Table S1. Summary of Study Characteristics

| Trial Acronym/ Author (Year) | Study Design/ Trial Phase | Treatment | Line of Therapy | Biomarker | Biomarker Cut-off Definition | Biomarker Assay Used | Outcomes Reported | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| OS | PFS | Response Rates |
| **NSCLC** | | | | | | | | | |
| BIRCH [S-[1-3](#_ENREF_1)] | Phase 2, single arm | ATEZO | 1, 2, or ≥ 3 | PD-L1 | ≥ 50%;1%-49% | SP142 IHC assay Ventana Medical Systems, Tucson, Arizona) | √ | √ | √ |
| *KRAS* | Mutant; wild type | √ | √ | √ |
| EGFR | Mutant; wild type |
| CheckMate 012 [S-[4](#_ENREF_4), [5](#_ENREF_5)] | Phase 1 study | NIVO | 1 | PD-L1 | ≥ 1%; < 1 % | NR | √ | √ | √ |
| EGFR | Mutant; wild type | NR | √ | √ | √ |
| *KRAS* | Mutant; wild type | NR | √ | √ | √ |
| CheckMate 017 [S-[6](#_ENREF_6)] | Phase 3 RCT | NIVO or DTX | 2 | PD-L1 | < 1%; ≥ 1%; < 5%; ≥ 5%; < 10%; ≥ 10% | IHC assay (Dako North America, Carpinteria, California) antihuman PD-L1 mAb (clone 28-8, Epitomics, Burlingame. California) | √ | √ | √ |
| CheckMate 017/057 [S-[7](#_ENREF_7), [8](#_ENREF_8)] | Follow-up of two phase 3 trials | NIVO or DTX | ≥ 1 | Cytoscore | High; low | Multivariate analyses of baseline serum cytokines | √ |  |  |
| PD-L1 | < 1%; ≥ 1%; ≥ 50% | NR | √ |  |  |
| CheckMate 026 [S-[9](#_ENREF_9), [10](#_ENREF_10)] | Phase 3 RCT | NIVO or platinum-based chemotherapy | 1 | PD-L1 | All: > 1%; ≥ 5%; ≥ 50% | Anti–PD-L1 antibody (28-8 antibody) | √ | √ | √ |
| TMB | High; low or medium | NR | √ | √ | √ |
| TMB and PD-L1 | High and PD-L1 ≥ 50%; high and PD-L1 1%-49%; low or medium and PD-L1 ≥ 50%; high and PD-L1 1%-49% |  |  | √ |
| CheckMate 057 [S-[11-13](#_ENREF_11)] | Phase 3 RCT | NIVO or DTX | ≥ 2 | PD-L1 | < 1%; ≥ 1%; < 5%  ≥ 5%; < 10%; ≥ 10% | IHC assay (Dako North America, Carpinteria, California) antihuman PD-L1 mAb (clone 28–8) | √ | √ | √ |
| EGFR | Positive; negative | NR | √ | √ |  |
| ALK | Translocation not detected | NR | √ | √ |  |
| *KRAS* | Positive | NR | √ | √ |  |
| CheckMate 063 [S-[14](#_ENREF_14)] | Phase 2 single arm | NIVO | ≥ 3 | PD-L1 | < 1%; ≥ 1%; < 5%  ≥ 5%;< 10%; 10% | IHC assay (Dako North America, Carpinteria, California) | √ | √ | √ |
| ALK translocation status | Negative; positive | NR | √ | √ |  |
| CheckMate 227 [S-[15](#_ENREF_15)] | Multipart phase 3 trial | NIVO + IPI, NIVO + platinum-based chemotherapy, NIVO monotherapy, or platinum-based chemotherapy alone | 1 | TMBa | ≥ 10 mutations per mb  < 10 mutations per mb | Foundation One CDx assay (Foundation Medicine, Cambridge, Massachusetts) |  | √ | √ |
| TMBa + PD-L1 | ≥ 10 mutations per mb + ≥ 1%  ≥ 10 mutations per mb + < 1%  ≥ 13 mutations per mb + ≥ 1% | FoundationOne CDx assay (Foundation Medicine, Cambridge, Massachusetts) |  | √ |  |
| CP1108 [S-[16-22](#_ENREF_16)] | A phase 1/2 escalation and dose-expansion study | DURVA | 1, 2, and ≥ 3 | PD-L1 and IFN-γ mRNA | None; all PD-L1 ≥ 25%; PD-L1 IHC < 25%; all IFN-γ+  IFN-γ+ and PD-L1 ≥ 25%; IFN-γ+ and PD-L1 < 25%; all IFN-γ–  IFN-γ– and PD-L1 ≥ 25%; IFN-γ– and PD-L1 < 25% | Analytically validated Ventana SP263 assay optimized for use on the automated BenchMark ULTRA platform (Ventana Medical Systems, Oro Valley, Arizona) and using Fluidigm Biomark for mRNA | √ |  | √ |
| PD-L1 | ≥ 25%; < 25% | √ | √ | √ |
| JAVELIN Solid Tumor [S-[23-32](#_ENREF_23)] | Dose-expansion cohort of an OL, phase 1 study | AVE | ≥ 2 | PD-L1 | < 1%; ≥ 1%; < 5%  ≥ 5%; < 10%; ≥ 10% | IHC assay (Dako North America, Carpinteria, California) anti–PD-L1 mAb clone 73–10 (Merck & Co. Inc., Kenilworth, New Jersey) | √ | √ | √ |
| EGFR | Wild type; mutant | NR | √ | √ |  |
| *KRAS* | Wild type; mutant | NR | √ | √ |  |
| KEYNOTE-001 [S-[33-40](#_ENREF_33)] | OL, phase 1, RCT | PEM | ≥ 1 | PD-L1 | ≥ 50%; 1%-49%; < 1%; positive; negative | IHC assay (early version of the PD-L1 22C3 IHC pharmDx assay; Dako North America, Carpinteria, California) | √ | √ | √ |
| *TP53* | *TP53* mutation | NR |  | √ |  |
| *KRAS* | Wild type; mutant |  | √ |  |
| EGFR | Wild type; mutant | √ |  |  |
| Baseline tumor size | Below median (10.2 cm); above median (10.2 cm) | NR |  |  | √ |
| *BRAF* | Wild type; mutant | NR | √ |  | √ |
| KEYNOTE-010 [S-[41-44](#_ENREF_41)] | Randomized, OL, phase 2/3 study | PEM or DTX | ≥ 1 | PD-L1 | ≥ 50%; 1%-49%; 1%‑24%; 25%-49%; 50%-74%; ≥ 75%; ≥ 1% | IHC assay with the murine 22C3 antihuman PD-L1 antibody | √ | √ | √ |
| EGFR | Mutant; wild type | NR | √ | √ |  |
| OAK [S-[45-49](#_ENREF_45)] | Randomized, OL, phase 3 study | ATEZO or DTX | > 1 | PD-L1 | ≥ 10%; ≥ 5%; ≥ 1%; < 1% | VENTANA SP142 PD-L1 IHC assay (Ventana Medical Systems, Tucson, AZ, USA) | √ | √ | √ |
| *KRAS* | Mutant; wild type | NR | √ |  |  |
| EGFR | Mutant; wild type | NR | √ |  |  |
| ≥ 2 | TMB | ≥ 10; ≥ 16; ≥ 20 | bTMB assay | √ |  |  |
| POPLAR [S-[49-54](#_ENREF_49)] | OL, phase 2 RCT | ATEZO or DTX | ≥ 2 | PD-L1 | ≥ 10%; ≥ 5%; ≥ 1%; < 1%; < median; ≥ median | VENTANA SP142 PD-L1 IHC assay (Ventana Medical Systems, Tucson, AZ, USA) | √ | √ | √ |
| PD-L2 | < Median; ≥ median | NR | √ |  |  |
| B7.1 | < Median; ≥ median | NR | √ |  |  |
| T effector- IFN-γ | < Median; ≥ median | NR | √ |  |  |
| TMB | ≥ 10; ≥ 16; ≥ 20 | NR | √ | √ |  |
| NCT00730639 Topalian et al. (2012) [S-[55](#_ENREF_55), [56](#_ENREF_56)] | Phase 1 dose-escalation, cohort-expansion study | NIVO | ≥ 2 | PD-L1 | ≥ 5%; < 5% | Murine antihuman PD-L1 monoclonal antibody, clone 5H1 | √ | √ | √ |
| EGFR | Mutant; wild type | NR |  |  | √ |
| *KRAS* | Mutant; wild type | NR |  |  | √ |
| NCT01375842 [S-[57](#_ENREF_57), [58](#_ENREF_58)] | Phase 1, single arm, dose escalation with expansion cohorts | ATEZO | NR | PD-L1 | < 1%; 1% to < 5%; 5% to < 10%; 1%-10%; ≥ 10%; ≥ 1% | SP142 assay (Ventana Medical Systems, Tucson, AZ, USA) |  | √ | √ |
| PD-L2 | Positive; positive and PD-L1 positive | SP142 assay (Ventana Medical Systems, Tucson, AZ, USA) |  |  | √ |
| ID01 | Positive | NR |  |  | √ |
| *LAG3* | Positive | NR |  |  | √ |
| TIM3 | Positive | NR |  |  | √ |
| CTLA-4 | Positive | NR |  |  | √ |
| B7-H3 | Positive | NR |  |  | √ |
| B7-H4 | Positive | NR |  |  | √ |
| ID01 | Positive and PD-L1+ | NR |  |  | √ |
| *LAG3* | Positive and PD-L1+ | NR |  |  | √ |
| TIM3 | Positive and PD-L1+ | NR |  |  | √ |
| CTLA-4 | Positive and PD-L1+ | NR |  |  | √ |
| B7-H3 | Positive and PD-L1+ | NR |  |  | √ |
| B7-H4 | Positive and PD-L1+ | NR |  |  | √ |
