Table SI. Summary of clinical trials evaluating the predictive value of tumor PD-L1 expression in anti-PD-1/PD-L1 treatments.

Author, year and phase	Tumor type and regimen	Cell type of PD-L1 positivity	Cut-off value of PD-L1 positivity	Percentage of PD-L1 positivity	Association with response and clinical outcome	(Refs.)
Nivolumab						
Weber *et al*, (2013) Phase I	Ipilimumab-refractory/naive melanoma; Nivolumab with or without vaccine	Tumor cells	≥1% or ≥5%	52% (23/44) for ≥1% in tumors available for PD-L1 staining; 27% (12/44) for ≥5% in tumors available for PD-L1 staining	PD-L1-positive (≥5% or ≥1%) vs. PD-L1-negative (<5% or <1%) ORR: 67% (8/12) vs. 19% (6/32), 39% (9/23) vs. 23% (5/21), respectively	(21)
Larkin *et al*, (2015) Phase III	Melonoma; Nivolumab and/or ipilimumab	Tumor cells	≥5%	23.6% (223/945) in all selected; with 10.8% (102/945) that could not be determined/evaluated	PD-L1-positive vs. PD-L1-negative ORR: 57.5% (46/80) vs. 41.3% (86/208 in the nivolumab group; 72.1% (49/68) vs. 54.8% (115/210) in the nivolumab-plus-ipilimumab group; 21.3% (16/75) vs. 17.8% (36/202) in the ipilimumab group; mPFS: 14 months vs. 5.3 months in the nivolumab group; 14 months vs. 11.2 months in the nivolumab-plusipilimumab group; 3.9 months vs. 2.8 months in the ipilimumab group	(6)
Robert *et al*, (2015) Phase III	Melanoma without a *BRAF* mutation; Nivolumab vs. dacarbazine	Tumor cells	≥5%	35.4% (148/418) in all selected	PD-L1-positive vs. PD-L1-negative/indeterminate ORR: 52.7% vs. 33.1% in the nivolumab group; 10.8% vs. 15.7% in the dacarbazine group	(7)
Weber *et al*, (2015) Phase III	Melanoma failed in ipilimumab and/or *BRAF* inhibition; Nivolumab vs. chemotherapy	Tumor cells	≥5%	49.6% (201/405) in all selected	PD-L1-positive vs. PD-L1-negative ORR: 43.6% (24/55) vs. 20.3% (13/64 in the nivolumab group; 9.1% (2/22) vs. 13% (3/23) in the chemotherapy group	(30)
Rizvi *et al*, (2015) Phase II	Squamous NSCLC; Nivolumab	Tumor cells	≥5%	33% (25/76) in tumors which could be assessed for PD-L1 expression	PD-L1-positive vs. PD-L1-negative ORR: 24% (6/25) vs. 14% (7/51) in the nivolumab group	(31)
Brahmer *et al*, (2015) Phase III	Squamous NSCLC failed first-line chemotherapy; Nivolumab vs. docetaxel	Tumor cells	≥1%, ≥5% or ≥10%	43.8% (119/272) for ≥1%; 29.8% (81/272) for ≥5%; 25.4% (69/272) for ≥10% with 17.3% (47/272) that could not be evaluated	PD-L1-positive (≥1% or ≥5% or ≥10%) vs. PD-L1-negative (<1% or <5% or <10%) ORR: 17% (11/63) vs. 17% (9/54), 21% (9/42) vs. 15% (11/75), 19% (7/36) vs. 16% (13/81) in the nivolumab group; mOS: 9.3 months vs. 8.7 months, 10 months vs. 8.5 months, 11 months vs. 8.2 months in the nivolumab group; mPFS: 3.3 months vs. 3.1 months, 4.8 months vs. 2.2 months, 3.7 months vs. 2.3 months in the nivolumab group	(9)

Table SI. Continued.

