

Intra-tumor and inter-tumor heterogeneity of PD-L1 expression

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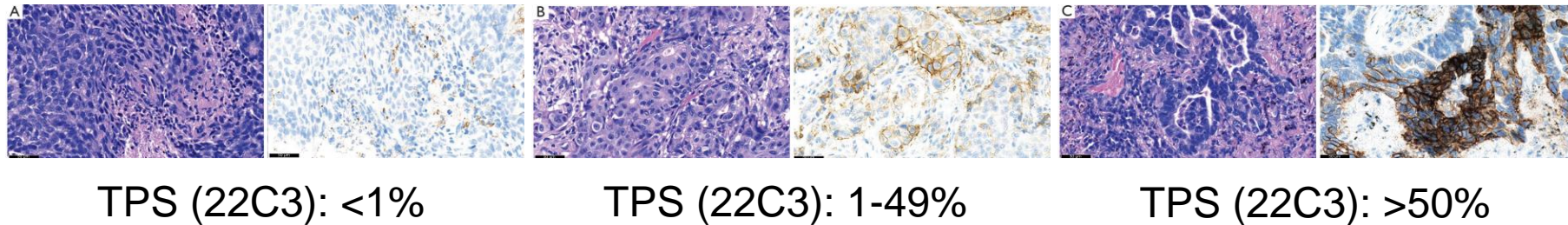
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DISCLOSURES

Commercial Interest	Relationship(s)
None	

- Programmed cell death ligand 1 (PD-L1) 22C3 pharmDx was approved by the US Food and Drug Administration, as a companion diagnostic test for pembrolizumab (Keytruda, Merck, Kenilworth, NJ, USA) in non-small cell lung cancer.



- Although increased PD-L1 expression levels can be associated with greater therapeutic efficacy, pembrolizumab is considered for patients according to PD-L1 expression.
- it is unknown whether which tissues is better for evaluation of PD-L1 expression
- Heterogeneity of PD-L1 expression is a significant practical issue between primary and secondary tumor (Inter-tumor heterogeneity).



Objective



The aim of this study was to investigate the difference of PD-L1 expression between primary tumor and paired metastatic lymph nodes in non-small cell lung cancer

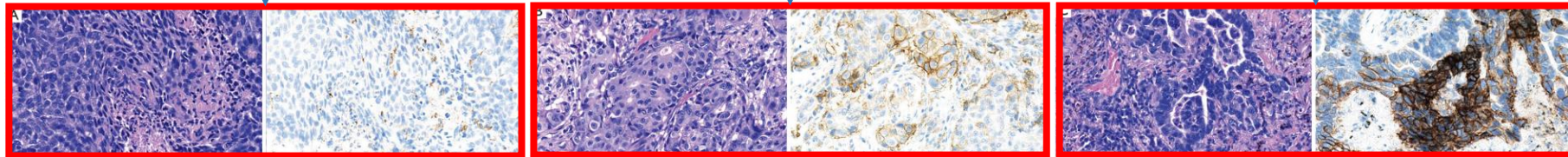
Methods

Surgical cases at Saitama Cardiovascular and Respiratory Center (Nov 2016~Dec 2020)

Surgical cases for primary lung cancer

- ✓ No biopsy by bronchoscopy before surgery
- ✓ No informed consent
- ✓ Limited surgery
- ✓ pN0
- ✓ Insufficient specimen for PD-L1 IHC

Only cases with preoperative bronchoscopy were selected



TPS (22C3): <1%
No expression

TPS (22C3): 1-49%
Low expression

TPS (22C3): >50%
High expression

Table 1. Characteristics of 18 patients

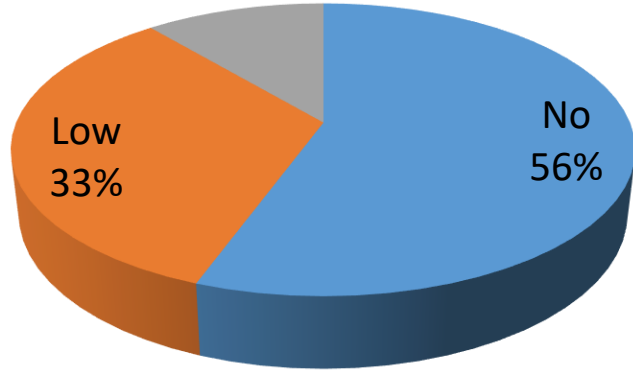
Age, year	65.4 ± 12.4
Gender	
Male	9 (50.0%)
Female	9 (50.0%)
Side	
Right	11 (61.1%)
Left	7 (38.9%)
Smoking status	
never	8 (44.4%)
former	10 (55.6%)
current	0 (0%)
Surgical procedure	
Lobectomy	16 (88.9%)
Bi-lobectomy	1 (5.6%)
Pneumonectomy	1 (5.6%)
pT factor	
1b	4 (22.2%)
1c	3 (16.7%)
2a	4 (22.2%)
2c	4 (22.2%)
3	3 (16.7%)
pN factor	
1	5 (27.8%)
2	12 (66.7%)
3	1 (5.6%)

Data on age: mean ± SD.

