

Clinical trials of immune checkpoint inhibition for lung cancer (metastatic) in first line

TrialResults-center www.trialresultscenter.org

1 anti-PD-1

Trial	Treatments	Patients	Trials design and methods
nivolumab vs platinum-based CT			
CheckMate 026 , 2016 [NCT02041533] n=271/270 follow-up:	Nivolumab solution for Injection 3 mg/kg Intravenous every 2 weeks until disease progression versus platinum-based chemotherapy (administered once every 3 weeks for up to six cycles).	patients with previously untreated advanced non-small cell lung cancer (NSCLC) whose tumors expressed PD-L1 at >5% (>1% ???). Patients with EGFR activating mutations and ALK translocations, which are sensitive to targeted therapy, were excluded.	Parallel groups open design
CheckMate 227 (nivolumab alone) , 2018 ongoing [NCT02477826] n=NA follow-up:	-	Subjects With Chemotherapy-Nave Stage IV or Recurrent Non-Small Cell Lung Cancer	No masking
pembrolizumab vs platinum-based CT			
Keynote 024 , 2015 [NCT02142738] n=154/151 follow-up: 11.2 months (median)	Pembrolizumab (200 mg, administered as intravenous (IV) infusion on Day 1 of each 21-day cycle for up to 35 cycles or until documented PD versus standard of care (SOC) platinum-based chemotherapies	previously untreated advanced NSCLC with PD-L1 expression on at least 50% of tumor cells and no sensitizing mutation of the epidermal growth factor receptor gene or translocation of the anaplastic lymphoma kinase gene	Parallel groups open label
Keynote 042 (>=1%) , 2018 [NCT02220894] n=637/637 follow-up: 12.8-mo median	pembrolizumab 200 mg every 3 wk for 35 cycles or until disease progression, intolerable toxicity versus investigator's choice of carboplatin plus paclitaxel or carboplatin plus pemetrexed for a maximum of 6 cycles	Treatment Nave Subjects With PD-L1 Positive Advanced or Metastatic Non-Small Cell Lung Cancer	Parallel groups open label 28 countries in Asia, Canada, Europe, and South America
Keynote 042 (>=20%) , 2018 [NCT02220894] n=413/405 follow-up: 12.8-mo median	pembrolizumab versus SOC Treatment (Platinum-based Chemotherapy)	Treatment Nave Subjects With PD-L1 Positive Advanced or Metastatic Non-Small Cell Lung Cancer	Parallel groups open label china

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Trial	Treatments	Patients	Trials design and methods
Keynote 042 ($\geq 50\%$), 2018 [NCT02220894] n=299/300 follow-up: 12.8-mo median	pembrolizumab versus SOC Treatment (Platinum-based Chemotherapy)	Treatment Nave Subjects With PD-L1 Positive Advanced or Metastatic Non-Small Cell Lung Cancer	open label china

References

CheckMate 026, 2016:

Carbone DP, Reck M, Paz-Ares L, Creelan B, Horn L, Steins M, Felip E, van den Heuvel MM, Ciuleanu TE, Badin F, Ready N, Hiltermann TJN, Nair S, Juergens R, Peters S, Minenza E, Wrangle JM, Rodriguez-Abreu D, Borghaei H, Blumenschein GR Jr, Villaruz LC, Ha First-Line Nivolumab in Stage IV or Recurrent Non-Small-Cell Lung Cancer. N Engl J Med 2017;376:2415-2426 [28636851]

CheckMate 227 (nivolumab alone), 2018:

Hellmann MD Nivolumab plus Ipilimumab in Lung Cancer with a High Tumor Mutational Burden. N Engl J Med 2018;378:2093-2104 [29658845] 10.1056/NEJMoa1801946

Keynote 024, 2015:

Reck M, Rodriguez-Abreu D, Robinson AG, Hui R, Csozsi T, Flp A, Gottfried M, Peled N, Tafreshi A, Cuffe S, O'Brien M, Rao S, Hotta K, Leiby MA, Lubiniecki GM, Shentu Y, Rangwala R, Brahmer JR Pembrolizumab versus Chemotherapy for PD-L1-Positive Non-Small-Cell Lung Cancer. N Engl J Med 2016 Oct 8;: [27718847] 10.1056/NEJMoa1606774

Keynote 042 ($\geq 1\%$), 2018:

Keynote 042 ($\geq 20\%$), 2018:

Keynote 042 ($\geq 50\%$), 2018:

