Réseau de cancérologie Rossy
Rossy Cancer Network

PD-L1 testing of EBUS-TBNA samples acquired for the diagnosis and staging of NSCLC

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Introduction

- Lung cancer is the leading cause of cancer death worldwide
- Immune checkpoint inhibitors targeting either programmed death receptor 1 (PD-1) or programmed death receptor-ligand 1 (PD-L1) have become an integral part of management of advanced NSCLC
- PD-L1 expression in at least 50% of tumour cells on tissue biopsy samples has been correlated with improved efficacy of the PD-1 inhibitor pembrolizumab[1,2]
- Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is frequently the first and only invasive diagnostic procedure performed in patients with advanced lung cancer
- Limited studies to date have examined the suitability of EBUS-TBNA specimens for the assessment of PD-L1 status[3,4,5]

Objectives

1. Assess the feasibility and results of PD-L1 testing in EBUS-TBNA specimens acquired for the diagnosis and/or staging of NSCLC
2. Compare the results of PD-L1 testing in EBUS-TBNA samples with additional histological samples tested for PD-L1, where available
3. Examine turnaround time (TAT) from test request to availability of PD-L1 results for clinical decision-making
4. To examine the impact of PD-L1 results based on EBUS-TBNA samples on patient management (*in progress*)

Materials & Methods

- Retrospective review between JUN-2016 and DEC-2017
- Patients identified from prospective pathology database
- Patient and procedural characteristics extracted OACIS
- Aspirated specimens placed in CytoLyt® (methanol-water solution)
- Sample centrifuged into pellet, fixed with B-Plus Fixative (37% formaldehyde) and cell block embedded in paraffin
- PD-L1 immunohistochemistry performed using Dako's 22C3 antibody, and expressed as tumour proportion score (TPS)
- TPS ≥ 50% considered PD-L1 positive
- H&E slides reviewed by cytopathologist to categorize cellularity between <100, 100-500 and >500 viable tumour cells

