Comparative Analysis of a New IHC Assay for PD-L1 Expression in Non-Small Cell Lung Carcinomas

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Background & Objective

Lung cancer is one of the leading causes of cancer-related mortalities globally and especially the United States.[1] The level of Program Death Ligand-1 (PD-L1) IHC expression is used to select patients with non-small cell lung carcinoma (NSCLC) for immunotherapy with anti-PD1 drugs such as pembrolizumab.[2] PD-L1 protein expression is determined by the tumor proportion score (TPS), where a TPS score ≥ 1% is eligible for treatment.[3-4] Since patient stratification for anti-PD1 drugs is based on IHC alone, our purpose is to determine the overall agreement between the widely applied and well-characterized PD-L1 IHC 22C3 pharmDx and a newly developed PD-L1 IHC Assay (clone RM320) in NSCLC.

Methods

104 human formalin-fixed paraffin-embedded (FFPE) NSCLC cases in a tissue microarray were analyzed with two different IHC assays: (1) PD-L1 IHC 22C3 pharmDx, Agilent and (2) PD-L1 IHC Assay RM320, Sakura Finetek USA. Evaluation of PD-L1 IHC results was performed by a pathologist and a certified external reviewer using the Tumor Proportion score (TPS) based on the official recommended scoring guidelines and related cut-off levels at 1% and 50%.[3-4] Representative photomics were taken with the Olympus VS200 SlideView.

Results

Using the PD-L1 IHC 22C3 pharmDx as a benchmark, 57.7% of the NSCLC cases (n=60) were classified as TPS-negative (<1%), 24.0% as TPS-low (≥1-49%, n=25) and 18.3% as TPS-high (≥50%, n=19). An overall agreement of 92% between the two methods was observed.

Cutoff	22C3		RM320	
	PPA	NPA	PPA	NPA
≥ 1%	100% (44/44)	100% (60/60)	97.7% (43/44)	95.0% (57/60)
≥ 50%	100% (19/19)	100% (85/85)	89.5% (17/19)	98% (83/85)

Table 1. Agreement for PD-L1 Expression: Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) were calculated when comparing PD-L1 Clone RM320 to PD-L1 IHC 22C3 pharmDx using a 2x2 table analysis. *PPA and NPA values for RM320 were updated from the abstract.

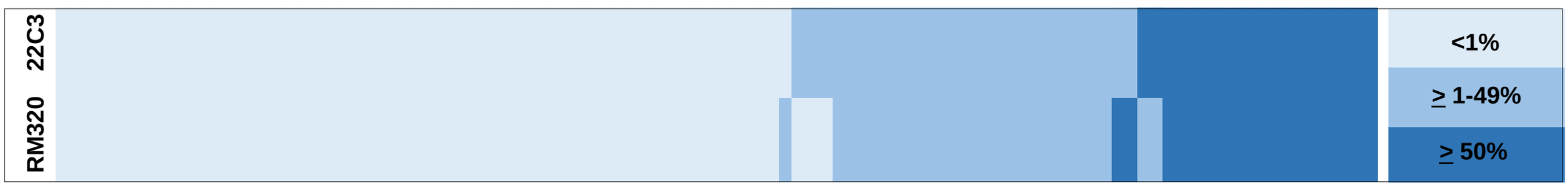

Fig 1. Distribution of PD-L1 scores: Map that depicts PD-L1 TPS scores for NSCLC (n=104)

