

**S3 Table.** Quality assessment of the 22 studies (23 RCTs)<sup>a)</sup> [1-22]

Author, year	Adequate random sequence generation	Allocation concealment	Blinding method	Adequate assessment of each outcome	Free of selective reporting	Modified Jadad score <sup>b)</sup>
Weber 2013 [1]	U	U	Y	Y	Y	5
Kwon 2014 [2]	Y	Y	Y	Y	Y	7
Brahmer 2015 [3]	U	U	N	Y	Y	3
Broghaei 2015 [4]	U	U	N	Y	Y	3
Reck 2016 [5]	Y	Y	Y	Y	Y	7
Eggermont 2016 [6]	U	U	Y	Y	Y	5
Weber 2017 [7]	U	Y	Y	Y	Y	6
Ascierto 2017 [8]	Y	Y	Y	Y	Y	7
Larkin 2018 [9]	Y	Y	Y <sup>c)</sup>	Y	Y	7
Govindan 2017 [10]	U	U	Y	Y	Y	5
Horn 2017 [11]	U	U	Y	Y	Y	5
Armand 2018 [12]	Y <sup>c)</sup>	Y <sup>c)</sup>	Y <sup>c)</sup>	Y	Y	7
Kelly 2018 [13]	Y <sup>c)</sup>	Y <sup>c)</sup>	Y <sup>c)</sup>	Y	Y	7
Larkin 2019 [14]	U	U	Y	Y	Y	5
Geoerger 2020 [15]	Y <sup>c)</sup>	Y <sup>c)</sup>	Y <sup>c)</sup>	Y	Y	7
Fradet 2019 [16]	U	N	Y <sup>c)</sup>	Y	Y	5
Tomita 2020 [17]	U	N	Y <sup>c)</sup>	Y	Y	5

Lebbé 2019 [18]	U	U	Y	Y	Y	5
Sharma 2020 [19]	U	N	Y <sup>c)</sup>	Y	Y	5
Morse 2019 [20]	Y <sup>c)</sup>	Y <sup>c)</sup>	Y <sup>c)</sup>	Y	Y	7
Carneiro 2019 [21]	Y <sup>c)</sup>	Y <sup>c)</sup>	Y <sup>c)</sup>	Y	Y	7
Horinouchi 2019 [22]	Y <sup>c)</sup>	Y <sup>c)</sup>	Y <sup>c)</sup>	Y	Y	7

N, no; RCT, randomized controlled trial; U, unclear; Y, yes. <sup>a)</sup>Quality assessment was based on the original study, possible updated study and supplementary materials but not the study protocol, <sup>b)</sup>Modified Jadad scale rates the adequacy of generation of random sequence, allocation concealment, blinding method, and drop out/loss of follow-up; high-quality studies had a score  $\geq 4$ ; low-quality,  $\leq 3$ , <sup>c)</sup>Application of the blinding method is impracticable in these studies due to unavoidable reasons, such as special study designs (single-arm trial), treatment plans requiring the involvement of clinicians (investigator's choice of chemotherapy), evidently different drug administration (oral medication and intravenous injection), and so on. For reasons that were clearly stated in their contents, these studies were still rated as "Y."

## References

1. Weber JS, Dummer R, de Pril V, Lebbe C, Hodi FS, Investigators MDX. Patterns of onset and resolution of immune-related adverse events of special interest with ipilimumab: detailed safety analysis from a phase 3 trial in patients with advanced melanoma. *Cancer*. 2013;119:1675-82.
2. Kwon ED, Drake CG, Scher HI, Fizazi K, Bossi A, van den Eertwegh AJ, et al. Ipilimumab versus placebo after radiotherapy in patients with metastatic castration-resistant prostate cancer that had progressed after docetaxel chemotherapy (CA184-043): a multicentre, randomised, double-blind, phase 3 trial. *Lancet Oncol*. 2014;15:700-12.
3. Brahmer J, Reckamp KL, Baas P, Crino L, Eberhardt WE, Poddubskaya E, et al. Nivolumab versus docetaxel in advanced squamous-cell non-small-cell lung cancer. *N Engl J Med*. 2015;373:123-35.

