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## 2017 San Antonio Breast Cancer Symposium

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### Questionnaire

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**Title:** The TRANSERI project: effect of eribulin (E) in patients with metastatic breast cancer (mBC) on circulating TGF $\beta$  and TNF $\alpha$ . Relationship with outcome

**Body:** Background: E is approved for the treatment of mBC patients (pts) after failure of at least 2 previous chemotherapy (CT) regimens containing anthracyclines and taxanes. Its mechanism of action interferes with microtubule leading to cell cycle arrest in G2/M phase and cell apoptosis. An in vitro study in triple negative BC cell lines shows that exposure to E reverses epithelial mesenchymal transition (EMT) phenotype toward an epithelial morphology and induces changes of gene profiling and protein expression. Accordingly in mice E reduces metastatization and can reverse EMT. TGF $\beta$  is an immunosuppressive cytokine and a growth factor for cancer-associated fibroblasts (CAFs). In addition it drives EMT. TNF $\alpha$  synergizes with TGF $\beta$  to promote EMT. While CAFs pave the way for metastatization, EMT permits cancer cells trafficking through the blood flow following CAFs and finally developing metastases. The purpose of the study is to investigate whether E interferes with TGF $\beta$  and TNF $\alpha$  levels and if the changes correlate with the outcome and the metastatic spread.

**Methods:** Pts with mBC, after failure of at least 2 previous CT lines were treated with E delivered at 1.23 mg/m<sup>2</sup>, d 1–8 every 21 d. Blood levels of TGF $\beta$  and TNF $\alpha$  were determined at baseline, before cycle 3, 5 and at disease progression. The changes observed were correlated with the outcome and the metastatic spread.

**Results:** The study is ongoing. Here we report preliminary data on 16 pts who completed 3 cycles of E. No change

of TNF $\alpha$  level was observed during treatment. On the contrary, TGF $\beta$  levels changed during treatment. Basal levels of TGF $\beta$  were divided in upper or lower the median (m) value. We did not observe any difference in m PFS between high or low values (137 d vs 141). However the m TGF $\beta$  value in pts was much higher than that observed in 3 healthy volunteers (m concentrations: 205 pg/ml [C.I. 115-920] vs 108 pg/ml [C.I. 85-120] respectively).

In 5 pts, TGF $\beta$  increased between cycle 1 and cycle 3, while diminished in 11 pts. We observed a numerical difference in PFS between the pts with decreased and increased values (150 d vs 85, p=NS).

We then divided the population in 3 groups: pts with TGF $\beta$  increased more than 25% of their basal levels (increased), pts with changes between +25% and -25% compared to their basal levels (stable) and pts with decreased values more than 25% of their basal levels (decreased). Comparing "increased" vs "stable" + "decreased" we observed a trend toward longer PFS favouring the latter group (77 d vs 144 p=0.12).

We collected the third determination in 14 pts. We did not analyse these data yet. However we observed that in 6 pts, TGF $\beta$  continues to decline. None of these pts progressed. In these pts the m value of TGF $\beta$  approaches healthy controls value (m concentrations: 180 pg/ml [C.I. 200-100] vs 108 pg/ml [C.I. 85-120]).

**Conclusions:** TNF $\alpha$  does not change during E treatment. On the contrary, TGF $\beta$  changes compared to basal levels. In pts with increased TGF $\beta$  between cycle 1 and 3 the PFS is lower than that observed in pts with stable or decreased levels (p=0.12). Pts with continue decline of TGF $\beta$  at cycle 5, approach the values of the healthy volunteers. None of them progressed. Updated results will be presented.

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#### Disclosures by Author:

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**3. - Daniele Lingua.**

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**4. - Anna Maria Vandone.**

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