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Clinicopathological and genomic correlates of programmed cell death ligand 1 (PD-L1) expression in nonsquamous non-small cell lung cancer

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Dana-Farber Cancer Institute

Disclosures

- Nothing to disclose

Background

- Increasing expression of PD-L1 (encoded by the *CD274* gene) correlates with improved outcomes to immunotherapy in NSCLC
- PD-L1 tumor proportion score (TPS) groups in NSCLC:
  - negative (<1%)
  - low (1-49%)
  - high (≥50%)
- Factors associated with PD-L1 expression in NSCLC are not well understood

Methods

- We aimed to investigate clinicopathological and genomic characteristics associated with PD-L1 expression in nonsquamous NSCLC.

- Nonsquamous NSCLC with PD-L1 assessment and targeted NGS at the Dana-Farber Cancer Institute

- We analyzed association of PD-L1 expression levels with:
  - Clinicopathological characteristics
  - Gene mutations
  - Gene and arm copy number variations (CNVs)
  - Immunotherapy outcome implications

Patient characteristics by PD-L1 expression levels

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	N=909	PD-L1 <1% (N=304, 33%)	PD-L1 1-49% (N=326, 36%)	PD-L1 ≥50% (N=279, 31%)	*p*
Age	**Median (range)**	66 (35-91)	64 (22-88)	67 (29-92)	0.21
Sex	**Female (N=549)**	179 (59%)	196 (60%)	174 (62%)	
Smoking status	**Never (N=185)**	68 (22%)	68 (21%)	49 (18%)	0.34
	Current/former (N=724)	236 (78%)	258 (79%)	230 (82%)	
Pack-years	**Median (IQR)**	20 (1.2-40.0)	20 (3.5-37.0)	25 (7.5-40.5)	***0.01***
Stage at diagnosis	**I-IIIA (N= 297)**	120 (39%)	109 (33%)	68 (24%)	***<0.001***
	IIIB-IV (N=612)	184 (61%)	217 (67%)	211 (76%)	
Histology	**Adenocarcinoma (N=851)**	287 (94%)	311 (95%)	253 (91%)	***0.047***
	Other (N=58)	17 (6%)	15 (5%)	26 (9%)	
Biopsy tumor site*	**Primary (N=180)**	55 (34%)	70 (37%)	67 (37%)	0.81
	Metastasis (N=345)	108 (66%)	121 (63%)	116 (63%)	
TMB (mut/Mb)	**Median (range)**	10.6 (7.3-14.5)	10.6 (6.8-15.2)	12.2 (8.4-18.2)	***<0.001***