| Bagley et al. (2017) [S-[59](#_ENREF_59)] | Retrospective cohort study | NIVO | NR | Neutrophil-to-lymphocyte ratio | ≥ 5; < 5 | NR | √ | √ |  |
| De Castro et al. (2017) [S-[60](#_ENREF_60)] | Retrospective evaluation | Nonspecified anti–PD-1 and anti–PD-L1 | NR | LDH | Baseline ≥ 400; baseline < 400; < baseline at ≥ 3 evaluations; > baseline at ≥ 3 evaluations | NR | √ |  | √ |
| Gettinger (2015a) [S-[61](#_ENREF_61)] | Phase 1 study | NIVO | 1 | PD-L1 | ≥ 5%; < 5% | NR |  |  | √ |
| Kaderbhai et al. (2017) [S-[62](#_ENREF_62)] | Retrospective cohort study | NIVO | 2 and 3 | PD-L1 | ≥ 1%; < 1% | IHC using SP142 mAb | √ | √ | √ |
| EGFR | Mutant; wild type |  |  | √ |
| *KRAS* | Mutant; wild type |  |  | √ |
| Nomizo et al. (2017) [S-[63](#_ENREF_63)] | Retrospective medical record review | NIVO | ≥ 2 | PD-L1 SNPs | Different intron/ missense mutation | TaqMan® genotyping assay (Applied Biosystems, Foster City, California) analyzed with Applied Biosystems 7300 Real-Time PCR System |  | √ | √ |
| Pabla et al. (2017) [S-[64](#_ENREF_64)] | NR | ≥ 1 nonspecified checkpoint inhibitors | NR | PD-L1 | > 50% + inflamed; ≤ 50% + inflamed; ≤ 50% | PD-L1 (22C3) IHC and custom NGS cancer immune gene expression assay |  |  | √ |
| Roach et al. (2016) [S-[65](#_ENREF_65)] | Retrospective of phase 1 trial | PEM | NR | PD-L1 | ≥ 50% | PD-L1 IHC 22C3 pharmDx assay |  |  | √ |
| Sabari et al. (2017) [S-[66](#_ENREF_66)] | NR | NIVO, PEM, ATEZO, DURVA, IPI + NIVO | NR | PD-L1 | ≥ 50%; 0% | IHC |  |  | √ |
| Sorensen et al. (2016) [S-[67](#_ENREF_67)] | Retrospective study | PEM + platinum-based chemotherapy | 1 | PD-L1 | ≥ 50%; 1%-49%; < 1%; ≥ 1% | Prototype IHC assay with anti–PD-L1 22C3 antibody (Merck & Co., Inc., Kenilworth, New Jersey) | √ |  |  |
| Yaghmour et al. (2016) [S-[68](#_ENREF_68)] | Retrospective database search | NIVO, PEM, or IPI | ≥ 1 | Tumor mutational load | Top quintile; other quintiles combined | NGS cancer immune gene expression assay | √ |  |  |
| B‑F1RST [S-[69](#_ENREF_69)] | Phase 2 single-arm trial | ATEZO | 1 | Blood-based TMB | ≥ 12; < 12; ≥ 14; < 14; ≥ 16; < 16; ≥ 20; < 20 | NR |  | √ | √ |
| **SCLC** | | | | | | | | | |
| CheckMate 032 [S-[70](#_ENREF_70), [71](#_ENREF_71)] | Multicenter, phase 1/2 | NIVO and/or IPI | ≥ 2 | PD-L1 | < 1%; ≥ 1% | IHC assay (Dako North America, Carpinteria, California) antihuman PD-L1 mAb (clone 28–8) |  |  | √ |
| **Melanoma** | | | | | | | | | |
| CA184004 [S-[72](#_ENREF_72)] | Phase 2 trial | IPI | NR | Gene expression profiles | NR | NR | √ |  |  |
| CA209-004 [S-[73](#_ENREF_73)] | Phase 1 study | NIVO, IPI | Mixed | PD-L1 | ≥ 5%; < 5% | IHC assay (Dako North America, Carpinteria, California) antihuman PD-L1 mAb (clone 28–8) |  |  | √ |
| ALC | ALC < 1.0 × 103 cells/L at weeks 5-7)  ALC ≥ 1.0 × 103 cells/L at weeks 5-7) | NR |  |  | √ |
| CheckMate 037 [S-[74](#_ENREF_74)] | Phase 3 RCT | NIVO or chemotherapy | ≥ 2 | *BRAF* | Mutant; wild type | NR |  |  | √ |
| PD-L1 | Positive; negative | Automated Bristol-Myers Squibb/Dako IHC assay (Bristol-Myers Squibb, New York City, New York; Dako North America, Carpinteria, California) |  |  | √ |
| CheckMate 066 [S-[75](#_ENREF_75)] | Phase 3 RCT | NIVO or dacarbazine | 1 | PD-L1 | ≥ 5%; < 5% | IHC assay (Bristol-Myers Squibb, New York City, New York; Dako North America, Carpinteria, California) | √ |  | √ |
| CheckMate 066/067/069 [S-[76](#_ENREF_76)] | Phase 2 and phase 3 trials | NIVO +IPI or NIVO | NR | PD-L1 | ≥ 5%; < 5% | Dako IHC (Dako North America, Carpinteria, California) |  | √ | √ |
| CheckMate 067 [S-[77-79](#_ENREF_77)] | Phase 3 RCT | NIVO or IPI | 1 | PD-L1 | ≥ 5%; < 5% | IHC assay (Dako North America, Carpinteria, California) antihuman PD-L1 mAb (clone 28–8) |  | √ | √ |
| *BRAF* | Wild type; mutant | NR |  | √ |  |
| CheckMate 069 [S-[80](#_ENREF_80), [81](#_ENREF_81)] | Phase 1 dose-escalation study | NIVO and IPI or IPI and PBO | 1 | PD-L1 | ≥ 5%; < 5% | IHC assay (Bristol-Myers Squibb, New York City, New York; Dako North America, Carpinteria, California) |  |  | √ |
| *BRAF* | Wild type; mutant | NR |  | √ | √ |
| KEYNOTE-001 [S-[33-40](#_ENREF_33), [82](#_ENREF_82)] | OL, phase 1, RCT | PEM | 2 | PD-L1 | ≥ 1%; < 1% | IHC assay (PD-L1 IHC 22C3 pharmDx; Dako North America, Carpinteria, California) | √ | √ | √ |
| KEYNOTE-002 [S-[83](#_ENREF_83)] | Randomized, phase 2 trial | PEM or chemotherapy | ≥ 1 | *BRAF* | Mutant; wild type | NR |  | √ |  |
| KEYNOTE-006 [S-[84-86](#_ENREF_84)] | Randomized, OL, phase 3 trial | PEM or IPI | 1 and 2 | PD-L1 | Positive; negative | IHC analysis, 22C3 antibody (Merck & Co. Inc., Kenilworth, New Jersey) | √ | √ |  |
| *BRAF* | Wild type; mutant | NR | √ | √ |  |
| MDX010-020 [S-[87](#_ENREF_87)] | Randomized study | IPI and tremelimumab | ≥ 1 | CTLA-4 | *BRAF* (V600) or *NRAS* mutation; *BRAF*/*NRAS* wild type; *BRAF* and *NRAS* mutated | NR | √ |  |  |
| NCT00257205 Ribas et al. (2013) [S-[88](#_ENREF_88)] | Phase 3 RCT | Tremelimumab or SOC | 1 | LDH | ≤ ULN; 1-2 × ULN; > 2 × ULN | NR | √ |  |  |
| HLA | A2; Other | NR | √ |  |  |
| NCT00324155 Robert et al. (2011) [S-[89](#_ENREF_89)] | Randomized, DB, phase 3 study | IPI + dacarbazine or dacarbazine + PBO | 1 | LDH | > ULN; < ULN; > 2 × ULN; < 2 × ULN | NR | √ |  |  |
| NCT01176461 Weber et al. (2013) [S-[90](#_ENREF_90)] | Phase 1 study | NIVO | ≥ 2 | PD-L1 | ≥ 5%; < 5%; ≥ 1%; < 1% | IHC assay (Dako North America, Carpinteria, California) antihuman PD-L1 mAb (clone 28–8) |  |  | √ |
| Algazi et al. (2016) [S-[91](#_ENREF_91)] | Retrospective medical record review | PEM, NIVO, ATEZO | Multiple | LDH | Normal; elevated | NR | √ | √ |  |
| Arenberger et al. (2017) [S-[92](#_ENREF_92)] | Prospective single-arm study | IPI | Multiple | MAGE-3 | > 1 and ≤ 10; > 10 and ≤ 100; > 100 | Quantitative real-time RT-PCR: MIA, Melan-A/MART-1, MAGE-3, and gp100 (glycoprotein) | √ |  |  |
| Melan-A, gp100, MAGE-3, and melanoma inhibitory antigen | Increase in marker levels at visit 3 compared to visit 1  Significant mean reduction by more than 30% |  |  | √ |
| Chakravarti et al. (2017) [S-[93](#_ENREF_93)] | Prospective single-arm study | IPI | NR | Baseline ALC/U | NR | NR | √ | √ |  |
| Baseline LDH/100U | NR | NR | √ | √ |  |
| Tumor CTLA-4 percentage | < 20% (negative);  ≥ 20% (positive) | Antibody against CTLA-4, PD-1, and PD-L1 (Abcam, Cambridge, Massachusetts), FASL (Santa Cruz Biotechnologies, Santa Cruz, California), p-S6 and p-AKT (Cell Signaling, Danvers, Massachusetts), and BRAF-V600E (Ventana Medical Systems, Tucson, Arizona) | √ | √ |  |
