A PHASE I STUDY OF THERMALLY SENSITIVE (TS) LIPOSOMES CONTAINING DOXORUBICIN (THERMODOX™;TDOX) IN COMBINATION WITH HYPERTHERMIA (HT) IN BREAST CANCER PATIENTS WITH CHEST WALL (CW) RECURRENCE

Jones Ellen L. [1*], Dewhirst Mark W[1*], Craciunescu Oana[1], Vujaskovic Zeljko[1*], Stauffer Paul[1], Prosnitz Leonard R[1*], Liotcheva Vlayka[1], Sims Dakya[2], Massa Lisa[3], Kimmick Gretchen[2], Hicks David[4] and Blackwell Kimberly[1,2]

[1]*Department of Radiation Oncology, Duke University Medical Center (DUMC) Durham NC, USA*

[2]*Divison of Medical Oncology, Department of Medicine, DUMC Durham, NC USA*

[3]*Department of Physicial Therapy, DUMC Durham, NC USA*

[4]*Celsion Corporation Columbia, MD USA*

PURPOSE: Pre-clinically, TS liposomes containing chemotherapy improve drug delivery and tumor control when combined with HT compared to non-liposomal formulations or TS liposomes without HT. As the CW is a common site for breast cancer recurrence, this phase I study utilized TS liposomes containing doxorubicin [TDox, Celsion] in combination with CW HT to define a dose schedule for this multimodality therapy.

METHODS: Patients with bx proven breast adenocarcinoma (>1 cm diameter/<3 cm thick) on the CW and having progressed on chemo and (if ER+) hormonal therapy were eligible. Prior CW radiation therapy was not required and distant mets were allowed. Prior anthracycline dose was limited to < 450mg/m^2 (Doxorubicin) or 900mg/m^2 (Epirubicin). Dose escalation of TDox followed a standard 3+3 design (20, 30, 40, 50, 60mg/m^2 q 21 d for up to 6 cycles). After TDox infusion (30 min), HT was administered for 1 hr using the BSD 500 (Salt Lake City) for a goal of 40–42°C. Response was measured using CT, digital photos, and infrared (IR) imaging prior to cycles 3, 5, and post cycle 6.

RESULTS: To date, 7 pts have accrued (6 pts with prior anthracycline tx) and no dose limiting toxicities have been seen. In the heated areas, 1 CR, 2 PR, 3 SD have been seen. One patient had a PR in the heated area but progressed in the non-heated area after 2 cycles. Infared imaging prior to cycles 3 and 5 correlated with disease response.

CONCLUSION: TDox combined with HT offers a potential treatment option for CW recurrence. Activity to date suggests that the combination of a TS liposome with HT improves anti-tumor effects on the CW compared to non-liposomal chemotherapy alone.

Supported in part by P01 CA42745-14