Распространенность экспрессии PD-L1 при IIIB и IV стадиях немелкоклеточного рака легкого. Данные из реальной практики

Real-World Prevalence of PD-L1 Expression in Locally Advanced or Metastatic Non–Small-Cell Lung Cancer
The Global, Multicenter EXPRESS Study

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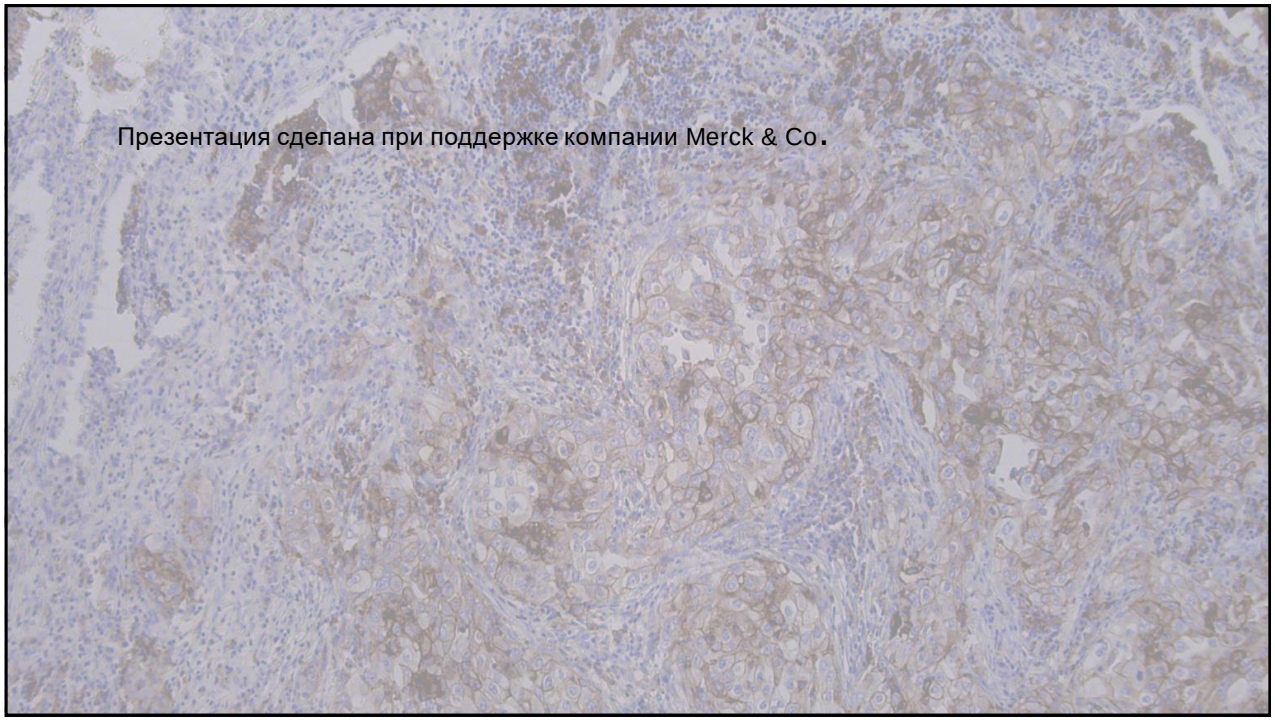


Презентация сделана при поддержке компании Merck & Co.

Background (I)

- Pembrolizumab (as monotherapy[1,2] and in combination with chemotherapy[3]) has demonstrated clinical benefit versus standard of care for patients with:
  - Previously treated advanced NSCLC expressing PD-L1 on ≥1% of tumor cells[1]
  - Treatment-naive advanced NSCLC expressing PD-L1 on ≥50% of tumor cells[2]
  - Treatment-naive advanced NSCLC irrespective of tumor PD-L1 expression[3]
  - *EGFR* mutations and *ALK* translocations were either exclusion criteria in these studies (treatment-naive) or were infrequently present in tumors among these patients (previously treated)

1. Herbst RS, et al. *Lancet*. 2016;387:1540-50. 2. Reck M, et al. *N Eng J Med.* 2016; 375:1823-33. 3. Langer CJ, et al. *Lancet Oncol*. 2016;17:1497-508.

