Detection of apoptosis and relationship to ventricular function in patients with early stage breast cancer receiving anthracycline-based chemotherapy.

Olexiy Aseyev[1] MD, PhD; Kathryn Ascah[2], MD; Girish Dwivedi[2], PhD, MD; Glenn Wells[2], PhD; John Hilton[1], MD; Jeffrey Sulpher[1], MD; Terrence Ruddy[2], MD; Susan Dent[1], MD

1. Department of Medicine (Medical Oncology), University of Ottawa,

2. The University of Ottawa Heart Institute

Background. Breast cancer (BC) patients (pts) treated with anthracycline based chemotherapy (Chemo) are at risk of developing cardiotoxicity (Ctox) which may occur years after completion of treatment. Left ventricular ejection fraction (LVEF) detects Ctox usually after cardiac damage is present and potentially irreversible. Annexin is a small protein that can be labeled with technetium-99m to detect apoptosis of cardiac myocytes. Animal models have demonstrated annexin-V changes prior to drops in LVEF. We recently completed a phase I evaluation of ^{99m}Tc rh-Annexin-V128 (ANX) in 12 adult volunteers and demonstrated the radiotracer was safe. The primary objective of this study is investigate ANX imaging of apoptosis in the evaluation of doxorubicin-induced Ctox in pts with early stage BC.

Methods. This is a single centre, prospective pilot study, designed to enrol 30 pts with Stage I-III BC receiving (neo) adjuvant anthracycline based Chemo (adriamycin/cyclophosphamide [AC]q2 weeks x 4; paclitaxel q2 weeks x 4) at The Ottawa Hospital Cancer Centre. Pts will have ANX imaging at baseline, early (at the end of 2 courses) and later (at the end of 4 courses) during Chemo. CMR imaging will be carried out at baseline, early (at the end of 2 courses) and later (at the end of 4 courses). Pts will have CMRI and ANX imaging 12 weeks after 4th cycle of AC. The 2 and 4 week uptake of ANX will be compared to changes in CMR LV function parameters measured after 4 courses of AC compared to baseline. Ten pts will be recruited during a Proof of Concept (PoC) phase to assess the potential of ANX in terms of imaging quality, uptake and medical relevance. A further 20 pts will be recruited based on the outcome of the PoC phase.

Results. This study is now open to accrual. Anticipated enrolment of the first patient is expected in July 2016. Preliminary results including pts` demographics and PoC data will be presented.

Conclusions. Serial imaging of apoptosis with ANX may be useful for early detection of anthracycline induced cardiotoxicity. Breast cancer patients identified with early cardiotoxicity may benefit from primary prevention strategies.