Editorial Commentary

Adjuvant therapy for mucosal melanoma in the era of immune checkpoint inhibitors

Yasuhiro Nakamura, Tatsuhiko Mori

Department of Skin Oncology/Dermatology, Saitama Medical University International Medical Center, Saitama, Japan

Correspondence to: Yasuhiro Nakamura, MD, PhD. Department of Skin Oncology/Dermatology, Saitama Medical University International Medical Center, 1397-1 Yamane, Hidaka, Saitama 350-1298 Japan. Email: ynakamur@saitama-med.ac.jp.

Comment on: Lian B, Si L, Chi ZH, *et al.* Toripalimab (anti-PD-1) versus High-Dose Interferon-α2b as Adjuvant Therapy in Resected Mucosal Melanoma: A Phase II Randomized Trial. Ann Oncol 2022;33:1061-70.

Keywords: Melanoma; immunotherapy; programmed cell death 1 receptor

Submitted Jun 30, 2023. Accepted for publication Sep 08, 2023. Published online Oct 09, 2023.
doi: 10.21037/cco-23-61
View this article at: https://dx.doi.org/10.21037/cco-23-61

Introduction

The management of patients with mucosal melanoma (MM) is challenging in both adjuvant and advanced stage due to its poorer prognosis compared to cutaneous melanoma. The reported 5-year overall survival (OS) rate for MM is approximately 25%, which is much lower than that for cutaneous melanoma (50–80%) (1,2). The poorer prognosis of MM than cutaneous melanoma is derived from multiple factors, such as aggressive nature of MM, delayed medical examination, and difficulties in complete excision due to the tumor invasion or metastasis to other adjacent anatomical structures (3). Even with advances in development of immune checkpoint inhibitors (ICIs), the therapeutic effect of ICIs is not as effective in patients with MM, even if resected in early stages, as that in patients with cutaneous melanoma in advanced stages.

Therefore, effective and safe postoperative adjuvant therapies are urgently required for patients with resected MMs. Before the advent of ICIs, clinical trials demonstrated that high-dose interferon (IFN)-α2b (HDI-α2b) therapy may improve relapse-free survival (RFS) and OS of high-risk resected patients with cutaneous melanoma in Western countries (4). Additionally, a phase II randomized trial demonstrated that adjuvant therapy with HDI improved both RFS and OS in patients with resected MM compared to observation alone arm after resected surgery (median RFS: 9.4 *vs.* 5.4 months; median OS: 40.4 *vs.* 21.2 months, respectively) (5), but did not impact on the adjuvant treatment of MM in Western countries. The therapeutic effect and safety of adjuvant ICIs in patients with MM have not been examined.

Is toripalimab anti-programmed cell death protein-1 antibody (PD1ab) superior to HDI-α2b for MM in adjuvant setting?

Lian *et al.* (6) performed a phase II randomized trial for investigation of the therapeutic effect of toripalimab, an anti-PD1ab versus HDI-α2b for MM in adjuvant setting. The study included Chinese patients with MM who underwent complete tumor resection and had an Eastern Cooperative Oncology Group performance status of 0 or 1 with adequate organ and bone marrow function (6). Patients who received systemic adjuvant therapies including PD1ab, anti-programmed death-ligand (PD-L) 1, or anti-PD-L2 antibodies for MM after surgery or had autoimmune disorders prior to enrollment were excluded from the study. The enrolled patients were randomly assigned to two treatment arms, toripalimab or HDI administration for one year. In total, 145 patients with MM after complete resection were enrolled, including 73 patients randomized to the toripalimab arm and 72 patients randomized to the HDI arm. The baseline patient characteristics of both treatment arms were well-balanced.

The results of this trial demonstrated no statistical difference in RFS, the primary endpoint of this study,

between the toripalimab arm and HDI arm {median RFS: 13.6 [95% confidence interval (CI): 8.31–19.02] *vs.* 13.9 (95% CI: 8.28–19.61) months, hazard ratio (HR): 1.05 (95% CI: 0.69–1.61), stratified P=0.811}. There was also no significant difference in distant metastasis-free survival (DMFS) and OS between the two arms {median DMFS: 16.3 (95% CI: 10.94–21.09) *vs.* 14.6 (95% CI: 8.34–21.26) months, HR: 1.00 (95% CI: 0.65–1.549), stratified P=0.994; median OS: 35.1 [95% CI: 27.93–not reached (NR)] *vs.* NR (95% CI: 28.29–NR) months, HR: 1.11 (95% CI: 0.66–1.84)}. Although the median RFS was approximately 6 months longer in the toripalimab arm than in the HDI arm in PD-L1 positive patients, the difference was statistically insignificant. Meanwhile, the incidence of ≥ grade 3 toxicities was much lower in the toripalimab arm than in the HDI arm (27.4% *vs.* 87.5%). Based on these trial results, the authors concluded that toripalimab might be a better option for the adjuvant treatment of MM. To our knowledge, this is the first randomized trial comparing the therapeutic effect of an PD1ab with HDI in an adjuvant treatment setting for patients with MM.

