Supplementary

Table S1 The ongoing trials of neoadjuvant immunotherapy

Study title	NCT.no	Key inclusion and exclusion criteria	Drug	Control group	Primary and secondary endpoint
A Single-arm, Phase II Study of Neoadjuvant MPDL3280A, Nab-paclitaxel and Carboplatin (MAC) in Resectable Non-small Cell Lung Cancer (NSCLC)	NCT02716038	Eligible patients were aged 18 years or older and had resectable American Joint Committee on Cancer-defined stage IB-IIIA non-small-cell lung cancer, an ECOG performance status of 0-1, and a history of smoking exposure	Atezolizumab; carboplatin; nab-paclitaxel	Carboplatin + nab-paclitaxel	The primary endpoint was major pathological response, defined as the presence of 10% or less residual viable tumour at the time of surgery
Randomized, Open-label, Controlled Phase III Trial Comparing Pembrolizumab-platinum Based Chemotherapy Combination With Pembrolizumab Monotherapy in First Line Treatment of Non-small-cell Lung Cancers (NSCLC) With PDL1 Expression ≥50%	NCT04547504	Advanced NSCLC molecularly defined by a PDL1 expression ≥50% of tumour cells and no EGFR mutations or ALK rearrangement	Pembrolizumab; cisplatin; carboplatin AUC	Pembrolizumab alone	The primary endpoint was PFS. The secondary endpoints were PFS, iPFS, ORR, OS, DOT, DOR, AE and AESI
A Phase 3, Randomized, Double-blind Trial of Pembrolizumab (MK-3475) With or Without Lenvatinib (E7080/MK-7902) in Participants With Treatment-naïve, Metastatic Non-small Cell Lung Cancer (NSCLC) Whose Tumors Have a Tumor Proportion Score (TPS) Greater Than or Equal to 1% (LEAP-007)-China Extension Study	NCT04676412	No prior systemic therapy for their metastatic NSCLC whose tumors has a PD-L1 TPS ≥1%	Lenvatinib; pembrolizumab	Pembrolizumab + placebo	The primary endpoints were PFS and OS. The secondary endpoints were ORR, AE, GHS, QoL, EORTC and TTD
A Phase 3, Randomized, Double-blind Trial of Pembrolizumab (MK-3475) With or Without Lenvatinib (E7080/MK-7902) in Participants With Treatment-naïve, Metastatic Non-small Cell Lung Cancer (NSCLC) Whose Tumors Have a Tumor Proportion Score (TPS) Greater Than or Equal to 1% (LEAP-007)	NCT03829332	No prior systemic therapy for their metastatic NSCLC whose tumors has a PD-L1 TPS ≥1%	Lenvatinib; pembrolizumab	Pembrolizumab + placebo	The primary endpoints were PFS and OS. The secondary endpoints were ORR, AE, GHS, QoL, EORTC and TTD
A Randomized, Phase 3 Trial With Anti-PD-1 Monoclonal Antibody Pembrolizumab (MK-3475) Versus Placebo for Patients With Early Stage NSCLC After Resection and Completion of Standard Adjuvant Therapy (PEARLS)	NCT02504372	Stage IB/II–IIIA NSCLC who have undergone surgical resection	Pembrolizumab	Placebo	The primary endpoint was DFS. The secondary endpoints were OS and LCSS
A Phase 3, Randomized, Placebo-Controlled Clinical Study to Evaluate the Safety and Efficacy of Stereotactic Body Radiotherapy (SBRT) With or Without Pembrolizumab (MK-3475) in Participants With Medically Inoperable Stages I or IIA Non Small Cell Lung Cancer (NSCLC) (KEYNOTE-867)	NCT03924869	Medically inoperable Stage I or IIA NSCLC	Pembrolizumab; SBRT	SBRT + placebo	The primary endpoints were EFS and OS. The secondary endpoints were TDDM, AE and EORTC QLQ-LC13/-C30 SCORE