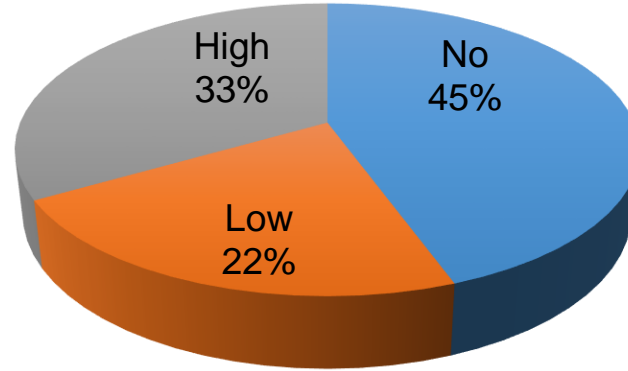
pStage		
IIB	5	(27.8%)
IIIA	9	(50.0%)
IIIB	3	(16.7%)
IVA	1	(5.6%)
Histology		
Adenocarcinoma	13	(72.2%)
Squamous cell carcinoma	3	(16.7%)
Other	2	(11.1%)
EGFR		
wild type	11	(61.1%)
mutated	7	(38.9%)
B-TPS		
No expression	10	(55.6%)
Low expression	6	(33.3%)
High expression	2	(11.1%)
T-TPS		
No expression	8	(44.4%)
Low expression	4	(22.2%)
High expression	6	(33.3%)
L-TPS		
No expression	11	(61.1%)
Low expression	6	(33.3%)
High expression	1	(5.6%)

Data on age: mean ± SD. B-TPS: Tumor Proportion Score of tumor tissue by Transbronchial biopsy, T-TPS: Tumor proportion Score of main tumor tissue, L-TPS: Tumor Proportion Score of metastatic lymph node tissue

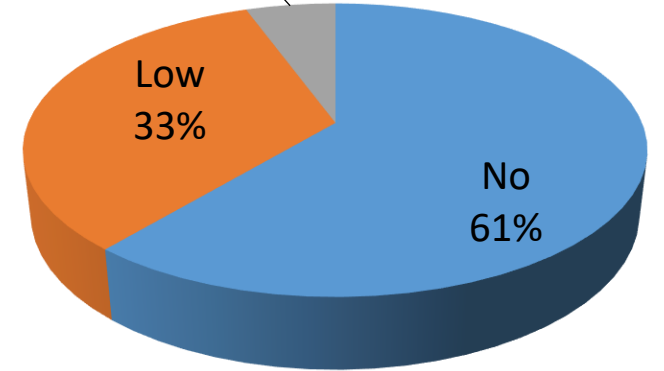
High **B-TPS**
11%



T-TPS



High **L-TPS**
6%



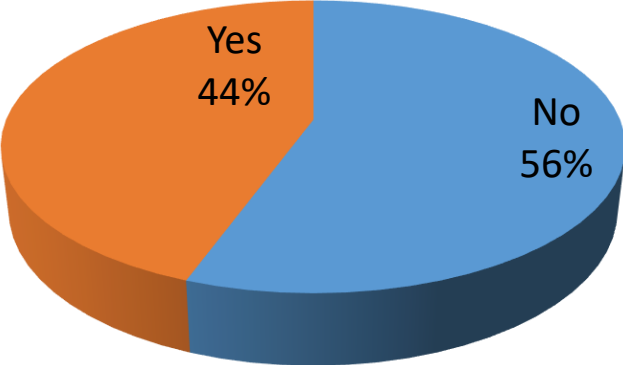
Concordance Rate

0.556
0.500
0.556

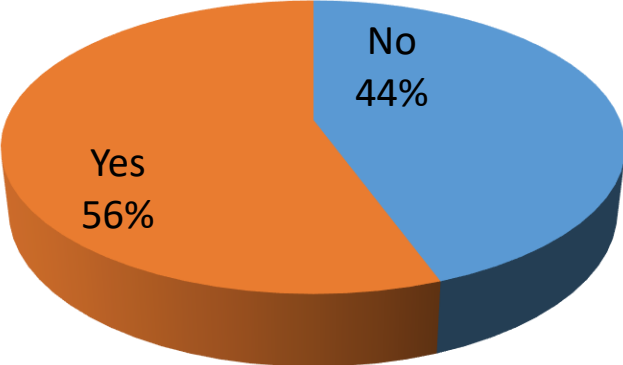
Case Num	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
B-TPS	No	No	No	No	No	No	No	No	No	No	Low	Low	Low	Low	Low	Low	High	High
T-TPS	No	No	No	No	No	No	Low	Low	High	High	No	No	Low	Low	High	High	High	High
L-TPS	No	No	No	No	No	Low	No	Low	No	Low	No	Low	No	Low	No	No	Low	High