What do we know about adjuvant ICI therapy for melanoma?

The most important clinical question in the field of melanoma is whether adjuvant PD1ab treatment truly improves OS compared with no adjuvant treatment (so-called "wait and see") or not. Major clinical trials on the adjuvant treatment of melanoma have not yet provided a definitive answer to this question. The phase III clinical trial CheckMate 238 indicated that the adjuvant use of nivolumab significantly improved RFS and DMFS but did not improve OS compared with adjuvant ipilimumab in patients with stage IIIB–C or stage IV melanoma after complete tumor resection at a minimum follow-up of 62 months (7). However, this trial could not evaluate the superiority of nivolumab over no treatment in terms of OS, because the comparator arm was ipilimumab. In the phase III clinical trial EORTC 1325/KEYNOTE-054, the use of pembrolizumab as adjuvant improved RFS and DMFS with statistical significance in comparison to the placebo arm in patients with resected high-risk stage III melanoma. However, OS results have not yet been published (8). As for high-risk stage IIB–C melanoma, the phase III clinical trial KEYNOTE-716 demonstrated that pembrolizumab significantly improved RFS and DMFS versus placebo in this population (9). Likewise, the phase III clinical trial CheckMate-76K demonstrated significant improvements in RFS and DMFS with adjuvant nivolumab compared with the placebo arm (10). However, the OS results of those two trials have not yet been published.

How does the therapeutic effect of anti-PD1ab monotherapy for advanced MM predict the outcome of adjuvant therapy for MM?

Currently, PD1ab monotherapy is the only ICI available as adjuvant therapy; however, its therapeutic effect in MM is not clear. Therefore, inferences must be drawn from the results of PD1ab monotherapy in advanced settings. Meanwhile, there have been few prospective clinical trials and several subgroup and retrospective studies evaluating PD1ab alone, particularly targeting patients with MM, even in advanced settings (*Table 1*). A pooled analysis of multiple clinical trial cohorts, reported by D'Angelo *et al.* (11), including 86 patients with MM and 326 patients with cutaneous melanoma clearly demonstrated a worse prognosis in MM compared to cutaneous melanoma in advanced setting [objective response rate (ORR): 23.3% (95% CI: 14.8–33.6%) and 40.9% (95% CI: 37.1–44.7%); median PFS: 3.0 (95% CI: 2.2–5.4) *vs.* 6.2 (95% CI: 5.1–7.5) months]. In a post-hoc analysis of CheckMate 067 reported by Shoushutari *et al.* (12) the patients with MM (23 patients) demonstrated lower PFS and OS than intent-to-treat population (316 patients with cutaneous melanoma) in the nivolumab alone arm (ORR: 30% *vs.* 45%; median PFS: 3.0 *vs.* 6.9 months; median OS: 20.2 *vs.* 36.9 months, respectively). These subgroup analyses had a very limited sample size for MM owing to the rarity of MM in the Caucasian population. Among all, the results of reported retrospective studies, the therapeutic effect of PD1abs in patients with MM is shown to be lower than that in patients with cutaneous melanoma (*Table 1*). In two larger representative real-world datasets, the Japanese Mucosal Melanoma (JMAC) study reported by Nakamura *et al.* (13) investigated 329 Japanese patients with advanced MM who were treated with ICIs, including 263 patients treated with PD1ab alone (nivolumab or pembrolizumab). The therapeutic effects of the PD1ab alone group showed downward trend (ORR: 26%; median PFS: 5.9 months; median OS: 20.4 months) than those in the phase III clinical trials such as CheckMate 067 and KEYNOTE-001 (13). Another larger international retrospective study by Dimitriou *et al.* (14) also investigated 545 patients with advanced MM treated with ICIs, including 348 patients treated with PD1ab

Table 1 Summary of studies for anti-PD-1 antibody monotherapy for advanced mucosal melanoma