*among metastatic patients at diagnosis

Oncogenic driver mutations

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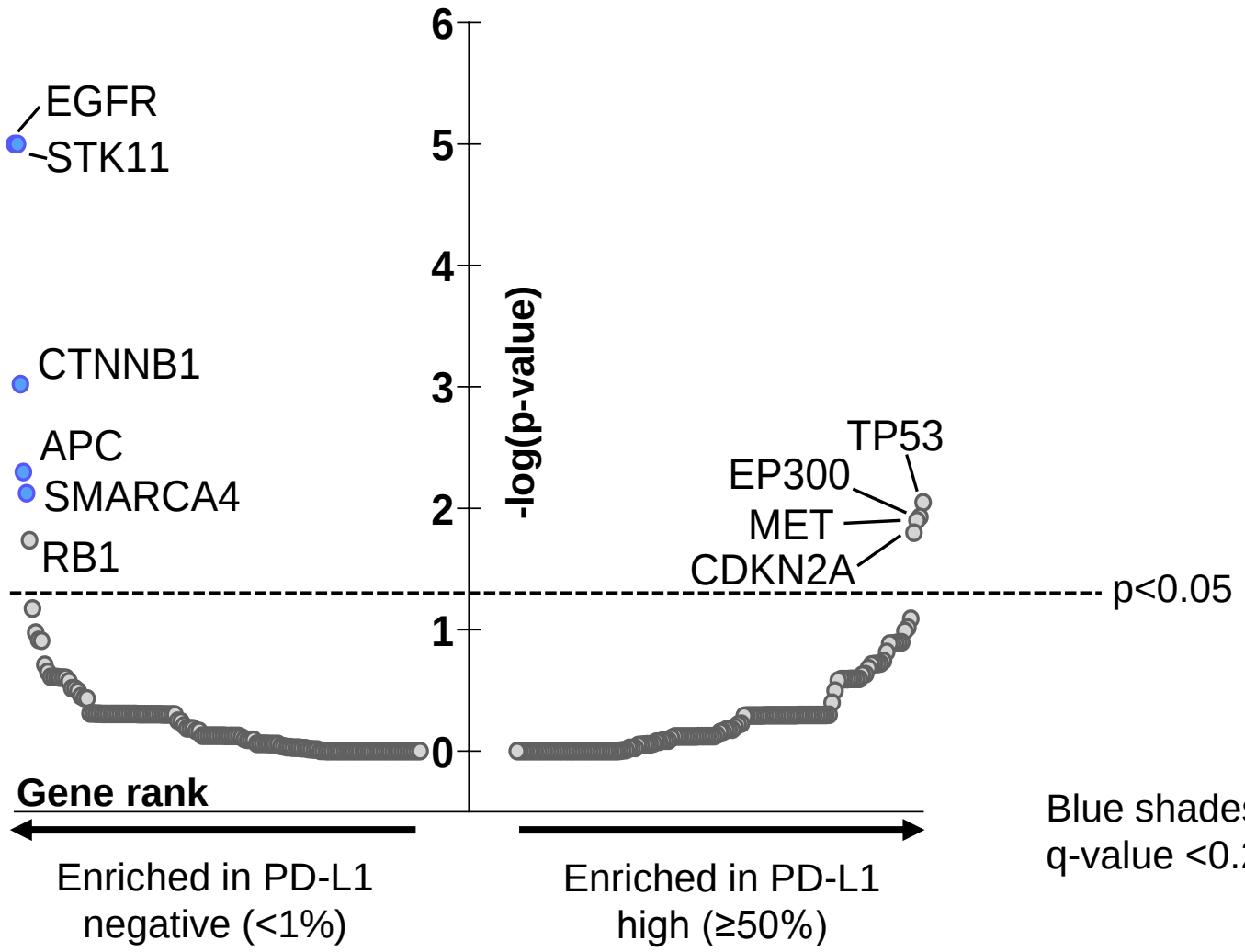
PD-L1 <1% N=304

PD-L1 1-49% N=326

PD-L1 ≥50% N=279

Gene	P

Mutations associated with PD-L1 expression levels



Blue shades indicate q-value <0.25.

