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Interim safety analysis of a randomized phase III study evaluating pegylated liposomal doxorubicin (PLD) versus capecitabine as first line chemotherapy for metastatic breast cancer (MBC) – The PELICAN study

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Background: MBC is still an incurable disease. Effective single agent chemotherapy is increasingly used in the frontline setting to lower toxicity and maintain patient's quality of life (QoL). The phase III PELICAN trial was designed to evaluate efficacy and safety of first-line PLD (50 mg/m^2, q28 days) vs. capecitabine (1250 mg/m^2 BID x 14 days, q21 days) as approved dose for both agents.

Methods: Pts with MBC were eligible. They received either PLD 50 mg/m^2 iv every 28 days or capecitabine 1250 mg/m^2 orally twice daily for 14 days followed by a 7-day rest period (qd21) as a first line treatment. Toxicity was evaluated continuously, efficacy and quality of life every 3months; cycles were repeated until disease progression or unacceptable toxicity.

Results: The PELICAN trial is actively enrolling pts. 79 pts (PLD n = 40; capecitabine n = 39) were analyzed for safety. Median age was 61 years (range, 35−80. Pts received a median of 4 cycles (1−20). Both drugs were associated with comparable rates of grade 1−3 hand foot syndrome (HFS) (PLD, 43%; Capecitabine, 49%); Capecitabine was associated with more diarrhea (35.9% v 5%) and more grade 3 or 4 thromboembolic events (7.7% v 0%). All other grade 3 or 4 toxicities affected less than 5% of pts in both arms. Altogether, 27 pts discontinued treatment: 15 for disease progression, 4 for toxicity, 2 died, and 6 for other reasons. Dose reductions related to HFS or diarrhea were documented in 34% of pts and treatment delay >1 week in 19%. Serious adverse events were reported in 19 pts.

Conclusions: These preliminary results showed no unanticipated toxicity. The toxicity observed was manageable and did not lead to treatment discontinuation. Thus, the IDMC recommended the continuation of patient accrual to the pre-set target of 346.

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Activity and safety of vinorelbine and capecitabine as first-line treatment in patients with metastatic breast cancer – a phase II trial

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Background: Both vinorelbine and capecitabine have shown significant activity as single agents in patients with advanced BC, and recent data suggest the feasibility of this drug combination in patients pretreated with anthracycline- and/or taxane-based chemotherapy. A prospective phase II study was designed to verify the activity and safety a combined regime of vinorelbine and capecitabine as first-line treatment in metastatic breast cancer (BC) patients.

Patients and methods: Thirty-eight consecutive patients with histologically confirmed, measurable advanced and/or metastic BC, entered the study. Median age was 54 years (range 30−72), 91% of them had previously received anthracyclines as neoadjuvant or adjuvant treatment, and 24% had been treated with taxanes; no patient had prior chemotherapy for the metastatic disease. Visceral metastases were present in most patients (liver 65%, lung 43%). Treatment consisted of capecitabine given at the fixed dose of 1000 mg/m^2 orally twice/daily for 14 consecutive days followed by one week rest plus vinorelbine given intravenously at 25 mg/m^2 on day 1 and 8 of a 21-day cycle.

Results: A total of 166 cycles of treatment were administered (median 6 per patient range 4−12). Neutropenia was the main toxicity, with grade 2−3 NCI-CTC occurring in 19 and 9% of patients, respectively, with no severe documented infection; grade 2 hand&foot syndrome occurred in 2 patients, gr.1−2 diarrhea in 4 patients; alopecia did not exceed gr.2. Twenty-three out of 32 valuable patients achieved a documented objective response, for an overall response rate of 72% (95% CI 54%-84%) including 4 complete responses (3 in the liver, 1 in the lung); 6 additional patients obtained a stable disease. Median time to progression was 9.1 months, median overall survival has not been reached.

Conclusions: Our results confirm that the vinorelbine/capecitabine combination has significant activity in non-pretreated metastatic BC patients, with manageable toxicity and good patient compliance, also after anthracycline- and/or taxane-based chemotherapy in the neoadjuvant or adjuvant setting. The recently reported activity of the same combination as all oral formulation need to be further investigated in such a patient population.

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Comparison of weekly and every-3-week nab-paclitaxel in elderly patients with metastatic breast cancer

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Background: Although variable toxicity and efficacy data exist for solvent-based taxanes in elderly patients (aged ⩾65 years), widespread use has been limited. However, when taxanes are used in elderly patients, solvent-based paclitaxel is usually administered weekly and docetaxel is administered every 3 weeks. Overall, in patients with metastatic breast cancer (MBC), nanoparticle albumin-bound (nab)-paclitaxel demonstrated significantly higher response rates and improved safety compared with solvent-based paclitaxel in a phase III trial and compared with docetaxel in a phase II trial. The current retrospective analysis compares the safety and efficacy of weekly and every-3-week (q3w) regimens of nab paclitaxel in elderly patients with MBC from these 2 trials.

Materials and Methods: This subset analysis of patients aged ⩾65 years in the nab-paclitaxel arms of 2 large, randomized phase II (CA-024) and III (CA-012; Gradishar et al. J Clin Oncol. 2005;23:7794–7803) trials that compared nab-paclitaxel with either paclitaxel or docetaxel in patients with MBC. Patients in the phase II trial received first-line therapy with nab-paclitaxel 300 mg/m^2 intravenously (IV) q3w, 100 mg/m^2 IV weekly 3 out of 4 (qw 3/4), or 150 mg/m^2 IV qw 3/4 and first- or second-line therapy with nab-paclitaxel 260 mg/m^2 IV q3w in the phase III trial. All doses were administered over 30 minutes without corticosteroid or antihistamine premedication or special tubing sets.

Results: See the Table.

Conclusions: Overall response rates were more than double in patients who received nab paclitaxel weekly compared with q3w in elderly patients. Patients who received nab paclitaxel weekly received a higher cumulative dose compared with the q3w group. Based on the favorable efficacy and safety profile, nab-paclitaxel administered weekly offers a beneficial treatment option for elderly patients with MBC.

	Nab-paclitaxel			
	Every 3 weeks		Weekly	
	300 mg/m^2 (N = 9)	260 mg/m^2 (N = 30)	150 mg/m^2 (N = 10)	100 mg/m^2 (N = 14)
Received nab-paclitaxel as first-line therapy, %	100	47	100	100
Overall response rate, %	22	26.7	60	64
Median progression-free survival, months	13.8	5.6	18.9	9.2
Mean cumulative dose, mg/m^2	1966.7	1151.3	2703.0	2500.0
Discontinuation because of progressive disease, %	22	31	22	46
Neutropenia, %				
Grade 3	44	28	40	29
Grade 4	22	7	10	7
Sensory neuropathy, %				
Grade 3	11	17	20	21
Grade 4	0	0	0	0