

P11

TRASTUZUMAB-INDUCED CARDIOTOXICITY: CAN BIOMARKERS AID DIAGNOSIS?

doi:10.1136/heartjnl-2012-303148a.16

²M Harbinson,* ¹P Forrest, ²A Clayton, ²M Campbell, ¹D Bell. ¹*School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, UK;* ²*Belfast Health and Social Care Trust*

Introduction HER2-positive breast cancer therapy with Trastuzumab, typically with the anthracycline, Epirubicin, increases survival but may decrease left ventricular ejection fraction (LVEF) asymptotically; serial echocardiograms are needed. Increased Brain Natriuretic Peptide (BNP) and precursor fragment, N-Terminal (NT)-proBNP, are plasma biomarkers for systolic dysfunction and heart failure. Adrenomedullin levels relate inversely to ventricular function and correlate with heart failure severity.

Aims To (i) assess the relationship between LVEF and plasma NT-proBNP in patients receiving Trastuzumab; (ii) compare changes in BNP and Adrenomedullin levels in human cardiomyocytes (HCM) following Trastuzumab treatment.

Methods 100 patients receiving Trastuzumab had LVEF measured by radionuclide ventriculography and plasma NT-proBNP levels assessed (Roche Multianalyser) every 3 months. HCM were treated with Epirubicin (2 h, 100 ng/ml) followed by Trastuzumab (150 µg/ml) for varying times. Cellular viability was determined using Trypan blue, Adrenomedullin and BNP were assessed by

semi-quantitative immunofluorescence staining; qRT-PCR confirmed mRNA production.

Results In patients receiving Trastuzumab adjuvant therapy, LogNT-proBNP correlated inversely with LVEF ($R^2=0.014$). Treatment with Trastuzumab and Epirubicin decreased viable HCM numbers. Intracellular Adrenomedullin content decreased 8 h after treatment, returning to baseline at 24 h; mRNA remained unchanged. BNP mRNA increased 8 h after therapy; protein level was unchanged.

Discussion Short term decreases in intracellular Adrenomedullin may indicate increased secretion with restored levels occurring due to increased breakdown of stored precursor. Increased BNP transcription may maintain intracellular BNP levels. Measuring plasma Adrenomedullin 8 h after Trastuzumab therapy may identify patients at risk of cardiotoxicity; BNP assessment may be more useful later.