Chromosomal arm and gene CNVs

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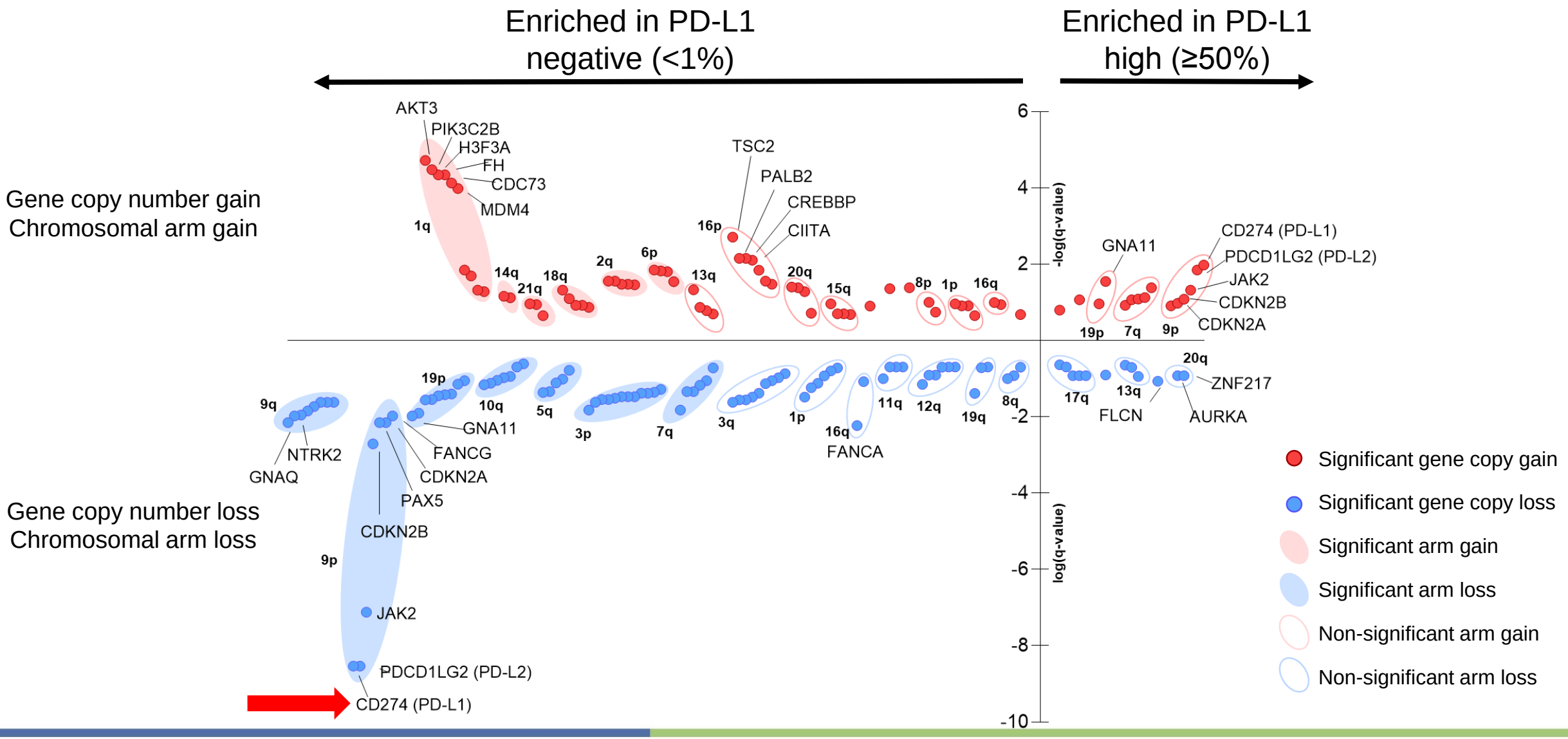
