Essai Clinique

Généré le 05 mai 2024 à partir de

Titre	Étude de phase 1b évaluant l'ASP1951, un anticorps agoniste du récepteur du TNF induit par glucocorticoïde (GITR), en monothérapie et en association avec le pembrolizumab chez des sujets atteints de tumeurs solides au stade avancé
Protocole ID	1951-CL-0101 (KEYNOTE KN-B02)
ClinicalTrials.gov ID	NCT03799003
Type(s) de cancer	Tumeurs solides
Phase	Phase I
Stade	Maladie avancée ou métastatique
Type étude	Clinique
Médicament	ASP1951 seul et en association avec le pembrolizumab
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Ville	
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But étude	The primary purpose of this study is to evaluate the tolerability and safety profile of ASP1951 when administered as a single agent and in combination with pembrolizumab in participants with locally advanced (unresectable) or metastatic solid tumors; characterize the pharmacokinetic profile of ASP1951 when administered as a single agent and in combination with pembrolizumab; and determine the recommended phase 2 dose (RP2D) of ASP1951 and/or maximum tolerated dose (MTD) when administered as a single agent and in combination with pembrolizumab. This study will also evaluate the anti-tumor effect of ASP1951 when administered as a single agent and in combination with pembrolizumab.

Critères d'éligibilité	• Subject has locally-advanced (unresectable) or metastatic solid tumor malignancy (no limit to the number of prior treatment regimens) that is confirmed by available pathology records or current biopsy as well as the following:
	  • Subject in the escalation cohort has received all standard therapies (unless the therapy is contraindicated or intolerable) felt to provide clinical benefit the subject's specific tumor type. OR
	  • Subject in an expansion cohort has received at least 1 standard therapy for the subject's specific tumor type.
	• Subject has an Eastern Cooperative Oncology Group (ECOG) Performance Status of 0, 1 or 2.
	• Subject's last dose of prior antineoplastic therapy, including any immunotherapy, was 21 days or 5-half-lives, whichever is shorter, prior to initiation of study drug administration. A subject with epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) mutation-positive NSCLC is allowed to remain on EGFR tyrosine kinase inhibitor (TKI) or ALK inhibitor therapy until 4 days prior to the start of study drug administration.
	• Subject has completed any radiotherapy (including stereotactic radiosurgery) at least 2 weeks prior to study drug administration.
	• Subject's AEs (excluding alopecia) from prior therapy have improved to grade 1 or baseline within 2 weeks prior to start of study treatment.
	• Subject with metastatic castration-resistant prostate cancer (mCRPC) (positive bone scan

and/or soft tissue disease documented by computed tomography [CT]/magnetic resonance imaging [MRI]) meets both of the following:
    - Subject has serum testosterone ≤ 50 ng/dL at Screening.
    - Subject has had a bilateral orchiectomy or plans to continue androgen deprivation therapy (ADT) for the duration of study treatment.
- Subject has adequate organ function prior to start of study treatment. If a subject has received a recent blood transfusion, the laboratory tests must be obtained ≥ 4 weeks after any blood transfusion.
- A female subject is eligible to participate if she is not pregnant and at least 1 of the following conditions applies:
    - Not a woman of childbearing potential (WOCBP); OR
    - WOCBP who agrees to follow the contraceptive guidance throughout the treatment period and for at least 6 months after the final study drug administration.
- Female subject must agree not to breastfeed starting at Screening and throughout the study treatment, and for 6 months after the final study drug administration.
- Female subject must not donate ova starting at Screening and throughout the study treatment, and for 6 months after the final study drug administration.
- A male subject with female partner(s) of childbearing potential must agree to use contraception during the treatment period and for at least 6 months after the final study drug administration.
- A male subject must not donate sperm during the treatment period and for at least 6 months after the final study drug administration.
- Male subject with a pregnant or breastfeeding partner(s) must agree to remain abstinent or use a condom for the duration of the pregnancy or time partner is breastfeeding throughout the study period and for 6 months after the final study drug administration.
- Subject agrees not to participate in another interventional study while receiving study drug (Subjects who are currently in the follow-up period of an interventional clinical trial are allowed).

Additional Inclusion Criteria for Subjects in the Expansion Cohorts:

- Subject has at least 1 measureable lesion per RECIST 1.1. Lesions situated in a previously irradiated area are considered measurable if progression has been demonstrated in such lesions. Subjects with mC RPC who do not have measurable lesions must have at least 1 of the following:
    - Progression with 2 or more new bone lesions; or
    - Prostate-specific antigen (PSA) progression (defined as a minimum of 3 rising PSA levels with an interval of ≥ 1 week between each determination) within 6 weeks prior to study drug administration and a PSA value at the screening visit ≥ 2 ng/mL.
- Subject consents to provide available tumor specimen in a tissue block or unstained serial slides obtained within 56 days prior to first dose of study treatment. Note: This does not apply to subjects with mCRPC who do not have measurable disease.
- Subject is an appropriate candidate for tumor biopsy and consents to undergoing a tumor biopsy (core tissue biopsy or excision) during the treatment period as indicated in the Schedule of Assessments. Note: This does not apply to subjects with mCRPC who do not have measurable disease.
- Subject meets one of the following:
    - Subject has the tumor type for which a confirmed response was observed in a monotherapy or combination therapy cohort; or
    - Subject has SCCHN and a combination therapy expansion cohort is opened due to achieving the predicted efficacious exposure or
    - Subject has NSCLC, SCCHN, colorectal cancer, melanoma or cervical cancer and RP2D combination therapy expansion cohorts are opened.

