Ipilimumab for melanoma brain metastases

- Combined immunotherapy with nivolumab and ipilimumab with and without sequential or concomitant stereotactic radiotherapy in patients with melanoma brain metastasis: An international retrospective study
- Molecular analysis of immune checkpoint inhibitor associated erythema nodosum-like toxicity
- Management of metastatic melanoma with combinations including PD-1 inhibitors
- Sustained Immunotherapy Response in Metastatic Brain Melanoma Through 2 Pregnancies
- Presence of brain metastasis differentially impacts long-term survival after first-line therapy in melanoma depending on BRAF mutation status
- Ipilimumab plus nivolumab versus nivolumab alone in patients with melanoma brain metastases (ABC): 7-year follow-up of a multicentre, open-label, randomised, phase 2 study
- MHC class II: a predictor of outcome in melanoma treated with immune checkpoint inhibitors
- Radiomic analysis of patient and interorgan heterogeneity in response to immunotherapies and BRAF-targeted therapy in metastatic melanoma

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Treatment of a melanoma brain metastasis with ipilimumab appears to cause measurable biological changes in the tumor that can be correlated with post-treatment diffusion-weighted MRI imaging, suggesting both a mechanism of action and a possible surrogate marker of efficacy [1].

Case series

2017

In a retrospective cohort of consecutive MM patients (pts) with BMs, all systematically upfront treated by Gamma-Knife (GK) at first BM and retreated in case of new BMs, from 2010 to 2015 at the time when ipilimumab BRAF ± MEK inhibitors and anti-PD-1 were introduced in practice. Survival after 1st GK (OSGK1) according to prognostic factors and treatment.

Among 179 consecutive pts treated by GK, 109 received IT and/or TT after the 1st GK. Median OSGK1 was 10.95 months and 1- and 2-year survival rates were 49.5% and 27.4%, respectively, versus a median overall survival (OS) of 2.29 months ($p < .001$) in those who did not receive IT or TT. In pts who initially had a single BM, median OS and 1- and 2-year survival rates were 14.46 months, 66.7% and 43.4%, respectively; in pts with 2-3 BMs: 8.85 months, 46.4% and 31%, respectively; in pts with >3 BMs: 7.25 months, 37.2% and 11.9%, respectively. Multivariate analysis for OSGK1 confirmed that IT and TT were significantly and highly protective. Best OSGK1 was observed in BRAF-wild-type pts receiving anti-PD-1 or in BRAF-mutated pts receiving BRAF-inhibitors and anti-PD-1 (12.26 and 14.82 months, respectively).

In real-life MM pts with BMs, a strategy aiming at controlling BM with GK together with TT and/or TT seems to achieve unprecedented survival rates [2].

Case reports

a 50-year-old woman previously treated with nivolumab-ipilimumab combination therapy for metastatic melanoma. Despite premature discontinuation of these immune checkpoint inhibitors (ICIs) after 2 cycles due to severe immune-related hepatitis, the patient achieved a complete response. Nine months later, brain magnetic resonance imaging (MRI) showed the progression of a single cerebral lesion, and the patient was referred for stereotactic radiosurgery. Unexpectedly, the brain MRI acquired one month later as part of radiosurgery planning showed a spontaneous regression of this lesion, allowing for radiosurgery cancellation. Follow-up imaging showed a sustained response, although the patient did not receive any other oncological treatment. We discuss here the potential immune mechanisms involved in this unusual course and the importance of better understanding the behavior of tumors in the era of ICIs [3].

1)
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2)
Gaudy-Marqueste C, Dussouil AS, Carron R, Troin L, Malissen N, Loundou A, Monestier S, Mallet S, Richard MA, Régis JM, Grob JJ. Survival of melanoma patients treated with targeted therapy and immunotherapy after systematic upfront control of brain metastases by radiosurgery. Eur J Cancer. 2017 Aug 4;84:44-54. doi: 10.1016/j.ejca.2017.07.017. [Epub ahead of print] PubMed PMID: 28783540.
3)
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