Background (II)

- Evaluation of PD-L1 tumor proportion score (TPS) in pembrolizumab clinical trials was conducted centrally using PD-L1 IHC 22C3 pharmDx (Agilent Technologies, Carpinteria, CA, USA)
- Prevalence of PD-L1 expression has largely been evaluated in clinical trials
  - **To date, little is known about global, real-world prevalence of PD-L1 expression in tumor cells of patients with advanced NSCLC, determined using PD-L1 IHC 22C3 pharmDx**
- Real-world assessment of eligibility for pembrolizumab treatment relies on local PD-L1 IHC testing by trained pathologists using the PD-L1 IHC 22C3 pharmDx assay or another comparable validated assay[1]

1. Comparable assays include the CE-marked Ventana SP263 assay or validated 22C3 antibody-based LDTs, such as that reported in Ilie, M et al. *PLoS ONE* 2017;12(8):e0183023.

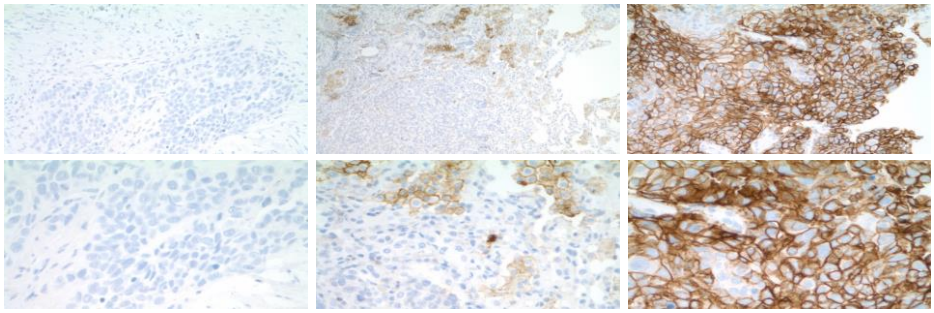
Study Methods

- Global, multicenter, retrospective observational study to determine real-world prevalence of tumor PD-L1 expression in advanced NSCLC
  - 18 countries
  - 45 centers
- Key eligibility criteria
  - Patients aged ≥18 years
  - Stage IIIB/IV NSCLC
  - ≤5-year old tumor tissue block obtained before treatment for advanced disease[a]
- PD-L1 evaluation performed locally using PD-L1 IHC 22C3 pharmDx

[a]Slides freshly cut from archived tumor blocks.

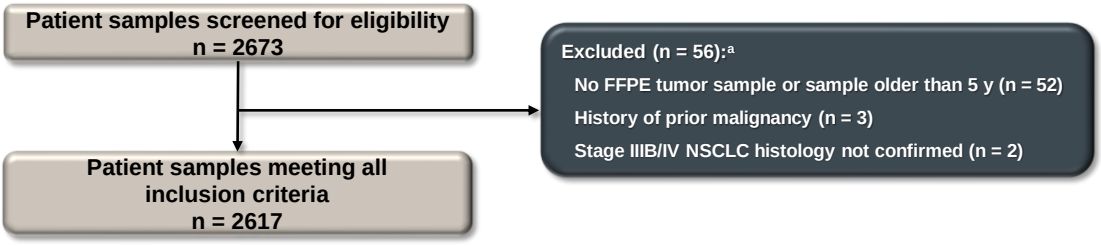
PD-L1 Evaluation

- Pathologists at each site were trained in a Merck-sponsored pathologist training program for the correct scoring and interpretation of PD-L1 TPS
- PD-L1 TPS cutpoints were rigorously determined using independent NSCLC training and validation sets derived from KEYNOTE-001[1]