A Phase 3, Multicenter, Randomized, Open-label Trial to Compare the Efficacy and Safety of Pembrolizumab (MK-3475) in Combination With Lenvatinib (E7080/MK-7902) Versus Docetaxel in Previously Treated Participants With Metastatic Non-small Cell Lung Cancer (NSCLC) and Progressive Disease (PD) After Platinum Doublet Chemotherapy and Immunotherapy (LEAP-008)	NCT03976375	Metastatic NSCLC and progressive disease (PD) after platinum doublet chemotherapy and treatment with one prior anti-PD-1/PD-L1	Pembrolizumab; lenvatinib; docetaxel	Docetaxel	The primary endpoints were OS and PFS. The secondary endpoints were ORR, DOR, AE, EORTC QLQ-LC13/-C30 SCORE and TTD in EORTC QLQ-LC13 Cough (Item 31) Scale Score
A Randomized, Double-Blind, Phase 3 Study of Pemetrexed + Platinum Chemotherapy With or Without Pembrolizumab (MK-3475) in TKI-resistant EGFR-mutated Tumors in Metastatic Non-squamous Non-small Cell Lung Cancer (NSCLC) Participants (KEYNOTE-789)	NCT03515837	Adults with the following types of TKI-resistant, EGFR-mutated, metastatic NSCLC tumors: (I) TKI-failures (including osimertinib [TAGRISSO®] failure) with T790M-negative mutation tumors, (II) T790M-positive mutation tumors with prior exposure to osimertinib, and (III) first-line osimertinib failure regardless of T790M mutation status	Pembrolizumab; pemetrexed; carboplatin; cisplatin	Placebo + pemetrexed + carboplatin+ cisplatin	The primary endpoints were OS and PFS. The secondary endpoints were ORR, DOR, AE, EORTC QLQ-LC13/-C30 SCORE and TTD in the EORTC Questionnaire Composite Endpoint of Cough, Chest Pain or Dyspnea
An Adaptive Phase III, Multicenter, Randomized, Open-Label, Controlled Study of M7824 (Bintrafusp Alfa) Versus Pembrolizumab as a First-line Treatment in Patients With PD-L1 Expressing Advanced Non-small Cell Lung Cancer	NCT03631706	Advanced NSCLC with high PD-L1-tumor expression, with no EGFR mutation or ALK translocation	M7824; pembrolizumab	Pembrolizumab	The primary endpoints were OS and PFS. The secondary endpoint were TEAEs, NCI-CTCAE, CR, PR and Immunogenicity
A Phase III, Randomized, Double-blind Trial of Platinum Doublet Chemotherapy +/-Pembrolizumab (MK-3475) as Neoadjuvant/Adjuvant Therapy for Participants With Resectable Stage II, IIIA, and Resectable IIIB (T3-4N2) Non-small Cell Lung Cancer (NSCLC) (KEYNOTE-671)	NCT03425643	Resectable stage II, IIIA, and resectable IIIB (T3-4N2) NSCLC	Pembrolizumab; cisplatin; gemcitabine; pemetrexed	NAC + neoadjuvant/adjuvant placebo	The primary endpoints were EFS and OS. The secondary endpoints were mPR rate, pCR rate, AE and EGHS/QoL SCORE
A Randomized, Double-blind, Placebo-controlled, Phase III Study Evaluating the Efficacy and Safety of Pembrolizumab Plus Platinum-based Doublet Chemotherapy With or Without Canakinumab as First Line Therapy for Locally Advanced or Metastatic Non-squamous and Squamous Non-small Cell Lung Cancer Subjects (CANOPY-1)	NCT03631199	Previously untreated locally advanced or metastatic non-squamous and squamous NSCLC subjects	Canakinumab; pembrolizumab; carboplatin; cisplatin; paclitaxel; nab-paclitaxel; pemetrexed	Canakinumab matching-placebo	The primary endpoint were DLTs, PFS and OS. The secondary endpoints were ORR, DCR, DOR and TTR
A Phase 3 Randomized, Placebo-controlled Study to Evaluate the Safety and Efficacy of Pemetrexed + Platinum Chemotherapy + Pembrolizumab (MK-3475) With or Without Lenvatinib (E7080/MK-7902) as First-line Intervention in Participants With Metastatic Nonsquamous Non-small Cell Lung Cancer (LEAP-006)	NCT03829319	Adults with metastatic nonsquamous NSCLC	Pembrolizumab; carboplatin; cisplatin; pemetrexed; lenvatinib	Pemetrexed + platinum chemotherapy + pembrolizumab + placebo	The primary endpoints were DLTs, AES, PFS and OS. The secondary endpoints were ORR, DOR and EORTC QLQ-LC13/-C30 SCORE
