Efficacy of immunotherapy in melanoma patients with brain metastases treated with steroids – The MEMBRAINS trial.

Objectives and endpoints

The primary objective is to evaluate 6 months progression-free survival rate and 6 months overall survival rate.

Main secondary objectives are to evaluate overall progression-free survival, overall survival, overall response rate, and blood and tissue biomarkers of response and progression.

Target population

Patients with histologically confirmed melanoma with radiologically verified brain metastasis and in treatment with prednisolone equivalent > 10 mg daily (dexamethasone > 1.6 mg daily, hydrocortisone > 40 mg daily or equivalent).

See main inclusion criteria.

Treatment plan

Eligible patients will be allocated to either treatment with pembrolizumab alone or the combination of ipilimumab and nivolumab at the discretion of the treating physician and according to patient's preferences.

Pembrolizumab 2 mg/kg is administered every three weeks for up to two years. Ipilimumab 3 mg/kg and nivolumab 1 mg/kg is administered every three weeks for four doses followed by administration of nivolumab 6 mg/kg (max 480 mg) every four weeks for up to two years in total.

Patients will be recruited from and treated at the three participating centers in Herlev, Aarhus or Odense.

Co-ordinating investigator

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Main inclusion criteria

- ≥ 18 years of age.
- The patient has histologically confirmed metastatic melanoma with radiologically verified brain metastasis.
- The patient has a need for systemic steroid treatment prednisolone > 10 mg or equivalent.
- The patient has a measurable parameter according to RECIST 1.1.
- The patient has an ECOG performance status of 0-2.
- The patient has no significant toxicities from previous treatments.
- The patient must have adequate hematological and organ function.
- Prior treatment with BRAF/MEK inhibitor is allowed.

Main exclusion criteria

- Another malignancy or concurrent malignancy unless disease-free for 3
- years.
- The patient has ocular melanoma.
- Any medical condition that will interfere with patient compliance or safety.
- Prior treatment with anti-PD-1/PD-L1/PD-L2/CTLA-4 antibodies in the metastatic setting.
- Prior systemic treatment with anti-PD-1/PD-L1/PD-L2/CTLA-4 antibodies in the adjuvant setting, unless completed more than 6 months before enrolment in this study.
- Concurrent treatment with other experimental drugs.