Letters to the Editor

The best dosage of nivolumab plus ipilimumab combination for melanoma brain metastases

ARTICLE INFO

Keywords

Melanoma
Ipilimumab
Nivolumab

ABSTRACT

Tawbi et al. (2021) have recently reported that nivolumab 1 mg/kg plus ipilimumab 3 mg/kg every 3 weeks for four doses (N1I3) provided durable survival for patients with active melanoma brain metastases without symptoms as first-line regimen [1]. While we believe in the usefulness of the regimen proposed by Tawbi et al., we thought to investigate whether the nivolumab 3 mg/kg plus ipilimumab 1 mg/kg every 3 weeks for four doses (N3I1) regimen might lead to better safety profile. This is because Tawbi et al. stated, in their previous report of CheckMate 204, that "the currently available evidence does not suggest that lower doses of ipilimumab are superior to the doses used in our study" [2].

To compare the risk of adverse events caused by these two regimes, we have recently conducted a random-model meta-analysis using a generic inverse variance method and the data of patients with both melanoma and the other malignancies (RevMan ver 5.4. Cochrane Collaboration, London, UK) [3]. This analysis suggested that N3I1 regimen caused less adverse events [3].

According to the CheckMate 511 and OpACIN-neo, the N3I1 regimen is sufficiently effective for melanoma. Besides, our analyses revealed safety superiority of the N3I1 regimen [Fig. 1] [3]. The data from Tawbi et al. are valuable in demonstrating the efficacy of the nivolumab plus ipilimumab combination [1], and we appreciate the authors for their contribution. We hope that there will be further discussion on the best dosage of the combination therapy.

Funding source

None.

CRediT authorship contribution statement

Takeshi Fukumoto: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. Nobuyuki Horita: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

None.
Acknowledgments

This work was supported by Japan Society for the Promotion of Science KAKENHI (grant number 22K16262), The Nakatomi Foundation, Hoansha Foundation and SGH Cancer Research Grant (TF).

References

[1] H.A. Tawbi, P.P. Forsyth, P.F. Hodi, et al., Long-term outcomes of patients with active melanoma brain metastases treated with combination nivolumab plus ipilimumab (CheckMate 204): final results of an open-label, multicentre, phase 2 study, Lancet Oncol. (2021), https://doi.org/10.1016/S1470-2045(21)00545-3.

[2] H.A. Tawbi, P.A. Forsyth, A. Algazi, et al., Combined nivolumab and ipilimumab in melanoma metastatic to the brain, N. Engl. J. Med. 379 (8) (2018) 722–730.

[3] K. Somekawa, N. Horita, A. Kaneko, et al., Adverse events induced by nivolumab and ipilimumab combination regimens, Ther. Adv. Med. Oncol. (2022) [in press].

[4] C. Lebbé, N. Meyer, L. Mortier, 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. 37 (11) (2019) 867–875.

[5] E.A. Rozeman, A.M. Menzies, A.C.J. van Akkooi, et al., Identification of the optimal combination dosing schedule of neoadjuvant ipilimumab plus nivolumab in macroscopic stage III melanoma (OpaCIIN-neo): a multicentre, phase 2, randomised, controlled trial, Lancet Oncol. 20 (7) (2019) 948–960.

Takeshi Fukumoto, Nobuyuki Horita

a Division of Dermatology, Department of Internal Related, Kobe University Graduate School of Medicine, 7-5-1 Kusunokicho Hyogo Chuo-ku, Kobe, 650-0017, Japan

b Chemotherapy Center, Yokohama City University Hospital, Yokohama, Japan

* Corresponding author.

E-mail address: fuku@med.kobe-u.ac.jp (T. Fukumoto).