LIBRETTO-431: A Multicenter, Randomized, Open-Label, Phase 3 Trial Comparing Selpercatinib to Platinum-Based and Pemetrexed Therapy With or Without Pembrolizumab as Initial Treatment of Advanced or Metastatic RET Fusion-Positive Non-Small Cell Lung Cancer	NCT04194944	Participants with RET fusion-positive non-squamous NSCLC that has spread to other parts of the body	Selpercatinib; carboplatin; cisplatin; pemetrexed; pembrolizumab	Pemetrexed with or without pembrolizumab	The primary endpoint was PFS. The secondary endpoints were ORR, DCR, PFS, OS, DOR and Time to Deterioration of Pulmonary Symptoms
A Randomized, Double-Blind, Phase III Study of Carboplatin-Paclitaxel/Nab-Paclitaxel Chemotherapy With or Without Pembrolizumab (MK-3475) in First Line Metastatic Squamous Non-small Cell Lung Cancer Subjects (KEYNOTE-407)	NCT03875092	Chinese adults with first line metastatic squamous NSCLC	Pembrolizumab; paclitaxel; nab-paclitaxel; carboplatin	Chemotherapy	The primary endpoints were PFS and OS. The secondary endpoints were ORR, DOR and AE
A Phase 3 Study of Pembrolizumab in Combination With Carboplatin/Taxane (Paclitaxel or Nab-paclitaxel) Followed by Pembrolizumab With or Without Maintenance Olaparib in the First-line Treatment of Metastatic Squamous Non-small Cell Lung Cancer (NSCLC)	NCT03976362	Have not received prior systemic treatment for their advanced/metastatic NSCLC	Pembrolizumab; carboplatin; paclitaxel; nab-paclitaxel; olaparib	Pembrolizumab + carboplatin + taxane + olaparib placebo	The primary endpoints were PFS and OS. The secondary endpoints were AE, EORTC QLQ-C30/LC13 score and TTD in EORTC QLQ-C30/LC13
PD-1 Inhibitors and Chemotherapy With Concurrent Irradiation at Varied Tumour Sites in Advanced Non-small Cell Lung Cancer	NCT03774732	Patients with advanced (stage IIIB/IV) NSCLC	Radiotherapy; pembrolizumab; chemotherapy	Pembrolizumab + chemotherapy	The primary endpoint was OS. The secondary endpoints were Tumour response, PFS, Acute/Late toxicities and Quality of life of the patients using EORTC-QLQ-C30
A Phase 3 Study of Pembrolizumab (MK-3475) in Combination With Concurrent Chemoradiation Therapy Followed by Pembrolizumab With or Without Olaparib *vs.* Concurrent Chemoradiation Therapy Followed by Durvalumab in Participants With Unresectable, Locally Advanced, Stage III Non-Small Cell Lung Cancer (NSCLC)	NCT04380636	Participants with unresectable, locally advanced NSCLC	Pembrolizumab; olaparib; etoposide; carboplatin; cisplatin; paclitaxel; pemetrexed; thoracic radiotherapy; durvalumab	Chemoradiation→durvalumab	The primary endpoints were PFS and OS. The secondary endpoints were AE, DOR, ORR and EORTC-QLQ-C30 score
A Phase 3 Study of Pembrolizumab in Combination With Pemetrexed/Platinum (Carboplatin or Cisplatin) Followed by Pembrolizumab and Maintenance Olaparib *vs.* Maintenance Pemetrexed in the First-Line Treatment of Participants With Metastatic Nonsquamous Non-Small-Cell Lung Cancer	NCT03976323	Advanced NSCLC with no EGFR mutation, ALK translocation or ROS1-directed therapy	Pembrolizumab; pemetrexed; carboplatin; cisplatin; olaparib	Pembrolizumab + pemetrexed + platinum therapy + pemetrexed	The primary endpoints were PFS and OS. The secondary endpoints were AE, EORTC-QLQ-C30 score and TTD in EORTC QLQ-LC13 Cough (Item 31) Scale Score
A Randomized Trial of Consolidative Immunotherapy With *vs.* Without Thoracic Radiotherapy and / or Stereotactic Body Radiation Therapy (SBRT) After First-Line Systemic Therapy for Metastatic NSCLC	NCT03867175	Stage IV NSCLC with no EGFR mutation, ROS1 or ALK gene rearrangements	Stereotactic body radiation therapy; pembrolizumab	Body radiation therapy	The primary endpoint was PFS. The secondary endpoints were Time of Progression, AE, Rate of Failure and Number of Participants with New Sites of Disease
