Clinical trials of immune checkpoint inhibition for melanoma in all type of patients

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1 anti-PD-1 antibody

Trial	Treatments	Patients	Trials design and methods
nivolumab vs chemotherapy			
CheckMate 037 (Weber) , 2015 [NCT01721746] n=272/133 follow-up:	ntravenous infusion of nivolumab 3 mg/kg every 2 weeks until progression or unacceptable toxic eff ects versus investigators choice of chemotherapy (dacarbazine 1000 mg/m every 3 weeks or paclitaxel 175 mg/m combined with carboplatin area under the curve 6 every 3 weeks)	patients with advanced melanoma who progressed after ipilimumab, or ipilimumab and a BRAF inhibitor if they were BRAFV mutation-positive (second-line or later-line treatment)	Parallel groups open-label
pembrolizumab 10mg/kg vs chemotherapy			
KEYNOTE 002 (10mg/kg Q3W) , 2015 [NCT01704287] n=181/179 follow-up:	intravenous pembrolizumab 10 mg/kg every 3 weeks versus investigator-choice chemotherapy (paclitaxel plus carboplatin, paclitaxel, carboplatin, dacarbazine, or oral temozolomide)	patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAFV600 mutation positive, a BRAF inhibitor	Parallel groups open design
pembrolizumab 2mg/kg vs chemotherapy			
KEYNOTE 002 (2mg/kg Q3W) , 2015 [NCT01704287] n=180/179 follow-up:	Pembrolizumab 2 mg/kg IV Q3W versus investigator-choice chemotherapy (paclitaxel plus carboplatin, paclitaxel, carboplatin, dacarbazine, or oral temozolomide)	patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAFV600 mutation positive, a BRAF inhibitor	Parallel groups open design
nivolumab vs dacarbazine			
CheckMate 066 (Robert) , 2015 [NCT01721772] n=418 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:	nivolumab versus Ipilimumab alone	Previously Untreated Advanced Melanoma	Parallel groups double-blind

continued...

Trial	Treatments	Patients	Trials design and methods
CheckMate 238 , 2017 [NCT02388906] n=453/453 follow-up:	nivolumab at a dose of 3 mg per kilogram of body weight every 2 weeks versus ipilimumab at a dose of 10 mg per kilogram every 3 weeks for four doses and then every 12 weeks	patients with Complete Resection of Stage IIIb/c or Stage IV Melanoma	Parallel groups double-blind US
nivolumab + ipilimumab vs ipilimumab			
CheckMate 067 (nivo + ipi vs ipi) , 2015 [NCT01844505] n=314/315 follow-up:	Nivolumab + ipilumab versus Ipilimumab alone	Previously Untreated Advanced Melanoma	Parallel groups double-blind
Postow , 2015 [NCT01927419] n=NA follow-up:	-	patients with metastatic melanoma who had not previously received treatment,	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 oPembrolizumab 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 + ipilumab versus nivolumab alone	Previously Untreated Advanced Melanoma	Parallel groups double-blind
pembrolizumab 2mg/kg vs pembrolizumab 10mg/kg			
KEYNOTE-001 , 2014 [NCT01295827] n=89/84 follow-up:	intravenous pembrolizumab at 2 mg/kg every 3 weeks versus intravenous pembrolizumab at 10 mg/kg every 3 weeks	patients (aged 18 years) with advanced melanoma whose disease had progressed after at least two ipilimumab doses	Parallel groups open-label
pembrolizumab vs placebo			

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Trial	Treatments	Patients	Trials design and methods
KEYNOTE-054 *ongoing* [NCT02362594] n=NA follow-up:	Pembrolizumab (Participants receive pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle for up to 1 year) versus placebo	patients with complete Resection of High-Risk Stage III Melanoma	Parallel groups double-blind

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CheckMate 037 (Weber), 2015:

Weber JS, Minor D, DAngelo SP, et al. A phase 3 randomized, open-label studyof nivolumab (anti-PD-1; BMS-936558;ONO-4538) versus investigators choicechemotherapy (ICC) in patients with advancedmelanoma with prior anti-CTLA-4 Presented at the European Society for Medical Oncology 2014 Congress, Madrid, September 2630, 2014. abstract.

