

## **Piotr Rutkowski**

Department of Soft-Tissue/Bone Sarcomas and Melanomas the Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland

## Introduction

Melanoma is one of the malignant tumors that most frequently metastasize to the central nervous system. New treatment methods introduced into daily clinical practice have significantly improved the prognosis of this group of patients [1]. Metastases in the central nervous system are increasingly diagnosed at an asymptomatic stage. Currently, most of the new systemic therapies are available in Poland under drug programs (vemurafenib with cobimetinib, dabrafenib with trametinib, encorafenib with binimetinib, ipilimumab with nivolumab, nivolumab and relatlimab, pembrolizumab, and nivolumab). Data from clinical trials indicate, that the median overall survival in patients with metastatic melanomas with *BRAF* mutations receiving anti-PD-1 immunotherapy or combined treatment with BRAF and MEK inhibitors is currently about 2 years, which is about 4 times longer than 7 years ago [2]. In each patient with confirmed metastases to the central nervous system, it is mandatory to assess *BRAF* gene status, if it has not been done before, in order to select the appropriate therapy.

The presented educational issue of Oncology in Clinical Practice includes review article and a series of clinical case reports concerning the efficacy of molecularly targeted therapies in the treatment of patients with melanoma with the V600 mutation in the *BRAF* gene and metastases to the central nervous system, with particular emphasis on the use of the latest combination of BRAF and MEK inhibitors — encorafenib with binimetinib. It should be noted, that according to current guidelines, in patients with *BRAF*-mutant melanoma and metastases in the central nervous system (especially asymptomatic and less than 3 cm in size), dual immunotherapy with nivolumab and ipilimumab is recommended; however, depending on the clinical situation, the use of BRAFi and MEKi should be considered in the first line treatment (especially in symptomatic cases) [1]. Recently published real-world evidence and the results of clinical trials also confirm that in patients with metastatic melanoma with *BRAF* mutations, the use of anti-PD-1 with anti-CTLA-4 combination as frontline therapy leads to a reduced rate and delay in the occurrence of central nervous system metastases compared to BRAF and MEK inhibitors in first line treatment [3, 4]. The basic principle in the management of patients with melanoma metastases to the central nervous system should be providing care by multidisciplinary teams whose members are experienced in the diagnosis and treatment of patients with melanoma.

## References

- 1. Rutkowski P, Kiprian D, Świtaj T, et al. Management of melanoma central nervous system metastases. Oncology in Clinical Practice. 2023, doi: 10.5603/ocp.2023.0042.
- Rutkowski P, Wysocki P, Kozak K, et al. Expert recommendations on diagnostic-therapeutic management of melanoma patients. Oncology in Clinical Practice. 2022; 18(6): 357–392, doi: 10.5603/ocp.2021.0042.
- Franklin C, Mohr P, Bluhm L, et al. Brain metastasis and survival outcomes after first-line therapy in metastatic melanoma: a multicenter DeCOG study on 1704 patients from the prospective skin cancer registry ADOREG. J Immunother Cancer. 2023; 11(4), doi: 10.1136/jitc-2022-005828, indexed in Pubmed: 37028819.
- Ascierto PA, Mandalà M, Ferrucci PF, et al. 1083MO Brain metastases and survival evaluation in the SECOMBIT trial. Annals of Oncology. 2023; 34: S653, doi: 10.1016/j.annonc.2023.09.2217.

Translation and republished by permission from: Rutkowski P. Wstęp. Onkol Prakt Klin Edu 2023; 9(supl. E): E1.