A Randomized, Phase 3, Open-Label Study of Combinations of REGN2810 (Anti-PD-1 Antibody), Platinum-based Doublet Chemotherapy, and Ipilimumab (Anti-CTLA-4 Antibody) Versus Pembrolizumab Monotherapy in First-Line Treatment of Patients With Advanced or Metastatic Non-Small Cell Lung Cancer With Tumors Expressing PD-L1 ≥50%	NCT03515629	Patients with advanced squamous or non-squamous NSCLC whose tumors express PD-L1 in ≥50% of tumor cells	REGN2810/ipi; REGN2810/chemo/ipi; Pembrolizumab	Pembrolizumab	The primary endpoint was PFS. The secondary endpoints were OS, ORR, TEAEs, SAEs, DLTs and Quality of life
QUILT 2.023: A Phase 3, Open-Label, 3-Cohort Randomized Study of N-803, in Combination With Current Standard of Care *vs.* Standard of Care as First-Line Treatment for Patients With Advanced or Metastatic NSCLC.	NCT03520686	Stage III/IV advanced or metastatic NSCLC	N-803; pembrolizumab; carboplatin; nab-paclitaxel	Control A: pembrolizumab; Control B: carboplatin + nab-paclitaxel or paclitaxel + pembrolizumab; control c: cisplatin or carboplatin + pembrolizumab + pemetrexed	The primary endpoint was PFS. The secondary endpoints were OS, ORR, PFS, DCR and Quality of life
A Randomized, Open-Label, Phase 3 Study of Pralsetinib Versus Standard of Care for First Line Treatment of RET Fusion-positive, Metastatic Non-Small Cell Lung Cancer	NCT04222972	Patients with RET fusion-positive metastatic NSCLC who have not previously received systemic anticancer therapy for metastatic disease	Pralsetinib; carboplatin; cisplatin; pemetrexed; pembrolizumab; gemcitabine	Platinum doublet with or without pembrolizumab	The primary endpoint was PFS. The secondary endpoints were OS, ORR, AE, DCR and CBR
A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study Comparing Niraparib Plus Pembrolizumab Versus Placebo Plus Pembrolizumab as Maintenance Therapy in Participants Whose Disease Has Remained Stable or Responded to First-Line Platinum Based Chemotherapy With Pembrolizumab for Stage IIIB or IV Non-Small Cell Lung Cancer	NCT04475939	Participants with Stage IIIB or IV NSCLC who have achieved Stable disease (SD), Partial response (PR), or complete response (CR) following completion of platinum-based first-line induction chemotherapy with pembrolizumab	Niraparib; pembrolizumab	Placebo + pembrolizumab	The primary endpoints were PFS and OS. The secondary endpoints were AE, TTD in Lung Symptoms and TPP
A Randomized Non-inferiority Trial Evaluating the Length of Treatment With PD-1/PD-L1 Inhibitors in Patients With Advanced Solid Tumors	NCT04157985	Patients who have disease stability to stop treatment at 1 year or continue treatment until disease progression	Pembrolizumab; nivolumab; atezolizumab; ipilimumab	Continue Treatment with PD-1/PD-L1 inhibitor	The primary endpoint was Time to next treatment. The secondary endpoints were OS, irAEs and BOR
An Open-label, Randomized Phase III Study of Early Switch Maintenance *vs.* DElayed Second-line Nivolumab in Advanced Stage Squamous Non Small-cell Lung Cancer (NSCLC) Patients After Standard First-line Platinum-based Chemotherapy - EDEN Trial	NCT03542461	Patients with advanced stage squamous NSCLC without immunotherapy	Nivolumab	Best supportive care	The primary endpoint was OS. The secondary endpoints were PFS, TTF, OSind and PFSind