Authors (year)	Trial number	Study design	Sample size	Anti-PD-1 antibody	Treatment line	ORR (%)	Median PFS (months)	Median OS (months)	Locations
Shoushtari 2016	NA	Multi-center, retrospective	35	Nivolumab or pembrolizumab	1+	23	3.9	12.4	US
Yamazaki 2017	NCT02180061	Phase Ib	8	Pembrolizumab	1+	25	3.4	NR	Japan
D'Angelo 2017	NCT00730639, NCT01621490, NCT01721772, NCT01721746, NCT01844505	Pooled analysis of CA209-003, CA209-038, CheckMate 066, CheckMate 037, and CheckMate 067	86	Nivolumab	1+	23.3	3.0	NA	US, Europe, Australia
Schaefer 2017	NA	Single-center, retrospective	7	Nivolumab or pembrolizumab	NA	28.6	NA	NA	Germany
Hamid 2018	NCT01295827, NCT01704287, NCT01866319	Post-hoc analysis of KEYNOTE-001, 002, 006	84	Pembrolizumab	1+	19	2.8	11.3	North America, Europe, Australia
Kiyohara 2018	NA	Prospective, postmarketing surveillance observational	208	Nivolumab	2+	NA	NA	11.3	Japan
Quereux 2018	NA	Single-center, retrospective	8	Nivolumab	1+	50	9	NA	France
Mignard 2018	NA	Multi-center, retrospective	75	Nivolumab or pembrolizumab	1+	20	NA	NA	France
Yamazaki 2019	JapicCTI142533	Single-arm, open-label, multi-center phase II	6	Nivolumab	1	33.3	NA	12	Japan
Nathan 2019	NCT02156804	Single-arm, openlabel, multi-center phase II	63	Nivolumab	2+	NA	NA	11.5	Europe
Si 2019	NCT02821000	Phase Ib	15	Pembrolizumab	2	13.3	NA	NA	China
Moya-Plana 2019	NA	Single-center, prospective	20	Pembrolizumab	1	35	5	16.2	France
Maeda 2019	NA	Single-center, retrospective	24	Nivolumab	NA	20.8	7.5	14.1	Japan
Kondo 2019	NA	Single-center, retrospective	22	Nivolumab	1+	9.5	NA	NA	Japan
Tang 2020	NCT03013101	Single-arm, open-label, multi-center phase II	22	Toripalimab	2+	0	1.9	10.3	China
Nomura 2020	UMIN000015845	Single-arm, open-label, multi-center phase II	17	Nivolumab	1+	23.5	1.4	12	Japan
Otsuka 2020	NA	Single-center, retrospective	27	Nivolumab	1+	30	NA	NA	Japan
Shoushtari 2020	NCT01844505	Post-hoc analysis of CheckMate 067	23	Nivolumab	1	30	3.0	20.2	US, Europe, Australia
Yamazaki 2021	NA	Multi-center single-cohort, prospective observational	25	Nivolumab	1+	16	3.3	17.5	Japan
Ogata 2021	NA	Single-center, retrospective	59	Nivolumab or pembrolizumab	1+	15.2	3.0	20.1	US
Umeda 2021	NA	Multi-center retrospective	115	Nivolumab or pembrolizumab	1	26	6.2	19.2	Japan
Nakamura 2021	NA (JMAC study)	Multi-center retrospective	263	Nivolumab or pembrolizumab	1	26	5.9	20.4	Japan
Dimitriou 2022	NA	Multi-center retrospective	348	Anti-PD-1 antibody	1	29	5	19	Australia, US, Europe, Asia

PD-1, programmed death 1; ORR, objective response rate; PFS, progression-free survival; OS, overall survival; NA, not available; NR, not reached; JMAC, Japanese Mucosal Melanoma.

alone. Similarly, the therapeutic effects of the PD1ab alone group demonstrated a downward trend (ORR: 29%; median PFS: 5 months; median OS: 19 months) than those in those in the aforementioned trials (14).

Several research studies have indicated that MM is molecularly different from cutaneous melanoma showing lower mutation rate of BRAF V600, lower tumor mutational burden (TMB), and higher rate of copy-number alterations (CNA), leading to lower response to ICIs (15,16). It is also generally known that the incidence rate of MM in East Asians is higher than that in Caucasians (17,18). Furthermore, a recent study reported by Liu *et al.* (19) shows lower TMB in the Chinese population. Additionally, rates of selected gene mutations, including those in the MAPK signaling pathway, variegate between the different races. NRAS Q61 and NF1 gene alterations, and preexisting T cell inflammation markers were observed to be less frequent in the Chinese population. Those data will lead to the hypothesis of the lower therapeutic effect of PD1ab in the advanced setting in East Asians than in Caucasian population (20). These observations suggest lower therapeutic effect of adjuvant PD1ab monotherapy in MM than in cutaneous melanoma.