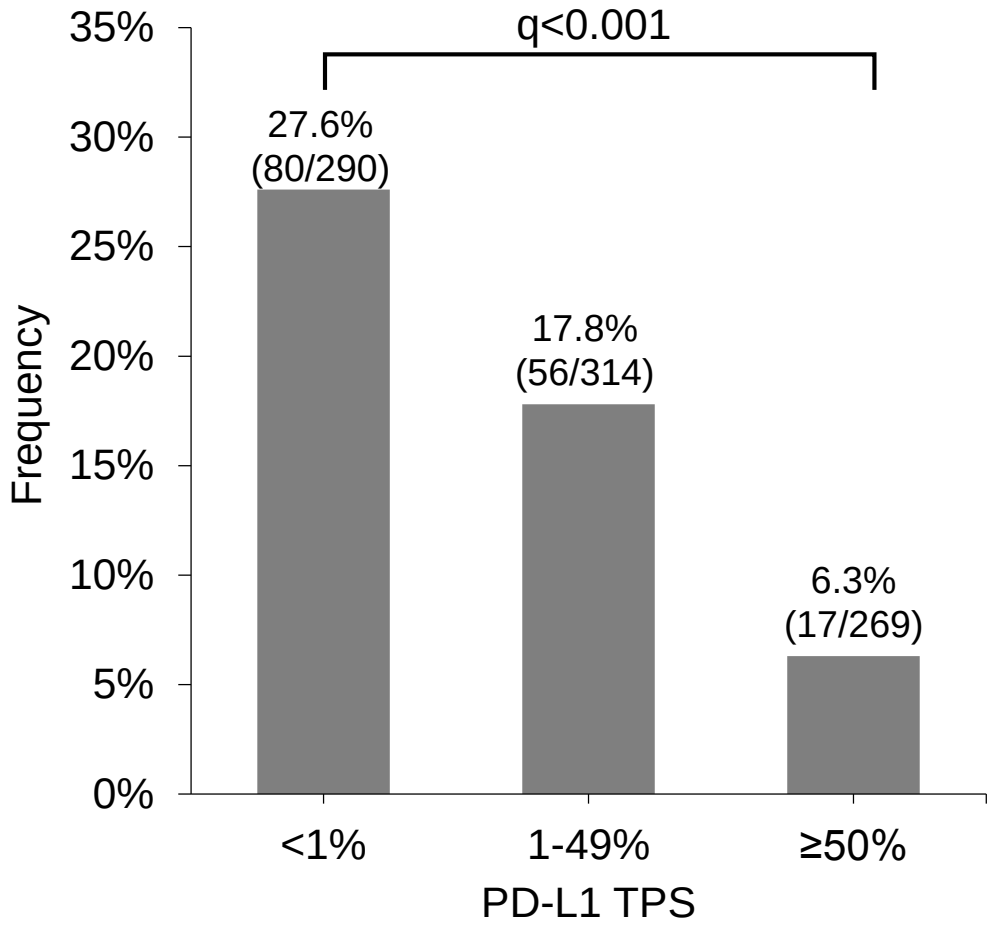
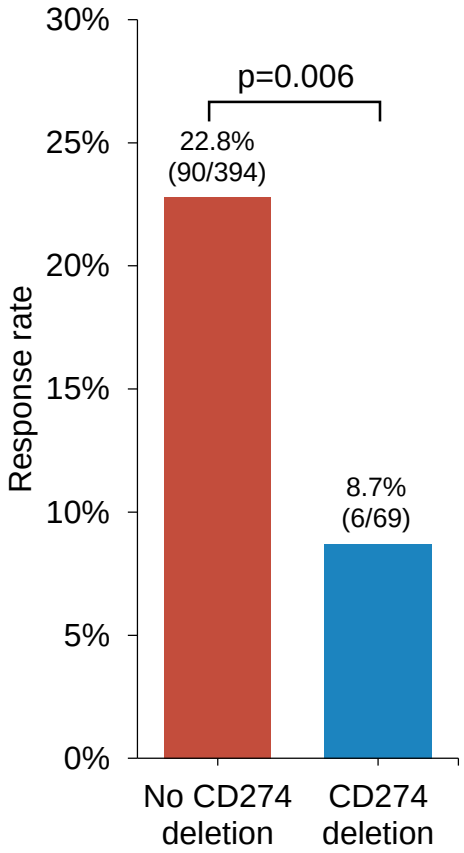
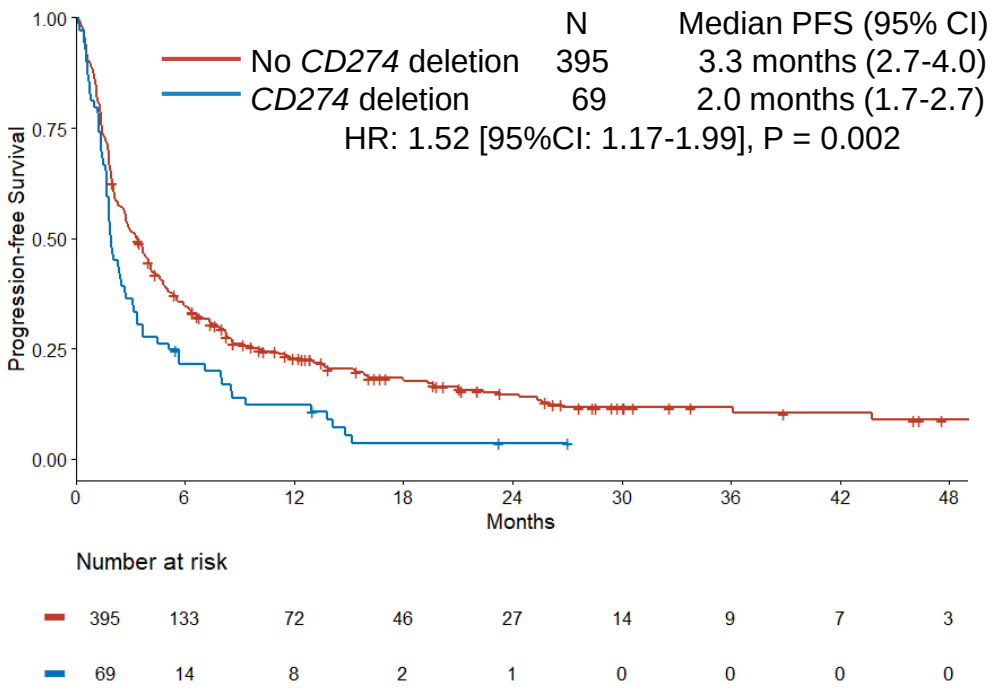


