Essai Clinique

Généré le 19 mai 2024 à partir de

Titre	An Open Label Phase II Randomized Trial of BNT113 in Combination With Pembrolizumab Versus Pembrolizumab Monotherapy as a First Line Therapy in Patients With Unresectable Recurrent, or Metastatic Head and Neck Squamous Cell Carcinoma (HNSCC) Which is Positive for Human Papilloma Virus 16 (HPV16+) and Expresses PD-L1
Protocole ID	AHEAD-MERIT
ClinicalTrials.gov ID	NCT04534205
Type(s) de cancer	ORL
Phase	Phase II
Type étude	Clinique
Médicament	BNT113 en association avec pembrolizumab versus pembrolizumab seul
Institution	CENTRE UNIVERSITAIRE DE SANTE MCGILL H SITE GLEN 1001 boul. Décarie , Montréal, QC, H4A 3J1
Ville	
Investigateur principal	Dr Nathaniel Bouganim
Coordonnateur	Anna Lysina 514-934-1934 poste 35391
Statut	Actif en recrutement
Date d'activation	14-10-2023
But étude	An open-label, controlled, multi-site, interventional, 2-arm, Phase II trial of BNT113 in combination with pembrolizumab vs pembrolizumab monotherapy as first line treatment in patients with unresectable recurrent or metastatic HPV16+ HNSCC expressing programmed cell death ligand -1 (PD-L1) with combined positive score (CPS) ≥1.**This trial has two parts :** **Part A**, an initial non-randomized Safety Run-In Phase to confirm the safety and tolerability at the selected dose range level of BNT113 in combination with pembrolizumab. **Part B**, the Randomized part of the trial to generate pivotal efficacy and safety data of BNT113 in combination with pembrolizumab versus pembrolizumab monotherapy in the first line setting in patients with unresectable recurrent or metastatic HPV16+ HNSCC expressing PD-L1 with CPS ≥1For Part B, an optional pre-screening phase is available for all patients where patients' tumor samples may be submitted for central HPV16 DNA and central PD-L1 expression testing prior to screening into the main trial.
Critères d'éligibilité	**Pre-screening phase (optional - patients can alternatively perform tumor biomarker testing as part of the main screening phase):** • Patients must sign the written pre-screening informed consent form (ICF) before any pre-screening procedures. • Patients must have histologically confirmed recurrent or metastatic HNSCC with no prior systemic anticancer therapy administered in the recurrent or metastatic (R/M) setting. • Patients have a clinical situation at a relatively high risk of developing R/M disease. • Patients do not meet any exclusion criteria for the main clinical trial, except for time-dependent (e.g., prior systemic treatment in the prior 6 months) or potentially reversible conditions that in the opinion of the investigator will be resolved prior to potential enrollment into the main phase. **Main trial:** • Patients must sign the written informed consent form before any screening procedure. Informed consent must be documented before any trial-specific screening procedure is performed.

- Patients must be aged ≥18 years on the date of signing the informed consent.
- Patients must be willing and able to comply with scheduled visits, treatment schedule, laboratory tests, and other requirements of the trial.
- Patients who present histologically confirmed recurrent or metastatic HPV16+ HNSCC that is considered incurable by local therapies.
- Patients who have a tumor that expresses PD-L1 [CPS ≥1] as determined by the approved test PD-L1 IHC 22C3 pharmDx kit performed and evaluated according to the manufacturer's specifications and relevant regulatory approvals.
- The eligible primary tumor locations are oropharynx, oral cavity, hypopharynx, and larynx.
- Patients must not have had prior systemic anticancer therapy administered in the incurable recurrent or metastatic setting. Systemic therapy which was completed more than 6 months prior to randomization, if given as part of multimodal treatment for locally advanced disease, is allowed.
- Patients who have measurable disease based on RECIST 1.1 as determined by the site and confirmed by BICR. Tumor lesions situated in a previously irradiated area may be considered measurable, if progression has been demonstrated in such lesions disease by RECIST 1.1.
- Patients have Eastern Cooperative Oncology Group (ECOG) performance status ≤1.
- Patients have adequate bone marrow function as defined by hematological parameters.
- Patients have adequate hepatic function.
- Patients should have adequate kidney function, assessed by the estimated glomerular filtration rate (eGFR) ≥30 mL/min/1.73m^2 using the Chronic Kidney Disease Epidemiology Collaboration (CPK-EPI) equation.
- Patients should be stable with adequate coagulation, as determined by the investigator.
- All patients must provide a tumor tissue sample (formalin fixed paraffin embedded [FFPE] blocks or both slides and curls) from archival tissue, or fresh biopsy if a biopsy is performed as part of the patient's standard clinical practice before the first dose of trial treatment.
- Women of childbearing potential (WOCBP) must not be pregnant. WOCBP, male patients who are sexually active with WOCBP and female partners of male patients should use a highly effective method of contraception up to at least 6 months after receiving the last dose of trial treatment, and should agree not to donate eggs (ova, oocytes) or sperm.

