

Circulating Tumor Microemboli (CTM) as Prognostic Factor for Patients with Head and Neck Advanced Squamous Cell Carcinoma (HNSCC)

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BACKGROUND: Head and Neck Squamous Cell Carcinoma (HNSCC) patients comprise a very heterogeneous group and many prognostic factors were studied to attempt to stratify risk. Circulating tumor cells (CTC) detection, kinetics, and characterization are defined as prognostic factors, but little is known regarding Circulating Tumor Microemboli (CTM). CTMs are defined as clusters of 3 or more cancer cells detected in peripheral blood.

OBJECTIVE: To determine the influence of CTMs in progression free survival (PFS) and overall survival (OS) in locally advanced HNSCC patients. The prospective trial was designed to analyze influence of CTM in survival and its role as an independent prognostic factor at beginning of therapy.

METHODS: there were enrolled 44 patients with locally advanced HNSCC positive for CTCs in this trial since December/2013 until August/2015, when the last patient was included for analysis. The trial is still ongoing. CTCs and CTMs were detected by ISET (Isolation by Size of Epithelial Tumor Cells, Rarecells, France®) technique. All patients had locally advanced disease and underwent standard treatment with surgery, radiotherapy or radiochemotherapy, according to individual factors. The analysis included frequencies, demographic characterization and survival variables, including PFS and OS. The PFS and OS were calculated based on the date of first CTC collection and first progression after collection (PFS) or death (OS).

RESULTS: From the 44 patients analyzed, mostly had extensive T or N disease; 30 (68.2%) were at least T3 and 27 (61.4%) were at least N2. No patients were metastatic at diagnosis. CTM was demonstrated in 16 (36.3%) patients. 18 patients (40.9%) relapsed during follow-up. Regarding groups, there were 8 (28.6%) relapses in the CTM negative group and 10 (62,5%) in the CTM positive group. At the end of the analysis, 36 (81.8%) patients were still alive; 2 of 28 (7.1%) patients died in the CTM negative group, in contrast with 6 of 16 (37.5%) patients in the CTM positive group. The presence of CTM was demonstrated as an independent factor for worst prognosis regarding PFS and OS. Median time for PFS was 16.97 x 7.73 months ($p = 0,024$) comparing CTM negative and CTM positive patients, respectively. The result was confirmed for OS, although the median was not reached for both groups, but significant difference was demonstrated by curves, with worst OS for CTM positive patients ($p = 0.035$).

CONCLUSIONS: our initial analysis of our ongoing study showed that CTM can be considered a significant prognostic factor for PFS and OS in patients with locally advanced, not metastatic, HNSCC. This data can aid to identify patients at a higher risk for relapse at baseline treatment. The sample is still small, and the trial is still recruiting patients.