| CTLA-4 intensity | 0; > 0 | √ |  |  |
| Tumor p-AKT intensity | ≤ 1 (negative); > 1 (positive) | √ |  |  |
| Tumor p-AKT/FAS-L intensity | –/–; +/–; +/+ | √ | √ |  |
| Tumor p-AKT/ CTLA-4 percentage | –/–; –/+; +/–; +/+ | √ | √ |  |
| Tumor p-AKT/p-S6 intensity | –/– |  | √ |  |
| Dick et al. (2016) [S-[94](#_ENREF_94)] | Retrospective database analysis | IPI | NR | LDH | Change in value after two cycles  Normal compared to elevated | NR | √ | √ |  |
| Diem et al. (2016) [S-[95](#_ENREF_95)] | Retrospective analysis | PEM or NIVO | NR | LDH | Normal; > ULN; > 10% CFB; ≤ 10% CFB | Serum LDH | √ |  | √ |
| Felix et al. (2016) [S-[96](#_ENREF_96)] | Prospective single-arm study | IPI | NR | LDH | < 500 U/L; ≥ 500 U/L | NR | √ |  |  |
| S100B | ≤ 0.15 µg/L; > 0.15 µg/L | S100 ELISA kit (DiaSorin, Stillwater, Minnesota) | √ |  |  |
| Anti-MICA | < 2; ≥ 2 | LABScreen assay | √ |  |  |
| Soluble MICA | ≤ 45 pg/mL; > 45 pg/mL | Human soluble MICA ELISA kit (Bamomab, Grafelfing, Germany) | √ |  |  |
| MIA | < 7.5 µg/L; ≥ 7.5 µg/L | MIA ELISA kit (Roche, Mannheim, Germany) | √ |  |  |
| Heppt et al. (2017) [S-[97](#_ENREF_97)] | Retrospective exploratory analysis | NIVO or IPI | NR | LDH | Normal; > ULN | NR | √ |  |  |
| CRP | Normal; > ULN | NR | √ |  |  |
| RLC | < 17.5%; ≥ 17.5% | NR | √ |  |  |
| REC | < 1.5%; ≥ 1.5% | NR | √ |  |  |
| Johnson et al. (2015) [S-[98](#_ENREF_98)] | Retrospective medical study | IPI | NR | PD-L1 | *NRAS* mutant; *BRAF* mutant; wild type | IHC assay (Dako North America, Carpinteria, California) antihuman PD-L1 mAb (clone 28-8) | √ | √ | √ |
| Johnson et al. (2016) [S-[99](#_ENREF_99)] | Retrospective medical study | NIVO, PEM, or ATEZO | ≥ 1 | TML | High (> 23.1 mutations per mb)  Intermediate (3.3-23.1 mutations per mb)  Low (< 3.3 mutations per mb) | Amendments-certified, hybrid capture-based NGS platform (FoundationOne, Foundation Medicine, Cambridge, Massachusetts) | √ | √ | √ |
| Ku et al. (2010) [S-[100](#_ENREF_100)] | Prospective, single-arm, compassionate use study | IPI | ≥ 2 | ALC | ≥ 1000/µL; < 1000/µL | NR | √ |  |  |
| Larkin et al. (2015b) [S-[101](#_ENREF_101)] | Pooled analysis of four clinical trials | NIVO | Multiple | *BRAF* | Wild type; Mutant | NR |  |  | √ |
| LDH | ≤ ULN and *BRAF* wild type; > ULN and *BRAF* wild type; ≤ ULN and *BRAF* mutation; > ULN and *BRAF* mutation | NR |  |  | √ |
| PD-L1 | ≥ 5% and *BRAF* mutation; < 5% and *BRAF* mutation; ≥ 5% and *BRAF* wild type; < 5% and *BRAF* wild type | NR |  |  | √ |
| Martens et al. (2016) [S-[102](#_ENREF_102)] | Cohort study | IPI | Multiple | LDH | ≤ 1.2; > 1.2; > 2.3 | NR | √ |  |  |
| RLC | < 10.5%; ≥ 10.5% | NR | √ |  |  |
| AMC | < 650/µL; ≥ 650/µL | NR | √ |  |  |
| AEC | < 50/µL; ≥ 50/µL | NR | √ |  |  |
| REC | < 1.5%; > 1.5% | NR | √ |  |  |
| CD4 + *CD25* + *FoxP3* + regulatory T cell | < 1.5%; ≥ 1.5% | NR | √ |  |  |
| *CD14*+ monocytes | < 28%; ≥ 28% | NR | √ |  |  |
| Lin-*CD14*+ HLA-DR/low MDSCs | < 5.1%; ≥ 5.1%; ≥ 9.5% | NR | √ |  |  |
| Morrison et al. (2017) [S-[103](#_ENREF_103)] | NR | One or more nonspecified checkpoint inhibitors | ≥ 1 | PD-L1 | PD-L1 positive + inflamed phenotype;  PD-L1 negative + inflamed phenotype;  PD-L1 negative | PD-L1 IHC and custom NGS immune gene expression assay |  |  | √ |
| Roh et al. (2017) [S-[104](#_ENREF_104)] | Longitudinal cohort study | IPI | NR | Mutational load/burden of copy number loss | High mutation + low copy loss;  High mutation + high copy loss;  Low mutation + low copy loss;  Low mutation + high copy loss | NR |  |  | √ |
| Roszik et al. (2016) [S-[105](#_ENREF_105)] | Retrospective samples | IPI or PEM | NR | Predicted TML | ≤ 100; > 100 | NR | √ | √ |  |
| Sade-Feldman et al. (2016) [S-[106](#_ENREF_106)] | Controlled clinical trial | IPI | ≥ 2 | MDSC | MDSCs > 55.5%; MDSCs < 55.5% | FACSCalibur using Cell Quest software (BD Biosciences, San Jose, California) | √ |  |  |
| LDH | LDH > 480 U/I; LDH < 480 U/I | √ |  |  |
| MDSC/LDH | High; MDSCs/LDH; low MDSCs/LDH | √ |  |  |
| Saenger et al. (2014) [S-[107](#_ENREF_107)] | Retrospective samples of phase 2 and phase 3 trials | Tremelimumab | ≥ 1 | Risk score | Low risk; intermediate risk; high risk | NR | √ |  |  |
| Sim and Elsheikh (2016) [S-[108](#_ENREF_108)] | Retrospective cohort study | NR | NR | PD-L1 | Tumor-infiltrating lymphocytes; melanoma tumor cells | NR |  | √ |  |
| Wilgenhof et al. (2013) [S-[109](#_ENREF_109)] | Prospective observational study | IPI | ≥ 2 | CRP | Baseline CRP ≤ 5 × ULN; Baseline CRP > 5 × ULN | NR | √ |  |  |
| ALC | ALC ≥ 800/mm3;ALC < 800/mm3; ALC at week 6 (2 doses);  800/mm3;ALC at week 6 (2 doses); < 800/mm3;ratio ALC ; 1  Ratio ALC ≤ 1 | NR | √ |  |  |
| Wistuba-Hamprecht et al. (2017) [S-[110](#_ENREF_110)] | Retrospective medical samples | IPI | NR | CD4 T cells | TCM ≤ 26.5%; TCM > 26.5%; TEM1 ≤ 17.5%; TEM1 > 17.5%; TEM3 ≤ 3.9%; TEM3 > 3.9%; TEM4 ≤ 0.2%; TEM4 > 0.2% | NR | √ |  |  |
| CD8 T cells | Naive ≤ 23.3%;  naive > 23.3%;  TCM ≤ 2.5%;  TCM > 2.5%;  TEM1 ≤ 13.0%; TEM1 > 13.0%; TEM3 ≤ 1.5%;  TEM3 > 1.5%;  TEM4 ≤ 1.9%;  TEM4 > 1.9%; TEMRA ≤ 23.8%; TEMRA > 23.8% | NR | √ |  | √ |
| Wu et al. (2017) [S-[111](#_ENREF_111)] | Retrospective medical samples | Various | ≥ 1 | ANGPT2 | Pretreatment:  > 3175 pg/mL; ≤ 3175 pg/mL; fold change:  ≥ 1.25 pg/mL; < 1.25 pg/mL | ANGPT2 plasma/serum samples measured using Magnetic Luminex Screening Assay kits (R&D Systems, Minneapolis, Minnesota) | √ |  | √ |
| Yaghmour et al. (2016) [S-[68](#_ENREF_68)] | Retrospective database search | NIVO, PEM, or IPI | ≥ 1 | TML | Top quintile; other quintiles combined | NGS reports generated from tissue biopsy specimens | √ |  |  |
| Yuan et al. (2014) [S-[112](#_ENREF_112)] | Retrospective medical samples | IPI | NR | VEGF | VEGF < 43 pg/mL; VEGF ≥ 43 pg/mL | MSD SECTOR Imager 2400 instrument (Meso Scale Discovery, Inc., Rockville, Maryland) | √ |  | √ |
| Zhou et al. (2017) [S-[113](#_ENREF_113)] | Retrospective medical samples | IPI + BEV or IPI or IPI + sargramostim or PEM | NR | Soluble PD-L1 | Soluble PD-L1 all < 1.4 ng/mL;  Soluble PD-L1 all ≥ 1.4 ng/mL;  Soluble PD-L1 < 0.5 ng/mL;  Soluble PD-L1 ≥ 0.5 ng/mL | NR |  |  | √ |
