DELTA-RADIOMICS PREDICTS RESPONSE AND OVERALL SURVIVAL IN ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS TREATED WITH DURVALUMAB

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Background Immune checkpoint inhibitors (ICI) are the standard of care for advanced non-small cell lung cancer (NSCLC). However, the response rates to these immuno-oncology agents remain modest (~45% in the frontline setting and ~20% in the second line setting). The ability to determine early response during treatment is important to allow early adjustment of treatment regimens. Currently, there is a lack of objective methods for early evaluation of clinical benefits from ICI treatments. In this study, we evaluated the performance of a CT-based delta-radiomics model for predicting early response in advanced NSCLC patients enrolled in CP1108 durvalumab nonrandomized phase 1/2 trial (NCT01693562) as an independent validation set. Change of feature statistics between baseline and post-treatment scans was defined as the delta radiomic features.

Methods Baseline and first post-treatment chest CT scans from 225 NSCLC patients were acquired from 3 sites. A maximum of 2 lung lesions were annotated on both scans as per RECIST v1.1 and patients with objective response were defined as ‘responders’, and those with progressive disease or stable disease were defined as ‘non-responders’. Patients lacking follow-up scans or measurable lung lesions were excluded. A previously trained classifier on D1=111 patients from two institutions (Cleveland Clinic Foundation and University of Pennsylvania Health System) was validated on D2=114 cases from CP1108 durvalumab study to assess the probability of treatment response using ROC curve as AUC. 454 intratumoral and 7426 peritumoral texture features were extracted from the scans and relative radiomic differences were computed to yield a set of ‘delta-radiomic’ features. A Cox regression model that was previously trained was used to evaluate the overall survival on CP1108 durvalumab study and relative HR with 95% confidence intervals (CI) was reported. A blinded validation was performed by AstraZeneca.

Results A combination of peritumoral and intratumoral delta radiomic features yielded an AUC of 0.77 ± 0.07 in D1 and a corresponding AUC of 0.7 in D2, respectively. Univariate Cox regression analysis indicated that delta-radiomic signature was significantly associated with OS in D1 set [HR: 1.95; 95% CI, 1.5–2.5; P<0.001; C-index=0.70] and D2 set [HR: 1.34; 95% CI, 1.05–1.7; P=0.018; C-index=0.55].

Conclusions We validated that a delta-radiomics based prediction model enables the identification of advanced NSCLC patients who respond to durvalumab treatment. Our study demonstrates the potential of radiomics and delta-radiomics as non-invasive imaging biomarkers to assess response and overall survival to immune checkpoint inhibitors including durvalumab.

REFERENCES

Ethics Approval The study included de-identified data from human participants. An exempt determination was made by Case Western Reserve University under the Exempt category ‘(4) Secondary research on data or specimens (no consent required)’.