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Prognostic and predictive value of CD8 intratumoral density in relation to transcriptional subtype and spatial transcriptomics in SCLC

S. Elings[1], D. Naves[1], Y.M. Kim[1], Z. Tsourti[2], F. Griesinger[3], J. Andrade[4], S. Popat[5], M. Reck[6], D. De Ruysscher[7], J. Cadranel[8], I. Houda[9], B. Lissenberg-Witte[10], I. Bahce[11], Y. Kim[12], A. Vervita[13], R. Kammler[14], S.P. Finn[15], R.A. Stahel[16], S. Peters[17], T. Radonic[1]

[1] Cancer Center Amsterdam, Department of Pathology, Amsterdam UMC - Vrije University Medical Centre (VUmc), Amsterdam, Netherlands, [2] ETOP Statistical Center, Frontier Science Foundation Hellas, Zografou, Greece, [3] Department of Oncology, Pius Hospital, Oldenburg, Germany, [4] Department of Medical Oncology, Hospital Virgen de la Salud, Toledo, Spain, [5] Department of Medicine, The Royal Marsden Hospital - NHS Foundation Trust, London, United Kingdom, [6] Thoracic Oncology Department, LungenClinic Grosshansdorf, Grosshansdorf, Germany, [7] Radiation Oncology Department, Maastro Clinic, Maastricht, Netherlands, [8] Thoracic Oncology Unit, Service de Pneumonologie, Hospital Tenon, Paris, France, [9] Lung Oncology, Amsterdam UMC - Vrije University Medical Centre (VUmc), Amsterdam, Netherlands, [10] Department of Epidemiology and Data Science, Amsterdam UMC, locatie VUmc, Amsterdam, Netherlands, [11] Pulmonary Diseases Department, Amsterdam UMC - Vrije University Medical Centre (VUmc), Amsterdam, Netherlands, [12] Cancer Center Amsterdam, Amsterdam UMC, locatie VUmc, Amsterdam, Netherlands, [13] ETOP Statistical Center, FSF-H - Frontier Science Foundation Hellas, Athens, Greece, [14] Translational Research Coordination Department, ETOP IBCSG Partners Foundation, Bern, Switzerland, [15] Cancer Molecular Diagnostics and Histopathology, St James's Hospital, Dublin, Ireland, [16] Department of Medical Oncology and Hematology, ETOP IBCSG Partners Foundation, Bern, Switzerland[17] Oncology Department, CHUV - Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

Background

Small Cell Lung Cancer (SCLC) is an aggressive neuroendocrine carcinoma notable for early dissemination + poor survival. Although CD8 emerged as a potential predictive biomarker for immunotherapy response, the prognostic + predictive value of intratumoral cytotoxic T-cell have to be confirmed.

Methods

Intratumoral CD8+ cytotoxic T-cell density (CD8%, computationally measured in immunohistochemistry (IHC)) and MHCI IHC expression in a historical cohort of 170 pts diagnosed b/w 2000-2024 [29% limited stage(LS) and 71% extensive stage (ES)] treated w/chemo +/- radiation + 87 ETOP/IFCT 4-12 STIMULI trial LS pts of whom 57 were randomized to consolidation nivolumab + ipilimumab or observation after chemoradiation. ES and LS CD8% were stratified by transcriptional subtype by IHC for ASCL1 (A-SCLC), NEUROD1 (N-SCLC), POU2F3 (P-SCLC), + all negative (I-SCLC). In 19 ES pts, we performed spatial transcriptomics.

Results

Median age of the historical cohort was 67 yrs (61-74). In ES median CD8% was 0.95%; in LS median CD8% was significantly higher 2.11% ($p<0.05$), thresholds of 1% and 2% were chosen; Significant difference in survival was found b/w CD8 excluded (CD8<respective threshold) + CD8 infiltrated patients in ES and LS (HR 0.45; CI 0.31-0.67; $p<0.001$ and HR 0.38; CI 0.2-0.74; $p=0.004$, respectively). P-SCLC showed worst OS. However, CD8% was prognostic in P-, A-, and I-SCLC, but not in N-SCLC. In a multivariable analysis, CD8% remained significantly prognostic (aHR=0.45, CI 0.22-0.92; $p=0.028$). Of 12 paired samples, in 7 pts CD8% was reduced after chemo+/- radiation ($p=0.07$). Median age of ETOP/IFCT 4-12 STIMULI pts was 62 yrs (38-77), and 28 of the 57 randomized pts received immunotherapy as consolidation, 29 chemoradiation only. Median CD8% was 2.6%, no prognostic effect of CD8% was detected ($p=0.76$). Among the randomized pts no predictive value for treatment response was found (interaction $p=0.58$). Results of cell state analysis w/spatial transcriptomics MH and CI results will also be presented.

Conclusions

Intratumoral CD8 density is higher in LS than ES SCLC and is prognostic for SCLC chemotherapy+/-radiation treated pts, except in SCLC-N subtype. No predictive value of CD8 density was found in STIMULI pts.

Legal entity responsible for the study

ETOP IBCSG Partners Foundation.

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Disclosure

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