Results Overview

120
Patients

64
Women

68.1
Mean age
(±10.5y)

92%
Samples suitable
for PD-L1 testing

48%
PD-L1
positive

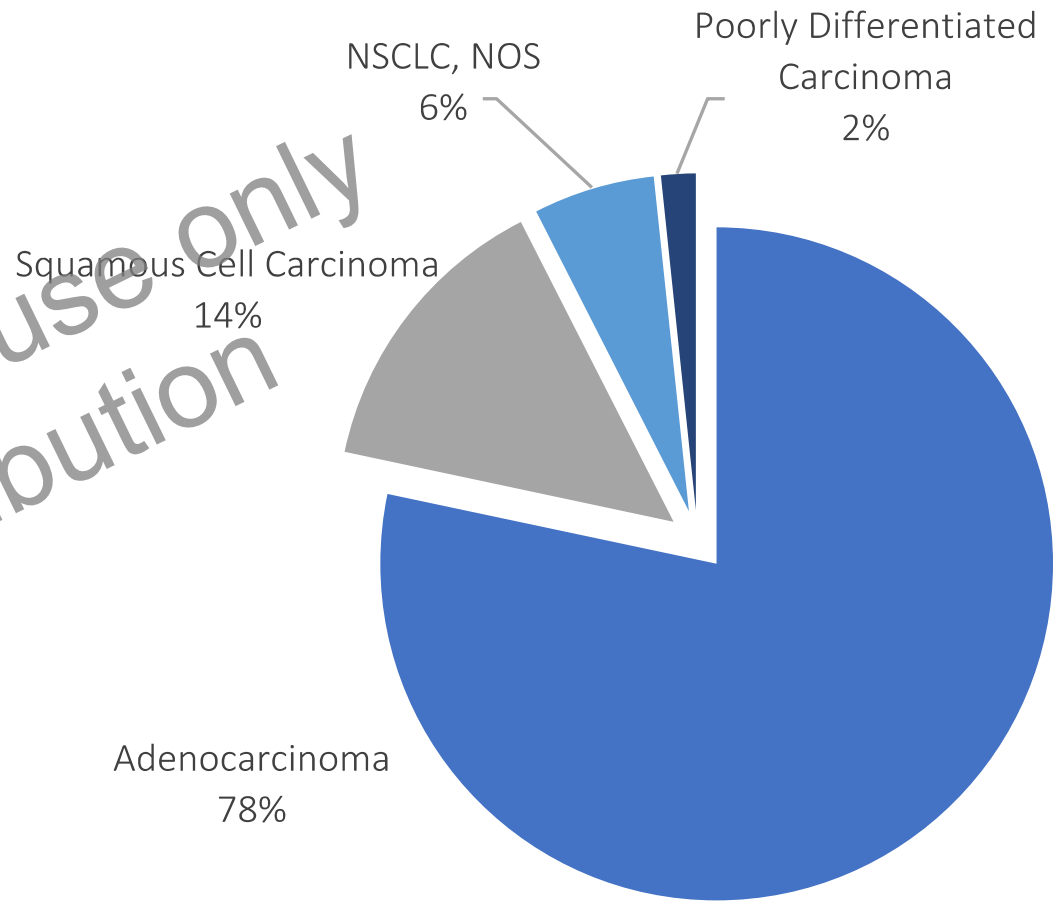
15/20
Concordant,
histology

100%
Sensitivity,
EBUS vs. histology

55%
Specificity,
EBUS vs. histology

Patient Characteristics

Patient Characteristics		n=120
Mean age in years		68.1±10.5
Sex	Female	64 (53.3%)
	Male	56 (46.7%)
NSCLC subtype		
	Adenocarcinoma	94 (78.3%)
	Squamous cell carcinoma	17 (14.2%)
	NSCC, NOS	7 (5.8%)
	Poorly differentiated carcinoma	2 (1.7%)
Disease stage		
	Stage I-II	9 (7.5%)
	Stage III-IV	111 (92.5%)

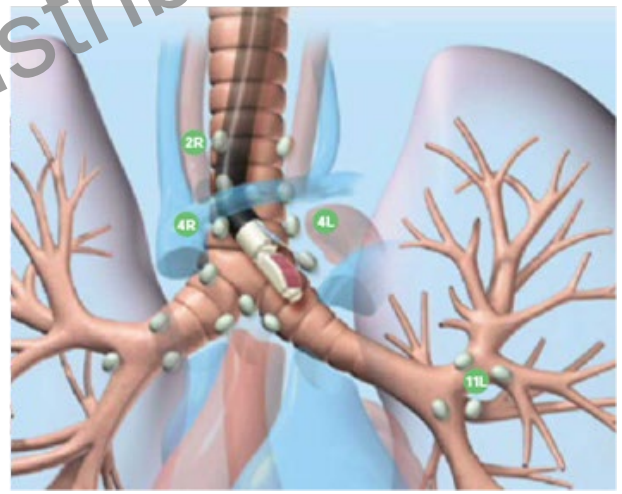


Procedural Characteristics

Procedural Characteristics		n=120
Needle gauge	22G	118 (98.3%)
	19G	2 (1.7%)
Median number of needle passes (range)		4 (2-8)
Availability of ROSE	Presence	6 (5.0%)
	Absence	114 (95.0%)
Site of nodal sample tested for PD-L1	Subcarinal	29 (24.2%)
	Hilar	52 (43.3%)
	Paratracheal	39 (32.5%)

Specimen Cellularity*	Total n=120	Feasibility of PD-L1 Testing
< 100 cells	10 (8.3%)	No+
100-500 cells	34 (28.3%)	Yes
>500 cells	76 (63.3%)	Yes

*H&E slides (100X)
+Cancelled in 8/10 patients



PD-L1 Expression according to EBUS-TBNA specimen cellularity

	Specimen cellularity*		
Tumor Proportion Score (TPS)**	**100-500 cells (n=34)**	**>500 cells (n=76)**	**Combined samples with >100 cells**
< 1%	8	14	23 (20.9%)
1-49%	7	28	35 (31.8%)
≥50% (Positive)	19	34	54 (49.1%)
TOTAL	**34 (30.9%)**	**76 (69.1%)**	**110**

* H&E slides (100X); no testing performed on 10 samples with < 100 cells
**PD-L1 staining using Dako's 22C3 PharmDx