What do we know about adjuvant PD1ab monotherapy for MM?

Few retrospective studies have investigated the therapeutic effect of adjuvant PD1ab monotherapy for MM. Muto *et al.* (21) retrospectively compared the therapeutic effect of adjuvantPD1ab monotherapy in 78 patients with different clinical melanoma. Contrary to expectations, patients with MM (n=11) showed no significant difference in RFS compared to those with cutaneous melanoma (n=31) (21), which may be due to the small sample sizes and follow-up periods (less than 12 months). Since there was no "wait and see" arm in this study, it is still unclear whether adjuvant PD1ab monotherapy truly improves RFS. Another retrospective study by Jacques *et al.* (22) compared adjuvant PD1ab monotherapy arm (55 patients) with "without adjuvant" matched control arm (28 patients) in patients with resected MM. No statistical significance were found in RFS and OS between the two arms [median RFS: 12.9 (95% CI: 6.7–28.2) *vs.* 17.4 (95% CI: 7–34.5) months, P=0.38; median OS: >36 *vs.* >54 months, P=0.84] and they concluded that there is no clear benefit of adjuvant PD1ab monotherapy for MM (22).

How should we interpret the results of adjuvant toripalimab versus HDI in MM?

Several study limitations should be considered, as addressed by the authors in this paper (6). First, HDI is currently not considered the standard-of-care adjuvant treatment for surgically resected melanoma in the era of ICIs, which compromises the significance of setting HDI as a competitive arm and prevents setting a placebo control group for ethical issues. Second, a previous randomized phase II trial for comparing two cohort of adjuvant HDI and complete resection alone without adjuvant therapy in patients with resected MM demonstrated 100% relapse rate in patients who underwent complete resection alone, while the HDI arm showed improved RFS and OS compared to surgery alone (5). The authors used those data from the complete resection alone arm for comparison. However, it should be highlighted that OS, the primary goal of clinical trials for adjuvant therapy, may be improved in the current era of ICIs, compared to previous data employing ICIs following recurrence in the surgery-alone arm. Additionally, the potential superiority of median RFS in the toripalimab arm in PD-L1 positive patients is that this analysis was likely underpowered given the smaller overall sample size of the study. While PD-L1 positivity is not clinically an impactful biomarker for cutaneous melanoma, it can be a potentially significant marker for an adequately stratified and/or sub-group powered for analysis in patients with MM. Finally, since only Chinese patients were included in this study, it is unclear whether the findings can be extrapolated to other ethnic groups or whether the same drug can be used, given that Caucasians have a lower incidence of MM than Asians.

Despite such limitations, this randomized phase II study reveals similar survival outcomes between toripalimab and HDI with more safe and tolerable profiles for toripalimab in patients with MM after complete resection. The validation of adjuvant PD1ab monotherapy for MM in a prospective trial, though still tentative, is a significant contribution to the field of this rare clinical subtype of melanoma. This study will lead to future clinical trials in which the PD1ab monotherapy arm can be used as the control arm comparing with other novel adjuvant therapies for MM; however, further evidence is required to fully accept that PD1ab should be set as a standard-of-care. In fact, a very recent prospective trial reported by Lian *et al.* (23) compared the therapeutic effect of temozolomide plus

Table 2 Summary of ongoing clinical trials of neoadjuvant and/or adjuvant immunotherapy targeting on mucosal melanoma

Trial number	Phase	Enrollment	Intervention	Status	Study start (year/month)	Study completion (year/month)	Locations
NCT04462965	Phase II	294	Toripalimab + temozolomide	Recruiting	2020/6	2025/6	China
NCT03241186	Phase II	36	Nivolumab + ipilimumab, followed by nivolumab	Active, not recruiting	2017/9	2023/9	US
NCT05545969	Phase II	44	Neoadjuvant: pembrolizumab + lenvatinib	Not yet recruiting	2023/5	2030/10	Australia
			Adjuvant: pembrolizumab + lenvatinib				
NCT03313206	Phase II	60	Neoadjuvant: pembrolizumab	Recruiting	2018/5	2026/11	France
			Adjuvant: pembrolizumab ± lenvatinib				
NCT04318717	Phase II	16	Pembrolizumab + hypofractionated radiation therapy	Recruiting	2020/5	2027/7	US
NCT05111574	Phase II	99	Nivolumab	Recruiting	2022/6	2023/12	US
			Nivolumab + cabozantinib				
NCT04879654	Phase II	45*	Multimodality treatment including radiotherapy, toripalimab, and/or chemotherapy	Recruiting	2021/6	2026/5	China

