

Clinical trials of immune checkpoint inhibition for melanoma in first line

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1 anti-CTLA-4

Trial	Treatments	Patients	Trials design and methods
ipilimumab + dacarbazine vs dacarbazine			
Robert , 2011 [NCT00324155] n=NA follow-up:	ipilimumab (10 mg per kilogram) plus dacarbazine (850 mg per square meter of body-surface area) versus dacarbazine (850 mg per square meter)	patients with previously untreated metastatic melanoma (stage III (unresectable) or stage IV)	Parallel groups double blind

References

Robert, 2011:

Robert C, Thomas L, Bondarenko I, O'Day S, Weber J, Garbe C, Lebbe C, Baurain JF, Testori A, Grob JJ, Davidson N, Richards J, Maio M, Hauschild A, Miller WH Jr, Gascon P, Lotem M, Harmankaya K, Ibrahim R, Francis S, Chen TT, Humphrey R, Hoos A, Wolchok JD Ipilimumab plus dacarbazine for previously untreated metastatic melanoma. N Engl J Med 2011;364:2517-26 [21639810]

2 anti-PD-1

Trial	Treatments	Patients	Trials design and methods
nivolumab vs dacarbazine			
CheckMate 066 (Robert) , 2015 [NCT01721772] n=210/208 follow-up:	nivolumab at a dose of 3 mg per kilogram of body weight every 2 weeks versus dacarbazine at a dose of 1000 mg per square meter of body-surface area every 3 weeks	previously untreated patients who had unresectable metastatic melanoma without a BRAF mutation (stage III or IV)	Parallel groups double-blind
nivolumab vs ipilimumab			
CheckMate 067 (nivo vs ipi) , 2015 [NCT01844505] n=316/315 follow-up:	3 mg of nivolumab per kilogram of body weight every 2 weeks versus 3 mg of ipilimumab per kilogram every 3 weeks for 4 doses	Previously Untreated Advanced Melanoma	Parallel groups double-blind
nivolumab + ipilimumab vs ipilimumab			

continued...

Trial	Treatments	Patients	Trials design and methods
CheckMate 067 (nivo + ipi vs ipi) , 2015 [NCT01844505] n=314/315 follow-up:	1mg of nivolumab per kilogram every 3 weeks plus 3 mg of ipilimumab per kilogram every 3 weeks for 4 doses, followed by 3 mg of nivolumab per kilogram every 2 weeks for cycle 3 and beyond versus 3 mg of ipilimumab per kilogram every 3 weeks for 4 doses	Previously Untreated Advanced Melanoma	Parallel groups double-blind
pembrolizumab (every 2W) vs ipilimumab			
KEYNOTE-006 (every 2W) , 2015 [NCT01866319] n=NA follow-up:	pembrolizumab (at a dose of 10 mg per kilogram of body weight) every 2 weeks or every 3 weeks versus four doses of ipilimumab (at 3 mg per kilogram) every 3 weeks	patients with advanced melanoma who had received no more than one previous systemic therapy for advanced disease	Parallel groups open-label
pembrolizumab (every 3W) vs ipilimumab			
KEYNOTE-006 (every 3W) , 2015 [NCT01866319] n=277/278 follow-up:	Pembrolizumab Every 3 Weeks versus Ipilimumab (Participants receive ipilimumab, 3 mg/kg IV, once every 3 weeks for a total of Pembrolizumab Every 2 Weeks (Participants receive pembrolizumab, 10 mg intravenously (IV), once every 2 weeks for up to 2 years) 2/ Pembrolizumab Every 3 Weeks (P	patients with unresectable stage III or IV advanced melanoma and who had received no more than one previous systemic therapy for advanced disease	Parallel groups open label
nivolumab + ipilimumab vs nivolumab			
CheckMate 067 (nivo + ipi vs nivo) , 2015 [NCT01844505] n=314/316 follow-up:	Nivolumab + ipilimumab versus nivolumab alone	Previously Untreated Advanced Melanoma	Parallel groups double-blind

References

CheckMate 066 (Robert), 2015:

Robert C, Long GV, Brady B, Dutriaux C, Maio M, Mortier L, Hassel JC, Rutkowski P, McNeil C, Kalinka-Warzocha E, Savage KJ, Hernberg MM, Lebb C, Charles J, Mihalciou C, Chiarion-Sileni V, Mauch C, Cognetti F, Arance A, Schmidt H, Schadendorf D, Gogas H, Nivolumab in previously untreated melanoma without BRAF mutation. *N Engl J Med* 2015 Jan 22;372:320-30 [25399552] [10.1056/NEJMoa1412082](https://doi.org/10.1056/NEJMoa1412082)

CheckMate 067 (nivo vs ipi), 2015:

Larkin J, Chiarion-Sileni V, Gonzalez R, Grob JJ, Cowey CL, Lao CD, Schadendorf D, Dummer R, Smylie M, Rutkowski P, Ferrucci PF, Hill A, Wagstaff J, Carlino MS, Haanen JB, Maio M, Marquez-Rodas I, McArthur GA, Ascierto PA, Long GV, Callahan MK, Postow MA, Combined Nivolumab and Ipilimumab or Monotherapy in Untreated Melanoma. *N Engl J Med* 2015;373:23-34 [26027431]

CheckMate 067 (nivo + ipi vs ipi), 2015:

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KEYNOTE-006 (every 2W), 2015:

Robert C, Schachter J, Long GV, Arance A, Grob JJ, Mortier L, Daud A, Carlino MS, McNeil C, Lotem M, Larkin J, Lorigan P, Neyns B, Blank CU, Hamid O, Mateus C, Shapira-Frommer R, Kosh M, Zhou H, Ibrahim N, Ebbinghaus S, Ribas A Pembrolizumab versus Ipilimumab in Advanced Melanoma. N Engl J Med 2015 Apr 19;: [25891173] [10.1056/NEJMoa1503093](https://doi.org/10.1056/NEJMoa1503093)

Schachter J, Ribas A, Long GV, Arance A, Grob JJ, Mortier L, Daud A, Carlino MS, McNeil C, Lotem M, Larkin J, Lorigan P, Neyns B, Blank C, Petrella TM, Hamid O, Zhou H, Ebbinghaus S, Ibrahim N, Robert C Pembrolizumab versus ipilimumab for advanced melanoma: final overall survival results of a multicentre, randomised, open-label phase 3 study (KEYNOTE-006). Lancet 2017;: [28822576]

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Schachter J, Ribas A, Long GV, Arance A, Grob JJ, Mortier L, Daud A, Carlino MS, McNeil C, Lotem M, Larkin J, Lorigan P, Neyns B, Blank C, Petrella TM, Hamid O, Zhou H, Ebbinghaus S, Ibrahim N, Robert C Pembrolizumab versus ipilimumab for advanced melanoma: final overall survival results of a multicentre, randomised, open-label phase 3 study (KEYNOTE-006). Lancet 2017;: [28822576]

CheckMate 067 (nivo + ipi vs nivo), 2015:

Larkin J, Chiarion-Sileni V, Gonzalez R, Grob JJ, Cowey CL, Lao CD, Schadendorf D, Dummer R, Smylie M, Rutkowski P, Ferrucci PF, Hill A, Wagstaff J, Carlino MS, Haanen JB, Maio M, Marquez-Rodas I, McArthur GA, Ascierto PA, Long GV, Callahan MK, Postow MA, Combined Nivolumab and Ipilimumab or Monotherapy in Untreated Melanoma. N Engl J Med 2015;373:23-34 [26027431]

3 About TrialResults-center.org

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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.

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