| Chasseuil et al. (2018) [S-[114](#_ENREF_114)] | Pilot monocentric retrospective study | NIVO | ≥ 1 | Leukocyte count | Univariate analysis;  multivariate analyses | NR | √ | √ | √ |
| Lymphocyte count |
| Leukocyte/ lymphocyte ratio |
| Neutrophil count |
| Neutrophil/ lymphocyte ratio |
| Monocyte count |
| Eosinophil count |
| Lactate dehydro-genase |
| C-reactive protein |
| Gaudy-Marqueste et al. (2017) [S-[115](#_ENREF_115)] | Retrospective cohort study | No targeted or immune therapy  *BRAF* ± MEK inhibitor alone  *BRAF* ± MEK inhibitor and immuno-therapy  Immuno-therapy alone  No immuno-therapy  Anti–PD-1 alone  IPI alone  IPI + anti–PD-1 | ≥ 1 | *BRAF* | Mutation; wild type | NR | √ |  |  |
| **Merkel cell carcinoma** | | | | | | | | | |
| JAVELIN Merkel 200 [S-[116](#_ENREF_116), [117](#_ENREF_117)] | Prospective, single-group, OL, phase 2 trial | AVE | ≥ 2 | PD-L1 | Positive; negative | Proprietary research-use-only assay (Dako North America, Carpinteria, California) based on anti–PD-L1 mAb (clone 73-10; Merck KGaA, Darmstadt, Germany) |  |  | √ |
| MCPyV | Positive; negative; not evaluable | mAb specific for Merkel cell polyomavirus large T antigen (Clone *CM2B4*; Santa Cruz Biotechnology, Dallas, Texas) |  |  | √ |
| PD-L1 and MCPyV | Positive/positive;  Positive/negative;  Negative/positive;  Negative/negative |  |  | √ |
| **Renal cell carcinoma** | | | | | | | | | |
| CheckMate 025 [S-[118](#_ENREF_118)] | Phase 3 RCT | NIVO or platinum-based chemotherapy | ≥ 2 | PD-L1 | ≥ 5%; < 5% | IHC assay (Dako North America, Carpinteria, California) antihuman PD-L1 mAb (clone 28–8) | √ |  |  |
| MDX-1106 [S-[87](#_ENREF_87)] | Blinded, randomized, phase 2 trial | NIVO | ≥ 1 | PD-L1 | < 5%; ≥ 5% | IHC assay (Dako North America, Carpinteria, California) antihuman PD-L1 mAb (clone 28–8) | √ | √ | √ |
| IMMotion-150 [S-[119](#_ENREF_119), [120](#_ENREF_120)] | Phase 2 RCT | ATEZO + BEV, ATEZO, or sunitinib | 1 | PD-L1 | Positive | IC SP142 IHC assay |  | √ | √ |
| NCT01375842 McDermott et al. (2016) [S-[121](#_ENREF_121)] | Phase 1, single arm, dose escalation | ATEZO | NR | PD-L1 | ≥ 1%; < 1% | SP142 assay | √ | √ | √ |
| CheckMate 214 [S-[122](#_ENREF_122)] | Phase 3 | NIVO + IPI or sunitinib | 1 | PD-L1 | < 1%; ≥ 1% | NR | √ | √ | √ |
| **Gastric or gastroesophageal cancer** | | | | | | | | | |
| ATTRACTION-02 [S-[123](#_ENREF_123)] | Phase 3 RCT | NIVO or PBO | ≥ 3 | PD-L1 | ≥ 1%; < 1% | 28-8 pharmDx assay | √ |  |  |
| KEYNOTE-059 [S-[124](#_ENREF_124)] | Global, multicohort, phase 2 study | PEM | 3 and 4 | PD-L1 | Positive; negative | IHC (22C3 antibody) |  |  | √ |
| **Colorectal cancer** | | | | | | | | | |
| CheckMate 142 [S-[125](#_ENREF_125), [126](#_ENREF_126)] | Phase 2 nonrandomized study | NIVO + IPI | ≥ 2 | PD-L1 | ≥ 1%; < 1% | Dako 28-8 pharmDx assay (Dako North America, Carpinteria, California) |  |  | √ |
| *BRAF* | Mutant | NR |  |  | √ |
| *KRAS* | Mutant |  |  | √ |
| *BRAF*/*KRAS* | Wild type |  |  | √ |
| KEYNOTE-164 [S-[127](#_ENREF_127), [128](#_ENREF_128)] | Global, multicenter, multicohort, phase 2 study | PEM | ≥ 3 | MSI-H | Positive tumors | IHC and/or PCR | √ | √ | √ |
| KEYNOTE-158 [S-[127](#_ENREF_127), [128](#_ENREF_128)] | Global, multicenter, multicohort, phase 2 study | PEM | ≥ 2 | MSI-H | Positive tumors | IHC and/or PCR | √ | √ | √ |
| **Urothelial cancer** | | | | | | | | | |
| CheckMate 032 [S-[129](#_ENREF_129), [130](#_ENREF_130)] | Phase 1/2 | NIVO | ≥ 2 | PD-L1 | ≥ 1%; < 1% | IHC assay (Dako North America, Carpinteria, California) antihuman PD-L1 mAb (clone 28–8) |  | √ | √ |
| CheckMate 275 [S-[131](#_ENREF_131), [132](#_ENREF_132)] | Single-arm, phase 2 study | NIVO | ≥ 2 | PD-L1 | < 1%; ≥ 1%; < 5%; ≥ 5% | Dako PD-L1 IHC 28-8 pharmDx kit (Dako North America, Carpinteria, California) | √ |  | √ |
| CP1108 [S-[133-136](#_ENREF_133)] | Phase 1/2 dose-escalation and dose‑expansion study | DURVA | Mixed | PD-L1 | ≥ 25%; < 25%; Low/negative | Ventana SP263 assay optimized for use on automated BenchMark ULTRA platform (Ventana Medical Systems, Tucson, Arizona) |  |  | √ |
| IFNGS | Positive: top tertile of IFNGS (*LAG3*, PD-L1, *CXCL9*, and IFN‑γ mRNAs)  Negative: not top tertile of IFNGS (*LAG3*, PD-L1, *CXCL9*, and IFN-γ mRNAs) | NR | √ | √ | √ |
| IMvigor-210 [S-[137-139](#_ENREF_137)] | Single-arm phase 2 study | ATEZO 1200 mg | 1  ≥ 2 | PD-L1 | IC 2/3 (≥ 5%); IC 1/2/3; IC 1 (≥ 1%, < 5%); IC 0 (< 1%) | VENTANA SP142 IHC assay (Ventana Medical Systems, Tucson, Arizona) | √ | √ | √ |
| IMvigor211 [S-[136](#_ENREF_136)] | Multicenter, OL, phase 3, randomized controlled trial | ATEZO or chemotherapy (physician's choice: vinflunine, paclitaxel, or DTX) | ≤ 3 | PD-L1 | IC 2/3 ≥ 5%; IC 1/2/3 ≥ 1% | VENTANA SP142 PD-L1 immunohistochemistry assay (Ventana Medical Systems, Tucson, Arizona) | √ | √ | √ |
| TMB | High (at or above median); low (less than median) | DNA extraction and preparation done with HistoGeneX NV (Antwerp, Belgium), DNA sequencing, genomic alteration detection, and FoundationOne test done by Foundation Medicine (Cambridge, Massachusetts) | √ |  |  |
| PD-L1 + TMB | IC 2/3 + high (at or above median);  IC 0/1 + high (at or above median) | VENTANA SP142 PD-L1 immunohistochemistry assay (Ventana Medical Systems, Tucson, Arizona)  DNA extraction and preparation done with HistoGeneX NV (Antwerp, Belgium) DNA sequencing, genomic alteration detection and FoundationOne test done by Foundation Medicine (Cambridge, Massachusetts) | √ |  |  |
| JAVELIN Solid Tumor [S-[140](#_ENREF_140)] | Dose-expansion cohort of a multicenter, OL, phase 1 study | AVE | ≥ 1 | PD-L1 | < 5%; ≥ 5% | Clone 73-10 |  |  | √ |
| KEYNOTE-045 [S-[141](#_ENREF_141), [142](#_ENREF_142)] | Randomized, OL, phase 3 trial | PEM or chemotherapy | 2 | PD-L1 | < 1%; ≥ 1%; < 10%; ≥ 10% | PD-L1 IHC 22C3 pharmDx assay (Dako North America, Carpinteria, California) | √ | √ | √ |
| KEYNOTE-052 [S-[143](#_ENREF_143), [144](#_ENREF_144)] | OL, multicenter, phase 2 study | PEM | 1 | PD-L1 | 18-gene expression profile and CPS; CPS ≥ 10%; CPS ≥ 1%; CPS ≥ 10% | NR |  |  | √ |
| NCT01375842 Petrylak et al. (2015) [S-[145](#_ENREF_145)] | Phase 1, single arm, dose escalation with expansion cohorts | ATEZO | NR | PD-L1 | IC 2/3; IC 0/1 | SP142 assay |  | √ | √ |
| CheckMate-032, IMvigor210, CA209-260 [S-[146](#_ENREF_146)] | Phase 2 randomized controlled trials | Anti–PD-1/ PD-L1 monotherapy | ≥ 1 | DNA damage response and repair | Deleterious; other; wild type | Memorial Sloan Kettering Integrated Molecular Profiling of Actionable Cancer Targets clinical sequencing assay | √ | √ |  |