A Phase 3, Randomized, Open Label Study to Compare Nivolumab Plus Concurrent Chemoradiotherapy (CCRT) Followed by Nivolumab Plus Ipilimumab or Nivolumab Plus CCRT Followed by Nivolumab *vs.* CCRT Followed by Durvalumab in Previously Untreated, Locally Advanced Non-small Cell Lung Cancer (LA NSCLC)	NCT04026412	Participants with untreated locally advanced NSCLC	Nivolumab; ipilimumab; durvalumab	Nivolumab/durvalumab + CCRT	The primary endpoints were PFS and OS. The secondary endpoints were AE, ORR and TTR
A Phase IIIb/IV Safety Trial of Nivolumab (BMS-936558) in Subjects With Advanced or Metastatic Non-Small Cell Lung Cancer Who Have Progressed During or After Receiving At Least One Prior Systemic Regimen	NCT02066636	Advanced or metastatic NSCLC (subjects with non-squamous histology must be tested for EGFR mutations and ALK rearrangement)	Nivolumab		The primary endpoint was AEs. The secondary endpoint were AEs and Median time to onset and median time to resolution
An Open-Label, Randomized Phase 3 Trial of Nivolumab, or Nivolumab Plus Ipilimumab, or Nivolumab Plus Platinum Doublet Chemotherapy Versus Platinum Doublet Chemotherapy in Subjects With Chemotherapy-Naïve Stage IV or Recurrent Non-Small Cell Lung Cancer (NSCLC)	NCT02477826	Stage IV or recurrent NSCLC, with no prior systemic anticancer therapy	Nivolumab; ipilimumab; carboplatin; cisplatin; gemcitabine; pemetrexed; paclitaxel	Platinum doublet chemotherapy	The primary endpoints were PFS and OS. The secondary endpoints were ORR and LCSS
Open-Label, Randomized Trial of Nivolumab (BMS-936558) Plus Pemetrexed/Platinum or Nivolumab Plus Ipilimumab (BMS-734016) *vs.* Pemetrexed Plus Platinum in Stage IV or Recurrent Non-Small Cell Lung Cancer (NSCLC) Subjects With Epidermal Growth Factor Receptor (EGFR) Mutation Who Failed 1L or 2L EGFR Tyrosine Kinase Inhibitor Therapy	NCT02864251	Patients with EGFR mutation, NSCLC who failed first line (1L) or second-line (2L) EGFR TKI therapy	Nivolumab; ipilimumab; pemetrexed; cisplatin; carboplatin	Platinum doublet chemotherapy	The primary endpoint was PFS. The secondary endpoints were PFS, ORR, OS and DOR
Randomized, OpenLabel, Phase 3 Trial of Nivolumab Plus Ipilimumab or Nivolumab Plus Platinum Doublet Chemotherapy Versus Platinum Doublet Chemotherapy in Early Stage NSCLC	NCT02998528	Early stage IB-IIIA, operable NSCLC	Nivolumab; cisplatin; vinorelbine; gemcitabine; docetaxel; pemetrexed; carboplatin; paclitaxel; ipilimumab	Platinum doublet chemotherapy	The primary endpoints were EFS and pCR. The secondary endpoints were OS, MPR and TTDM
An Open-Label Randomized Phase III Trial of BMS-936558 (Nivolumab) Versus Docetaxel in Previously Treated Advanced or Metastatic Squamous Cell Non-small Cell Lung Cancer (NSCLC)	NCT01642004	Subjects with squamous cell NSCLC, after failure of prior platinum-based chemotherapy	Nivolumab; docetaxel	Docetaxel	The primary endpoint was OS. The secondary endpoints were PFS, ORR, OS and TTR
Randomized Phase III Study Testing Nivolumab and Ipilimumab Versus a Carboplatin Based Doublet in First Line Treatment of PS 2 or Elderly (More Than 70 Years Old) Patients With Advanced Non-small Cell Lung Cancer	NCT03351361	Patients already have metastatic disease and a systemic, palliative treatment is the primary therapeutic option	Nivolumab; ipilimumab; chemotherapy	Chemotherapy	The primary endpoint was OS. The secondary endpoints were PFS, ORR, Quality of life score and PD-L1
