, n (%)	1 (3)	1 (4)
Partial response, n (%)	15 (39)	12 (50)
Progressive disease, n (%)	1 (3)	1 (4)
Stable disease, n (%)	21 (55)	10 (42)
Median TTP, days (range)	151 (64–244)	140 (46–252)

Results: Sixty two patients were included in the standard population, of which 38 received low-dose X, with an objective response rate of 42% (16/38), and 24 received standard-dose X, with a response rate of 54% (13/24). Median TTP was 151 and 140 days, respectively.
Conclusions: These results suggest that lower-dose X (1,000 mg/m^2 b.i.d.) has comparable efficacy to standard-dose X (1,250 mg/m^2 b.i.d.) when administered for $\geqslant$6 weeks to older patients with ABC.

5061 POSTER

Gemcitabine and carboplatin in heavily pretreated metastatic breast cancer: predictive value of breast cancer subtypes

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Background: Patients (pts) with breast cancer (BC) are increasingly exposed to anthracyclines and taxanes either as adjuvant treatment or during initial therapy of metastatic disease. This trial studied the efficacy and safety of gemcitabine and carboplatin (GC) in unfavorable subgroup of pts affected by heavily pretreated metastatic BC.
Patients and Methods: We included HER-2 negative metastatic BC refractory or resistant to previous anthracycline- and taxane-based chemotherapy, and HER-2 positive metastatic BC with at least two progressions of disease during protracted trastuzumab-based therapy. Other inclusion criteria were: age $\geqslant$18 years, ECOG PS of 0−2, RECIST-defined measurable MBC. Treatment consisted of gemcitabine (1000 mg/m^2 iv on days 1 and 8 and carboplatin (AUC 5 iv on day 1) applied every 3 weeks.
Results: Forty-two pts were registered. The 1-year disease control rate (PR + CR + SD) was 62%, with a median time to progression (TTP) of 7.0 mos (range 1−12 mos) and a median overall survival (OS) of 10.5 mos (range 1−34 mos). Overall, grade $\geqslant$3 toxicities included neutropenia (45%), and thrombocytopenia (7%). Other non-hematologic toxicities were irrelevant. We performed a subgroup analysis in order to evaluate the prognostic and predictive significance of immunohistochemically defined subsets of pts. According to the definition proposed by BCIRG trialists (Hugh J, et al. J Clin Oncol 2009; 27: 1168–1176), pts were grouped as triple negative (ER negative, PR negative, HER-2 negative), HER-2 (HER-2 positive, ER negative, PR negative), Luminal B (LB) (ER positive and/or PR positive and either HER-2 positive and/or Ki67^{high}), and Luminal A (LA) (ER positive and/or PR positive and HER-2 negative and Ki67^{low}). LA pts had lower 1-year disease control rate than other subtypes (LA 34% vs others 74%; Fisher's exact p = 0.02), shorter PFS (LA 2.4 mos vs others 6.3 mos, HR = 0.62; 95% CI = 0.28−1.39; Log-rank test p = 0.015), and shorter OS (LA 7.5 mos vs others 11.7 mos, HR = 0.52, 95% CI = 0.23−1.16; p = 0.034).
Conclusions: Chemotherapy with GC is an effective and generally well-tolerated treatment option for intensively pretreated pts with metastatic BC. Pts affected by LA subtype BC seem to fare poorly as compared to others subtypes. Specific gene-expression signature between LA and other subtypes might explain the different outcome.

5062 POSTER

Fulvestrant in heavily pre-treated ER-positive post-menopausal metastatic breast cancer patients: final update of a phase II study