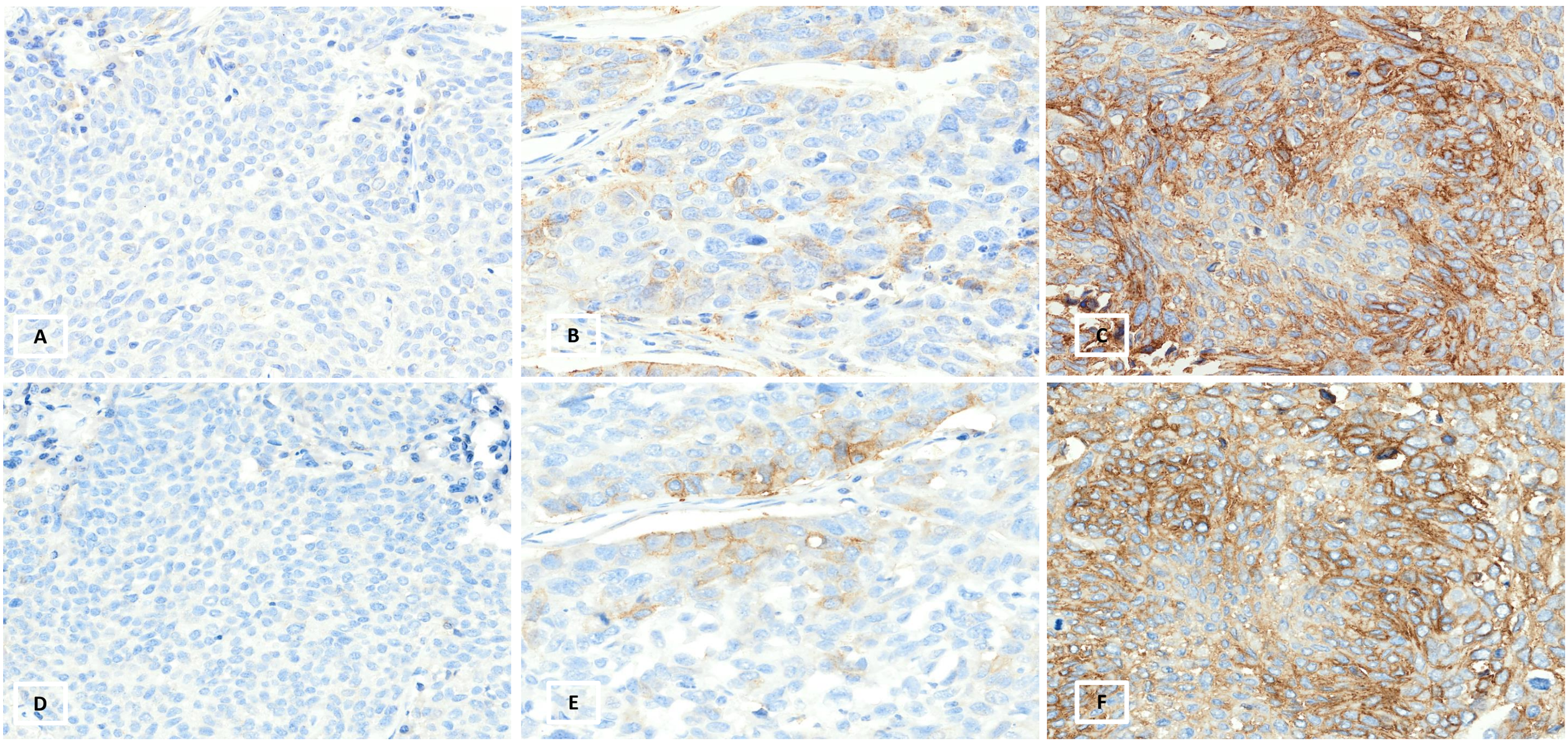

Fig 2. PD-L1 IHC Expression with TPS score
Representative photomics for PD-L1 IHC 22C3 pharmDx exhibiting a PD-L1 TPS-negative score (**A**, IHC 200x), TPS-low score (**B**, IHC 200x) and TPS-high score (**C**, IHC 400x) as well as PD-L1 IHC Assay using clone RM320 exhibiting a PD-L1 TPS-negative score (**D**, IHC 200x), TPS-low score (**E**, IHC 200x) and TPS-high score (**F**, IHC 400x).