*, sinonasal mucosal melanoma alone.

cisplatin with that of toripalimab in patients with resected MM in adjuvant setting. The temozolomide plus cisplatin arm showed significantly improved survivals compared with the toripalimab arm (median RFS: 28.2 *vs.* 12.0 months, P=0.04), DMFS (median DMFS: 42.0 *vs.* 19.0 months, P=0.02), and OS (median OS: 93.4 *vs.* 39.3 months, P=0.03). This data suggests that adjuvant temozolomide plus cisplatin may be a better option for resected MM than adjuvant PD1ab even in the era of ICIs.

Future perspectives: current ongoing clinical trials of ICIs for MM in neoadjuvant and/or adjuvant setting

Despite promising results of the current clinical trials of ICIs as an adjuvant treatment for cutaneous melanoma, they may be less effective in patients with MM. The difference in response to ICIs even in adjuvant setting may be due to the differences in the TMB, tumor immune microenvironment, or immune system not only between cutaneous melanoma and MM but also between other ethnic populations. The complexity in risk stratification for the location of MM may also carry the substantial risk for ineffectiveness of adjuvant therapies, even without regional nodal metastasis. Therefore, novel neoadjuvant and/or adjuvant combination therapies are warranted to obtain improved survival of patients with MM. Several clinical trials are presently ongoing to investigate the therapeutic effect and safety of various agents or treatment modalities in combination with PD1ab in patients with MM (*Table 2*). Those combination immunotherapies targeting different cancer-immunity cycles may be more promising strategy for resectable or resected MM.

Acknowledgments

Funding: This work was supported by the Japan Agency for Medical Research and Development (grant number JP23ck0106765h0002 to Y.N.) and the National Cancer Center Research and Development Fund (grant number 2023-J-3 to Y.N.).

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Chinese Clinical Oncology*. The article

has undergone external peer review.

Peer Review File: Available at https://cco.amegroups.com/article/view/10.21037/cco-23-61/prf

