Combination therapy with Nivolumab and PD-L1/IDO peptide vaccine to patients with metastatic malignant melanoma. MM1636

Objectives and endpoints

The primary objective is to assess tolerability and safety of the peptide vaccine containing the peptides Indolemamine 2,3-dioxygenase long (IDO long) and programmed death ligand-1 long1 (PD-L1 long1) with Montanide ISA 51 as adjuvant to patients with metastatic malignant melanoma (MM) in combination with the immune checkpoint blocking antibody Nivolumab.

Target population

Patients with metastatic malignant melanoma. Three patient cohort exists:
A) Anti PD-1/PD-L1 naïve patients (30 patients). These patients are candidates for Nivolumab monotherapy. B) An extension cohort (10 patients). Progressive disease ON anti-PD-1 monotherapy. C) An Extension cohort (10 patients). Progressive disease during follow up OFF anti-PD-1 after clinical benefit (SD/PR/CR) on anti-PD-1 therapy**.**
See main inclusion criteria.

Treatment plan

Patients included in the trial will be treated with Nivolumab IV infusions every second week. The PD-L1/IDO vaccine is given from the start of Nivolumab and every second week for the first 6 vaccines and thereafter every fourth week up 47 weeks. 15 vaccines will be given in total. At the end of vaccination, patients who are not excluded from the protocol because of progression will continue treatment with Nivolumab in accordance with the usual guidelines.

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Main inclusion criteria

- Age ≥ 18
- The patient has locally advanced or metastatic melanoma with progressive, persistent or recurrent disease on or following treatment with standard of care agents.
- Patients belonging to one of the following patient groups will be enrolled:
  Cohort A: Anti PD-1/PD-L1 naïve patients (30 patients). The patient is a candidate for Nivolumab monotherapy. Prior anti-PD-1/anti-PD-L1 antibody treatment is not allowed **OR:**
  Cohort B: Extension cohort (10 patients). Progressive disease ON anti-PD-1 monotherapy*** OR:**
  Cohort C: Extension cohort (10 patients). Progressive disease during follow up OFF anti-PD-1 after clinical benefit (SD/PR/CR) on anti-PD-1 therapy*****.
  *****Subjects should not have discontinued antibody therapy due to serious and/or life-threatening toxicity.
- At least one measurable parameter according to RECIST 1.1.
- The patient has an ECOG performance status of 0 or 1.

Main exclusion criteria

- The patient has not recovered to grade 0-1 from adverse events due to prior chemotherapy, radioactive, or biological cancer therapy.
- The patient has not recovered from surgery or is less than 4 weeks from surgery.
- The patient has an active infection requiring systemic therapy.
- The patient has a history of life-threatening or severe immune related adverse events on treatment with another immunotherapy and is at risk of not recovering.
- Any active autoimmune diseases or a history of severe clinical autoimmune disease.
- Significant medical disorder according to investigator; e.g. severe asthma or chronic obstructive lung disease, dysregulated heart disease, or dysregulated diabetes mellitus.
- The patient is expected to require any other form of systemic antineoplastic therapy while receiving the treatment.
- The patient requires systemic steroids for management of immune-related adverse events experienced on another immunotherapy.
- The patient has active CNS metastases and/or carcinomatous meningitis. However, patients with subclinical brain metastases < 1 cm can be included (maximum of 4 metastases < 1 cm). (Patients with previously treated brain metastases may participate provided they are clinically stable. Patients with untreated brain metastasis will be excluded).
- Concurrent treatment with other experimental drugs.
- Severe allergy or anaphylactic reactions earlier in life.