Author, year and phase	Tumor type and regimen	Cell type of PD-L1 positivity	Cut-off value of PD-L1 positivity	Percentage of PD-L1 positivity	Association with response and clinical outcome	(Refs.)
Borghaei *et al*, (2015) Phase III	Non-squamous NSCLC failed platinum-based doublet chemotherapy; Nivolumab vs. Docetaxel	Tumor cells	≥1%, ≥5% or ≥10%	42.3% (246/582) for ≥1%; 31.1% (181/582) for ≥5%; 28.4% (165/582) for ≥10% with 21.8% (127/582) that could not be quantified	PD-L1-positive (≥1% or ≥5% or ≥10%) vs. PD-L1-negative (<1% or <5% or <10%) ORR: 31% (38/123) vs. 9% (10/108), 36% (34/95) vs. 10% (14/136), 37% (32/86) vs. 11% (16/145) in the nivolumab group; mPFS: 4.2 months vs. 2.1 months, 5 months vs. 2.1 months, 5 months vs. 2.1 months in the nivolumab group; mOS: 17.7 months vs. 10.5 months, 19.4 months vs. 9.8 months, 19.9 months vs. 9.9 months in the nivolumab group	(8)
Motzer *et al*, (2015) Phase III	Previously treated RCC; Nivolumab vs. everolimus	Tumor cells	≥1% or ≥5%	24% (181/756) for ≥1%; 11% (85/756) for ≥5%	PD-L1-positive (≥1%) vs. PD-L1-negative (<1%) mOS: 21.8 months vs. 27.4 months in the nivolumab group; 18.8 months vs. 21.2 months in the everolimus group	(11)
Ferris *et al*, (2016) Phase III	Squamous-cell carcinoma of the head and neck failed platinum chemotherapy. Nivolumab vs. methotrexate, docetaxel, cetuximab	Tumor cells	≥1%, ≥5% or ≥10%	41.3% (149/361) for ≥1%; 26.9% (97/361) for ≥5%; 21.3% (77/361) for ≥10% with 28% (101/361) that could not be quantified	PD-L1-positive (≥1% or ≥5% or ≥10%) vs. PD-L1-negative (<1% or <5% or <10%) mOS: 8.7 months vs. 5.7 months, 8.8 months vs. 7 months, 8.7 months vs. 7.2 months in the nivolumab group; ORR: 17% (15/88) vs. 12.3% (9/73), 22.2% (12/54) vs. 11.2% (12/107), 27.9% (12/43) vs. 10.2% (12/118) in the nivolumab group	(32)
Carbone *et al*, (2017) Phase III	NSCLC with PD-L1 tumor expression level ≥1%; Nivolumab vs. chemotherapy	Tumor cells	≥5% or ≥50%	78.2% (423/541) for ≥5% in patients who underwent randomization (≥1%); 39.6% (214/541) for ≥50% in patients who underwent randomization (≥1%).	PD-L1-positive (≥50% and ≥5%) vs. all randomized (≥1%) ORR: 34% (55/211) and 26% (23/88 in the nivolumab group; mPFS: 5.4 months and 4.2 months vs. 4.2 months in the nivolumab group; mOS: 15.9 months and 14.4 months vs. 13.7 months in the nivolumab group	(33)
Hellmann *et al*, (2018) Phase III	Stage IV or recurrent NSCLC previously untreated with chemotherapy; Nivolumab plus ipilimumab	Tumor cells	≥1%	68.4% (1189/1739) for ≥1%	PD-L1-positive vs. PD-L1-negative 1-year PFS rate: 42% vs. 45% in the nivolumab plus ipilimumab group	(34)

Table SI. Continued.