Critères d'exclusion

Medical conditions:

- Patients are pregnant or breastfeeding.
- Patients present primary tumor site of nasopharynx (any histology).
- Patients with uncontrolled intercurrent illness, including but not limited to:
    - Ongoing or active infection which requires systemic treatment with antibiotics on the first dose of trial treatment.
    - Symptomatic congestive heart failure (Grade III or IV as classified by the New York Heart Association), myocardial infarction within 3 months before screening, unstable angina pectoris, or cardiac arrhythmia.
    - Arterial thrombosis or pulmonary embolism within ≤6 months before the start of trial treatment, if not on a stable dose of anticoagulants or if in the opinion of the investigator contra-indicates trial inclusion.
    - Evidence or history of interstitial lung disease that, in the opinion of the investigator, is a contraindication for treatment with pembrolizumab, or active non-infectious pneumonitis.
    - Uncontrolled hypertension defined as systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥100 mmHg, despite optimal medical management. Patients with arterial hypertension need to be on stable anti-hypertensive medication for at least 4 weeks prior to trial entry.
    - Known primary immunodeficiencies.
    - Evidence or history of significant autoimmune disease that (a) required treatment with systemic immunosuppressive treatments, (b) was associated with ongoing treatment with corticosteroids, or (c) was associated with a record of significant end-organ dysfunction (even if transient), which in the opinion of the investigator may suggest increased risk for immune-related AEs.
    - Patients with prior allogeneic stem cell or solid organ transplantation.
    - Any other disease, metabolic dysfunction, physical examination finding, and/or laboratory finding giving reasonable suspicion of a disease or condition that in the opinion of the investigator contraindicates the use of an investigational drug or may render the patient at high risk for complications.
- Patients with a known allergy, hypersensitivity, or intolerance to BNT113 or its excipients, or to pembrolizumab or its excipients.
- Patients who have had a splenectomy.
- Patients who have had major surgery (e.g., requiring general anesthesia) within 4 weeks before screening, or have not fully recovered from surgery, or have major surgery planned during the time of trial participation.
- Patients who have a known history or a positive test at screening of any of the following:
    1. Human immunodeficiency virus (HIV) 1 or 2. Inclusion is allowed if HIV 1/2 infection is adequately controlled and stable on a highly effective antiviral regimen.
    2. Hepatitis B infection, as defined by the presence of hepatitis B surface antigen (HbsAg) or hepatitis B virus (HBV) DNA positivity. Testing of HBV DNA is mandatory if hepatitis B core antibody is positive.
    3. Hepatitis C (unless considered cured).
- Patients with another primary malignancy that has not been in complete remission for at least 2 years, with the exception of those with a negligible risk of metastasis or death (such as

adequately treated carcinoma in situ of the cervix, non-invasive basal or non-invasive squamous cell skin cancer, localized prostate cancer, non-invasive superficial bladder cancer or breast ductal carcinoma in situ).
- Patients with any condition for which, in the opinion of the investigator, participation would not be in the best interest of the patient (e.g., compromise the well-being) or that could prevent, limit, or confound the protocol-specified assessments.

