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The risk factors for breast cancer (BC) related lymphedema (LE); is vascular endothelial growth factor (VEGF) one of them?

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Background: Arm LE is one of the major morbidities after surgery for BC. Although LE is related with patient', disease and treatment related factors, growth factors are suggested to cause LE. VEGF-C and D are critical regulators of lymphangiogenesis. The aims of this study were to determine risk factor of LE in patients underwent mastectomy for carcinoma and also demonstrate whether serum VEGF-C, D levels and VEGF-C/D ratios correlate with LE in patients with BC.
Materials and Methods: The serum levels of VEGF-C, VEGF-D are determined by ELISA in patients with BC before treatment (n = 68). All patients had level II or III axillary dissection (AD). Circumferential measurements were used and LE was accepted if differences between affected and contralateral arms showed greater than 2 cm in four different special points. Comparison of growth factor levels and clinicopathological variables between LE and non-LE patients, were analyzed using the Mann-Whitney U or Kruskal-Wallis and X^2 where appropriate.
Results: The mean age of the patients was 50.7±13.1 years. The mean follow up was 30.1±7.5 (8–58 months). LE was seen in 16 patients (23.5%). Forty-three (63.2%) patients underwent level II AD while 36.8% (n = 25) of them had level III AD. The mean number of dissected lymph node (LN) was 19.8±8.3 (7–46). The mean number of LN metastases was 8.6±9.6 in patients with LE while it was 3.1±6.8 in patients without LE (p = 0.002). The patients with 4 or more LN metastases have higher chance of LE than LN less than 4 (15.8–45.5%, p = 0.042). The mean BMI was not different in patients with LE than patients without LE (p > 0.05). The mean size of the tumor in the LE patients was 4.2±2.8 cm, while it was 2.7±1.5 cm in the patients without LE (p = 0.047). Patients with advanced stage tumors (p = 0.001), receiving adjuvant radiotherapy (p = 0.024) were more likely to have LE. The mean level of VEGF-D was significantly lower in patients with LE than the patients without LE (p = 0.038) while the mean VEGF-C was not different in patients with or without LE (p > 0.05). VEGF-C/D ratio was higher in patients with LE than without LE (p = 0.052).
Conclusion: The present study shows that decreased VEGF-D levels associated with presence of LE in patients underwent mastectomy for carcinoma. VEGF-D is one of the major players in promoting lymphatic vascular growth both during development and in pathological conditions. Decreased levels of VEGF-D may be cause decrease in lymphangiogenesis and end up with LE.

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Phase II study of an all-oral regimen combining oral vinorelbine with capecitabine as first-line chemotherapy (CT) of metastatic breast cancer (MBC)

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Background: Vinorelbine and Capecitabine are effective in MBC, both drugs are orally available and easy to administer. In the phase I part of the study, oral Vinorelbine 60 mg/m^2 weekly with capecitabine 1000 mg/m^2 bid days 1 to 14 q3wks was established as the recommended dose [F. Nolè et al, Ann Oncol, 2006; 17(2): 322–329]. We investigated this all-oral combination regimen in the phase II part of the study to test the activity and the tolerability of the combination in first line MBC patients (pts).
Methods: Fifty-two pts received the combination. Patients had to have one measurable lesion (WHO) and adequate baseline organ functions. The primary endpoint was response rate and secondary endpoints were progression free-survival, survival and safety.
Results: median age 60 years (range 29–77), PS 0–1: 96.2% pts, 42 pts (80.8%) had visceral metastasis and 82.6% had 2 or more organs involved, 41 pts (78.8%) received prior neo and/or adjuvant chemotherapy consisting of CMF and/or anthracyclines (38 pts), anthracyclines and taxanes (3 pts). All patients were evaluable for safety and 42 were evaluable for efficacy after panel review.
Results: A total of 396 cycles were given, median 7 (range 1–18). Grade 3–4 neutropenia occurred in 46.2% of pts and 14.1% of cycles with only one episode of febrile neutropenia. Grade 3 anemia and thrombocytopenia occurred in one patient each.The incidence of grade 3–4 related non-hematological toxicity was low; one patient (2%) experienced grade 4 abdominal pain. Grade 3 events were: thrombosis in 5 pts (9.6%), fatigue, vomiting and abdominal pain in 4 pts (7.7%), stomatitis in 3 pts (5.8%), dehydration, neurosensory in 2 pts (3.8%), nausea, HFS, anorexia, constipation, diarrhoea, chest pain, dyspnoea and weight loss in one pt (1.9), each. There were 2 CRs and 21 PRs, with an overall response (OR) of 44.2%, [95% CI: 30.5–58.7%] and 54.8% [95% CI: 38.7–70.2%] in the ITT and evaluable populations, respectively. Fifteen patients had stable disease, median duration: 6.1 months (range 2–10.3). After a median follow up of 13 months, median PFS and survival are not reached yet.
Conclusion: This combination is effective in first line MBC and offers the additional advantages of a better patient convenience without the stress of repeated injections and reduced time spent in hospital. The combination of oral Vinorelbine and Capecitabine can be considered as a valuable option for treatment of MBC.