Additional Inclusion Criteria for Re-treatment:

- Subject stopped initial treatment with ASP1951 or ASP1951 in combination with pembrolizumab after attaining a confirmed CR, PR or SD.
- Subject experienced an investigator-determined iCPD after stopping their initial treatment with ASP1951 or ASP1951 in combination with pembrolizumab.
- Subject did not receive any prohibited anti-cancer treatment since the last dose of ASP1951 or ASP1951 in combination with pembrolizumab.
- Subject did not experience a toxicity that met treatment discontinuation criteria during the initial treatment with ASP1951 or ASP1951 in combination with pembrolizumab or pembrolizumab alone.

Critères d'exclusion

- Subject weighs < 45 kg.
- Subject has received investigational therapy (other than an investigational EGFR TKI in a subject with EGFR activating mutations or ALK inhibitor in a subject with an ALK mutation) within 21 days or 5-half-lives, whichever is shorter, prior to start of study drug.
- Subject requires or has received systemic steroid therapy or any other immunosuppressive therapy within 14 days prior to study drug administration. Subjects using a physiologic replacement dose of hydrocortisone or its equivalent (defined as up to 30 mg per day of hydrocortisone, 2 mg per day of dexamethasone, or up to 10 mg per day of prednisone) are allowed.
- Subject has symptomatic central nervous system (CNS) metastases or subject has evidence of unstable CNS metastases even if asymptomatic (e.g., progression on scans). Subjects with previously treated CNS metastases are eligible, if they are clinically stable and have no evidence of CNS progression by imaging for at least 4 weeks prior to start of study treatment

and are not requiring immunosuppressive doses of systemic steroids (> 30 mg per day of hydrocortisone, > 2 mg per day of dexamethasone, or > 10 mg per day of prednisone or equivalent) for longer than 2 weeks.
- Subject has leptomeningeal disease as a manifestation of the current malignancy.
- Subject has an active autoimmune disease that has required systemic treatment in the past 2 years. Subjects with type 1 diabetes mellitus, endocrinopathies stably maintained on appropriate replacement therapy, and skin disorders (e.g., vitiligo, psoriasis or alopecia) not requiring systemic treatment are allowed.
- Subject was discontinued from prior immunomodulatory therapy due to a grade ≥ 3 toxicity that was mechanistically related (e.g., immune related) to the agent.
- Subject has known history of serious hypersensitivity reaction to a known ingredient of ASP1951 or pembrolizumab or severe hypersensitivity reaction to treatment with another monoclonal antibody.
- Subject with positive Hepatitis B virus (HBV) antibodies and surface antigen (indicating acute HBV or chronic HBV) or Hepatitis C ([HCV]; ribonucleic acid [RNA] detected by qualitative assay). Hepatitis C RNA testing is not required in subjects with negative Hepatitis C antibody testing. HBV antibodies are not required in subjects with negative HBV surface antigen.
- Subject has received a live vaccine against infectious diseases within 4 weeks prior to initiation of study treatment.
- Subject has a history of drug-induced pneumonitis (interstitial lung disease), a history of (non-infectious) pneumonitis that required steroids, radiation pneumonitis or currently has pneumonitis.
- Subject has an infection requiring systemic therapy within 2 weeks prior to study drug administration.
- Subject has received a prior allogeneic bone marrow or solid organ transplant.
- Subject is expected to require another form of antineoplastic therapy while on study treatment.
- Subject has had a myocardial infarction or unstable angina within 6 months prior to the start of study treatment or currently has an uncontrolled illness including, but not limited to symptomatic congestive heart failure, clinically significant cardiac disease, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements.
- Subject has received prior treatment with an anti-glucocorticoid-induced tumor necrosis factor receptor (GITR) antibody.
- Subject has had a major surgical procedure and has not completely recovered within 28 days prior to the start of study treatment.
- Subject has any condition which makes the subject unsuitable for study participation.

Additional Exclusion Criterion for Subjects in Expansion Cohorts:

- Subject has a prior malignancy, other than the current malignancy for which the subject is seeking treatment, active (i.e., requiring treatment of intervention) within the previous 2 years except for locally curable malignancies that have been apparently cured, such as basal or squamous cell skin cancer, superficial bladder cancer or carcinoma in situ of the cervix or breast.

Additional Exclusion Criteria for Re-treatment:

- Subjects who have completed 45 weeks in monotherapy or 57 weeks in combination therapy follow-up with disease control are not eligible for re-treatment.
- Subject currently has an ongoing AE related to ASP1951 or ASP1951 in combination with pembrolizumab that meets the criteria for treatment interruption or discontinuation.