2

2 combination

Trial	Treatments	Patients	Trials design and methods
durvalumab + tremelimumab vs platinum-based CT			
NEPTUNE <i>ongoing</i> [NCT02542293] n=NA follow-up:	MEDI4736 + tremelimumab versus platinum-based SoC chemotherapy	the first-line treatment of patients with epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) wild-type advanced or metastatic NSCLC	
nivolumab + ipilimumab vs platinum-based CT			
CheckMate 227 (High Tumor Mutational Burden), 2018 [NCT02477826] n=139/160 follow-up:	nivolumab plus ipilimumab versus chemotherapy	patients with stage IV or recurrent NSCLC that was not previously treated with chemotherapy and high tumor mutational burden (≥ 10 mutations per megabase), irrespective of PD-L1 expression level	Parallel groups No masking
durvalumab + tremelimumab vs Standard of Care			

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Trial	Treatments	Patients	Trials design and methods
MYSTIC (combination) ongoing [NCT02453282] n=NA follow-up:	MEDI4736 (Durvalumab)+Tremelimumab versus Standard of Care chemotherapy treatment	patients with advanced or metastatic NSCLC in the first-line treatment of patients with epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) wild-type locally advanced or metastatic NSCLC	open label Germany

References

NEPTUNE, :

CheckMate 227 (High Tumor Mutational Burden), 2018:

Hellmann MD, Ciuleanu TE, Pluzanski A, Lee JS, Otterson GA, Audigier-Valette C, Minenza E, Linardou H, Burgers S, Salman P, Borghaei H, Ramalingam SS, Brahmer J, Reck M, O'Byrne KJ, Geese WJ, Green G, Chang H, Szustakowski J, Bhagavatheeswaran P, Healey D Nivolumab plus Ipilimumab in Lung Cancer with a High Tumor Mutational Burden. *N Engl J Med* 2018;: [29658845]

MYSTIC (combination), 0:

3 IO + CT

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Trial	Treatments	Patients	Trials design and methods
atezolizumab + bevacizumab vs bevacizumab (on top platinum-based CT)			
IMpower150 (Teff) , 2018 [NCT02366143] n=155/129 follow-up:	atezo + bev + C + P versus bev + C + P	chemotherapy-naive patients with Stage IV non-squamous non-small cell lung cancer and expression of a tumour T-effector gene signature (Teff) and EGFR et ALK negative (wild type)	Parallel groups open label
IMpower150 (WT) , 2018 [NCT02366143] n=356/336 follow-up:	atezo + bev + C + P; versus bev + C + P	wild type chemotherapy-naive patients with Stage IV non-squamous non-small cell lung cancer (EGFR et ALK negative)	Parallel groups open label
atezolizumab + platinum-based CT vs platinum-based CT			
IMpower 132 ongoing [NCT02657434] n=NA follow-up:	Atezolizumab + Carboplatin or Cisplatin + Pemetrexed versus Carboplatin or Cisplatin + Pemetrexed)	Participants Who Are Chemotherapy-Naive and Have Stage IV Non-Squamous Non-Small Cell Lung Cancer (NSCLC) (IMpower 132)	Open Label
IMpower 133 ongoing [NCT02763579] n=NA follow-up:	Atezolizumab + Carboplatin + Etoposide versus Placebo + Carboplatin + Etoposide	Participants With Untreated Extensive-Stage Small Cell Lung Cancer	Participant, Investigator
nivolumab + CT vs platinum-based CT			

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Trial	Treatments	Patients	Trials design and methods
CheckMate 227 (nivolumab + CT) , 2018 [NCT02477826] n=177/186 follow-up:	Nivolumab + chemotherapy versus chemotherapy	Subjects With Chemotherapy-Nave Stage IV or Recurrent Non-Small Cell Lung Cancer <1% tumor PD-L1 expression	No masking
pembrolizumab + platinum-based CT vs platinum-based CT			
Keynote 189 , 2018 [NCT02578680] n=410/206 follow-up: 10.5 mo median	pemetrexed and a platinum-based drug plus 200 mg of pembrolizumab, followed by pembrolizumab for up to a total of 35 cycles plus pemetrexed maintenance therapy versus pemetrexed and a platinum-based drug plus placebo every 3 weeks for 4 cycles, followed by placebo	participants with advanced or metastatic nonsquamous non-small cell lung cancer (NSCLC) who have not previously received systemic therapy for advanced disease and without sensitizing EGFR or ALK mutations	Parallel groups double-blind
KEYNOTE-021 phase 2 , 2016 [NCT02039674] n=60/63 follow-up:	24 months treatment with pembrolizumab (200mg every three weeks)+ CT versus four cycles of carboplatin and pemetrexed (500 mg/m ² every three weeks)	patients with stage IIIB/IV, chemotherapy-naive, nonsquamous non-small-cell lung cancer	Parallel groups open design