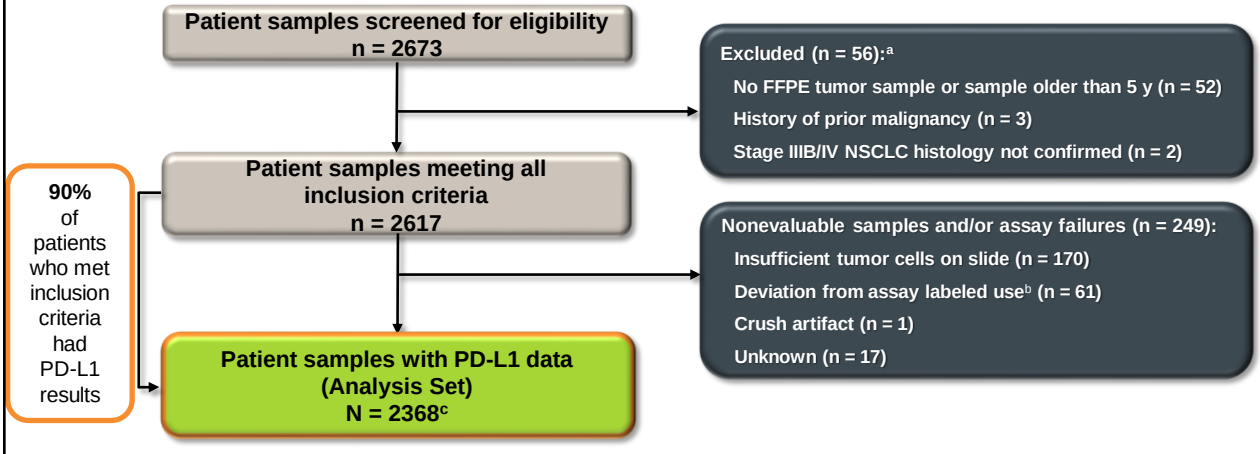
1. Garon EB et al. *N Engl J Med* 2015;372:2018-28.

Patient Sample Screening And Evaluation of PD-L1 Expression on Tumor Cells



[a]Reasons for exclusion are not mutually exclusive.
Data cutoff date September 21, 2017.

Patient Sample Screening And Evaluation of PD-L1 Expression on Tumor Cells



[a]Reasons for exclusion are not mutually exclusive. [b]Decalcified sample.
[c]After abstract submission, 67 additional patients were excluded due to violations of eligibility criteria or assay labeled use.
Data cutoff date September 21, 2017.

PD-L1 Prevalence in Tumor Cells by Demographics and Regions

	n	TPS ≥50%	TPS ≥1%	TPS <1%
All patients	2368	530 (22%)	1232 (52%)	1136 (48%)
Age, years				
≥75	450	105 (23%)	224 (50%)	226 (50%)
<75	1917	425 (22%)	1008 (53%)	909 (47%)
Sex				
Female	899	189 (21%)	471 (52%)	428 (48%)
Male	1468	340 (23%)	760 (52%)	708 (48%)
Region				
Asia-Pacific[a]	661	148 (22%)	351 (53%)	310 (47%)
Europe[b]	831	181 (22%)	428 (52%)	403 (48%)
The Americas[c]	363	77 (21%)	172 (47%)	191 (53%)
Other[d]	513	124 (24%)	281 (55%)	232 (45%)

Number of patients with specific characteristic (row total n) is denominator for % in TPS columns.
[a]Japan, Hong Kong, Korea, Singapore, Taiwan. [b]Denmark, France, Germany, Italy, Spain, Sweden, The Netherlands. [c]Argentina, Canada, and Colombia. [d]Russia, Saudi Arabia, and Turkey. Data cutoff date September 21, 2017.

PD-L1 Prevalence in Tumor Cells by Clinicopathologic Characteristics

	n	TPS ≥50%	TPS ≥1%	TPS <1%
Specimen type				
Surgical resection	610	127 (21%)	327 (54%)	283 (46%)
Core needle biopsy	1694	394 (23%)	880 (52%)	814 (48%)
Specimen source				
Primary	1735	377 (22%)	892 (51%)	843 (49%)
Metastases	565	133 (24%)	297 (53%)	268 (47%)
Histology				
Squamous	500	114 (23%)	286 (57%)	214 (43%)
Nonsquamous	1846	410 (22%)	934 (51%)	912 (49%)
Smoking status				
Never	532	98 (18%)	249 (47%)	283 (53%)
Former	642	154 (24%)	349 (54%)	293 (46%)
Current	740	184 (25%)	393 (53%)	347 (47%)

Number of patients with specific characteristic (row total n) is denominator for % in TPS columns. Data cutoff date September 21, 2017.