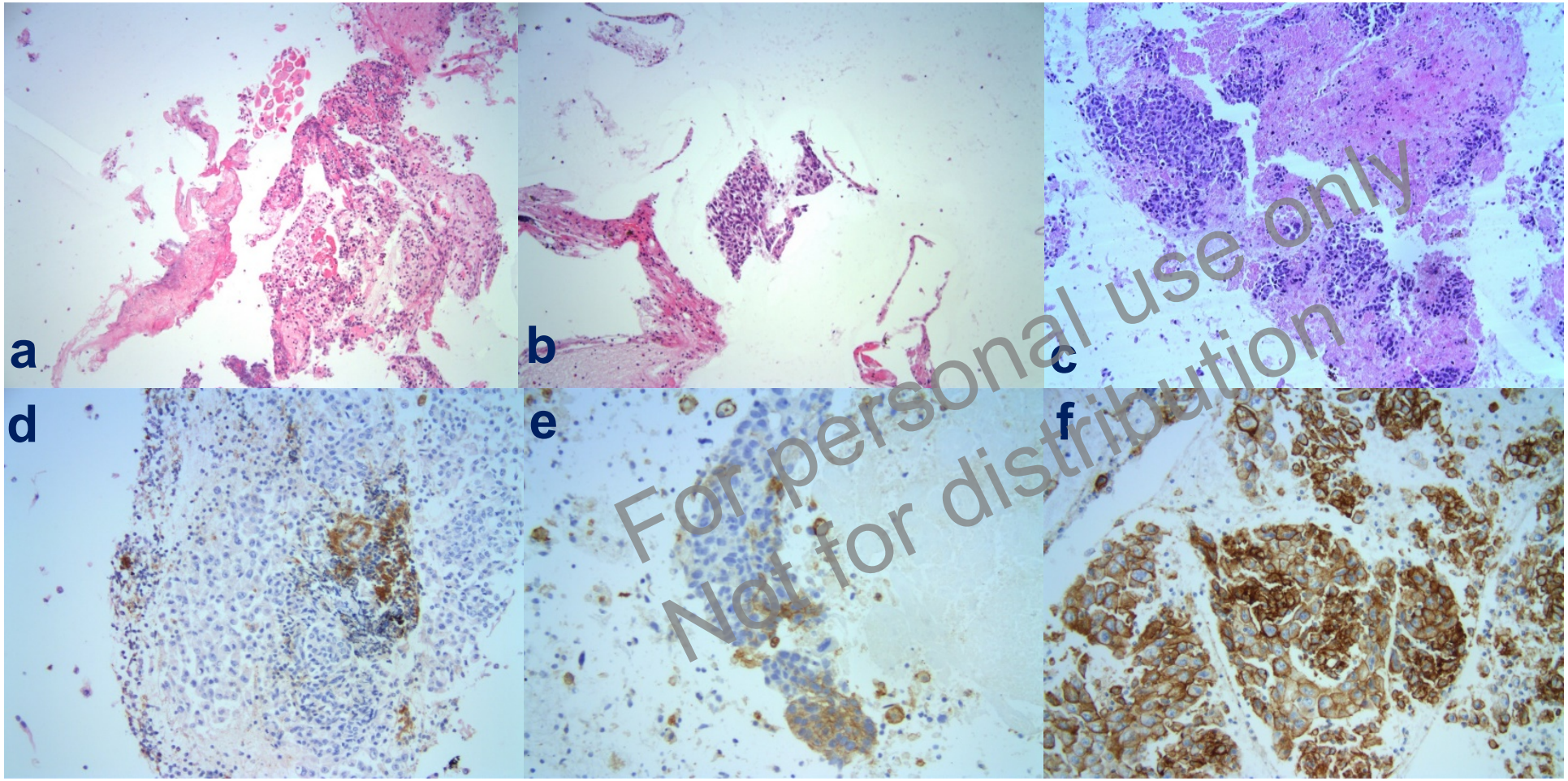
Comparison of EBUS PD-L1 results vs. additional histology samples

	Histology PD-L1 < 50%	Histology PD-L1 ≥ 50%	Total
EBUS PD-L1 < 50%	6	0	6
EBUS PD-L1 ≥ 50%	5	9	14
Total	11	9	20

Sensitivity: 100%
Specificity: 55%

	Histology PD-L1 < 1%	Histology PD-L1 < 1-49%	Histology PD-L1 ≥ 50%
EBUS PD-L1 < 1%	2	0	0
EBUS PD-L1 < 1-49%	2	2	0
EBUS PD-L1 ≥ 50%	0	5	9

