Essai Clinique

Généré le 02 mai 2024 à partir de

Titre	Étude de phase I/II sur le durvalumab (MEDI4736) + trémélimumab + radiothérapie stéréotaxique corporelle pour les carcinomes métastatiques de la tête et du cou
Protocole ID	OZM-088 / ESR-16-12361
ClinicalTrials.gov ID	NCT03283605
Type(s) de cancer	ORL
Phase	Phase I-II
Type étude	Traitement
Médicament	Durvalumab + Tremelimumab
Institution	CENTRE HOSPITALIER DE L'UNIVERSITE DE MONTREAL
Ville	Montréal
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Statut	Fermé
Date d'activation	17-07-2018
But étude	Immunotherapy targeting the PD-1/PD-L1 pathway had previously been shown to be efficacious in the treatment of patients with metastatic head and neck squamous cell carcinomas. Stereotactic Body Radiotherapy (SBRT) to metastatic lesions causes localized cancer cell killing and the release of cancer cell debris, which could stimulate the immune system in the presence of immunotherapy. The purpose of this study is to assess the tolerability and efficacy of combining Durvalumab (MEDI4736), Tremelimumab and SBRT in controlling cancer progression. SBRT will be administered to patients while they are receiving Durvalumab and Tremelimumab.
Critères d'éligibilité	• Pathologically (histologically or cytologically) confirmed diagnosis HNSCC at a metastatic site. This includes histologic variants of SCC such as spindle cell carcinoma, poorly differentiated keratin-positive carcinoma, and lymphoepithelioma. The pathology can come from the most accessible site. • ≥2 measurable metastatic extracranial lesions (using RECIST version 1.1) that are treatable by SBRT. • Failure of first line systemic treatment • ≤ 4 prior treatment lines with systemic therapy • ≥2 measurable disease (RECIST) consisting of extracranial metastatic lesions (no brain metastasis) that are treatable by SBRT. • ≤ 10 metastatic lesions • Life expectancy > 24 weeks • Evaluation by a radiation oncologist within 45 days prior to study registration • Evaluation by a medical oncologist within 45 days prior to study registration • Body weight >30kg • The following imaging workup to document metastases within 45 days prior to study registration: • CT scans of the chest, abdomen and pelvis OR whole body PET/CT • ≥ 18 years of age at time of study entry • Up to 4 prior treatment lines with systemic therapy are allowed • Eastern Cooperative Oncology Group/World Health Organisation (ECOG/WHO) performance status score of ≤ 1 • Patients with locoregional recurrence(s) can be included only if they have evidence of distant metastasis; patients with locoregional recurrences which are symptomatic and/or potentially

affect quality of life may undergo palliative radiation therapy to this region prior to enrollment on the protocol at the discretion of the treating physician. However, a minimum of 6 weeks must elapse before receiving protocol treatment.
- Adequate normal organ and marrow function as defined below:
- Haemoglobin ≥ 9.0 g/dL
- Absolute neutrophil count (ANC ≥ 1.5 (or 1.0) x (> 1500 per mm3)
- Platelet count ≥ 100 (or 75) x 109/L (>75,000 per mm3)
- Serum bilirubin ≤ 1.5 x institutional upper limit of normal (ULN). This will not apply to subjects with confirmed Gilbert's syndrome (persistent or recurrent hyperbilirubinemia that is predominantly unconjugated in the absence of hemolysis or hepatic pathology), who will be allowed only in consultation with their physician.
- AST (SGOT)/ALT (SGPT) ≤ 2.5 x institutional upper limit of normal unless liver metastases are present, in which case it must be ≤ 5x ULN
- Serum creatinine CL>40 mL/min by the Cockcroft-Gault formula (Cockcroft and Gault 1976) or by 24-hour urine collection for determination of creatinine clearance (calculated by study site staff)
- Evidence of post-menopausal status or negative urinary or serum pregnancy test for female pre-menopausal patients. Women will be considered post-menopausal if they have been amenorrheic for 12 months without an alternative medical cause. The following age-specific requirements apply:
- Women <50 years of age would be considered post-menopausal if they have been amenorrheic for 12 months or more following cessation of exogenous hormonal treatments and if they have luteinizing hormone and follicle-stimulating hormone levels in the post-menopausal range for the institution or underwent surgical sterilization (bilateral oophorectomy or hysterectomy).
- Women ≥50 years of age would be considered post-menopausal if they have been amenorrheic for 12 months or more following cessation of all exogenous hormonal treatments, had radiation-induced menopause with last menses >1 year ago, had chemotherapy-induced menopause with last menses >1 year ago, or underwent surgical sterilization (bilateral oophorectomy, bilateral salpingectomy or hysterectomy).
- Patient is willing and able to give written informed consent, prior to performing any protocol-related procedures, including screening evaluations.
- Patient is willing and able to comply with the protocol for the duration of the study including undergoing treatment and scheduled visits and examinations including follow up.
- Patients who have received prior anti-PD-1, anti PD-L1 or anti CTLA-4, including durvalumab and tremelimumab if the following are fulfilled:
- Must not have experienced a toxicity that led to permanent discontinuation of prior immunotherapy.
- All AEs of prior immunotherapy must have completely resolved or resolved to baseline prior to screening for this study.
- Must not have experienced a ≥ Grade 3 immune related AE or an immune related neurologic or ocular AE of any grade while receiving prior immunotherapy.
- Must not have required the use of additional immunosuppression other than corticosteroids for the management of an AE and not have experienced recurrence of an AE if re-challenged.