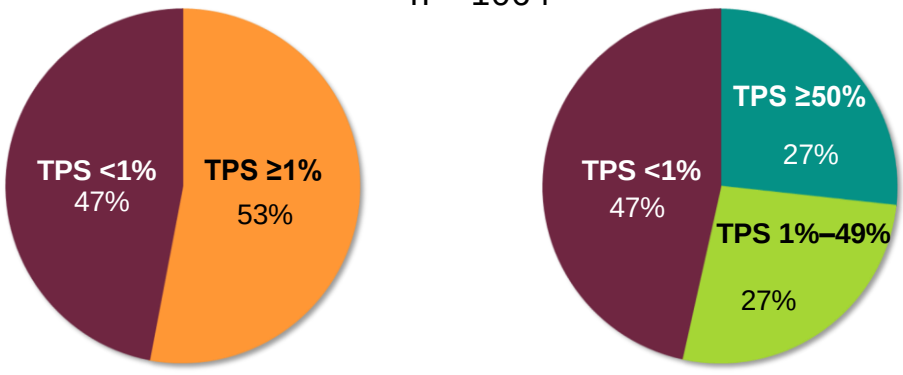
PD-L1 Prevalence in Tumor Cells by *ALK* Translocation and *EGFR* Mutation Status

	n	TPS ≥50%	TPS ≥1%	TPS <1%
ALK Translocation positive	74	15 (20%)	48 (65%)	26 (35%)
EGFR Mutation positive	448	60 (13%)	197 (44%)	251 (56%)
EGFR and *ALK* negative	1064	283 (27%)	569 (53%)	495 (47%)

Number of patients with specific characteristic (row total n) is denominator for % in TPS columns.
Data cutoff date September 21, 2017.

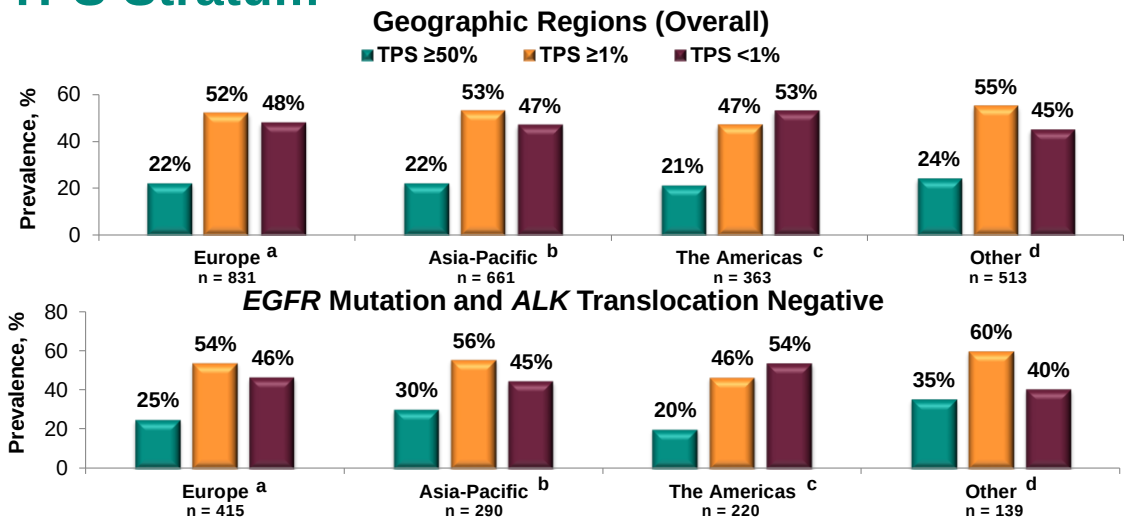
PD-L1 Prevalence[a] in Tumor Cells by TPS Stratum

***EGFR* Mutation and *ALK* Translocation Negative**
n = 1064



Rounding may result in total percentage >100%.
[a]Prevalence is defined as the proportion (%) of a population that is affected by a particular disease/feature at a given time.
Data cutoff date September 21, 2017.

PD-L1 Prevalence in Tumor Cells by TPS Stratum



[a]Denmark, France, Germany, Italy, Spain, Sweden, The Netherlands. [b]Japan, Hong Kong, Korea, Singapore, Taiwan. [c]Argentina, Canada, Colombia. [d]Russia, Saudi Arabia, Turkey.
Rounding may result in total percentage >100%.
Data cutoff date September 21, 2017.

Conclusions

- Largest **real-world study** in advanced NSCLC evaluating PD-L1 expression in tumor cells using PD-L1 IHC 22C3 pharmDx
- Prevalence of PD-L1 TPS ≥50% and TPS ≥1% was similar across geographic regions and between surgical specimens and biopsies
- Consistency in results across geographic regions also suggests high **overall reliability** of IHC-based PD-L1 analysis when performed by **experienced trained pathologists**
  - **High assay success rate** despite local evaluation in 45 sites across 18 countries

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