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Bevacizumab-based Treatment in Breast Cancer (BC) Patients With Cutaneous Metastases − a Subgroup Appropriate for Targeting Angiogenesis?

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Background:The value of targeting angiogenesis in BC has recently been questioned. Therefore, the identification of subgroups that might benefit from targeting angiogenesis is needed. Bevacizumab (BEV), the first inhibitor of angiogenesis, has been shown to improve outcome in metastatic BC. The results from patients with BC and skin dissemination are presented here.
Patients and Treatment: From 105 patients (pt) with advanced BC treated with BEV/paclitaxel (95pt) or BEV/docetaxel (10pt), 30pt (29 Female/ 1 Male, 33−75 years old, with median age 52 years) with cutaneous metastases exclusively [3pt] or in combination with other sites of metastases [27pt], were separately studied. In 9pt had extensive lymphatic dissemination while in 8pt de novo inflammatory BC with skin dissemination was present. Forteen and 16 pts were treated in 1st and 2nd line respectively.
Results: The overall response rate was 55%, 38% in 1st and 2nd line treatment respectively. Although complete clinical remission was not achieved in pt with cutaneous metastases, a major PR in 13/14 pt and 15/16 pt treated with 1st and 2nd line treatment respectively (dissociated response in 19pt) for >12 months in the majority of patients was observed. Yet, rechallenge of BEV in 1pt after a long BEV-free interval resulted in a new remission. All patients with inflammatory breast cancer responded (cPR, no pCR).
Conclusions: Although the small number of patients does not allow for firm conclusions, the almost uniform response observed in our patients with BC and cutaneous metastases (28/30pt, 93.3%) should be mainly attributed to BEV, given that the usual response rate to cytotoxics either in monotherapy or combinations is clearly inferior. Moreover, the dissociated response observed in 63% of patients corroborates this statement. If these findings are confirmed in more patients and by others, a subgroup of patients with advanced BC with antiangiogenic treatment "sensitivity" may emerge.
Also, the identification of predictive markers for targeting angiogenesis may be incited from such observations using prospective studies.

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Lapatinib (L) in Combination With Paclitaxel (P) is an Effective and Tolerable Treatment in HER2-overexpressing Metastatic Breast Cancer (MBC) Patients

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Background: The recently completed phase III randomized, double-blind EGF104535 study compared lapatinib plus paclitaxel (L+P) versus P alone in patients with HER2-positive (MBC). The study was conducted in the Asian-Pacific, Eastern European and South American regions.
Methods: Pts with centrally confirmed HER2-positive (FISH) MBC and measurable disease were randomized to L 1500 mg daily + P 80 mg/m^2/wk 3 out of 4 wk or to P 80 mg/m^2/wk 3 out of 4 wk alone. Pts were administered P for 6 cycles with additional cycles at investigator discretion, and continued on blinded randomized therapy until disease progression (PD). At time of PD, there was an optional monotherapy extension to allow pts on P alone arm to receive L monotherapy. The primary endpoint of the study was overall survival (OS); secondary endpoints included progression-free survival (PFS), overall response rate (ORR), clinical benefit rate (CBR) and safety.
Results: The intent-to-treat and safety populations included 444 pts (N = 222/arm) and 443 pts (N = 222 in L+P; 221 in P), respectively. Baseline demographics were well-balanced between treatment groups. The most frequent adverse events (AEs) were diarrhea (L+P, 77%, Grade 3/4 20/0; P, 29% Grade 3/4, <1/<1) and neutropenia (L+P, 77% Grade 3/4, 35/16; P, 47%, Grade 3/4, 15/5). As expected, the incidence was higher in L+P; however the majority of events resolved. Of note, only 4% in L+P reported febrile neutropenia. Cardiac events were of low grade, asymptomatic, and mostly reversible. The incidence of hepatic events was similar in each arm and none met the clinical definition of Hy's Law. There were no fatal AEs in the L+P arm. OS was significantly longer in L+P compared with P alone [Cox Regression: Treatment Hazard Ratio (HR) (95% CI) = 0.64 (0.49, 0.82), $p = 0.0005$, Kaplan–Meier estimates: median OS 27.8 mos (95% CI = 23.2, 32.2) vs. 20.5 mos (95% CI = 17.9, 24.3), respectively]. Median PFS was 9.7 mos (95% CI = 9.2, 11.1) compared with 6.5 mos (95% CI = 5.5, 7.3), in the L+P vs P, respectively [HR (95% CI) = 0.52 (0.42, 0.64), stratified log rank $p < 0.0001$].
Conclusion: The combination of L+P showed a statistically significant and clinically meaningful survival advantage. Secondary endpoints support the observed clinical benefit. The combination of L+P was well tolerated.

