Although patients with high tumor programmed death ligand-1 (PD-L1) expression benefit from PD-1/PD-L1 axis inhibitors, many studies have highlighted that a fraction of patients respond to these agents despite lacking detectable PD-L1 expression. Heterogeneity of tumor PD-L1 expression within the tumor has been postulated to be responsible for clinical benefit observed in test negative patients. To address this postulate experimentally, we compared the percentage of PD-L1 positive tumor cells (k.a., tumor proportion scores or TPS) by quantitative immunohistochemistry in paired whole tissue sections (WTS) and tissue microarray (TMA) cores from surgical non-small cell lung cancer (NSCLC) specimens.

METHODS

WTS and two 0.6mm TMA cores localized at least 3mm apart from each other were prepared from each formalin-fixed, paraffin-embedded surgically resected tumor specimens of 451 patients with stage I-IV NSCLC. Using quantitative immunofluorescence with the E7L1 anti-PD-1 antibody, TPS were generated in TMA and corresponding WTS and classified as 0%, 1-49% and ≥50%.

RESULTS

> High discordance was observed in PD-L1 TPS between paired WTS and TMA cores (discordance rate = 40.6%, 95% CI, 35.4%-45.9%; k = 0.26).

Case 1: Discordant

Case 2: Concordant

> Moderate discordance observed for the PD-L1 TPS scores amongst the two TMA cores (discordance rate = 10.2%, 95% CI, 7.6%-13.5%; k = 0.600).

CONCLUSIONS

> Discrepancies in PD-L1 expression between paired WTS and TMA core as well as between TMA cores themselves represent intratumoral heterogeneity of PD-L1.

Small needle aspirations or biopsies during endobronchial or CT-guided biopsy, which can be equated to TMA core, may not be representative of the true tumor PD-L1 expression.

It is imperative to obtain bigger or multiple needle biopsies from tumor to more accurately identify patients who could benefit from PD-1/PD-L1 axis inhibitors.

REFERENCES


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