An Open Label, Safety Study of Participants With Non-Small Cell Lung Cancer Receiving Second-Line Nivolumab Monotherapy in Asia	NCT03195491	Patients in Asia with NSCLC who are treated with Nivolumab monotherapy as a second line or third line treatment	Nivolumab		The primary endpoint was AE. The secondary endpoints were AE and Laboratory test abnormalities
A Randomized Phase 3 Study of Sitravatinib in Combination With Nivolumab Versus Docetaxel in Patients With Advanced Non-Squamous Non-Small Cell Lung Cancer With Disease Progression On or After Platinum-Based Chemotherapy and Checkpoint Inhibitor Therapy SAPPHIRE	NCT03906071	Patients with advanced non-squamous NSCLC who have previously experienced disease progression on or after platinum-based chemotherapy and checkpoint inhibitor therapy	Nivolumab; sitravatinib; docetaxel	Docetaxel	The primary endpoint was OS. The secondary endpoints were AEs, PFS and ORR
A Randomized Phase 3 Trial Comparing Continuation Nivolumab-Ipilimumab Doublet Immunotherapy Until Progression Versus Observation in Treatment-naive Patients With PDL1-positive Stage IV Non-Small Cell Lung Cancer (NSCLC) After Nivolumab-Ipilimumab Induction Treatment	NCT03469960	Stage IV NSCLC, with no prior systemic anticancer therapy, PD-L1 tumor content ≥1% and <50%	Ipilimumab; nivolumab	Standard treatment: 6 months of treatment by nivolumab + ipilimumab then nivolumab + ipilimumab then in case of progression platinum-based doublet recommended	The primary endpoint was PFS. The secondary endpoints were OS, PFS and Quality of life
Adjuvant Nivolumab in Resected Lung Cancers (ANVIL) - A Randomized Phase III Study of Nivolumab After Surgical Resection and Adjuvant Chemotherapy in Non-Small Cell Lung Cancers	NCT02595944	Patients with stage IB–IIIA NSCLC	Nivolumab	No intervention	The primary endpoints were DFS and OS. The secondary endpoint was AE
Randomized Phase III Trial of Local Consolidation Therapy (LCT) After Nivolumab and Ipilimumab for Immunotherapy-Naive Patients With Metastatic Non-Small Cell Lung Cancer (LONESTAR) -Strategic Alliance: BMS	NCT03391869	Patients with stage IV NSCLC	Radiation therapy; local consolidation therapy; nivolumab; ipilimumab	Ipilimumab + nivolumab	The primary endpoint was OS. The secondary endpoints were PFS, TANM and Quality of life
A Phase III Clinical Trial of Adjuvant Chemotherapy *vs.* Chemoimmunotherapy for Stage IB-IIIA Completely Resected Non-small Cell Lung Cancer (NSCLC) Patients.	NCT04564157	Stage IB–IIIA, completely resected, NSCLC patients	Carboplatin; paclitaxel; nivolumab	Carboplatin + paclitaxel	The primary endpoint was DFS. The secondary endpoints were OS and AE
A Phase 3, Randomized, Double-blind Study of Neoadjuvant Chemotherapy Plus Nivolumab Versus Neoadjuvant Chemotherapy Plus Placebo, Followed by Surgical Resection and Adjuvant Treatment With Nivolumab or Placebo for Participants With Resectable Stage II-IIIB Non-small Cell Lung Cancer	NCT04025879	Early-stage NSCLC with no prior systemic anti-cancer treatment	Nivolumab; carboplatin; cisplatin; paclitaxel; pemetrexed; docetaxel	Neoadj. Plac. + Pt-based doublet chemo followed by Adj.Plac.	The primary endpoint was EFS. The secondary endpoints were OS, pCR, MPR and AE
A Multicenter, Randomized, Double-Blind Trial in Subjects With Non-Squamous Non-Small Cell Lung Cancer (TASUKI-52)	NCT03117049	Stage IIIB/IV or recurrent non-squamous NSCLC unsuitable for radical radiation	ONO-4538; carboplatin; paclitaxel; bevacizumab	Placebo group	The primary endpoint was PFS. The secondary endpoints were OS, PFS, ORR and AE

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