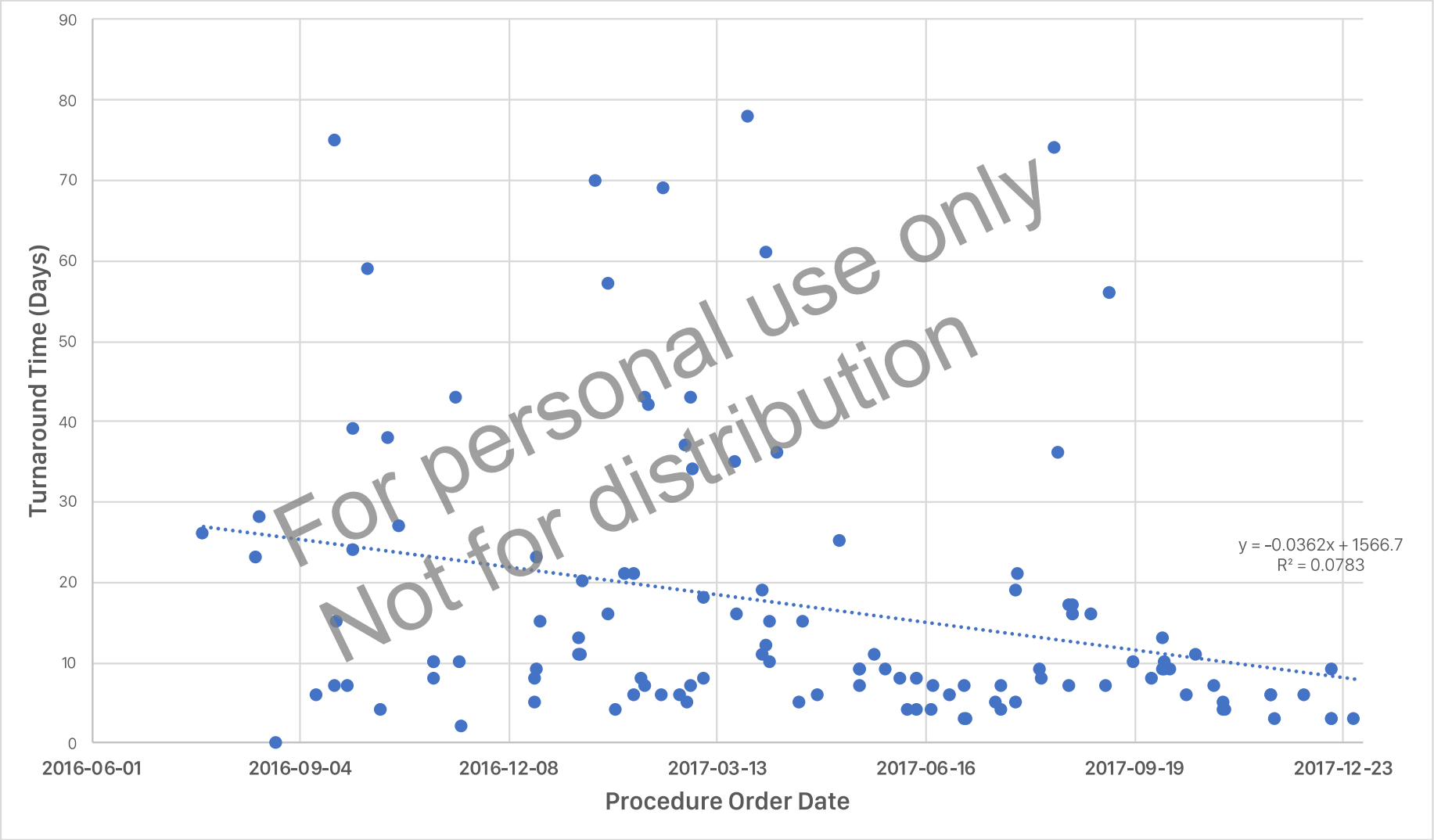
PD-L1 Staining



H&E, 100X: Cellularity scores of <100 viable tumor cells (**a**), 100-500 cells (**b**) and >500 cells (**c**)

PD-L1 IHC on EBUS-TBNA sample using 22C3PharmDx, 200X: TPS of <1% (**d**), 1-49% (**e**) and ≥ 50% (**f**)

