OVERALL SURVIVAL IN SMALL CELL LUNG CANCER DETECTED WITH EPITHELIAL, MESENCHYMAL AND STEM CELL BIOMARKERS


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Aim: Markers of epithelial to mesenchymal transition (EMT) and markers associated with cancer stem cells (CSC) have been associated with increased chemoresistance in small cell lung cancer (SCLC). We and others previously demonstrated that elevated circulating tumour cells (CTC) are associated with worse survival. In the current exploratory study we hypothesized that markers of EMT and CSC in tumour biopsies obtained at diagnosis were associated with overall survival in patients with SCLC.

Methods: Biopsies selected from small cell lung cancer pts study published previously by our group [Ann Oncol 2012;23:2937-42]. Epithelial markers [Cytokeratin 8,18,19 (CK, ab41825, Abcam), EPCAM (VU1D9, cellsignaling), E-cadherin (24E10, cellsignaling)] and mesenchymal markers [Vimentin (V9, Santa Cruz) and c-MET (EP1454Y, Abcam)] were used as biomarkers for EMT. SOX2 (L1D6A2, cellsignaling) and CD44 (IM7, Biolegend) were used as CSC markers. Scoring by two independent observers having no information about clinical outcome. Immuno-Reactive Score (IRS) was made by multiplying percentage (0-6) and intensity (0-3). IRS score >=5 was high, <5 low. Intensity was high >=2 low <2. Data expressed as median with range. Overall survival: Kaplan Meijer plots were made.

Results: From 38 patients (mean age 65 yrs [49-84], 18 female pts, ECOG performance score 1 [0-3], extensive disease stage 26 pts, CTC at baseline 19 [0-14040]) adequate material was available to cut at least 10 tumour containing slides for immunohistochemical staining. Staining intensity high/low: CK 10/27; Vimentin 23/15; CD44 19/19; SOX2 17/21; c-MET 19/19; IRS high/low EPCAM 20/18, E-cadherin 14/24. Combining primary tumour low c-MET intensity with high CK intensity and high E-Cadherin IRS resulted in a significantly worse survival vs the c-METhigh/CKlow/E-cadherinhigh group, OS 10 vs 24 month, p=0.040. A trend towards a positive correlation between CTC and primary tumor c-METlow was seen, p=0.062.

Conclusions: SCLC with an epithelial phenotype (E-Cadhigh, CKhigh, cMETlow) may give rise to more epithelial CTCs in circulation than those with an mesenchymal phenotype and have a worse prognosis.

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