| **SCCHN** | | | | | | | | | |
| CheckMate 141 [S-[147-150](#_ENREF_147)] | Phase 3, randomized controlled trial | NIVO or standard therapy | Mixed | PD-L1 | ≥ 1%; ≥ 5%; ≥ 10%; < 1%; < 5%; < 10% | IHC assay (Dako North America, Carpinteria, California) antihuman PD-L1 mAb (clone 28–8) | √ | √ | √ |
| p16 | Positive; negative | NR | √ |  | √ |
| p16 and PD-L1 | Positive and ≥ 1%; negative and ≥ 1%; positive and < 1%; negative and < 1% | NR | √ |  |  |
| KEYNOTE-012 [S-[151](#_ENREF_151), [152](#_ENREF_152)] | Phase 1b, multicenter, nonrandomized multicohort study | PEM | ≥ 1 | PD-L1 | ≥ 1%; < 1% | PD-L1 IHC 22C3 pharmDx assay (Dako North America, Carpinteria, California) 22C3 (Merck) anti–PD-L1 antibody | √ | √ | √ |
| **Classical Hodgkin's lymphoma** | | | | | | | | | |
| CheckMate 205 [S-[153](#_ENREF_153), [154](#_ENREF_154)] | Noncomparative, single-arm, phase 2 study | NIVO | ≥ 2 | 9p24·1 | Polysomy; copy gain; amplification | NR |  |  | √ |
| PD-L1 | Q1; Q2; Q3; Q4 | FISH with probes targeting PD-L1 (*CD274*), PD-L2 (*PDCD1LG2*) (both Empire Genomics, Williamsville, New York), and a centromeric region of chromosome 9 (*CEP 9*, control probe; Abbott Molecular, Des Plaines, Illinois) |  |  | √ |
| **Pancreatic** | | | | | | | | | |
| De Remigis et al. (2015) [S-[155](#_ENREF_155)] | Cohort study | GVAX or GVAX + IPI | NR | Thyroglobulin antibody seroconversion | Positive; negative | In-house ELISA and commercial ELISA QUANTA Lite and RIA KRONUS (Star, Idaho) thyroglobulin antibodies | √ |  |  |
| **Metastatic triple-negative breast cancer** | | | | | | | | | |
| KEYNOTE-086 [S-[156](#_ENREF_156)] | Phase 2, OL trial | PEM | ≥ 1 | PD-L1 | Positive and negative | NR | √ | √ | √ |
| **Multiple** | | | | | | | | | |
| ***Melanoma, renal cell carcinoma, and NSCLC*** | | | | | | | | | |
| NCT01375842 Herbst et al. (2014) [S-[57](#_ENREF_57), [58](#_ENREF_58), [121](#_ENREF_121), [145](#_ENREF_145)] | Phase 1, single arm, dose escalation with expansion cohorts | ATEZO | NR | PD-L1 | < 1%; 1% to < 5%; 5% to < 10%; ≥ 10%; increase in PD-L1 TC or IC of > 5% in patients with paired biopsies | SP142 assay |  | √ | √ |
| ***Metastatic tumors including breast, gastric, urothelial, and colorectal tumors*** | | | | | | | | | |
| Ayers et al. (2016) [S-[157](#_ENREF_157)] | Retrospective of KEYNOTE-012 and KEYNOTE-028 | PEM | NR | MSI-H | MSI-H; non-MSI-H | Microsatellite markers were analyzed by capillary electrophoresis |  |  | √ |
| ***SCLC, melanoma, and SCCHN*** | | | | | | | | | |
| Navarro et al. (2016) [S-[158](#_ENREF_158)] | Retrospective study | PEM, NIVO, or ATEZO | ≥ 1 | Immune gene signature | All signatures  T helper cells 1 high-tertile group  T helper cells 1 low-tertile group | RNA was analyzed using the NanoString PanCancer Immune Panel (NanoString Technologies, Seattle, Washington) |  | √ | √ |
| ***NSCLC, SCCHN, and melanoma*** | | | | | | | | | |
| Prat et al. (2017) [S-[159](#_ENREF_159)] | Retrospective of clinical trials | NIVO or PEM | ≥ 1 | Natural killer-cell expression | Low; high | Expression of 730 immune-related genes and 40 housekeeping genes using the nCounter platform (NanoString Technologies, Seattle, Washington) |  | √ |  |
| ***Any solid tumor with stage IV disease*** | | | | | | | | | |
| Yaghmour et al. (2016) [S-[68](#_ENREF_68)] | Retrospective database search | NIVO, PEM, or IPI | ≥ 1 | TML | Top quintile; other quintiles combined | NR | √ | √ | √ |
| PD-L1 | Positive; negative | IHC by the individual commercial labs | √ |  |  |
| PD-1 | Positive; negative | √ |  |  |
| ***NSCLC, mUC, or other advanced solid tumors*** | | | | | | | | | |
| FIR, BIRCH, POPLAR, OAK, IMVIGOR, PCD4989g [S-[160](#_ENREF_160)] | NR | ATEZO | ≥ 1 | Tissue TMB | ≥ 16 mutations per mb; < 16 mutations per mb | FoundationOne assay (Foundation Medicine, Cambridge, Massachusetts) |  |  | √ |

AEC = absolute eosinophil count; AKT = protein kinase B; ALC = absolute lymphocyte count; ALK = anaplastic lymphoma kinase; AMC = absolute monocyte count; ANGPT2 = angiopoietin-2 precursor; ATEZO = atezolizumab; AVE= avelumab; BEV= bevacizumab; bTMB = blood tumor mutational burden; CD25 = cluster of differentiation 25/interleukin 2 receptor alpha; CFB = change from baseline; CPS = combined positive score; CRP = C-reactive protein; CTLA-4 = cytotoxic T-lymphocyte–associated protein 4; *CXCL9* = chemokine (C-X-C) motif ligand 9; DB= double-blind; DNA = deoxyribonucleic acid; DTX = docetaxel; DURVA = durvalumab; EGFR = epidermal growth factor receptor; ELISA = enzyme-linked immunosorbent assay; FISH = fluorescence in situ hybridization; *FOXP3* = Forkhead Box P3; GVAX = pancreatic cancer vaccine; HLA = human leukocyte antigen; HLA-DR = human leukocyte antigen-D related; IC = immune cell; IFN-γ = interferon gamma; IFNGS = interferon gene signature; IHC = immunohistochemistry; IPI = ipilimumab; *KRAS* = KRAS Proto-Oncogene, GTPase; *LAG3* = lymphocyte-activation gene 3; LDH = lactate dehydrogenase; mAb = monoclonal antibody; MAGE-3 = melanoma-associated antigen 3; MART-1 = melanoma antigen recognized by T cells 1; mb= megabase; MCPyV = Merkel cell polyomavirus; MDSC = myeloid-derived suppressor cell; MEK = mitogen-activated protein kinase enzyme; MIA = multiplex immunoassay; MICA = major histocompatibility complex class I-related chain A; mRNA = messenger ribonucleic acid; MSI-H = high-level microsatellite instability; mUC = metastatic urothelial cancer; NGS = next-generation sequencing; NIVO= nivolumab; NR = not reported; NSCLC = non–small cell lung cancer; OL = open-label; OS = overall survival; p-AKT = phospho-AKT; p‑S6 = phospho-S6 ribosomal protein; PBO = placebo; PCR = polymerase chain reaction; PD-1 = programmed cell death protein 1; PD-L1 = programmed cell death ligand 1; PD-L2 = programmed cell death ligand 2; PEM= pembrolizumab; PFS = progression-free survival; Q = quarter; RCT= randomized controlled trial; REC = relative eosinophil count; RLC = relative lymphocyte count; RNA = ribonucleic acid; RT-PCR = reverse transcription polymerase chain reaction; SCCHN = squamous-cell carcinoma of the head and neck; SCLC = small cell lung cancer; SOC = standard of care; TC = tumor cell; TCM = central memory T cell; TEM1 = effector memory T cell-1; TEM3 = effector memory T cell-3; TEM4 = effector memory T cell-4; TEMRA = effector memory T cell RA; TIM3 = T‑cell immunoglobulin and mucin-domain containing-3; TMB = tumor mutational burden; TML = tumor mutational load; ULN = upper limit of normal; VEGF = vascular endothelial growth factor.