Prior/concomitant therapy:

- Patients who have received or currently receive the following therapy/medication:
    1. Chronic systemic immunosuppressive treatment including corticosteroid treatment (prednisone >10 mg daily orally [PO] or intravenously [IV], or equivalent) in the 7 days prior to the first dose of trial treatment.
    2. Prior treatment with other immune modulating agents that was (a) within fewer than 4 weeks (28 days) or 5 half-lives of the agent (whichever is longer) prior to the first dose of BNT113, or (b) associated with immune-mediated AEs that have not resolved prior to the first dose of BNT113 or that pose an additional risk of on-trial complications, per investigator's assessment, or (c) associated with toxicity that resulted in discontinuation of the immune-modulating agent and that poses an additional risk of on-trial complications, per investigator's assessment.
    3. Prior treatment with live attenuated vaccines within 4 weeks before the first dose of BNT113.
    4. Prior treatment with an investigational drug (including investigational vaccines) within 4 weeks or 5 half-lives of the agent (whichever is longer) before the planned first dose of BNT113.
    5. Ongoing treatment with therapeutic PO or IV antibiotics. • Note: Patients receiving prophylactic antibiotics (e.g., for prevention of a urinary tract infection or chronic obstructive pulmonary disease) may be enrolled.
- Prior treatment with anti-cancer immunomodulating agents, such as blockers of programmed death receptor-1 (PD-1), PD-L1, tumor necrosis factor receptor superfamily member 9 (TNRSF9, 4 1BB, CD137), OX 40, therapeutic vaccines, cytokine treatments, or any investigational agent within 4 weeks or 5 half-lives of the agent (whichever is longer) before the first dose of BNT113.
- Treatment with non-systemic anti-cancer therapy (e.g., radiotherapy or surgery) within 2 weeks prior to randomization.
    - Note: Prior treatment with bone resorptive therapy, such as bisphosphonates (e.g., pamidronate, zoledronic acid) and denosumab, is allowed.

Other comorbidities:

- Current evidence of Common Terminology Criteria for Adverse Events (CTCAE) v5.0 Grade >1 toxicity before the start of treatment, except for hair loss and those Grade 2 toxicities listed as permitted in other eligibility criteria. Patients with Grade 2 neuropathy may be eligible at investigator's discretion.
- Current evidence of new or growing brain or spinal metastases during screening. Patients with known brain or spinal metastases may be eligible if they:
    - had radiotherapy or another appropriate therapy for the brain or spinal metastases,
    - have no neurological symptoms (excluding Grade ≤2 neuropathy),
    - have no evidence of clinical or radiological progression within 4 weeks before signing the informed consent,
    - do not require steroid therapy within 7 days before randomization or are undergoing slow steroid tapering, currently at doses ≤10 mg and neurologically stable.
    - spinal bone metastases are allowed, unless imminent fracture or cord compression is anticipated.

Other exclusions:

- Patients who have previously been enrolled in this trial (rescreening is allowed once).
- Patients with substance abuse or known medical, psychological, or social conditions that in the opinion of the investigator may interfere with the patient's participation in the trial or evaluation of the trial results.
- Patients affiliated with the investigational site (e.g., a close relative of the investigator or dependent person, such as an employee or student of the trial site) or sponsor. For patients meeting this criterion, a prospective exception and eventual contingencies to be put in place may be defined on a case-by-case basis by the local Institutional Review Board.

Tumor-related conditions:

- Patients that have disease suitable for local therapy administered with curative intent.
- Patients that have a life expectancy of less than 3 months and/or have rapidly progressive disease, as assessed by the treating investigator.
- Patients with high-burden of visceral metastatic disease or location in anatomically critical areas (e.g., causing significant biliary or respiratory obstruction), that in the opinion of the investigator may benefit from treatment with chemotherapy.