4. Borghaei H, Paz-Ares L, Horn L, Spigel DR, Steins M, Ready NE, et al. Nivolumab versus docetaxel in advanced nonsquamous non-small-cell lung cancer. *N Engl J Med*. 2015;373:1627-39.
5. Reck M, Luft A, Szczesna A, Havel L, Kim SW, Akerley W, et al. Phase III randomized trial of ipilimumab plus etoposide and platinum versus placebo plus etoposide and platinum in extensive-stage small-cell lung cancer. *J Clin Oncol*. 2016;34:3740-8.
6. Eggermont AM, Chiarion-Sileni V, Grob JJ, Dummer R, Wolchok JD, Schmidt H, et al. Prolonged survival in stage III melanoma with ipilimumab adjuvant therapy. *N Engl J Med*. 2016;375:1845-55.
7. Weber J, Mandala M, Del Vecchio M, Gogas HJ, Arance AM, Cowey CL, et al. Adjuvant nivolumab versus ipilimumab in resected stage III or IV melanoma. *N Engl J Med*. 2017;377:1824-35.
8. Ascierto PA, Del Vecchio M, Robert C, Mackiewicz A, Chiarion-Sileni V, Arance A, et al. Ipilimumab 10 mg/kg versus ipilimumab 3 mg/kg in patients with unresectable or metastatic melanoma: a randomised, double-blind, multicentre, phase 3 trial. *Lancet Oncol*. 2017;18:611-22.
9. Larkin J, Minor D, D'Angelo S, Neyns B, Smylie M, Miller WH Jr, et al. Overall survival in patients with advanced melanoma who received nivolumab versus investigator's choice chemotherapy in CheckMate 037: a randomized, controlled, open-label phase III trial. *J Clin Oncol*. 2018;36:383-90.
10. Govindan R, Szczesna A, Ahn MJ, Schneider CP, Gonzalez Mella PF, Barlesi F, et al. Phase III trial of ipilimumab combined with paclitaxel and carboplatin in advanced squamous non-small-cell lung cancer. *J Clin Oncol*. 2017;35:3449-57.
11. Horn L, Spigel DR, Vokes EE, Holgado E, Ready N, Steins M, et al. Nivolumab versus docetaxel in previously treated patients with advanced non-small-cell lung cancer: two-year outcomes from two randomized, open-label, phase III trials (CheckMate 017 and CheckMate 057). *J Clin Oncol*. 2017;35:3924-33.
12. Armand P, Engert A, Younes A, Fanale M, Santoro A, Zinzani PL, et al. Nivolumab for relapsed/refractory classic Hodgkin lymphoma after failure of autologous hematopoietic cell transplantation: extended follow-up of the multicohort single-arm phase II CheckMate 205 trial. *J Clin Oncol*. 2018;36:1428-39.
13. Kelly K, Infante JR, Taylor MH, Patel MR, Wong DJ, Iannotti N, et al. Safety profile of avelumab in patients with advanced solid tumors: A

pooled analysis of data from the phase 1 JAVELIN solid tumor and phase 2 JAVELIN Merkel 200 clinical trials. *Cancer*. 2018;124:2010-7.

14. Larkin J, Chiarion-Sileni V, Gonzalez R, Grob JJ, Rutkowski P, Lao CD, et al. Five-year survival with combined nivolumab and ipilimumab in advanced melanoma. *N Engl J Med*. 2019;381:1535-46.

15. Georger B, Kang HJ, Yalon-Oren M, Marshall LV, Vezina C, Pappo A, et al. Pembrolizumab in paediatric patients with advanced melanoma or a PD-L1-positive, advanced, relapsed, or refractory solid tumour or lymphoma (KEYNOTE-051): interim analysis of an open-label, single-arm, phase 1-2 trial. *Lancet Oncol*. 2020;21:121-33.

16. Fradet Y, Bellmunt J, Vaughn DJ, Lee JL, Fong L, Vogelzang NJ, et al. Randomized phase III KEYNOTE-045 trial of pembrolizumab versus paclitaxel, docetaxel, or vinflunine in recurrent advanced urothelial cancer: results of >2 years of follow-up. *Ann Oncol*. 2019;30:970-6.

17. Tomita Y, Kondo T, Kimura G, Inoue T, Wakumoto Y, Yao M, et al. Nivolumab plus ipilimumab versus sunitinib in previously untreated advanced renal-cell carcinoma: analysis of Japanese patients in CheckMate 214 with extended follow-up. *Jpn J Clin Oncol*. 2020;50:12-9.

18. Lebbe C, Meyer N, Mortier L, Marquez-Rodas I, Robert C, Rutkowski P, et al. Evaluation of two dosing regimens for nivolumab in combination with ipilimumab in patients with advanced melanoma: results from the phase IIIb/IV CheckMate 511 trial. *J Clin Oncol*. 2019;37:867-75.

19. Sharma P, Sohn J, Shin SJ, Oh DY, Keam B, Lee HJ, et al. Efficacy and tolerability of tremelimumab in locally advanced or metastatic urothelial carcinoma patients who have failed first-line platinum-based chemotherapy. *Clin Cancer Res*. 2020;26:61-70.

20. Morse MA, Overman MJ, Hartman L, Khoukaz T, Brucher E, Lenz HJ, et al. Safety of nivolumab plus low-dose ipilimumab in previously treated microsatellite instability-high/mismatch repair-deficient metastatic colorectal cancer. *Oncologist*. 2019;24:1453-61.

21. Carneiro BA, Konda B, Costa RB, Costa RLB, Sagar V, Gursel DB, et al. Nivolumab in metastatic adrenocortical carcinoma: results of a phase 2 trial. *J Clin Endocrinol Metab*. 2019;104:6193-200.

22. Horinouchi H, Nishio M, Hida T, Nakagawa K, Sakai H, Nogami N, et al. Three-year follow-up results from phase II studies of nivolumab in Japanese patients with previously treated advanced non-small cell lung cancer: pooled analysis of ONO-4538-05 and ONO-4538-06 studies. *Cancer Med*. 2019;8:5183-93.