a Defined as the number of somatic, coding base substitutions and short insertions and deletions per megabase of genome examined.

Table S2. PD-L1: OS and PFS Data in NSCLC

| Trial Acronym/ Author (Year) | Population | Treatment | No. of Patients | OS | | PFS | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Median (95% CI), Months | HR (95% CI) | Median (95% CI), Months | HR (95% CI) |
| BIRCH [S-[1-3](#_ENREF_1)] | PD-L1 ≥ 50% | First-line ATEZO | 65 | NE (12-NE) | NR | 5.6 (2.7-8.3) | NR |
| Second-line ATEZO | 122 | 15.1 (12-NE) | NR | 4 (1.5-5.5) | NR |
| ≥ Third ATEZO | 115 | 17.5 (11.1-NE) | NR | 4.1 (2.8-5.6) | NR |
| PD-L1 10-49% | First-line ATEZO | 74 | 20.1 (NE) | NR | 5.3 (2.8-6.9) | NR |
| Second-line ATEZO | 146 | 15.5 (11.9-NE) | NR | 2.6 (1.4-2.8) | NR |
| ≥ Third ATEZO | 136 | 11 (7.5-14.9) | NR | 2.7 (1.5-2.8) | NR |
| PD-L1 TC 3 or IC 3 | First-line ATEZO | 65 | 26.9 (12-NE) | NR | 7.3 (4.9-12) | NR |
| PD-L1 TC 2 or IC 2b | 73 | 23.5 (18.1-NE) | NR | 7.6 (4-9.7) | NR |
| CheckMate 012 [S-[4](#_ENREF_4), [5](#_ENREF_5)] | PD-L1 ≥ 1% | NIVO 10 mg/kg | 23 | 20.2 (NR) | NR | 6 (NR) | NR |
| PD-L1 < 1 % | 21 | 19.2 (NR) | NR | 5.2 (NR) | NR |
| CheckMate 017 [S-[6](#_ENREF_6)] | PD-L1 < 1% | NIVO 3 mg/kg | 54 | 8.7 (NR) | 0.58 (0.58-0.92) | 3.1 (NR) | 0.66 (0.43-1.0) |
| DTX 75 mg/mg | 52 | 5.9 (NR) | 3 (NR) |
| PD-L1 ≥ 1% | NIVO 3 mg/kg | 63 | 9.3 (NR) | 0.69 (0.45-1.1) | 3.3 (NR) | 0.67 (0.44-1.0) |
| DTX 75 mg/m2 | 56 | 7.2 (NR) | 2.8 (NR) |
| PD-L1 < 5% | NIVO 3 mg/kg | 75 | 8.5 (NR) | 0.7 (0.47-1.0) | 2.2 (NR) | 0.75 (0.52-1.1) |
| DTX 75 mg/m2 | 69 | 6.4 (NR) | 2.9 (NR) |
| PD-L1 ≥ 5% | NIVO 3 mg/kg | 42 | 10 (NR) | 0.53 (0.31-0.89) | 4.8 (NR) | 0.54 (0.32-0.9) |
| DTX 75 mg/m2 | 39 | 6.1 (NR) | 3.1 (NR) |
| PD-L1 < 10% | NIVO 3 mg/kg | 81 | 11 (NR) | 0.7 (0.48-1.0) | 2.3 (NR) | 0.7 (0.49-0.99) |
| DTX 75 mg/m2 | 75 | 6.1 (NR) | 2.8 (NR) |
| PD-L1 ≥ 10% | NIVO 3 mg/kg | 36 | 8.2 (NR) | 0.5 (0.28-0.89) | 3.7 (NR) | 0.58 (0.33-1.0) |
| DTX 75 mg/m2 | 33 | 7.1 (NR) | 3.3 (NR) |
| CheckMate 026 [S-[9](#_ENREF_9), [10](#_ENREF_10)] | PD-L1 > 1% | NIVO 3 mg/kg | 271 | 13.7 (11.8-15.4) | 1.07 (0.86-1.33) | 4.2 (3.1-5.5) | 1.17 (0.95-1.43) |
| Platinum-based CT | 270 | 13.8 (11-17) | 5.8 (5.4-6.9) |
| PD-L1 ≥ 5% | NIVO 3 mg/kg | 211 | 14.4 (11.7-17.4) | 1.02 (0.8-1.3) | 4.2 (3.0-5.6) | 1.15 (0.91-1.45) |
| Platinum-based CT | 212 | 13.2 (10.7-17.1) | 5.9 (5.4-6.9) |
| PD-L1 ≥ 50% | NIVO 3 mg/kg | 88 | 15.9 (NR) | 0.9 (0.63-1.29) | 5.4 (NR) | 1.07 (0.77-1.49) |
| Platinum-based CT | 126 | 13.9 (NR) | 5.8 (NR) |
| CheckMate 057 [S-[11-13](#_ENREF_11)] | PD-L1 < 1% | NIVO 3 mg/kg | 108 | 10.5 (NR) | 0.9 (0.66-1.24) | 2.1 | 1.19 (0.88-1.61) |
| DTX 75 mg/m2 | 101 | 10.1 (NR) | 3.6 |
| PD-L1 ≥ 1% | NIVO 3 mg/kg | 123 | 17.7 (NR) | 0.59 (0.43-0.82) | 4.2 | 0.7 (0.53-0.94) |
| DTX 75 mg/m2 | 123 | 9 (NR) | 4.5 |
| PD-L1 < 5% | NIVO 3 mg/kg | 136 | 9.8 (NR) | 1.01 (0.77-1.34) | 2.1 | 1.31 (1.01-1.71) |
| DTX 75 mg/m2 | 138 | 10.1 (NR) | 4.2 |
| PD-L1 ≥ 5% | NIVO 3 mg/kg | 95 | 19.4 (NR) | 0.43(0.30-0.63) | 5 | 0.54 (0.39-0.76) |
| DTX 75 mg/m2 | 86 | 8.1 (NR) | 3.8 |
| PD-L1 < 10% | NIVO 3 mg/kg | 145 | 9.9 (NR) | 1 (0.76-1.31) | 2.1 | 1.24 (0.96-1.61) |
| DTX 75 mg/m2 | 145 | 10.3 (NR) | 4.2 |
| PD-L1 ≥ 10% | NIVO 3 mg/kg | 86 | 19.9 (NR) | 0.4 (0.26-0.59) | 5 | 0.52 (0.37-0.75) |
| DTX 75 mg/m2 | 79 | 8 (NR) | 3.7 |
| CP1108 [S-[16-22](#_ENREF_16)] | PD-L1 TC ≥ 25% | Second line, DURVA | 46 | 17.8 (7.9-22.4) | NR | NR | NR |
| PD-L1 TC < 25% | 24 | 8.2 (4.9-15.5) | NR | NR | NR |
| PD-L1 TC ≥ 25% | ≥ Third line, DURVA | 59 | 13 (6-NE) | NR | NR | NR |
| PD-L1 TC < 25% | 82 | 7.1 (4.3-10) | NR | NR | NR |
| IFN-ɣ mRNA any and PD-L1 IHC+ (≥ 25%) | Mixed line, DURVA | 43 | NE (8.8-NE) | 0.4 | NR | NR |
| IFN-ɣ mRNA any and PD-L1 IHC– | 20 | NE (6.5-NE) | 0.38 | NR | NR |
| IFN-ɣ mRNA any and PD-L1 IHC+ (≥25%) | 42 | 9.7 (8.8-NE) | 0.64 | NR | NR |
| IFN-ɣ mRNA any and PD-L1 IHC– | 52 | 5.9 (4.1-10.2) | NR | NR | NR |
| PD-L1 (high): ≥ 25% of TC expressed PD‑L1 | First line, DURVA | 109 | 15.4 (9.7-22.4) | NR | NR | NR |
| PD-L1 (low/negative): < 25% of TC | 108 | 7.6 (5.6-10) | NR | NR | NR |
| JAVELIN Solid Tumor [S-[23-32](#_ENREF_23)] | PD-L1 ≥ 1% positive | ≥ Second line, AVE | 122 | 8.9 (8-NE) | 0.64 (0.34-1.2) | 2.8 (2.4-4.1) | 0.4 (0.27-0.75) |
| PD-L1 ≥ 1% negative | 20 | 4.6 (2.8-NE) | 1.4 (1.3-1.6) |
| PD-L1 ≥ 5% positive | 84 | 10.6 (7.9-NE) | 1.14 (0.7-1.02) | 2.7 (1.5-4.2) | NR |
| PD-L1 ≥ 5% negative | 58 | 8.4 (5.6-NE) | 1.8 (1.4-2.8) | NR |
| PD-L1 ≥ 25% positive | 53 | 8.44 (6-NE) | 1.14 (0.7-1.85) | 2.7 (1.5-4.2) | 0.79 (0.53-1.18) |
| PD-L1 ≥ 25% negative | 89 | 8.57 (7.16-NE) | 2.5 (1.4-3.2) |
| PD-L1 ≥ 10% positive | 27 | 8.5 (3.9-NE) | 1.2 (0.68-2.14) | 1.9 (1.3-3.5) | 1.19 (0.74-1.92) |
| PD-L1 ≥ 10% negative | 115 | 8.9 (7.9-NE) | 2.6 (1.5-3.5) | NR |
| KEYNOTE-001 [S-[33-40](#_ENREF_33)] | PD-L1:  PS ≥ 50% training group | ≥ First line, PEM  2 mg/kg Q3W or 10 mg/kg Q3W or 10 mg/kg Q2W | 38 | 13.7 (6.9-NE) | NR | 4.5 (1.9-12.5) | NR |
| PD-L1:  PS 1%-49% training group | 43 | 5.9 (4.2-8.2) | NR | 2.1 (2-2.9) | NR |
| PD-L1:  PS < 1% training group | 40 | 6.7 (3.9-10) | NR | 2.1 (1.8-2.5) | NR |
| PD-L1: PS ≥ 50% validation group | 73 | NE (NE-NE) | NR | 6.4 (4.2-NE) | NR |
| PD-L1:  PS 1%-49% validation group | 103 | 10.6 (7.3-NE) | NR | 4.1 (2.3-4.4) | NR |
| PD-L1: PS < 1% validation group | 28 | 10.4 (7.3-NE) | NR | 4 (2.1-6.2) | NR |
| PD-L1 positive: overall | 101 | 22.1 (17.1-27.2) | NR | 6.2 (4.1-8.6) | NR |
| PD-L1 positive: TPS ≥ 50% | 27 | NE (22.1-NE) | NR | 12.5 (6.2-NE) | NR |
| PD-L1 positive:  TPS 1%-49% | 52 | 19.5 (10.7-22.2) | NR | 4.2 (3.1-6.4) | NR |
| PD-L1 positive: TPS < 1% | 12 | 14.7 (3.4-NE) | NR | 3.5 (2.1-19) | NR |
| PD-L1: TPS ≥ 1% | 79 | 22.2 (16.7-31.5) | NR | NR | NR |
| PD-L1: TPS ≥ 50% | 27 | 34.9 (20.3-NE) | NR | NR | NR |
| PD-L1:  TPS 1%-49% | 52 | 19.5 (10.7-26.3) | NR | NR | NR |
| PD-L1: TPS ≥ 1% | 306 | 11.1 (8.3-14) | NR | NR | NR |
| PD-L1: TPS ≥ 50% | 138 | 15.4 (10.5-18.5) | NR | NR | NR |
| PD-L1:  TPS 1%-49% | 90 | 8.5 (6-12.7) | NR | NR | NR |
| PD-L1: TPS < 1% | 90 | 8.6 (5.5-10.6) | NR | NR | NR |
