Real-world insights into treatment patterns and outcomes in stage III non-small cell lung cancer (NSCLC): KINDLE study India analysis

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Background: Heterogeneous nature and poor prognosis of stage III NSCLC, accounting for ~29% of NSCLC burden, cause substantial management challenges in India. We present retrospective results of Indian cohort from the real-world, multicountry, observational KINDLE study that explored treatment patterns and associated outcomes in the pre-immuno-oncology era.

Methods: Retrospective data from 15 sites in India were analyzed for stage III NSCLC patients diagnosed between 01Jan2013 and 31Dec2017 with at least 9 months (m) of documented follow-up. Descriptive analyses for demographics, clinical characteristics, and treatment modalities, and inferential statistics to correlate treatment with progression-free survival (PFS) and overall survival (OS) were conducted.

Results: Data for 494 patients: median age 60.0 years (range 25-84), 83.4% men, 58.7% current/former smokers, and 48.2% and 51.8% with stage IIIA and IIIB NSCLC (AICC 7th ed.), respectively; 84.9% had ECOG performance score of 0/1 at diagnosis. Squamous cell and adenocarcinoma represented 48.5% and 44.6%, respectively; 15.4% had EGFR mutations. Of the 18 first-line treatment modalities, the most frequent were concurrent chemoradiotherapy (cCRT) (29.5%), sequential CRT (13.6%), chemotherapy (CT) alone (13.3%), and radiotherapy alone (12.7%). Overall median PFS was 16.4m, 95% confidence interval (CI) 14.36-19.38 (stage IIIA: 19.4m, 95% CI 15.08-25.95; IIIB: 15.4m, 95%CI 12.45-19.78). Median overall OS was 66.0m, 95% CI 49.81-noncalculable (NC); (stage IIIA: NC, 95% CI 52.14-NC; IIIB: 15.4m, 95%CI 12.45-19.78). Overall median PFS and OS were better for India (16.4m and 66m) than in the global cohort (12.5m and 34.9m). cCRT was associated with improved survival in both stage IIIA and IIIB. Improved access to newer medicines and quality care will be key to further enhance patient outcomes.

Clinical trial identification: Protocol - D1313HR00004 NCT037252475.

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Chromatin accessibility reveals potential prognostic value of the peak set associated with smoking history in patients with lung adenocarcinoma

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Background: Considerable differences in molecular characteristics have been defined between non-smokers and smokers in patients with lung adenocarcinoma (LUAD). However, study of open chromatin patterns associated with LUAD progression caused by smoking is still lacking.

Methods: Here, we firstly constructed a novel network based on correlations between each ATAC-seq peak from TCGA data using our previously developed algorithm. Subsequently, principal component analysis was performed on LUAD samples with retained peaks filtered by the correlation network. Prognostic value of the significant ATAC-seq peak set with overall survival in these smoking related LUAD patients was assessed. Then, pathway analysis of the peak-related genes was conducted for potential pathways identification.

Results: We identified a set of peaks with significant correlation that clearly differentiated long-term smokers from those with short-term smoking history in LUAD patients and also significantly associated with overall survival of these patients. The gene set that were demonstrated to be related to those peaks, such as BGN3, ACTN4, and CLDN3, are strongly associated with LUAD development, which is consistent with the important roles for the associated pathways in LUAD oncogenesis induced by smoking, including glycosphingolipid biosynthesis and tight junction pathways.

Conclusions: Our study may provide valuable insights on exploration of ATAC-seq peaks and on smoking-related LUAD carcinogenesis from a perspective of open chromatin changes.

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