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Rechallenge With Docetaxel After a First Response in Metastatic Breast Cancer − a Significant Activity With Manageable Toxicity

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Background: Docetaxel (Dc) is a major drug in metastatic breast cancer (MBC). At progression, rechallenge with docetaxel can be discussed based on the previous efficacy and tolerance. No data on this pragmatic strategy are avalaible in MBC.
Methods: We identify 73 patients (pts) with the following criteria: (i) objective response or stable disease with a previous line of treatment with Dc in MBC, (ii) rechallenge with Dc (on a three weekly schedule) for progressive disease after a minimal Dc-free interval of 3 months. The main objectives were to evaluate the overall response, the time to progression (TTP) and toxicity at reintroduction of TXT.
Results: Median age was 57 years (34−84). Patients had already received 1, 2, 3, $\geqslant$ 4 lines of chemotherapy (including the first use of Dc) in 20%, 47%, 18% and 15% of cases, including capecitabine, anthracycline, and vinorelbine in 56%, 40% and 21% of cases, respectively. Visceral disease was described in 80% of cases. The median number of cycles was 6 (1−18). Overall, 57 pts (78%) obtained a symptomatic benefit from the treatment. Among the 32 pts (44%) with disease assessed according to RECIST criteria, 14 (44%) had a partial response and 11 (34%) had a stable disease >3 months. Among the 41 pts without an available evaluation according to RECIST, 22 (54%) experienced a biological partial response. The median TTP was 5.9 months (95% CI [4.9−6.9]). The median overall survival (OS) was 10.8 months (95% CI [9.1–12.5]). Toxicity was manageable. Forty seven pts (64%) reported grade 1/2 toxicity, mostly mucositis (37%), asthenia (34%) and nails toxicity (30%). Twenty six pts (36%) experienced grade 3/4 toxicity, mostly neutropenia (16%) and fluid retention (11%). Predictive factors of benefit at re-introduction of TXT are in progress.
Conclusion: This retrospective analysis supports the pragmatic strategy to retreat patients with MBC with Dc provided that this drug had shown previous activity and was stopped for other causes than progression.

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Improvement of Neoadjuvant Therapy Response by Using 4FE100C Vs 6FE100C in Locally Advanced Breast Cancer

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Background: Cytostatic agents such as antracyclines have showed to be effective in locally advanced breast cancer. Epirubicin used as a single agent or in combination can be used in higher dose without severe toxicity. Our main goal was to assess the difference between two schedule regimens based on $4FE_{100}C$ and $6FE_{100}C$.
Materials and Methods: Patients diagnosed with locally advanced breast cancer during 2003–2007 were included (n = 96). One group of patients (n = 48) received Cyclophosphamide 500 mg/m^2, Epirubicin 100 mg/m^2 and 5-Fluorouracil 500 mg/m^2 ($FE_{100}C$) during 4 cycles every 21 days. Other group of patients received 6 cycles of the same scheme. All patients were followed by surgery and radiotherapy.
Results: Objective Response (OR) was 62.5% for $4FE_{100}C$ group and 85.7% for $6FE_{100}C$ group ($p < 0.003$); we determined a complete response rate (CR) of 35.4% with $6FE_{100}C$ (CI 95%: 22−48%, n = 17) and complete pathologic response (pCR) for $6FE_{100}C$ was 20.8% vs 12.5% ($p = 0.04$; OR 1.57, CI 95%: 22−48%, n = 10). The toxicity by $6FE_{100}C$ was mild to moderate vomiting (52.4%, $p = 0.001$), hematologic toxicity was not significant ($p = 0.14$). There was not observed other toxicities.
Conclusions: In the analysis the clinical benefit was better in $6FE_{100}C$ group, the largest number of cycles was a predictor of OR. It was confirmed a significant improvement in the pCR and CR using intensified Epirubicin dose ($6FE_{100}C$). Surprisingly the toxicity in both schemes was similar and tolerable. Finally, we demonstrated that the use of $6FE_{100}C$ compare with $4FE_{100}C$ increase 1.6 folds the pCR in locally advanced breast cancer patients.

