MMP-9 as predictive factor for response and progression free survival in breast cancer patients treated with bevacizumab and pegylated liposomal doxorubicin.

Background

The benefit of bevacizumab (BV) has been shown in different tumors including colorectal cancer, renal cancer, pulmonary non-small cell cancer and also breast cancer. However, to date, there is no established test evaluating the angiogenic status of a patient and monitoring the effects of anti-angiogenic treatments.

Tumor angiogenesis is the result of a balance between multiple pro- and anti-angiogenic molecules. There is very little published clinical data exploring the impact of the anti-angiogenic therapy on the different angiogenesis-related molecules and the potential role of these molecules as prognostic or predictive factors.

We measured prospectively the levels of 6 angiogenesis-related molecules in the peripheral blood of breast cancer patients treated with a combination of BV and pegylated liposomal doxorubicin (PLD): VEGF, VEGFR-1, VEGFR-2, VEGFR-3, PlGF, and MMP-9.

Methods & Materials

Main-eligibility criteria for patients included in the SAKK 2406 trial:

- Cytologically or histologically proven breast cancer, either metastatic or locally recurrent inoperable and HER2-negative
- Normal heart function (LVEF > 50%)
- No previous chemotherapy for metastatic or inoperable locally recurrent breast cancer, no previous adjuvant or neo-adjuvant chemotherapy
- Cytologically or histologically proven breast cancer, either metastatic or locally recurrent inoperable and HER2-negative
- Blood sampling: 20 ml of blood were taken: 10 ml for serum and 10 ml for plasma (EDTA-K)
- Measurement of the angiogenesis-related molecules: Enzyme-linked immunosorbent assays (Quantikine, R&D Systems and Reliatech) were used to measure the molecules.
- The measurements were done centrally in our laboratory (CePO and ISREC, Epalinges, Switzerland).

Results

- **Figure 1: Box-plot of log-transformed plasma level of MMP-9 for best response**

- **Figure 2: Box-plot of log-transformed plasma level of sVEGFR-1 for best response**

- **Figure 3: Baseline plasma level of MMP-9 vs PD**

- **Figure 4: Survival function estimates vs PFS**

Objective

The objective of this substudy is to identify surrogate markers of angiogenesis in advanced breast cancer patients treated with the combination of PLD and BV.

Conclusion

Our exploratory results suggest that:

1. The baseline plasma level of MMP-9 was associated with tumor response and disease control to PLD-Bv.
2. The baseline plasma level of MMP-9 could predict PFS.
3. The baseline plasma level of sVEGFR-1 was associated with disease control.

Therefore, these results justify further assessment of MMP-9 and sVEGFR-1 as predictive or prognostic factors in breast cancer patients treated with anti-angiogenic therapies.

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References:

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