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First-line Bevacizumab Plus Taxane-based Chemotherapy for Metastatic Breast Cancer (mBC)

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Background: Combining Bevacizumab with first-line Taxane-based chemotherapy significantly improves progression-free survival (PFS) and response rate (RR) compared with taxanes alone in HER2-negative mBC, as shown in 3 phase III trials. Until recently docetaxel and paclitaxel were registered for routine use based on those results. The aim of this retrospective study was to assess the efficacy and safety of docetaxel–bevacizumab versus paclitaxel–bevacizumab in patients (pts) with HER2-negative mBC.
Material and Method: All pts with histologically/cytologically confirmed HER2-negative mBC treated between July 2006 and March 2010 by either bevacizumab plus docetaxel, or bevacizumab plus paclitaxel were studied. Bevacizumab was continued until disease progression or unacceptable toxicity. All pts were eligible if they have not received previous cytotoxic therapy for metastatic disease. Previous hormonal therapy for mBC or cytotoxic adjuvant chemotherapy was allowed.
A search for significant factors related to the length of progression free survival (PFS) was conducted. The following variables were studied: age, hormonal receptors status, liver involvement, number of metastatic sites involved, previous exposure to taxanes containing chemotherapy in adjuvant setting.
Results: Between July 2006 and March 2010, 217 pts were treated first-line bevacizumab plus taxane-based chemotherapy for mBC.
Demographic and baseline disease characteristics of this ITT population were generally well balanced between treatment arms. Preliminary results of 86 reported a similar PFS between two treatment arms, with median values of 10 months [8−13] (HR = 1.32 [95% CI 0.81–2.17], p = 0.26). Only hormonal receptors status positive was statistically significant for PFS (HR = 0.52 [95% CI 0.32–0.85], p = 0.005).
Conclusion: In our study, we found that two treatments were similarly effective in patients with HER2-negative mBC. The safety of Bevacizumab-Taxane therapy were consistent with results from randomized first-line trials. Further details and analysis will be presented during ECCO.

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Non Basal Like Phenotype: a Potential Predictive Factor for the Effectiveness of Neoadjuvant Chemotherapy in Triple Negative Breast Cancer

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Background: Triple negative breast cancer (TNBC) negative for estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2) is a distinct breast cancer subtype, which remains a great clinical challenge. TNBCs have been shown to respond to neoadjuvant chemotherapy (NAC) but it is an heterogeneous disease. In this study, we analyzed TNBC patients who were treated with NAC at Centre Jean Perrin (Clermont Ferrand, France) over a recent 9-year period to clarify the predictive factors for the effectiveness of the NAC.
Patients and Methods: Seventy TNBC patients underwent NAC with anthracyclines and taxanes from January 2002 to December 2010. Pre-therapeutical and surgical specimens were studied for expressions of ER, PgR, HER-2, epithelial growth factor receptor (EGFR), cytokeratin 5/6, Ki-67, by immunohistochemistry (IHC). We analyzed clinicopathological factors and molecular markers in regard to the response to NAC. Basal-like subtype was defined as CK5/6 positive and/or EGFR positive.
Results: The age of the patients ranged from 30 to 72 years old (median 50). The median tumour size before chemotherapy was 50 mm (range, 14–90 mm) and 40 patients had clinically positive nodes. Among the cases