MK-7902-003 - E7080-G000-312 / LEAP-003 (dernière mise à jour : 05/02/2020)

http://archimaid.fr/index.php?action=show&id=729

Informations générales

Titre de l'étude : A Phase 3 Randomized, Placebo-controlled Trial to Evaluate the Safety and Efficacy of Pembrolizumab (MK-3475) and Lenvatinib (E7080/MK-7902) Versus Pembrolizumab Alone as First-line Intervention in Participants With Advanced Melanoma

Traitement : Métastatique ou localement avancé

Type d'étude : Hors ciblage moléculaire

Phase : III **Stade** : Localement avancé à Métastasique **Ligne(s)** : 1

Schéma : The purpose of this study is to assess the safety and efficacy of pembrolizumab (MK-3475) combined with lenvatinib (MK-7902/E7080) compared to pembrolizumab alone (with placebo for lenvatinib) as first-line treatment in adults with no prior systemic therapy for their advance melanoma.

The primary study hypotheses are that: 1) The combination of pembrolizumab and lenvatinib is superior to pembrolizumab and placebo as assessed by Progression-free Survival (PFS) per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1), and 2) The combination of pembrolizumab and lenvatinib is superior to pembrolizumab and placebo as assessed by Overall Survival (OS). For this study, RECIST 1.1 has been modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ.

Spécialités / Localisations

Spécialité n°1 : Peau

CIM10 - Localisation n°1 : **C43** - Mélanome malin de la peau

Critères

Critères d'inclusion : - Has histologically or cytologically confirmed melanoma
- Has unresectable Stage III or Stage IV melanoma, as per American Joint Committee on Cancer guidelines, not amenable to local therapy
- Has been untreated for advanced or metastatic disease except as follows: a. proto-oncogene B-Raf (BRAF) V600 mutation-positive melanoma may have received standard of care targeted therapy as first-line therapy for advanced or metastatic disease. b. Prior adjuvant or neoadjuvant therapy, with targeted therapy or immunotherapy (such as anti-cytotoxic T-lymphocyte-associated protein 4 [CTLA-4], anti-programmed cell death 1 [anti-PD-1] therapy or Interferon) will only be permitted if relapse did not occur during active treatment or within 6 months of treatment discontinuation.
- Has an Eastern Cooperative Oncology Group (ECOG) performance status 0 to 1
- Has the presence of >=1 measurable lesion by computed tomography (CT) or magnetic resonance imaging (MRI) per RECIST 1.1
- Provides a tumor biopsy. Participants must submit tumor sample during Screening for confirmation of adequacy of tumor tissue at a central pathology laboratory. Participants who do not submit a tumor tissue sample will not be randomized. The tumor biopsy may not be obtained from a lone target lesion. Confirmation of presence of tumor tissue is not required prior to randomization.

- Has resolution of toxic effect(s) of the most recent prior therapy to Grade 1 or less (except alopecia). If participant received major surgery or radiation therapy of >30 Gray (Gy), they must have recovered from the toxicity and/or complications from the intervention.
- Male participants must agree to use contraception during the treatment period and for at least 120 days after the last dose of study treatment and refrain from donating sperm during this period
- Female participants must not be pregnant, not breastfeeding, and >=1 of the following conditions applies: a. Not a woman of childbearing potential (WOCBP) OR b. A WOCBP who agrees to use study-approved contraception during the treatment period and for at least 120 days after the last dose of study treatment
- Has adequately controlled blood pressure (BP) with or without antihypertensive medications, defined as BP <=150/90 mmHg at screening and no change in antihypertensive medications within 1 week before Cycle 1 Day 1
- Has adequate organ function

Critères de non-inclusion : - Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy (in dosing exceeding 10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within 7 days before the first dose of study treatment.
- Has a known additional malignancy that is progressing or requires active treatment. Exceptions include early stage cancers (carcinoma in situ or Stage 1, non-ulcerated primary melanoma <1 mm in depth with no nodal involvement) treated with curative intent, basal cell carcinoma of the skin, squamous cell carcinoma of the skin, in situ cervical cancer, or in situ breast cancer that has undergone potentially curative therapy.
- Has known active central nervous system metastases and/or carcinomatous meningitis
- Has ocular melanoma
- Has known hypersensitivity to active substances or any of their excipients including previous clinically significant hypersensitivity reaction to treatment with another monoclonal antibody
- Has an active autoimmune disease that has required systemic treatment in past 2 years (i.e., with use of disease-modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (e.g. thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment.
- Has an active infection requiring systemic therapy
- Has known history of human immunodeficiency virus (HIV) infection
- Has known history of or is positive for hepatitis B virus or hepatitis C virus infection
- Has a history of (non-infectious) pneumonitis that required steroids or current pneumonitis
- Has a history of active tuberculosis (Bacillus tuberculosis)
- Has presence of gastrointestinal condition including malabsorption, gastrointestinal anastomosis, or any other condition that might affect the absorption of lenvatinib
- Has had a major surgery within 4 weeks prior to Cycle 1 Day 1. Adequate wound healing after major surgery must be assessed clinically and have resolved completely prior to Cycle 1 Day 1.
- Has a pre-existing Grade >=3 gastrointestinal or non-gastrointestinal fistula
- Has radiographic evidence of major blood vessel invasion/infiltration
- Has clinically significant hemoptysis or tumor bleeding within 2 weeks prior to the first dose of study treatment
- Has clinically significant cardiovascular disease within 12 months of the first dose of study treatment including New York Heart Association Class III or IV congestive heart failure, unstable angina, myocardial infarction, cerebral vascular accident, or cardiac arrhythmia associated with hemodynamic instability
- Has received prior systemic treatment for unresectable or metastatic melanoma other than targeted therapy as noted in Inclusion Criteria above
- Has received prior therapy with a monoclonal antibody, chemotherapy, or an investigational agent or device within 4 weeks or 5 half-lives (whichever is longer) before administration of study treatment or not recovered (<=Grade 1 or at Baseline) from adverse events due to previously administered agents.

Exception to this rule would be use of denosumab, which is not excluded. Note: Participants with alopecia and <=Grade 2 neuropathy are an exception and may enroll.
- Has received prior radiotherapy within 2 weeks of first dose of study treatment (Cycle 1 Day 1) with the exception of palliative radiotherapy to bone lesions, which is allowed if completed 2 weeks prior to Cycle 1 Day 1. Participants must have recovered from all radiation-related toxicities, not require corticosteroids, and not have had radiation pneumonitis.
- Has received live vaccine within 30 days before the first dose of study treatment
- Is currently participating in or has participated in a study of an investigational agent or has used an investigational device within 4 weeks prior to the first dose of study treatment
- Has had an allogeneic tissue/solid organ transplant

Informations promoteur

Nom du promoteur : MERCK

Type de promoteur : Industriel

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Informations centre investigateur n°1

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Statut de l'essai : OUVERT

Liens utiles

ClinicalTrials.gov (anglais) : https://clinicaltrials.gov/ct2/show/NCT03820986