

INTER-TUMOR HETEROGENEITY OF PD-L1 EXPRESSION IN ADVANCED NON-SMALL CELL LUNG CANCER AND ADVANCED HEAD AND NECK SQUAMOUS CELL CARCINOMA AMONG PATIENTS IN ALEXANDRIA, EGYPT

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Introduction

In the year 2020, lung cancer was second only to female breast cancer as the most commonly diagnosed cancer in the world and the leading cause of cancer-related deaths. In Egypt, the Global Cancer Observatory (GLOBOCAN) 2020 report places lung cancer as the fifth in incidence (4.9%; 6,538 cases). In terms of mortality, lung cancer was the fourth-leading cause of cancer-related deaths in both sexes and accounted for 6.5% (5,817 cases). Non-small cell lung cancer (NSCLC) accounts for 85% of lung cancers. On the other hand, among Head and Neck Cancers (HNCs), the most common pathologic subtype is the squamous cell carcinoma (SCC). In 2018, Head and Neck Squamous Cell Carcinoma (HNSCC) was the seventh leading cause of cancer-related deaths globally. In 2020, Egypt reported laryngeal cancer as the most common HNC, ranking 17th in incidence (1.2%; 1,552 cases) and 15th in mortality (1.2%; 1,061 cases) among all cancers. Over time, the role of immunotherapy has been established in the management of both advanced NSCLC, as well as recurrent and metastatic HNSCC. PD-L1 is one of the markers of response to this treatment. Despite the great leaps in research about the effectiveness of anti-PD-L1 drugs in the management of advanced NSCLC and HNSCC, there are still debates about the recommended site(s) and number of biopsies to be taken when assessing tumors for the PD-L1 marker by immunohistochemistry (IHC). More weaknesses in PD-L1’s predictive power as a biomarker for response to anti-PD-L1 immunotherapy include: type of specimen (biopsy versus resection specimen), variation in staining techniques, difference in scoring systems to determining positivity, inter-observer variability, and heterogenic expression of the PD-L1.

Aim of the work

The primary objective of this study was to determine inter-tumor heterogeneity of PD-L1 expression in advanced Non-small Cell Lung Cancer and advanced Head and Neck Squamous Cell Carcinoma among patients managed at the Alexandria University Hospitals and Specialized Universal Network (SUN) Oncology Center in Alexandria, Egypt. The secondary objectives were to compare inter-tumor heterogeneity of PD-L1 expression as reported using different cut-off points, $\geq 1\%$, $\geq 25\%$, and $\geq 50\%$ of the Tumor Proportion Score (TPS) for Non-small Cell Lung Cancer and ≥ 1 or ≥ 20 of the Combined Positive Score (CPS) for Head and Neck Squamous Cell Carcinoma.

Patients and Methods

The study was conducted among patients treated in Alexandria University Hospitals and Specialized Universal Network (SUN) Oncology Center in Alexandria, Egypt. It included 15 patients with advanced NSCLC and 13 patients with advanced HNSCC, who presented at the aforementioned facilities between December, 2021 and June, 2023. Approval to conduct the study was sought from the Faculty of Medicine’s Ethics Committee and oral informed consent was obtained from the patients. Information on biodata, clinic-pathological characteristics, and treatment was retrieved from the patients’ medical records and compiled using a checklist. This was prospective study (quasi-experimental clinical trial) assessing concordance of PD-L1 expression in surgically resected paired or matched primary tumors and their respective lymph node metastases in both advanced NSCLC and HNSCC. Sections from Formalin-fixed paraffin-embedded (FFPE) block specimens of the patients underwent Hematoxylin and Eosin (H&E) staining and microscopic examination to confirm diagnosis. After which, staining for PD-L1 was done using Dako’s PD-L1 IHC 22C3 pharmDx within 6 months of sectioning.

Results

Table 1: Concordance rate and level of agreement of PD-L1 expression between paired/matched resection specimens at different TPS cut off points in NSCLC

PD-L1 Expression (TPS)	Concordance Rate (n=15)	Kappa value (k value)	Level of Agreement	Percentage of Reliable Data
TPS $\geq 1\%$	86.67%	0.722	Moderate	35-63%
TPS $\geq 25\%$	100%	1	Almost Perfect	82-100%
TPS $\geq 50\%$	86.67%	0.667	Moderate	35-63%

Table 2: Concordance rate and level of agreement of PD-L1 expression between paired/matched resection specimens at different CPS cut off points in HNSCC

PD-L1 Expression (CPS)	Concordance Rate (n=13)	Kappa value (k value)	Level of Agreement	Percentage of Reliable Data
CPS ≥ 1	92.3%	Could not be established	-	-
CPS ≥ 20	61.5%	0.235	Minimal	4-15%

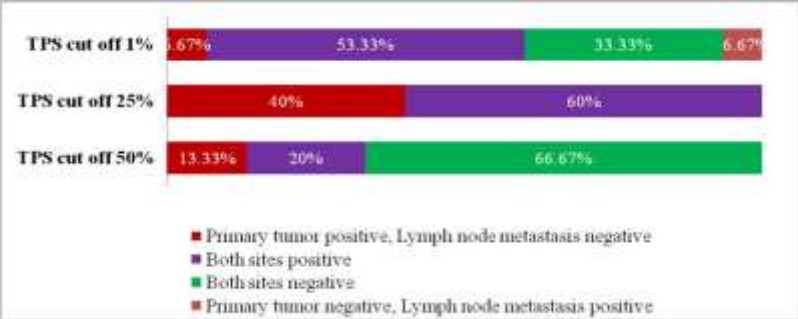


Figure 1: Comparison of PD-L1 expression between primary tumors and lymph node metastases at different TPS cut off points in NSCLC

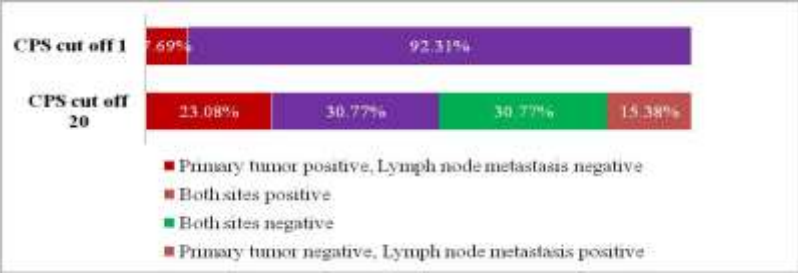


Figure 2: Comparison of PD-L1 expression between primary tumors and lymph node metastases at different TPS cut off points in HNSCC

Conclusion

There was statistically significant discordance demonstrated at all TPS cut offs. Based on the three clinically relevant clusters of PD-L1 TPS, up to a quarter of the patients’ results obtained from tests conducted on primary tumors were shifted to a different cluster when compared with results of PD-L1 tests ran on lymph node specimens. It would reduce the margin of error to test PD-L1 from at least two sites at the same time in each patient before making a treatment decision. Further studies are required to provide guidance on which of the two readings better predicts response to anti-PD-L1 therapy. In both primary and nodal subgroups, the proportions of positive LVI were statistically significantly higher in PD-L1 positive compared with PD-L1 negative subgroups. This supports the association of high PD-L1 expression with aggressive pathological features. In the HNSCC group, the number of positive PD-L1 tumors was higher in primary tumors than in lymph node metastases at both CPS cut offs of 1 and 20. In the paired primary-nodal HNSCC resection specimens, it was not possible to statistically prove the level of agreement at the CPS cut off of 1 while the minimal level of agreement demonstrated at CPS cut off of 20 was highly unreliable.