Author, year and phase	Tumor type and regimen	Cell type of PD-L1 positivity	Cut-off value of PD-L1 positivity	Percentage of PD-L1 positivity	Association with response and clinical outcome	(Refs.)
Hellmann *et al*, (2019) Phase III	Stage IV or recurrent NSCLC previously untreated with chemotherapy; Nivolumab plus ipilimumab	Tumor cells	≥1%	68.4% (1189/1739) for ≥1%	PD-L1-positive (≥1%) vs. negative ORR: 35.9% vs. 27.3%; mOS: 17.1 months vs. 17.2 months; DoR: 23.2 months vs. 18.0 months	(35)
Pembrolizumab						
Garon *et al*, (2015) Phase I	NSCLC; Pembrolizumab	Tumor cells	>50%	23.2% (191/824) in all screened; 22.7% (146/643) in previously treated; 24.9% (45/181) in treatmentnaive	PD-L1-positive vs. negative (1-49% and <1%) ORR: 34.2% (13/38) vs 9.3% (4/43) and 10% (4/40) in training set; 45.2% (33/73) vs. 16.5% (17/103) and 10.7% (3/28) in validation set; mPFS: 4.5 months vs. 2.1 months (both groups) in training set; 6.4 months vs. 4.1 months and 4 months in validation set; mOS: 13.7 months vs. 5.9 months and 6.7 months in training set; not reached vs. 10.6 months and 10.4 months in validation set	(10)
Herbst *et al*, (2016) Phase II/III	NSCLC with PD-L1 expression on ≥1% tumor cells; Pembrolizumab (2 or 10 mg/kg) vs. docetaxel	Tumor cells	≥50%	42.8% (442/1033) for ≥50% in all enrolled (≥1%).	PD-L1-positive vs. enrolled (≥1%) ORR: 30% (42/139) vs. 18% (62/344 in the pembrolizumab 2 mg/kg group; 29% (44/151) vs. 18% (64/345 in the pembrolizumab 10 mg/kg group.	(36)
Eggermont *et al*, (2018) Phase III	Melanoma; Pembrolizumab	Tumor cells and tumor-infiltrating immune cells	IHC score ≥2	83.7% (853/1019) for PD-L1 IHC score ≥2 in all selected with 4.9% (50/1019) that could not be determined	PD-L1-positive vs. PD-L1-negative 12-month PFS: 77.1% vs. 72.2% in the pembrolizumab group; 62.6% vs. 52.2% in the placebo group	(37)
Mok *et al*, (2019) Phase III	Treatment-naive, locally advanced or metastatic NSCLC with PD-L1 expression and without *EGFR* or *ALK*; Pembrolizumab vs. platinum-based chemotherapy	Tumor cells	TPS ≥50%, ≥20%, or ≥1%	47.0% (599/1274) for TPS ≥50% 64.2% (818/1274) for TPS ≥20% 100% (1274/1274) for TPS ≥1%	PD-L1 TPS ≥50% vs. ≥20% vs. ≥1% ORR: 39% (118/299) vs. 33% (138/413 vs. 27% (174/637) in the pem brolizumab group; mPFS: 7.1 months vs. 6.2 months vs. 5.4 months in the pembrolizumab group; mOS: 20 months vs. 17.7 months vs. 16.7 months in the pembrolizu mab group	(38)

Table SI. Continued.