| PD-L1: TPS ≥ 1% | 79 | 22.1 (16.7-27.2) | NR | NR | NR |
| PD-L1: TPS ≥ 50% | 27 | NE (22.1-NE) | NR | NR | NR |
| PD-L1:  TPS 1%-49% | 52 | 19.5 (10.7-22.2) | NR | NR | NR |
| PD-L1: TPS < 1% | 12 | 14.7 (3.4-NE) | NR | NR | NR |
| PD-L1: TPS ≥ 1% | 306 | 11.3 (8.3-14) | NR | NR | NR |
| PD-L1: TPS ≥ 50% | 138 | 15.4 (10.6-18.5) | NR | NR | NR |
| PD-L1:  TPS 1%-49% | 168 | 8.2 (6-12.7) | NR | NR | NR |
| PD-L1: TPS < 1% | 90 | 8.6 (5.5-12) | NR | NR | NR |
| PD-L1 ≥ 50% | 17 | NE (NE-NE) | NR | NE (2.4-NE) | NR |
| PD-L1 1%-49% | 31 | NE (8.6-NE) | NR | 4.4 (3.6-6.4) | NR |
| PD-L1 < 1% | 7 | 7.3 (3.4-NE) | NR | 3.4 (2.1-4.2) | NR |
| KEYNOTE-010 [S-[41-44](#_ENREF_41)] | PD-L1: TPS ≥ 1% | > First line, PEM 2 mg/kg Q3W | 344 | 10.4 (9.4-11.9) | 0.71 (0.58-0.88) | 3.9 (3.1-4.1) | 0.88 (0.74-1.05) |
| PD-L1: TPS ≥ 1% | > First line, PEM 10 mg/kg Q3W | 346 | 12.7 (10-17.3) | 0.61 (0.49-0.75) | 4 (2.7-4.3) | 0.79 (0.66-0.94) |
| PD-L1: TPS ≥ 1% | > First line, DTX 75 mg/m2 Q3W | 343 | 8.5 (7.5-9.8) | 4 (3.1-4.2) |
| PD-L1: TPS ≥ 50% | > First line, PEM 2 mg/kg Q3W | 139 | 14.9 (10.4-NE) | 0.54 (0.38-0.77) | 5.2 (4.1-8.1) | 0.59 (0.44-0.78) |
| PD-L1: TPS ≥ 50% | > First line, PEM 10 mg/kg Q3W | 151 | 17.3 (11.8-NE) | 0.5 (0.36-0.7) | 4.1 (3.6-4.3) | 0.59 (0.45-0.78) |
| PD-L1: TPS ≥ 50% | > First line, DTX 75 mg/m2 Q3W | 152 | 8.2 (6.4-10.7) | NR |
| PD-L1: TPS ≥ 50% | > First line, PEM and DTX, 2 mg/kg Q3W or 10 mg/kg Q3W or 75 mg/m2 Q3W | 442 | NR | 0.53 (0.4-0.7) | NR | 0.59 (0.46-0.74) |
| PD-L1:  TPS 1%-49% | 591 | NR | 0.76 (0.6-0.96) | NR | 1.04 (0.85-1.27) |
| PD-L1: TPS ≥ 50% | ≥ 1st line, PEM 2 mg/kg Q3W | NR | 14.9 (10.4-NR) | 0.54 (0.38-0.77) | NR | NR |
| PD-L1: TPS ≥ 50% | ≥ 1st line, DTX 75 mg/m2 Q3W | NR | 8.2 (6.4-10.7) | NR | NR |
| PD-L1:  TPS 1%-24% | ≥ 1st line, PEM  2 or 10 mg/kg Q3W | 324 | 9.7 (NR-NR) | NR | 2.6 (NR-NR) | NR |
| PD-L1:  TPS 25%-49% | 76 | 9.8 (NR-NR) | NR | 2.9 (NR-NR) | NR |
| PD-L1:  TPS 50%-74% | 106 | 15.8 (NR-NR) | NR | 4.3 (NR-NR) | NR |
| PD-L1: TPS ≥ 75% | 184 | 16.6 (NR-NR) | NR | 6.2 (NR-NR) | NR |
| PD-L1:  TPS 1%-24% | ≥ 1st line, PEM and DTX, 2 mg/kg Q3W or 10 mg/kg Q3W or 75 mg/m2 Q3W | 471 | NR | 0.74 (0.56-0.96) | NR | 1.08 (0.86-1.36) |
| PD-L1:  TPS 25%-49% | 120 | NR | 0.86 (0.51-1.45) | NR | 0.95 (0.6-1.5) |
| PD-L1:  TPS 50%-74% | 158 | NR | 0.58 (0.36-0.95) | NR | 0.78 (0.52-1.17) |
| PD-L1:  TPS ≥ 75% | 284 | NR | 0.51 (0.36-0.73) | NR | 0.52 (0.38-0.69) |
| PD-L1:  TPS 1%-24% | ≥ First line, DTX 75 mg/m2 Q3W | 147 | 8.5 (NR-NR) | NR | 4 (NR-NR) | NR |
| PD-L1:  TPS 25%-49% | 44 | 9.9 (NR-NR) | NR | 3.8 (NR-NR) | NR |
| PD-L1:  TPS 50%-74% | 52 | 8.2 (NR-NR) | NR | 4.3 (NR-NR) | NR |
| PD-L1: TPS ≥ 75% | 100 | 8.2 (NR-NR) | NR | 4 (NR-NR) | NR |
| PD-L1: TPS ≥ 50% (archival) | 119 | 11.5 (NR-NR) | NA | 3.9 (NR-NR) | NA |
| PD-L1: TPS ≥ 50% (new tissue) | ≥ First line, DTX 75 mg/m2 Q3W | 171 | NE (NR-NR) | NA | 6.3 (NR-NR) | NA |
| PD-L1: TPS ≥ 1% (archival) | 300 | 10.5 (NR-NR) | NA | 2.9 (NR-NR) | NA |
| PD-L1: TPS ≥ 1% (new tissue) | 390 | 12.6 (NR-NR) | NA | 4.1 (NR-NR) | NA |
| PD-L1: TPS ≥ 50% (archival) | ≥ First line, PEM and DTX, 2 mg/kg Q3W or 10 mg/kg Q3W or 75 mg/m2 Q3W | 184 | NA (NA-NA) | 0.6 (0.4-0.9) | NA | 0.64 (0.45-0.9) |
| PD-L1: TPS ≥ 50% (new tissue) | ≥ First line, PEM and DTX, 2 mg/kg Q3W or 10 mg/kg Q3W or 75 mg/m2 Q3W | 258 | NA (NA-NA) | 0.44 (0.29-0.66) | NA | 0.54 (0.39-0.75) |
| PD-L1: TPS ≥ 1% (archival) | 455 | NA (NA-NA) | 0.7 (0.54-0.89) | NA | 0.81 (0.65-1.01) |
| PD-L1: TPS ≥ 1% (new tissue) | 578 | NA (NA-NA) | 0.64 (0.5-0.83) | NA | 0.86 (0.7-1.07) |
| PD-L1: TPS ≥ 50% (archival) | ≥ First line, DTX 75 mg/m2 Q3W | 65 | 7.4 (NR-NR) | NA | 4 (NR-NR) | NA |
| PD-L1: TPS ≥ 50% (new tissue) | 87 | 8.3 (NR-NR) | NA | 4.3 (NR-NR) | NA |
| PD-L1: TPS ≥ 1% (archival) | 155 | 8.3 (NR-NR) | NA | 3.8 (NR-NR) | NA |
| PD-L1: TPS ≥ 1% (new tissue) | 188 | 8.6 (NR-NR) | NA | 4.2 (NR-NR) | NA |
| OAK [S-[45-49](#_ENREF_45)] | PD-L1 ≥ 50% | ATEZO | 72 | 20.5 (17.5-NE) | 0.41 (0.27-0.64) | 4.2 (2.9-7) | 0.63 (0.43-0.91) |
| DTX | 65 | 8.9 (5.6-11.6) | 3.3 (2.7-4.2) |
| PD-L1 ≥ 5% | ATEZO | 129 | 16.3 (13.3-20.1) | 0.67 (0.49-0.90) | 4.1 (2.8-5.3) | 0.76 (0.58-0.99) |
| DTX | 136 | 10.8 (8.8-12.7) | 3.6 (2.8-4.2) |
| PD-L1 ≥ 1% | ATEZO | 241 | 15.7 (12.6-18.0) | 0.74 (0.58-0.93) | 2.8 (2.6-4.0) | 0.91 (0.74-1.12) |
| DTX | 222 | 10.3 (8.8-12.0) | 4.1 (2.9-4.3) |
| PD-L1 < 1% | ATEZO | 180 | 12.6 (9.6-15.2) | 0.75 (0.59-0.96) | 2.6 (1.7-2.9) | 1 (0.8-1.25) |
| DTX | 199 | 8.9 (7.7-11.5) | 4 (3.1-4.2) |
| PD-L1 ≥ 50% (nonsquamous) | ATEZO | 49 | 22.5 (NR) | 0.35 (0.21-0.61) | NR | NR |
| DTX | 47 | 8.7 (NR) | NR | NR |
| PD-L1 ≥ 5% (nonsquamous) | ATEZO | 89 | 18.7 (NR) | 0.61 (0.42-0.88) | NR | NR |
| DTX | 99 | 11.3 (NR) | NR | NR |
| PD-L1 ≥ 1% (nonsquamous) | ATEZO | 171 | 17.6 (NR) | 0.72 (0.55-0.95) | NR | NR |
| DTX | 162 | 11.3 (NR) | NR | NR |
| PD-L1 < 1% (nonsquamous) | ATEZO | 140 | 14 (NR) | 0.75 (0.57-1.0) | NR | NR |
| DTX | 150 | 11.2 (NR) | NR | NR |
| PD-L1 ≥ 50% (squamous) | ATEZO | 23 | 17.5 (NR) | 0.57 (0.27-1.2) | NR | NR |
| DTX | 18 | 11.6 (NR) | NR | NR |
| PD-L1 ≥ 5% (squamous) | ATEZO | 40 | 10.4 (NR) | 0.76 (0.45-1.29) | NR | NR |
| DTX | 37 | 9.7 (NR) | NR | NR |
| PD-L1 ≥ 1% (squamous) | ATEZO | 70 | 9.9 (NR) | 0.71 (0.48-1.06) | NR | NR |
| DTX | 60 | 8.7 (NR) | NR | NR |
| PD-L1 < 1% (squamous) | ATEZO | 40 | 7.6 (NR) | 0.82 (0.51-1.32) | NR | NR |
| DTX | 49 | 7.1 (NR) | NR | NR |
| PD-L1 ≥ 1% (Japanese) | ATEZO | 11 | 21.3 (15-NE) | 0.81 (0.22-3.05) | 4.2 (2.9-10.2) | 1.18 (0.44-3.16) |
| DTX | 8 | NE (NE-NE) | 5.6 (4.2-8.8) |
| PD-L1 < 1% (Japanese) | ATEZO | 25 | 20.9 (7.8-NE) | 0.79 (0.36-1.73) | 4 (1.5-4.4) | 1.45 (0.78-2.69) |
| DTX | 20 | 17 (12-NE) | 4.2 (2.9-5.8) |
| POPLAR [S-[49-54](#_ENREF_49)] | PD-L1 ≥ 50% | ATEZO | 24 | 15.5 (9.8-NE) | 0.49 (0.22-1.07) | 7.8 (2.7-12.3) | 0.6 (0.31-1.16) |
| DTX | 23 | 11.1 (6.7-14.4) | 3.9 (1.9-5.7) |
| PD-L1 ≥ 5% | ATEZO | 50 | 15.1 (8.4-NE) | 0.54 (0.33-0.89) | 3.4 (1.4-6.9) | 0.72 (0.47-1.1) |
| DTX | 55 | 7.4 (6.0-12.5) | 2.8 (1.9-3.9) |
| PD-L1 ≥ 1% | ATEZO | 93 | 15.5 (11-NE) | 0.59 (0.40-0.85) | 2.8 (2.6-5.5) | 0.85 (0.63-1.16) |
| DTX | 102 | 9.2 (7.3-12.8) | 3 (2.8-4.1) |
| PD-L1 < 1% | ATEZO | 51 | 9.7 (6.7-12) | 1.04 (0.62-1.75) | 1.7 (1.4-4.2) | 1.12 (0.72-1.77) |
| DTX | 41 | 9.7 (8.6-12) | 4.1 (2.7-5.6) |