Results

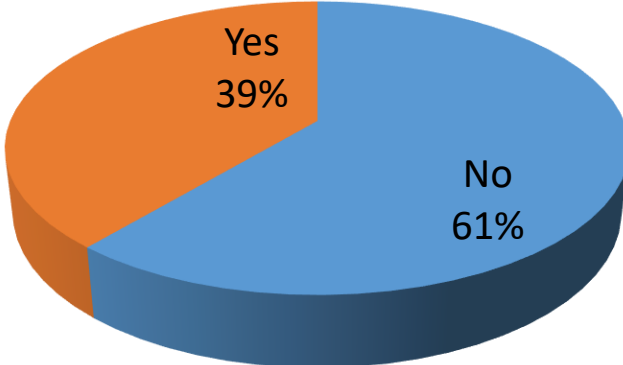
B-TPS (<1% or >=1%)



T-TPS (<1% or >=1%)



L-TPS (<1%, >=1%)



Concordance Rate

0.611
0.611
0.667

Case Num	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
B-TPS	No	No	No	No	No	No	No	No	No	No	YES	YES	YES	YES	YES	YES	YES	YES
T-TPS	No	No	No	No	No	No	YES	YES	YES	YES	No	No	YES	YES	YES	YES	YES	YES
L-TPS	No	No	No	No	No	YES	No	YES	No	YES	No	YES	No	YES	No	No	YES	YES

PD-L1 expression in non-small cell lung cancer: heterogeneity by pathologic types, tissue sampling and metastasis

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Comparison of Programmed Death Ligand-1 Immunohistochemical Staining Between Endobronchial Ultrasound Transbronchial Needle Aspiration and Resected Lung Cancer Specimens

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TABLE 3] EBUS-TBNA PD-L1 Expression \geq 1% Compared With Resected Tumor Specimen: n = 61

	PD-L1 \geq 1%	
	Tumor +	Tumor -
EBUS-TBNA +	21	0
EBUS-TBNA -	8	32

TABLE 5] EBUS-TBNA PD-L1 Expression \geq 50% Compared With Resected Tumor Specimen: n = 61

	PD-L1 \geq 50%	
	Tumor +	Tumor -
EBUS-TBNA +	7	3
EBUS-TBNA -	8	43

Comparison of tissue samples between preoperative EBUS-TBNA and surgery

61 cases: Adenocarcinoma: 39

Squamous cell carcinoma: 21

Large cell carcinoma: 1

Concordance rate: 87.0% (53/61, PD-L1 \geq % cutoff)

82.0% (50/61, PD-L1 \geq 50% cutoff)

Table 3 The heterogeneous PD-L1 expression between biopsy and matched resected specimens

PD-L1 status	Biopsy			Total (n=35)	Kappa value	P value
	TPS <1%	TPS 1-49%	TPS \geq 50%			
Resection						
TPS <1%	8	2	0	10	0.533	<0.001
TPS 1-49%	6	7	2	15		
TPS \geq 50%	0	1	9	10		
Total	14	10	11	35		

PD-L1, programmed cell death ligand-1; TPS, tumour proportion score.

Comparison between pre- and post-operative tissue samples

35 cases: Adenocarcinoma: 18

Squamous cell carcinoma: 17

Concordance rate: 68.6% (24/35)

- Concordance rate of TPS was 55.6% between tissue samples obtained by bronchoscopy and surgery for primary tumor.
- Concordance rate of TPS was 55.6% between tissue sample obtained by bronchoscopy for primary tumor and tissue sample obtained by surgery for metastatic lymph node.
- Concordance rate of TPS was 38.9% among tissue samples obtained by bronchoscopy or surgery for primary tumor, or that obtained by surgery for metastatic lymph node.

- Intra-tumor heterogeneity exists between tissue samples obtained by bronchoscopy and surgery for primary tumor.
- Inter-tumor heterogeneity exists between tissue samples obtained by bronchoscopy for main tumor and surgery for metastatic lymph node.
- In near future, we will report results of long-term outcome after surgical treatment by subgroups of tissue samples.



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