Expression of MRP-2 in circulating tumor cells (CTCs) of patients with locally advanced head and neck squamous cell carcinoma (LAHNSCC) and their relation with progression free survival.

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Background: Currently there are different treatment options for LAHNSCC patients: upfront surgery followed by radiotherapy (RT), RT concurrent with chemotherapy (CT) or cetuximab, preceded or not by induction CT (ICT). Despite efforts, no predictive biomarkers are available to guide therapy. **Hypothesis**: The aim of this study is to determine the prognostic role of circulating tumor cells (CTCs) in LAHNSCC patients treated with a curative intent and correlate its counts, kinetics and biomarkers expression, such as MRP-2, with treatment response and survival. **Methods**: Blood samples of 47 non-metastatic LAHNSCC patients, stages III/IV, were analyzed for CTCs using the isolation by size method (ISET - Isolation by Size of Epithelial Tumor Cells, Rarecells, France®), in two scenarios: curative surgical resection and adjuvant treatment (RT+/-CT) and candidates for a non-surgical strategy (unresectable/organ-preservation) based on combination of RT with CT or cetuximab, with or without ICT. The analysis included CTCs counts, kinetics and expression of biomarkers by immunocytochemistry. **Results**: The median number of baseline CTCs was 2.6 CTCs/ml and 30 of 47 patients had CTCs analyzed after treatment, with a median count of 3.2 CTCs/ml. Patients with CTCs kinetics always favorable had a better PFS in comparison with always unfavorable kinetics (11.9 x 8 months – p=0.14). Expression of MRP-2 in the CTCs after treatment was associated with a significant worse PFS (8.8 x 17.5 months – p<0,001) although no difference was observed for baseline expression (13.3 x 11.9 months – p=0,61). **Conclusions**: Favorable kinetics of CTCs was associated with an impact on survival in LAHNSCC patients treated with a curative intent, although without statistical significance. Expression of multidrug resistance protein 2 (MRP-2), involved in cisplatin resistance, in CTCs after treatment, was strongly correlated with worse PFS in this scenario.