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Annals of Oncology 29 (Supplement 10): x1–x10, 2018
doi:10.1093/annonc/mdy493

BIOMARKER DEVELOPMENT

10 Advanced CT imaging features reflect distinct tissue immune profiles and exhibit high prognostic impact on NSCLC

G. Mazzaschi[1], P. Pagano[1], G. Milanese[1], D. Madeddu[1], A. Falco[1], G. Armani[1], G. Bocchialini[1], D. Marturano[1], L. Ampollini[1], B. Lorusso[1], C. Lagrasta[1], N. Sverzellati[1], M. Silva[1], M. Tiseo[2], F. Quaini[1], G. Roti[1]

[1]Medicine and Surgery, University Hospital of Parma, Parma, Italy, [2]Medicine and Surgery, Università degli Studi di Parma - Facoltà di Medicina e Chirurgia, Parma, Italy

Background: Intersecting genetic, biologic and clinico-pathological features with high-throughput imaging may pave the way to precision oncology. We advanced the hypothesis that the tumor immune microenvironment (TIME) may imprint on CT scan parameters in a qualitative and quantitative (radiomics) fashion, providing a non-invasive approach to identify new prognostic factors in NSCLC patients.

Methods: In this study, we enrolled sixty (31 Adenocarcinoma, 29 Squamous Cell Carcinoma) surgically resected patients. We defined TIME by the quantitative assessment of PD-L1 expression and a detailed morphometric evaluation of Tumor Infiltrating Lymphocytes (TILs). Next, from each tumor associated images we extrapolated 841 CT radiomic features through an open-source (3d Slicer) software.

Results: We observed high levels of tissue PD-L1 in radiologic lesions displaying a solid texture and any effect on the surrounding parenchyma ($p < 0.05$), while well defined CT margins were seen in TILs-rich cases ($p < 0.05$). The combined analysis of predetermined risk factors from TIME and CT texture had a striking impact on clinical outcome. Patients with low PD-1 expression on CD8+ TILs and CT evidence of tumor effect on parenchyma had significantly increased ($p < 0.001$) OS with respect to their counterpart (median 50 vs 30 months, HR = 16.82). We also documented prolonged survival ($p < 0.05$) in cases with well defined CT margins and high CD8-to-CD3 TILs (46 vs 35 months, HR = 2.66). Intriguingly, when an unsupervised hierarchical clustering model was applied to radiomics data, we identified two clusters (A and B) with oppositely regulated features: the first of 57 cases (A), further branching into two continuous different clusters, the second (B) comprised only three patients sharing a mutual genetic (EGFR and KRAS mutations), immunologic (PD-L1, CD3+ and CD8+ TILs, PD-1/CD8 ratio), radiologic (shape, effect, texture and structure) and clinical (relapse and death) profile.

Conclusions: A highly significant prognostic score can be obtained in NSCLC by integrating TIME with CT features. Distinct tissue immune backgrounds may entail imaging textures potentially able to portray a radiologic signature of lung cancer.

Legal entity responsible for the study: University of Parma.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.