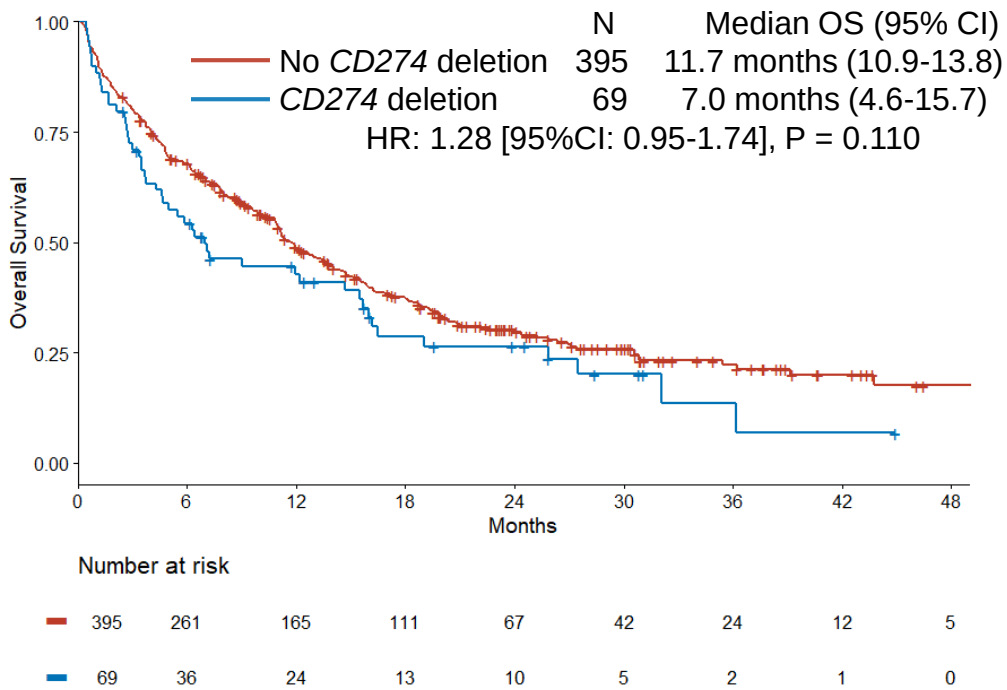
Prevalence of *CD274* deletion



Outcome on immunotherapy in patients without and with *CD274* deletion







Key message

- PD-L1 expression is highly variable and different PD-L1 expression levels are associated with clinicopathological and genomic characteristics.
- High PD-L1 expression (TPS ≥50%) in nonsquamous NSCLC is associated with tobacco exposure, advanced stage at diagnosis, and high TMB, as well as copy gain of *CD274 (PD-L1)*, *PDCD1LG2* (*PD-L2*) and *JAK2*.
- PD-L1 negative tumors (TPS <1%) are associated with mutations in *STK11*, *EGFR*, *CTNNB1 (β-catenin)*, *APC* and *SMARCA4*, copy loss of *CD274 (PD-L1)*, *PDCD1LG2 (PD-L2)* and *JAK2* (and the whole chromosomal arm 9p loss) and copy gain of *AKT3*, *PIK3C2B* and the whole chromosomal arm 1q gain.

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Thank you

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