TAXANE ASSOCIATED WITH TRASTUZUMAB INDUCED EARLY VENTRICULAR IMPAIRMENT: CORRELATION WITH BIOLOGICAL MARKERS OF CHRONIC INFLAMMATION AND OXIDATIVE STRESS

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Background: The concomitant administration of Taxanes enhances the efficacy of Trastuzumab (TZM), an anti HER-2 receptor monoclonal antibody, in the treatment of HER-2 overexpressing cancers. Currently, there are little data on the short and long term effects on the cardiac structure and function of TZM associated with Taxane in humans. Speckle Tracking (ST) imaging based deformation indexes have shown to be very sensitive identifying left ventricular dysfunction.

Methods: Inclusion criteria: histologically confirmed HER-2+ve breast cancer, candidates for TZM and Taxanes based regimen; LVEF ≥55%; ECOG PS score 0-2, no history of cardiac disease. The following assessments were carried out at baseline, after each TZM treatment and every 3 months during 1 year follow-up: ECOG PS score, conventional echocardiography and ST parameters (global circumferential, radial and longitudinal S and SR), chronic inflammation (IL-6 and TNF-alpha) and oxidative stress (reactive oxygen species and glutathione peroxidase) markers. The correlation between changes detected by echocardiography and chronic inflammation was studied.

Results: At May 2012, 20 patients (mean±SD age 53±10 yo) have been enrolled. A significant progressive reduction of the peak of longitudinal SR was observed throughout all treatment starting at 4th dose of TZM (0.81±0.16 s-1 vs respectively 0.65±0.18 s-1, p<0.005; vs 0.58±0.16 s-1, p<0.001; vs 0.53±0.24 s-1, p=0.005) as signs of systolic dysfunction. Furthermore, a significant reduction of the circumferential SR (0.51±0.14 s-1 vs 0.6±0.15 s-1; p<0.01) and of the rotation (1.45±0.57 vs 2.49±1.08; p<0.001) appeared at the first dose of TZM. At the 3rd dose of TZM, increased significantly (16.7±15.6 pg/ml vs 25±11.7; p=0.03), whilst the other laboratory parameters did not change significantly in comparison to baseline values.

Conclusions: The concomitant administration of Taxanes and TZM enhances the efficacy of TZM but proved to induce a subclinical early impairment of left ventricular function. These effects seem to be related to an increase of TNF alpha. Follow up data will show if this myocardial impairment will persist over time. The study is in progress.