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://cco.amegroups.com/article/view/10.21037/cco-23-61/coif). Y.N. has served as a consultant and/or received honoraria from Merck Sharp & Dohme (MSD), Novartis, Alexion Pharma, Bristol-Myers Squibb (BMS), Leo Pharma, Maruho, Ono Pharma, Sun Pharma, Kyowa Kirin, Torii, Sanofi and Tanabe-Mitsubishi Pharma. Y.N. reports support for this manuscript from the Japan Agency for Medical Research and Development (grant numbers JP23ck0106765h0002) and the National Cancer Center Research and Development Fund (grant number 2023-J-3). Y.N. also reports grants or contracts from Torii for his institution. T.M. received honoraria from Ono Pharma. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Cui C, Lian B, Zhou L, et al. Multifactorial Analysis of Prognostic Factors and Survival Rates Among 706 Mucosal Melanoma Patients. Ann Surg Oncol 2018;25:2184-92.
2. Chi Z, Li S, Sheng X, et al. Clinical presentation, histology, and prognoses of malignant melanoma in ethnic Chinese: a study of 522 consecutive cases. BMC Cancer 2011;11:85.
3. Chan RC, Chan JY, Wei WI. Mucosal melanoma of the head and neck: 32-year experience in a tertiary referral hospital. Laryngoscope 2012;122:2749-53.
4. Kirkwood JM, Strawderman MH, Ernstoff MS, et al. Interferon alfa-2b adjuvant therapy of high-risk resected cutaneous melanoma: the Eastern Cooperative Oncology Group Trial EST 1684. J Clin Oncol 1996;14:7-17.
5. Lian B, Si L, Cui C, et al. Phase II randomized trial comparing high-dose IFN-α2b with temozolomide plus cisplatin as systemic adjuvant therapy for resected mucosal melanoma. Clin Cancer Res 2013;19:4488-98.
6. Lian B, Si L, Chi ZH, et al. Toripalimab (anti-PD-1) versus high-dose interferon-α2b as adjuvant therapy in resected mucosal melanoma: a phase II randomized trial. Ann Oncol 2022;33:1061-70.
7. Larkin J, Del Vecchio M, Mandalá M, et al. Adjuvant Nivolumab versus Ipilimumab in Resected Stage III/IV Melanoma: 5-Year Efficacy and Biomarker Results from CheckMate 238. Clin Cancer Res 2023;29:3352-61.
8. Eggermont AMM, Blank CU, Mandalà M, et al. Adjuvant pembrolizumab versus placebo in resected stage III melanoma (EORTC 1325-MG/KEYNOTE-054): distant metastasis-free survival results from a double-blind, randomised, controlled, phase 3 trial. Lancet Oncol 2021;22:643-54.
9. Long GV, Luke JJ, Khattak MA, et al. Pembrolizumab versus placebo as adjuvant therapy in resected stage IIB or IIC melanoma (KEYNOTE-716): distant metastasis-free survival results of a multicentre, double-blind, randomised, phase 3 trial. Lancet Oncol 2022;23:1378-88.
10. Long GV, Del Vecchio M, Weber J et al: Adjuvant therapy with nivolumab versus placebo in patients with stage IIB/C melanoma (CheckMate 76K). 2023 Society fo Melanoma Research 2022 International Congress.
11. D'Angelo SP, Larkin J, Sosman JA, et al. Efficacy and Safety of Nivolumab Alone or in Combination With Ipilimumab in Patients With Mucosal Melanoma: A Pooled Analysis. J Clin Oncol 2017;35:226-35.
12. Shoushtari AN, Wagstaff J, Ascierto PA, et al. CheckMate 067: Long-term outcomes in patients with mucosal melanoma. J Clin Oncol 2020;38:abstr 10019.
13. Nakamura Y, Namikawa K, Yoshikawa S, et al. Anti-PD-1 antibody monotherapy versus anti-PD-1 plus anti-CTLA-4 combination therapy as first-line immunotherapy in unresectable or metastatic mucosal melanoma: a retrospective, multicenter study of 329 Japanese cases (JMAC study). ESMO Open 2021;6:100325.
14. Dimitriou F, Namikawa K, Reijers ILM, et al. Single-agent anti-PD-1 or combined with ipilimumab in patients with mucosal melanoma: an international, retrospective, cohort study. Ann Oncol 2022;33:968-80.

15. Hayward NK, Wilmott JS, Waddell N, et al. Whole-genome landscapes of major melanoma subtypes. Nature 2017;545:175-80.
16. Sakaizawa K, Ashida A, Uchiyama A, et al. Clinical characteristics associated with BRAF, NRAS and KIT mutations in Japanese melanoma patients. J Dermatol Sci 2015;80:33-7.
17. Namikawa K, Yamazaki N. Targeted Therapy and Immunotherapy for Melanoma in Japan. Curr Treat Options Oncol 2019;20:7.
18. Bai X, Kong Y, Chi Z, et al. MAPK Pathway and TERT Promoter Gene Mutation Pattern and Its Prognostic Value in Melanoma Patients: A Retrospective Study of 2,793 Cases. Clin Cancer Res 2017;23:6120-27.
19. Liu D, Schilling B, Liu D, et al. Integrative molecular and clinical modeling of clinical outcomes to PD1 blockade in patients with metastatic melanoma. Nat Med 2019;25:1916-27.
20. Shoushtari AN, Bao R, Luke JJ. PD-1 Blockade in Chinese versus Western Patients with Melanoma. Clin Cancer Res 2020;26:4171-3.
21. Muto Y, Kambayashi Y, Kato H, et al. Adjuvant Anti-PD-1 Antibody Therapy for Advanced Melanoma: A Multicentre Study of 78 Japanese Cases. Acta Derm Venereol 2022;102:adv00756.
22. Jacques SK, McKeown J, Grover P, et al. Outcomes of patients with resected stage III/IV acral or mucosal melanoma treated with adjuvant anti-PD-1 therapy. Ann Oncol 2022;33:S915-6.
23. Lian B, Tian H, Si L, et al. Temozolomide plus cisplatin versus toripalimab (anti-PD-1) as adjuvant therapy in resected mucosal melanoma. J Clin Oncol 2023;41:9508.

Cite this article as: Nakamura Y, Mori T. Adjuvant therapy for mucosal melanoma in the era of immune checkpoint inhibitors. Chin Clin Oncol 2024;13(1):13. doi: 10.21037/cco-23-61