Critères d'exclusion

- Involvement in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff at the study site)
- Nasopharyngeal carcinoma
- Concurrent enrolment in another clinical study, unless it is an observational (non-interventional) clinical study or during the follow-up period of an interventional study.
- >4 prior treatment lines with systemic therapy
- Receipt of the last dose of anti-cancer therapy (chemotherapy, immunotherapy, endocrine therapy, targeted therapy, biologic therapy, tumour embolization, monoclonal antibodies) ≤ 30 days prior to the first dose of study drug. If sufficient wash-out time has not occurred due to the schedule or PK properties of an agent, a longer wash-out period will be required, as agreed by AstraZeneca/MedImmune and the investigator.
- Any unresolved toxicity NCI CTCAE Grade ≥2 from previous anticancer therapy with the exception of alopecia, vitiligo, and the laboratory values defined in the inclusion criteria
- Patients with Grade ≥2 neuropathy will be evaluated on a case-by-case basis after consultation with the Study Physician.
- Patients with irreversible toxicity not reasonably expected to be exacerbated by treatment with durvalumab or tremelimumab may be included only after consultation with the Study Physician.
- Any concurrent chemotherapy, IP, biologic, or hormonal therapy for cancer treatment. Concurrent use of hormonal therapy for non-cancer-related conditions (eg. hormone replacement therapy) is acceptable.
- Radiotherapy treatment to more than 30% of the bone marrow or with a wide field of radiation within 4 weeks of the first dose of study drug
- Major surgical procedure (as defined by the Investigator) within 28 days prior to the first dose of IP. Note: Local surgery of isolated lesions for palliative intent is acceptable.
- History of allogenic organ transplantation.
- Active or prior documented autoimmune or inflammatory disorders (including inflammatory bowel disease [eg, colitis or Crohn's disease], diverticulitis [with the exception of diverticulosis], systemic lupus erythematosus, Sarcoidosis syndrome, or Wegener syndrome [granulomatosis with polyangiitis, Graves' disease, rheumatoid arthritis, hypophysitis, uveitis, etc]). The following are exceptions to this criterion:
- Patients with vitiligo or alopecia
- Patients with hypothyroidism (eg, following Hashimoto syndrome) stable on hormone

replacement
- Any chronic skin condition that does not require systemic therapy
- Patients without active disease in the last 5 years may be included but only after consultation with the study physician
- Patients with celiac disease controlled by diet alone
- Uncontrolled undercurrent illness, including but not limited to, ongoing or active infection, symptomatic congestive heart failure, uncontrolled hypertension, unstable angina pectoris, cardiac arrhythmia, interstitial lung disease, serious chronic gastrointestinal conditions associated with diarrhea, or psychiatric illness/social situations that would limit compliance with study requirement, substantially increase risk of incurring AEs or compromise the ability of the patient to give written informed consent
- History of another primary malignancy except for
- Malignancy treated with curative intent and with no known active disease ≥5 years before the first dose of IP and of low potential risk for recurrence
- Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease
- Adequately treated carcinoma in situ without evidence of disease
- History of leptomeningeal carcinomatosis
- Brain metastases or spinal cord compression. Patients with suspected brain metastases at screening should have an MRI (preferred) or CT each preferably with IV contrast of the brain prior to study entry.
- Current or prior use of immunosuppressive medication within 14 days before the first dose of durvalumab or tremelimumab. The following are exceptions to this criterion:
- Intranasal, inhaled, topical steroids, or local steroid injections (eg, intra articular injection)
- Systemic corticosteroids at physiologic doses not to exceed <<10 mg/day>> of prednisone or its equivalent
- Steroids as premedication for hypersensitivity reactions (eg, CT scan premedication)
- Receipt of live attenuated vaccine within 30 days prior to the first dose of IP. Note: Patients, if enrolled, should not receive live vaccine whilst receiving IP and up to 30 days after the last dose of IP.
- Female patients who are pregnant or breastfeeding or male or female patients of reproductive potential who are not willing to employ effective birth control from screening to 90 days after the last dose of durvalumab monotherapy or180 days after the last dose of durvalumab + tremelimumab combination therapy.
- Known allergy or hypersensitivity to any of the study drugs or any of the study drug excipients.
- Past medical history of ILD, drug-induced ILD, radiation pneumonitis which required steroid treatment, or any evidence of clinically active interstitial lung disease.
- Judgment by the investigator that the patient is unsuitable to participate in the study and the patient is unlikely to comply with study procedures, restrictions and requirements.
- Female patients who are pregnant or breastfeeding or male or female patients of reproductive potential who are not willing to employ effective birth control from screening to 180 days after the last dose of durvalumab + tremelimumab combination therapy or 90 days after the last dose of durvalumab monotherapy, whichever is the longer time period.