References

IMpower150 (Teff), 2018:

[10.1093/annonc/mdx760.002](https://doi.org/10.1093/annonc/mdx760.002)

Socinski MA, Jotte RM, Cappuzzo F, Orlandi F, Stroyakovskiy D, Nogami N, Rodriguez-Abreu D, Moro-Sibilot D, Thomas CA, Barlesi F, Finley G, Kelsch C, Lee A, Coleman S, Deng Y, Shen Y, Kowanetz M, Lopez-Chavez A, Sandler A, Reck M Atezolizumab for First-Line Treatment of Metastatic Nonsquamous NSCLC. N Engl J Med 2018;378:2288-2301 [29863955]

IMpower150 (WT), 2018:

Socinski MA Atezolizumab for First-Line Treatment of Metastatic Nonsquamous NSCLC. N Engl J Med 2018;: [29863955] [10.1056/NEJMoa1716948](https://doi.org/10.1056/NEJMoa1716948)

IMpower 132, :

IMpower 133, :

CheckMate 227 (nivolumab + CT), 2018:

Keynote 189, 2018:

Gandhi L, Rodriguez-Abreu D, Gadgeel S, Esteban E, Felip E, De Angelis F, Domine M, Clingan P, Hochmair MJ, Powell SF, Cheng SY, Bischoff HG, Peled N, Grossi F, Jennens RR, Reck M, Hui R, Garon EB, Boyer M, Rubio-Viqueira B, Novello S, Kurata T, Gray JE, Pembrolizumab plus Chemotherapy in Metastatic Non-Small-Cell Lung Cancer. N Engl J Med 2018;: [29658856]

KEYNOTE-021 phase 2, 2016:

Langer CJ, Gadgeel SM, Borghaei H, Papadimitrakopoulou VA, Patnaik A, Powell SF, Gentzler RD, Martins RG, Stevenson JP, Jalal SI, Panwalkar A, Yang JC, Gubens M, Sequist LV, Awad MM, Fiore J, Ge Y, Raftopoulos H, Gandhi L Carboplatin and pemetrexed with or without pembrolizumab for advanced, non-squamous non-small-cell lung cancer: a randomised, phase 2 cohort of the open-label KEYNOTE-021 study. Lancet Oncol 2016;17:1497-1508 [27745820]

4 PD-L1 inhibitors

Trial	Treatments	Patients	Trials design and methods
atezolizumab vs platinum-based CT			
GO29432 <i>ongoing</i> [NCT02409355] n=NA follow-up:	-	patients with chemotherapy-naive, Stage IV squamous non-small cell lung cancer	open label
IMpower 110 <i>ongoing</i> [NCT02409342] n=NA follow-up:	Atezolizumab (MPDL3280A) versus dual regimen of carboplatin or cisplatin plus pemetrexed	chemotherapy-naive patients with Stage IV NSCLC	open label
avelumab vs platinum-based CT			
JAVELIN Lung 100 <i>ongoing</i> [NCT02576574] n=NA follow-up:	avelumab versus platinum-based doublet	a First-line Treatment of Recurrent or Stage IV non-small cell lung cancer with Programmed death ligand 1+ tumors	
durvalumab vs Standard of Care			
MYSTIC (monotherapy) <i>ongoing</i> [NCT02453282] n=NA follow-up:	durvalumab versus Standard of Care chemotherapy treatment	patients with advanced or metastatic NSCLC in the first-line treatment of patients with epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) wild-type locally advanced or metastatic NSCLC	open label Germany

References

GO29432, 0:

IMpower 110, 0:

JAVELIN Lung 100, :

MYSTIC (monotherapy), 0:

5 About TrialResults-center.org

TrialResults-center is an innovative knowledge database that collects the results of RCTs and provides dynamic interactive systematic reviews and meta-analysis in the field of all major heart and vessels diseases.

The TrialResults-center database provides a unique view of the treatment efficacy based on all data provided directly from clinical trial results, offering a valuable alternative to personal bibliographic search, published meta-analysis, etc. Furthermore, it would allow comparing easily the various concurrent therapeutic for the same clinical condition.

Rigorous meta-analysis method is used to populate TrialResults-center: widespread search of published and non published trials, study selection using pre-specified criteria, data extraction using standard form.

TrialResults-center is continually updated on a weekly basis. We continually search all new results (whatever their publication channel) and these news results are immediately added to the database with a maximum of 1 week.

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