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Randomized phase 3 clinical trial comparing 130-nanometer albumin bound paclitaxel with solvent-based paclitaxel in Chinese patients with metastatic breast cancer

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Background: The results of a large clinical study comparing solvent-based paclitaxel (Taxol®) 175 mg/m^2 with 130-nM-albumin-bound (nab-) paclitaxel (Abraxane®) 260 mg/m^2 demonstrated that nab-paclitaxel had greater efficacy and a favorable safety profile in patients (pts) with metastatic breast cancer (MBC; Gradishar et al., JCO, 2005; 23:7794). The maximum tolerated dose of nab-paclitaxel was 300 mg/m^2 infused over 30 minutes without premedication in Chinese pts with solid tumors (Teng et al., Ai Zheng, 2004;23:1431). The aim of the current randomized study is to compare the response rate, time to progression (TTP), progression-free survival (PFS), and safety of nab-paclitaxel with those of solvent-based paclitaxel in Chinese pts with MBC.
Methods: In this open-label, multicenter study, 210 pts with MBC were assigned to receive either solvent-based paclitaxel 175 mg/m^2 intravenously (IV) over 3 hours every 3 weeks (q3w) with standard premedication or nab-paclitaxel 260 mg/m^2 IV over 30 minutes q3w with no premedication for 1–6 cycles. The primary endpoints were the overall response rate (ORR, complete or partial response) and toxicity. Stable disease (SD) at ⩾16 weeks, TTP, and PFS were also measured. All pts who received at least 1 dose of study drug were evaluable for study endpoints.
Results: 210 pts (median age, 50 years; 70% postmenopausal) were enrolled from 29 June 2005 to 1 August 2006. Efficacy results are summarized in the Table. The common toxicities occurring at ⩾20% were alopecia (79%), peripheral neuropathy (PN; 75%, 6% grade 3), neutropenia (66%), leucopenia (61%), myalgia (39%), arthralgia (24%), and nausea (23%) and were similar between groups (P = NS).

	nab-paclitaxel 260 mg/m^2 (n = 104)	P-value	Solvent-based paclitaxel 175 mg/m^2 (n = 106)
ORR	56 (54%)	<0.001*	31 (29%)
Median TTP (months)	8.5	0.033**	6.5
95% CI	7.3–15.7		4.7–10.3
Median PFS (months)	8.1	0.046**	6.2
95% CI	6.9–10.4		4.7–8.0

*CMH; **log rank test.

Conclusions: Compared to solvent-based paclitaxel, treatment with nab-paclitaxel was associated with a higher response rate and longer TTP and PFS without increased toxicity. These comparative data in Chinese pts are similar to results previously reported in Caucasian pts (Gradishar et al, JCO, 2005). In Chinese patients PN was similar between groups in contrast with a higher incidence in Caucasian pts receiving nab-paclitaxel. Mature PFS data will be presented; at this time only 49% of events have occurred.