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Background: Fulvestrant (F), an estrogen receptor down-regolator drug, is effective in ER +ve post-menopausal metastatic breast cancer (MBC) progressing on Tamoxifen (Howell A., 1995) and has demonstrated overall response rates (OORR), time to progression (TTP) and overall survival (OS) comparable with Anastrozole (Howell A., 2000 and Mauriac L., 2003). The aim of the study was to evaluate efficacy and toxicity of F in ER+ve post-menopausal metastatic breast cancer patients (pts) heavily pre-treated both with hormonal agents and chemotherapy.
Materials and Methods: From 5/2006 to 12/2008, F 250 mg i.m. q 28 days was administered to 27 ER+ve post-menopausal MBC pts, median age 64 (range 39−81). Fifteen pts (55.5%) had received prior chemotherapy for MBC, and all pts had received prior hormonal therapy (median 2 drugs: range 1−4). Metastatic sites were: 20 bone, 8 liver, 8 lung, 9 nodes, 5 skin, 5 breast. A total of 186 cycles of F were delivered, median 6 cycles/pt. (range 2−24). All pts were valuable for toxicity and for efficacy.
Results: Overall response rate (OORR) was 13.7% (0/27CR, 4/27PR) and stable disease (SD) was observed in 9 pts (33.3%); clinical benefit (OORR + SD) was obtained in 13/27 pts. (48.1%). Median TTP in all pts was 7+ mos (range 2−30+ mos.) and in pts obtaining clinical benefit was 9+ mos (range 4−30+ mos). Median OS was 14 mos. (range 3−41+ mos) and 20 mos. (range 9−41+) in pts obtaining clinical benefit. No G3−4 toxicities were observed: G1−2 coetaneous rash occurred in 3/27 (11.1%) pts. and G1−2 asthenia in 3/27 (11.1%) pts.
Conclusions: This phase II study demonstrated that F is safe and effective in heavily pre-treated ER+ve post-menopausal MBC pts. Results from this phase II trial are comparable with those observed in pivotal trials, when F was used as 2nd line treatment, suggesting F has comparable efficacy in heavily pretreated MBC pts.

5063 POSTER

Paclitaxel combined with ifosfamide in anthracycline- and docetaxel-pretreated metastatic breast cancer

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Background: The aim of this study was to evaluate the efficacy and tolerability of paclitaxel and ifosfamide in anthracycline-/docetaxel-pretreated breast cancer.
Materials: Advanced breast cancer patients who had received prior anthracycline- and docetaxel-based chemotherapy were eligible. Paclitaxel (175 mg/m^2 i.v. in a 3-hour infusion) on day 1 and ifosfamide (1.5 g/m^2 i.v. in a 15-min infusion) on days 1−3 were given every 3 weeks for a maximum of 9 cycles. Tumor response was assessed by using RECIST criteria every 2 cycles.
Results: Thirty-four patients (33 with metastatic and 1 with locoregional disease) were enrolled. Anthracycline- and docetaxel-based chemotherapy were previously given to 1/17/13 and 1/12/21 patients in neoadjuvant/adjuvant/metastatic settings, respectively. Three patients did not previously receive anthracycline due to abnormal cardiac function. The response rate under the intent-to-treat analysis was 27.6% (8/34; all partial responses) with the median response duration of 14 months. The median disease control rate was 70.6%. The median progression-free and overall survival was 5.9 and 8.5 months, respectively. A total of 174 cycles of chemotherapy were delivered with median 6 cycles. In terms of toxicities, grade III/IV neutropenia was 46.6% (81/174 cycles) with febrile neutropenia of only 1.7% (3/174 cycles). Grade III/IV nonhematological toxicities were peripheral neuropathy (17.6%; 6/34 patients), infection (11.8%; 4/34 patients) and liver enzyme elevation (2.9%; 1/34 patients). There was one treatment-related death from sepsis.
Conclusions: Paclitaxel combined with ifosfamide was effective and tolerable in anthracycline-/docetaxel-pretreated advanced breast cancer. Overcoming docetaxel resistance by using paclitaxel in combination with ifosfamide needs to be addressed via further investigation.

5064 POSTER

Zoledronic acid in breast cancer patients with bone metastasis

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Background: Zoledronic acid is a nitrogen containing bisphosphonate that has been proven to reduce oestoprosis and cancer induced osteolysis. Zometa has been the treatment of choice for the prevention of skeletal complication of bone metastasis (pain, pathological fracture) in patients with breast cancer, which have a significant impact on the quality of life of patients. The aim of the study is to evaluate the efficacy and tolerability of Zometa in improving pain scores and quality of life in patients with bone metastasis secondary to breast cancer.
Material & Methods: 150 patients with bone metastasis and pathologically confirmed carcinoma of the breast during the period between January 2004 and January 2006 were enrolled, ECOG PS 0−2, and adequate renal function. Treatment consisted of Zometa 4 mg IV over 15 minutes repeated every 3−4 weeks concurrently with chemotherapy and/or hormonal therapy or radiotherapy if treatment was needed. Zometa administered continuously until impairment in the performance status, progression of the disease or severe adverse events. Pain was evaluated by present pain intensity from McGill Melzack (PPI) questionnaire, quality of life (QOL) was assessed with functional assessment of cancer therapy (FACT) questionnaire.
Results: The median age was 48 years (range 30−65 years), median PS 1, extent of disease (metastasis): 60 patients (40%) had only one bone