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Breast Cancer Subtype and Survival in Metastatic Patients Treated With Bevacizumab

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Background: HER2 negative breast cancer is classified into 3 distinct subtypes known as triple negative, luminal A and luminal B, which differ for gene expression profile, prognosis and treatment outcome. Patients with luminal B early breast cancer weakly respond to primary hormono- and chemo-therapy and present poor clinical outcome. This study aimed to analyze the implication of breast cancer subtype on survival of HER2 negative metastatic breast cancer (MBC) patients treated with bevacizumab at any time.
Methods: Retrospective survival analyses were performed in HER2 negative MBC patients treated with bevacizumab between July 2005 and June 2010, according to clinical characteristics and breast cancer subtypes. Patients were classified as triple negative (ER and PR negative), luminal A (ER and/or PR positive and Ki67 < 14%) and luminal B (ER positive and PR negative or Ki67 >14% or grade III). Survival estimates were analyzed according to each breast cancer subtype.
Results: A total of 132 patients were identified. Six patients were excluded for incomplete information. Median age at diagnosis was 48 years (range, 27−79 years). Median overall survival (OS) was 41.8 months (CI 95%: 36.62–46.98). According to breast cancer subtype, OS was 32.38 months (CI 95%: 24.23–41.43), 40.8 months (CI 95%: 33.11–48.49), and 48.27 months (CI 95%: 37.47–59.06) in patients with triple negative (n = 39), luminal B (n = 45) and luminal A (n = 42) MBC, respectively. A trend toward worse survival was observed for triple negative breast cancer patients ($p = 0.06$).
Conclusions: This analysis on the use of bevacizumab in a daily clinical practice setting shows high OS rate across all breast cancer subtype. These findings might help on the design of future studies with antiangiogenics in breast cancer treatment.

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Trastuzumab Responder Will Show Good Repose to Lapatinib

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Background: Combination of Lapatinib (L) plus capecitabine (C) is commonly used in patients (pts) with trastuzumab (T)-pretreated HER2-positive metastatic breast cancer (HER2+MBC), although, it is difficult to estimate one's response to L+C therapy in practice.
Materials and Methods: HER2+MBC pts resistant to T-based regimen(s) received L+C. L was administered 1250 mg/body daily and C was given 2000 mg/m^2/day from day 1 to 14 in a 3-week cycle. Clinical efficacy was assessed by 2 (or 3) courses.
Results: Thirty-two female, T-resistant HER2+MBC pts (31 immunohistochemically HER2-positive, 1 FISH-positive), median age of 57 (range 33−72) were treated with L+C. Twenty-six pts (81.3%) had visceral lesion(s) and 8 pts (25.0%) had histories of central nervous system involvement. Median T-based regimens pts received prior to L+C was 2 (range 1−7), and 15 pts (46.9%) were heavily (>2) pretreated. Of 28 pts who have complete history of previous therapies, exposed to T from 56 to 2226 (median 837) days prior to L+C. Twenty-three pts discontinued therapy because of disease-progression (21 pts) or toxicity (2 pts). Of 21 resistant pts, 9 re-challenged T-based therapies, 3 received HER2-nonspecific regimens including clinical trials and 9 underwent supportive care. Of 29 evaluable pts, 1 (3.1%) achieved complete response (CR), 3 (9.4%) showed partial response (PR) and 15 (46.9%) maintained stable disease (SD) for more than 16 weeks. Median progression-free (PF) was 154.0 days (95% confidence interval 103.9–204.1), and median overall survival (OS) was 426.0 days (95% CI 305.5–546.5). Pts heavily pretreated (2 > T-based regimens) showed a trend of inferior PF (202.0 vs. 151.0), although, it was not statistically significant ($p = 0.23$). Furthermore, numbers of prior T-based regimens did not affect OS ($p = 0.72$). Interestingly, pts who showed a minor response, less than 360 days of treatment duration, to prior T-based regimen(s) had a trend of inferior PF (median 108.0 vs. 161.0, $P = 0.18$) and OS (337.0 vs. 448.0, $P = 0.01$).
Conclusions: Within our observation, lapatinib plus capecitabine showed a clinical effectiveness against patients with trastuzumab-pretreated