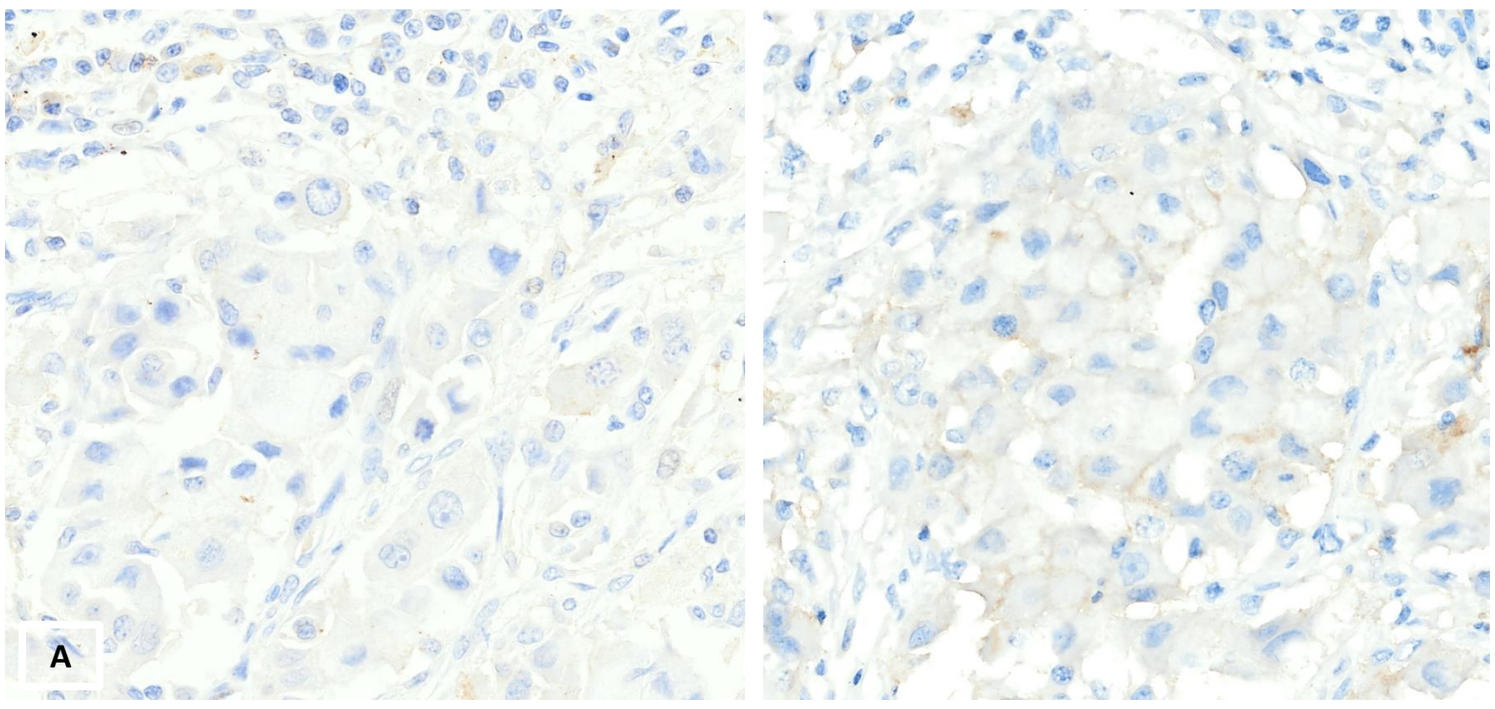

Fig 3. PD-L1 IHC Expression with TPS Negative and TPS Low score
Representative photomics for PD-L1 IHC 22C3 pharmDx exhibiting a PD-L1 TPS-negative score (**A**, IHC 200x) and PD-L1 IHC Assay using clone RM320 exhibiting a PD-L1 TPS-low score (**B**, IHC 200x)

Conclusion

- A high overall agreement for PD-L1 expression was found with IHC PD-L1 assay with clone RM320 using the applied cut-off values and guidelines for TPS in NSCLC when compared to PD-L1 IHC 22C3 pharmDx.
- More studies using NSCLC cases with positive PD-L1 expression levels are required to further evaluate the overall agreement of the PD-L1 IHC assay developed on the Tissue-Tek Genie® Advanced Staining System when compared to PD-L1 IHC 22C3 pharmDx using the TPS system.

Disclaimer: This study does not promote any *in-vitro* diagnostic use.

References:

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