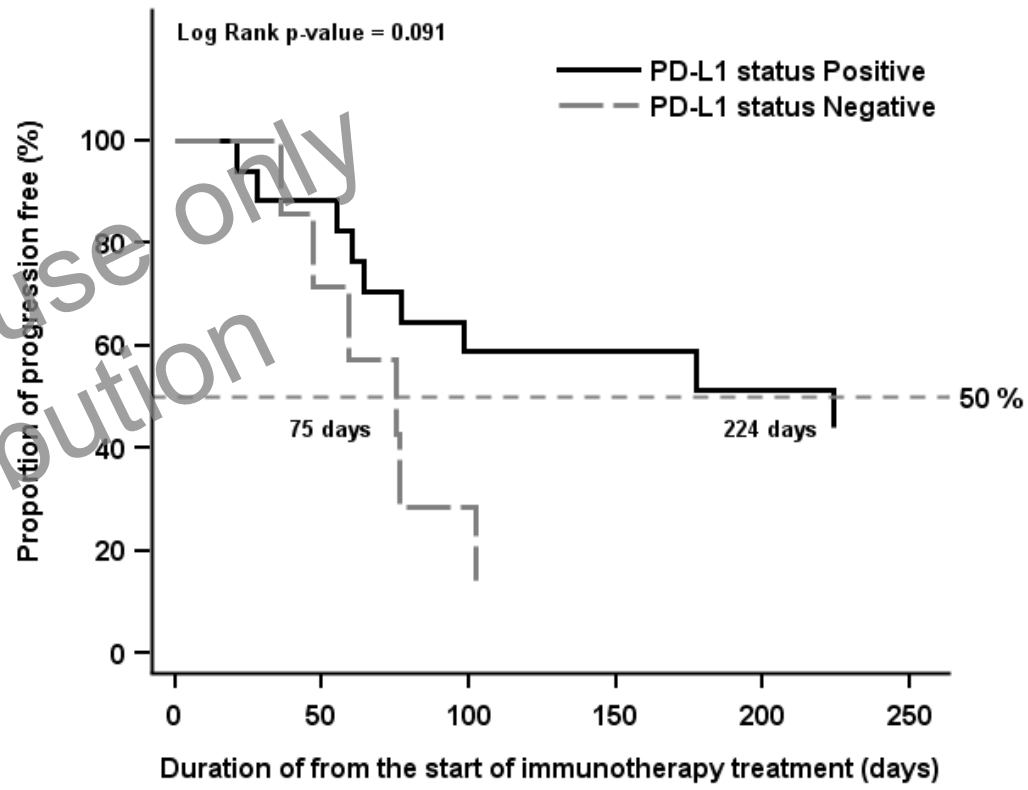
Turnaround time vs. procedure order date



Impact of EBUS results on patient management (*very* preliminary results)

	PDL-1 positive	PDL-1 negative
Pembrolizumab, 1st line	4	0
Pembrolizumab, 2nd line	11	0
Nivolumab, 2nd line	2	6

- 2 patients PDL-1 positive on EBUS samples received > 2nd line pembrolizumab
- 1 patient PDL-1 negative on EBUS sample received 5th line nivolumab
- 2 patients with unknown PDL-1 status (insufficient EBUS sample) received 2nd line nivolumab



Discussion

- Only EBUS-TBNA samples available for PD-L1 testing in majority of patients
- Feasibility of PD-L1 testing in EBUS samples consistent with recently published, smaller series (Biswas, Stoy, Fernandez-Bussy)
- Rate of positive PD-L1 expression overall higher than previously reported, although consistent with other reports (Lerner et al)
- Sakata et al. Comparison of PD-L1 immunohistochemical staining between EBUS-TBNA and resected lung cancer specimens (Chest 2018)
  - Concordance rate for PD-L1 ≥50% was 82%
  - Sensitivity and specificity of EBUS samples were 47% and 93%, respectively
- Current disconnect between specimens required for clinical trials vs. tissue samples acquired in routine clinical practice (Beattie et al, ATS 2018)

Conclusion

- PD-L1 testing was feasible in 92% of EBUS-TBNA samples acquired for diagnosis & staging of NSCLC
- The prevalence of positive PD-L1 staining (TPS≥50% with Dako's 22C3 antibody) was 48%
- Where tissue was available, the results of PD-L1 testing in EBUS samples were concordant with histological samples in 15/20 (75%) patients
- To date, 29 patients have been treated with pembrolizumab or nivolumab, on the basis of PD-L1 results in EBUS samples
- Future work will review the impact of these results on patient outcomes

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Thank you !