Weber JS, D'Angelo SP, Minor D, Hodi FS, Gutzmer R, Neyns B, Hoeller C, Khushalani NI, Miller WH Jr, Lao CD, Linette GP, Thomas L, Lorigan P, Grossmann KF, Hassel JC, Maio M, Sznol M, Ascierto PA, Mohr P, Chmielowski B, Bryce A, Svane IM, Grob JJ, Krackha Nivolumab versus chemotherapy in patients with advanced melanoma who progressed after anti-CTLA-4 treatment (CheckMate 037): a randomised, controlled, open-label, phase 3 trial. Lancet Oncol 2015 Apr;16:375-84 [25795410] 10.1016/S1470-2045(15)70076-8

KEYNOTE 002 (10mg/kg Q3W), 2015:

Ribas A, Puzanov I, Dummer R, Schadendorf D, Hamid O, Robert C, Hodi FS, Schachter J, Pavlick AC, Lewis KD, Cranmer LD, Blank CU, O'Day SJ, Ascierto PA, Salama AK, Margolin KA, Loquai C, Eigentler TK, Gangadhar TC, Carlino MS, Agarwala SS, Moschos SJ, Sos Pembrolizumab versus investigator-choice chemotherapy for ipilimumab-refractory melanoma (KEYNOTE-002): a randomised, controlled, phase 2 trial. Lancet Oncol 2015;16:908-18 [26115796]

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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, Mihalcioiu 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

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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

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KEYNOTE-054, :

2 antiCTLA-4 antibody

Trial	Treatments	Patients	Trials design and methods
ipilimumab 10mg/kg plus dacarbazine vs dacarbazine			
Robert (Ipilimumab) , 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) orstage IV)	Parallel groups double blind
ipi + gp100 vs gp100			
Hodi (ipi + gp100) , 2010 [NCT00094653] n=403/136 follow-up:	Ipilimumab, at a dose of 3 mg per kilogram of body weight, was administered with gp100 every 3 weeks for up to four treatments versus gp100 alone	patients with previously treated metastatic melanoma patients with unresectable stage III or IV melanoma, whose disease had progressed while they were receiving therapy for metastatic disease	Parallel groups open-label

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Trial	Treatments	Patients	Trials design and methods
ipilimumab 3 mg/kg vs gp100			
Hodi (ipi alone) , 2010 [NCT00094653] n=137/136 follow-up:	ipilimumab 3mg/kg every 3 weeks up to 4 treatments versus gp100 alone	patients with previously treated metastatic melanoma patients with unresectable stage III or IV melanoma, whose disease had progressed while they were receiving therapy for metastatic disease	Parallel groups open-label
ipilimumab vs placebo			
EORTC 18071 , 2015 [NCT00636168] n=475/476 follow-up:	ipilimumab at a dose of 10 mg per kilogram every 3 weeks for four doses, then every 3 months for up to 3 years or until disease recurrence or an unacceptable level of toxic effects occurred versus placebo	high risk patients who had undergone complete resection of stage III melanoma	Parallel groups double-blind

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Hodi (ipi + gp100), 2010:

Hodi FS, O'Day SJ, McDermott DF, Weber RW, Sosman JA, Haanen JB, Gonzalez R, Robert C, Schadendorf D, Hassel JC, Akerley W, van den Eertwegh AJ, Lutzky J, Lorigan P, Vaubel JM, Linette GP, Hogg D, Ottensmeier CH, Lebb C, Peschel C, Quirt I, Clark JI, Wol Improved survival with ipilimumab in patients with metastatic melanoma. N Engl J Med 2010;363:711-23 [20525992]

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Eggermont AM, Chiarion-Sileni V, Grob JJ, Dummer R, Wolchok JD, Schmidt H, Hamid O, Robert C, Ascierto PA, Richards JM, Lebb C, Ferraresi V, Smylie M, Weber JS, Maio M, Bastholt L, Mortier L, Thomas L, Tahir S, Hauschild A, Hassel JC, Hodi FS, Taitt C, d Prolonged Survival in Stage III Melanoma with Ipilimumab Adjuvant Therapy. N Engl J Med 2016;375:1845-1855 [27717298]

3 About TrialResults-center.org

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