Author, year and phase	Tumor type and regimen	Cell type of PD-L1 positivity	Cut-off value of PD-L1 positivity	Percentage of PD-L1 positivity	Association with response and clinical outcome	(Refs.)
Atezolizumab						
Fehrenbacher *et al*, (2016) Phase II	NSCLC failed plati num chemotherapy; Atezolizumab vs. docetaxel	Tumor cells and tumor-infiltrating immune cells	Tumor cells: ≥1% or ≥5% or ≥50%; tumor-infiltrating immune cells ≥1% or ≥5% or ≥10%	16% for tumor cells ≥50% or tumor-infiltrating immune cells ≥10% (G1); 37% for tumor cells ≥5% or tumor-infiltrating immune cells ≥5% (G2); 68% for tumor cells ≥1% or tumor-infiltrating immune cells ≥1% (G3); 32% for tumor cells <1% and tumor-infiltrating immune cells <1% (G4).	PD-L1-positive (G1, G2, G3) vs. PD-L1-negative (G4) mOS: 15.5 months, 15.1 months, 15.5 months vs. 9.7 months in the atezolizumab group	(17)
Rosengerg *et al*, (2016) Phase II	Urothelial carcinoma failed in platinum based chemotherapy; Atezolizumab	Tumor-infiltrating immune cells	≥1% or ≥5%	66.8% (207/310) for ≥1%; 32.3% (100/310) for ≥5%.	PD-L1-positive (≥5% and 1-5%) vs. PD-L1-negative ORR: 27% (27/100) and 17% (18/ vs. 13% (13/100) in the atezolizumab group; mOS: 11.4 months and 6.7 months vs. 6.5 months in the atezolizumab group	(39)
Balar *et al*, (2017) Phase II	Cisplatin-ineligible urothelial carcinoma; Atezolizumab	Tumor-infiltrating immune cells	≥1% or ≥5%	67% (80/119) for ≥1%; 27% (32/119) for ≥5%.	PD-L1-positive (≥5% and 1-5%) vs. PD-L1-negative ORR: 28% (9/32) and 21% (10/48) vs. 21% (8/39) in the atezolizumab group; mPFS: 4.1 months and 2.1 months vs. 2.6 months in the atezolizumab group; PD-L1-high (≥5%) vs. PD-L1-low (<5%) mOS: 12.3 months vs. 19.1 months in the atezolizumab group	(40)
Petrylak *et al*, (2018) Phase I	Urothelial carcinoma; Atezolizumab	Tumor-infiltrating immune cells	≥5%	53% (50/95) in all selected (40% of patients were enrolled based on a requirement for positive PD-L1 expression).	PD-L1-positive vs. PD-L1-negative ORR: 40% (26/55) vs. 11% (4/25) in the atezolizumab group; mOS: 14.6 months vs. 7.6 months in the atezolizumab group.	(41)

Table SI. Continued.

Author, year and phase	Tumor type and regimen	Cell type of PD-L1 positivity	Cut-off value of PD-L1 positivity	Percentage of PD-L1 positivity	Association with response and clinical outcome	(Refs.)
Socinski *et al*, (2018) Phase III	Metastatic nonsquamous NSCLC previously untreated with chemotherapy; Atezolizumab plus bevacizumab plus carboplatin plus paclitaxel	Tumor cells and tumor-infiltrating immune cells	Tumor cells: ≥50% or ≥1%; tumor-infiltrating immune cells ≥10% or ≥1%	20% for tumor cells ≥50% or tumor-infiltrating immune cells ≥10% (G1); 51% for tumor cells ≥1% or tumor-infiltrating immune cells ≥1% (G2); 32% for >50% tumor cells ≥1% or >10% tumor-infiltrating immune cells ≥1% (G3); 80% for >50% tumor cells and >10% tumor-infiltrating immune cells (G4); 49% for >1% tumor cells and >1% tumor-infiltrating immune cells (G5)	mPFS: 12.6 months for G1; 11 months for G2; 8.3 months for G3; 8 months for G4; 7.1 months for G5.	(42)
Durvalumab						
Powles *et al*, (2017) Phase I/II	Urothelial carcinoma failed first-line chemotherapy; Durvalumab	Tumor cells and tumor-infiltrating immune cells	High: ≥25%; Low and negative: <25%	High: 51.3% (98/191); Low. and negative: 41.4% (79/191); Unknown: 7.3% (14/191) (40 of enrolled patients had PD-L1 expression of ≥5% on tumor cells)	PD-L1-high vs. low and negative ORR: 27.6% (27/98) vs. 5.1% (4/79) in the durvalumab group; DCR: 44.9% (44/98) vs. 21.5% (17/79) in the durvalumab group; DoR: not reached vs. 12.5 months in the durvalumab group; mPFS: 2.1 months vs. 1.4 months in the durvalumab group; mOS: 20 months vs. 8.1 months in the durvalumab group	(43)

PD-1, programmed death-1; PD-L1, PD ligand-1; NSCLC, non-small cell lung cancer; RCC, renal cell carcinoma; IHC, immunohistochemistry; mPFS, median progression-free survival; PFS, progression-free survival; mOS, median overall survival; TPS, tumor proportion score; DCR, disease control rate including CR; PR, or SD ≥6 weeks; DoR, duration of response; CR, complete response; PR, partial response; SD, stable disease.