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Locoregional hyperthermia combined with chemotherapy for metastatic breast cancer patients – preliminary results of the Mammatherm-trial

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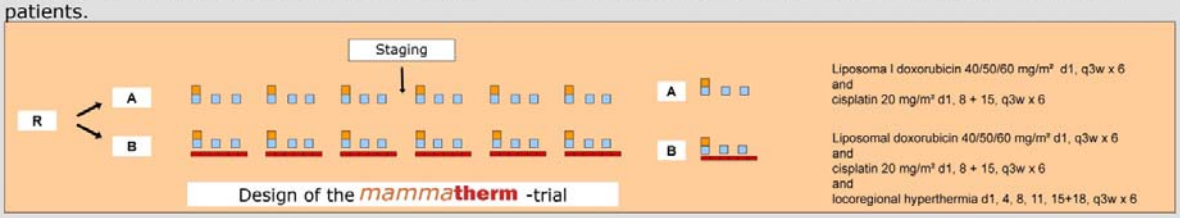
Background

Treatment options for patients with metastatic breast cancer should be as effective and preferably as little toxic as possible. To date there is no standard therapy available and treatment regimens for metastatic breast cancer vary largely. Locoregional hyperthermia might show additive effects to chemotherapy due to an increased perfusion and a simultaneous occurrence of interstitial acidosis in tumor tissue. In randomized clinical trials the addition of hyperthermia to radiation in advanced breast cancer was associated with improved outcome. To our knowledge so far there are no randomized clinical trials evaluating the effect of a combination of hyperthermia and chemotherapy in breast cancer patients.



Design of the mammatherm -trial

Fig. 1: Hyperthermia devices in the study

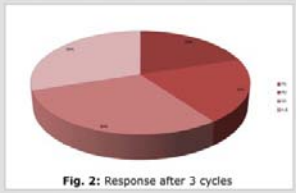


Fig. 2: Response after 3 cycles

Patients and Methods

Phase I of the multicenter German Mammatherm-trial was a dose-finding-study for liposomal doxorubicin administered in combination with cisplatin (20mg/m2) and locoregional hyperthermia. Patients received 6 cycles of therapy according to the following regimen:
liposomal doxorubicin 40 or 50mg/m2 i.v. d1 q22d and cisplatin 20 mg/m2 i.v. d1, 8, 15 q22d in combination with locoregional hyperthermia administered at d1, 4, 8, 11, 15, 18 q22d. Dosage escalation levels for liposomal doxorubicin were at 40/50mg/m2; an escalation up to 60mg/m2 was planned but not effected due to dose limiting toxicities (DLTs).
DLTs were defined as non-hematological toxicities > grade 2 NCI CTCAE (National Cancer Institute Common Terminology Criteria of Adverse Events), - except of nausea and vomiting -, or hematological side effects grade 3 or 4 NCI CTCAE leading to treatment postponement of more than 7 days, if those adverse events were at least possibly associated with the study therapy.
Here first results of the trial concerning the observed DLTs are presented.

Results

A total number of 10 patients were recruited into the trial between August 2007 and May 2011. The therapy was prematurely stopped in 6 patients. Therapy was discontinued in only one patient due to toxicity (adiponecrosis); all other discontinuations were required because of tumor progression. Dose limiting toxicities (DLTs) were observed in 2 patients and comprised liver toxicity in a patient with liver metastases, and, probably, but not proven, tumor-associated bone pain. A causal link to the administered chemotherapy could not be ruled out but appeared to be rather unlikely in both cases. None of these adverse events required treatment discontinuation. There were neither hematological nor hyperthermia related DLTs seen.

	grade 3	grade 4
leukopenia	6	
Neutropenia	3	
thrombopenia	-	
anemia	-	
GOT ↑		1
GGT ↑		1
Total of non-hematological toxicity	12	2
Burns	1	
SAE's	6	

Table 1: Incidence of grade 3/4-toxicities

Conclusion

The combination of locoregional hyperthermia and chemotherapy in pretreated metastatic breast cancer patients showed a tolerable toxicity profile. Data concerning the final toxicity analysis are pending.

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