| NCT00730639  Topalian et al. (2012) [S-[55](#_ENREF_55), [56](#_ENREF_56)] | PD-L1 ≥ 5% | NIVO 1.0, 3.0, or 10.0 mg/kg Q2W | 33 | 7.8 (5.6-21.7) | NR | 3.3 (1.8-7.5) | NR |
| PD-L1 < 5% | 35 | 10.5 (5.2-14.8) | NR | 1.8 (1.7-2.3) | NR |
| NCT01375842 [S-[57](#_ENREF_57), [58](#_ENREF_58)] | PD-L1 < 1% | ATEZO 0.01, 0.03, and 0.1 mg and 0.3, 1, 3, 10, and 20 mg/kg Q3W | 20 | NR | NR | 13 (6-37) | NR |
| PD-L1 1 ≤ 5% | 13 | NR | NR | 6 (5-43) | NR |
| PD-L1 5%-10% | 7 | NR | NR | 11 (1-17) | NR |
| PD-L1 ≥ 10% | 6 | NR | NR | NE (5-NE) | NR |
| Kaderbhai (2017) [S-[62](#_ENREF_62)] | PD-L1 ≥ 1% | NIVO | 33 | NR | 1.4 (0.63-3.09) | NR | 0.97 (0.55-1.69) |
| PD-L1 < 1% | 33 | NR | NR |
| Sorensen et al. (2016) [S-[67](#_ENREF_67)] | PD-L1 ≥ 50%, all patients | PEM + platinum-doublet chemotherapy as initial therapy | 51 | 9 (6.4-11.1) | 1.36 (0.9-2.06) | NR | NR |
| PD-L1 ≥ 50%, adenocarcinoma | NR | 10.9 (6.9-13.3) | 1.31 (0.76-2.27) | NR | NR |
| PD-L1 ≥ 50%, squamous-cell carcinoma | NR | 7.2 (0.9-10.2) | 3.87 (1.05-14.26) | NR | NR |
| PD-L1 1%-49%, all patients | 102 | 9.8 (8.2-12.3) | 1.09 (0.76-1.58) | NR | NR |
| PD-L1 1%-49%, adenocarcinoma | NR | 12.1(8.5-15.0) | 0.84 (0.53-1.34) | NR | NR |
| PD-L1 1%-49%, squamous-cell carcinoma | NR | 8.8 (6.1-12.2) | 2.36 (0.84-6.63) | NR | NR |
| PD-L1 < 1%, all patients | 51 | 7.5 (6.4-12.4) | NR | NR | NR |
| PD-L1 < 1%, adenocarcinoma | NR | 10.7 (7.1-16.4) | NR | NR | NR |
| PD-L1 < 1%, squamous-cell carcinoma | NR | 19.9 (3.3-NE) | NR | NR | NR |
| PD-L1 ≥ 1%, all patients | NR | 9.3 (7.8-11.0) | 1.17 (0.83-1.66) | NR | NR |
| PD-L1 ≥ 1%, adenocarcinoma | NR | 11.1(9.2-13.3) | 0.96 (0.62-1.48) | NR | NR |
| PD-L1 ≥ 1%, squamous-cell carcinoma | NR | 8.4 (6.6-9.8) | 2.4 (0.87-6.6) | NR | NR |
| Yaghmour (2016) [S-[68](#_ENREF_68)] | PD-1 positive | ≥ First line, NIVO or IPI | 50 overall patients | 7.5 (NR-NR) | 1.53 (0.38-7.58) | NR | NR |
| PD-1 negative | Undefined  (NR-NR) | NR | NR |
| PD-L1 positive | 7.5 (NR-NR) | 1.76 (0.5-6.85) | NR | NR |
| PD-L1 negative | Undefined (NR-NR) | NR | NR |

ATEZO = atezolizumab; AVE= avelumab; CI = confidence interval; CT = chemotherapy; DTX = docetaxel; DURVA = durvalumab; HR = hazard ratio; IC = immune cell; IFN = interferon; IFN-γ = interferon gamma; IHC = immunohistochemistry; IPI = ipilimumab; mRNA = messenger RNA; NA =not applicable ; NE = not estimable/not reached; NIVO= nivolumab; NR = not reported; OS = overall survival; PD-1 = programmed cell death protein 1; PD-L1 = programmed cell death ligand 1; PEM = pembrolizumab; PFS = progression-free survival; PS = proportion score; Q2W = every 2 weeks; Q3W = every 3 weeks; TC = tumor cell; TPS = tumor proportion score.

Table S3. PD-L1 and TMB: OS and PFS Data in NSCLC

| Trial Acronym | Population | Treatment | No. of Patients | OS | | PFS | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Median (95% CI), Months | HR (95% CI) | Median (95% CI), Months | HR (95% CI) |
| CheckMate 227 [S-[15](#_ENREF_15)] | ≥ 10 mutations per megabase + PD-L1 ≥ 1% | Chemotherapy | 112 | NR | NR | NR | NR (NR-NR) |
| NIVO + IPI | 101 | NR | NR | 7.1 (5.5-13.5) | 0.75 (0.53-1.07) |
| NIVO | 102 | NR | NR | 4.2 (2.6-8.3) |
| ≥ 10 mutations per megabase + PD-L1 < 1% | NIVO + IPI | 38 | NR | NR | NR | 0.48 (0.27-0.85) |
| Chemotherapy | 48 | NR | NR | NR |
| ≥ 13 mutations per megabase + PD-L1 ≥ 1% | NIVO | 71 | NR | NR | 4.2 (2.7-8.3) | 0.95 (0.64-1.4) |
| Chemotherapy | 79 | NR | NR | 5.6 (4.5-7) |

CI = confidence interval; HR = hazard ratio; IPI = ipilimumab; NIVO = nivolumab; NR = not reported; NSCLC = non–small-cell lung cancer; OS = overall survival; PD-L1 = programmed cell death ligand 1; PFS = progression-free survival; TMB = tumor mutational burden.

Supplementary Table S4. PD-L1: OS and PFS Data in Melanoma

| Trial Acronym | Population | Treatment | No. of Patients | OS | | PFS | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Median (95% CI), Months | HR (95% CI) | Median (95% CI), Months | HR (95% CI) |
| CheckMate 066 [S-[75](#_ENREF_75)] | PD-L1 ≥ 5% | NIVO 3 mg/kg Q2W | 74 | NE (NE) | NR | NR | NR |
| PD-L1 < 5% | 128 | NE (NE) | NR | NR | NR |
| PD-L1 ≥ 5% | Dacarbazine 100 mg/m2 Q3W | 74 | 12.4 (9.2 -NE) | NR | NR | NR |
| PD-L1 < 5% | 126 | 10.2 (7.6-11.8) | NR | NR | NR |
| CheckMate 066/067/069 [S-[76](#_ENREF_76)] | PD-L1 ≥ 5% | NIVO 1 mg/kg + IPI 3 mg/kg Q3W | 832 (overall patients) | NR | NR | NE | 0.99 (0.66-1.46) |
| NIVO 3 mg/kg Q2W | NR | NR | 22 |
| PD-L1 < 5% | NIVO 1 mg/kg + IPI 3 mg/kg Q3W | NR | NR | 11.1 | 0.7 (0.57-0.87) |
| NIVO 3 mg/kg Q2W | NR | NR | 4.9 |
| CheckMate 067 [S-[77-79](#_ENREF_77)] | PD-L1 ≥ 5% | NIVO 3 mg/kg Q2W | 80 | NR | NR | 14 (9.1-NE) | NR |
| NIVO 1 mg/kg + IPI 3 mg/kg Q3W | 68 | NR | NR | 14 (9.7-NE) | NR |
| IPI 3 mg/kg Q3W | 75 | NR | NR | 3.9 (2.8-4.2) | NR |
| PD-L1 < 5% | NIVO 3 mg/kg Q2W | 208 | NR | NR | 5.3 (2.8-7.1) | NR |
| NIVO 1 mg/kg + IPI 3 mg/kg Q3W | 210 | NR | NR | 11.2 (8.0-NE) | NR |
| IPI 3 mg/kg Q3W | 202 | NR | NR | 2.8 (2.8 to NE) | NR |
| KEYNOTE-001 [S-[33-40](#_ENREF_33), [82](#_ENREF_82)] | PD-L1 ≥ 1% | PEM 2 mg/kg Q3W or 10 mg/kg Q2W or Q3W | 344 | 29.9 (24.6-NE) | 0.5 (0.37-0.67) | 5.6 (4.4-8.1) | 0.51 (0.4-0.65) |
| PD-L1 < 1% | 107 | 12.6 (7-18.5) | 2.8 (2.7-2.8) |
| PD-L1 positive | PEM for measurable disease at baseline | 535 | NR | < 0.001 | NR | NR |
| PD-L1 negative | 106 | NR | NR | NR |
| KEYNOTE-006 [S-[84-86](#_ENREF_84)] | PD-L1 ≥ 1% | PEM 10 mg/kg Q2W | 450 | NR | 0.55 (0.4-0.76) | NR | 0.53 (0.41-0.67) |
| PD-L1 < 1% | 96 | NR | 0.91 (0.49-1.69) | NR | 0.67 (0.41-1.11) |
| PD-L1 ≥ 1% | PEM 10 mg/kg Q3W | 456 | NR | 0.58 (0.42-0.79) | NR | 0.52 (0.4-0.66) |
| PD-L1 < 1% | 101 | NR | 1.02 (0.56-1.85) | NR | 0.76 (0.47-1.24) |
| PD-L1 ≥ 1% | First- or second-line PEM vs. IPI | 671 | NR | 0.56 (0.43-0.74) | NR | 0.52 (0.43-0.64) |
| PD-L1 < 1% | 150 | NR | 0.94 (0.56-1.6) | NR | 0.83 (0.55-1.26) |
| PD-L1 ≥ 1% | First-line PEM vs. IPI | 667 | NR | 0.56 (0.43-0.73) | NR | 0.52 (0.43-0.64) |
| PD-L1 < 1% | 150 | NR | 0.95 (0.56-1.62) | NR | 0.83 (0.55-1.26) |

CI = confidence interval; IPI= ipilimumab; NE= not estimable/not reached; NIVO = nivolumab; NR= not reported; HR = hazard ratio; OS = overall survival; PEM= pembrolizumab; PD-L1 = programmed cell death ligand 1; PFS = progression-free survival; Q2W = every 2 weeks; Q3W = every 3 weeks.

# References

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