

Abstract 1186

Breast Cancer Recurrences at the Chest Wall (BCRCW) When Standard Treatments (Tx) Have Failed: Lyso-thermosensitive liposomal doxorubicin (LTLT) + Mild Local Hyperthermia (MLH)

Type: Abstract

Category: Breast cancer, locally advanced

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Body

Background: BCRCW has a poor prognosis, with disfigurement, pain, and restriction of movement. Study treatment consisted of LTLT that releases high concentrations of doxorubicin (Dox) in areas treated with mild hyperthermia at > 39.5°C. MLH kills tumor cells, selectively increases liposomal permeability in tumor microvasculature, releases Dox from LTLT, and promotes Dox tumor uptake.

Methods: We conducted a phase I study of LTLT + MLH in patients (pts) with BCRCW tumors < 3 cm deep who had failed all standard Tx including surgery, radiation, and chemotherapy (CTx). Pts received up to 6 LTLT/MLH Txs every 21 days. Dosing cohorts started at 40 mg/m² and stopped escalation at 50 mg/m². LTLT was infused IV over 30 minutes (min); then MLH was given by microwave or ultrasound. The thermal dose goal was 40°C-42°C for 60 min. Pharmacokinetic samples for total plasma Dox and doxorubicinol (Doxol) were taken at 0.5, 5, 10 and 24 hours after starting infusion.

Results: Eleven pts with a median of 4 prior CTx (range 2 – 12) were enrolled; 10 had recurred after prior anthracycline (AC). All pts received > 2 cycles. The within subject variability in Dox and Doxol exposure was small with mean Cycle 2 vs Cycle 1 ratios ranging from 0.99 to 1.06.

		Cycle 1	Cycle 2
Cmax/dose (ng/ml)/(mg/m ²)	Dox	499.82	512.00
	Doxol	0.46	0.45
AUClast/dose ((ng*hr/ml)/(mg/m ²))	Dox	1,338.18	1,381.82
	Doxol	7.96	8.04

Two types of grade 3/4 toxicity were seen in > 5% of 42 cycles given: reversible neutropenia in 17 (40.5%) and reversible leukopenia in 9 (21.4%). One case (each) of mucositis (grade 1), chest wall thermal burn, and chest wall cellulitis (both grade 4) occurred, and no cases of cardiomyopathy or hand-foot toxicity were seen. The rate of clinically-significant (> 6 point) QoL improvement on the FACT-B after 2 cycles was 54.5% (95% CI: 25.1% - 83.9%), including 1 lasting > 3 months. The local objective response rate was 45.5% (95% CI: 16.1% - 74.9%), with 1 complete and 4 partial local responses.

Conclusion: LTLT + MLH is safe and active in BCRCW pts with prior radiation and AC exposure. A phase II study is underway.

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