Essai Clinique

Généré le 29 avr. 2024 à partir de

Titre	Étude de phase 3 à répartition aléatoire comparant le nivolumab périopératoire à l'observation chez des patients atteints d'un carcinome rénal subissant une néphrectomie
Protocole ID	REC4
ClinicalTrials.gov ID	NCT03055013
Type(s) de cancer	Rein
Phase	Phase III
Stade	Métastatique
Type étude	Traitement
Médicament	Nivolumab
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But étude	Cette étude de phase III compare la néphrectomie (ablation chirurgicale d'un rein ou d'une partie d'un rein) avec ou sans nivolumab dans le traitement de patients atteints d'un cancer du rein limité à une certaine partie du corps (localisé). L'immunothérapie au moyen d'anticorps monoclonaux, comme le nivolumab, peut aider le système immunitaire de l'organisme à attaquer le cancer et peut entraver la capacité des cellules tumorales à croître et à se propager. L'administration de nivolumab avant une néphrectomie peut réduire la taille de la tumeur et diminuer la quantité de tissu normal à retirer, tandis qu'après une néphrectomie, elle peut augmenter la survie. On ignore encore si le nivolumab et la néphrectomie sont plus efficaces que la néphrectomie seule dans le traitement du cancer du rein.
Critères d'éligibilité	**ELIGIBILITY CRITERIA FOR PREREGISTRATION (STEP 0):** • Patients with a renal mass consistent with a clinical stage >= T2Nx renal cell carcinoma (RCC) or TanyN+ RCC for which radical or partial nephrectomy is planned • Patients must have no clinical or radiological evidence of distant metastases (M0) unless the presumed M1 disease can be resected/definitively treated (e.g., thermal ablation, stereotactic radiation) at the same time or within a 12 week window from the date of the initial procedure such that the patient is considered "no evidence of disease" (M1 NED) • Permitted sites of oligo-metastases: lung, adrenal, nodes, pancreas, soft tissue or skin; liver or bone metastases are not permitted • No more than 3 metastases are permitted and all must be able to be removed or definitively treated within 12 weeks of the primary tumor resection • If histological confirmation of RCC has not been done within 12 months prior to pre-registration (Step 0), patient must be willing to undergo a core biopsy for this purpose if randomized to Arm H • NOTE: This can be a (1) standard of care diagnostic biopsy or (2) a research biopsy following assignment to Arm H or a planned metastasectomy before or after randomization; if the biopsy performed following pre-registration (Step 0) clearly demonstrates a benign condition, oncocytoma or a different type of cancer that is not RCC, the patient is not eligible for registration (Step 1); a non-diagnostic biopsy is considered a good faith effort and does not need to be repeated unless deemed clinically necessary by the treating investigator • NOTE: Patients randomized to Arm O (Observation) are permitted to register to Step 1 (Arm B)

immediately following pre-registration assignment to Arm O, regardless of whether or not they have had a standard of care diagnostic biopsy
- No prior systemic or local anti-cancer therapy for the current RCC is permitted
- Partial nephrectomy for prior RCC
- Metastasectomy for the current RCC diagnosis is not allowed unless performed to render patient NED (in addition to the planned nephrectomy) within 6 months of the current diagnosis
- Radiation therapyto the bilateral kidney or any distant metastatic sites, is not allowed unless administered to render patient NED within 6 months of the current diagnosis
- Current or past antineoplastic systemic therapies for RCC are not allowed: i.e., chemotherapy, hormonal therapy, immunotherapy, or standard or investigational agents for treatment of RCC
- Prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-CTLA-4 antibody, or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways
- Eastern Cooperative Oncology Group (ECOG) performance status: 0 or 1
- Patient must have no prior history of RCC that was resected with curative intent within the past 5 years
- Patients with a prior RCC that was treated > 5 years before, are eligible if the current tumor is consistent with a new primary in the opinion of the treating investigator
- Patients with bilateral synchronous RCCs are eligible if they can be resected or definitively treated at the same time or within a 12 week window from time of initial nephrectomy (partial or radical) or procedure and maintain adequate residual renal function; the patient is not eligible if both kidneys are completely removed and subsequent hemodialysis is required
- Permitted forms of local therapy for second tumor:
- Partial or radical nephrectomy
- If tumor is =< 3cm: thermal ablation (e.g., radiofrequency ablation, cryoablation or stereotactic radiosurgery)
- Patients cannot have concurrent malignancies, with the following exceptions:
- Adequately treated basal cell or squamous cell skin cancer
- In situ cervical cancer
- A history of superficial Ta urothelial cancer is permitted (as long as not currently undergoing treatment) whereas T1 or greater disease is excluded if < 3 years from diagnosis; concurrent persistent disease is not permitted
- Adequately treated stage I or II cancer from which the patient is currently in complete remission
- Any other cancer and stage from which the patient has been disease-free for at least 3 years prior to the time of pre-registration and as long as they are not receiving any current treatment (e.g. adjuvant or maintenance systemic or local therapy)
- Concurrent low risk prostate cancer on active surveillance
- No active known or suspected autoimmune disease; the following autoimmune disorders are permitted: patients with vitiligo, type I diabetes mellitus, controlled/stable hypothyroidism due to autoimmune or non-autoimmune conditions (hormone replacement is allowed), psoriasis not requiring systemic treatment, or other conditions not expected to recur
- No ongoing condition requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalent) or other immunosuppressive medications with the exceptions outlined below; no treatment with other immunosuppressive agents within 14 days prior to the first dose of study drug with the following exceptions:
- Topical, ocular, intra-articular, intranasal, inhaled steroids and adrenal replacement steroid doses > 10 mg daily prednisone or the equivalent are permitted in the absence of active autoimmune disease
- A brief (less than 3 weeks) course of corticosteroids (any amount) for prophylaxis (for example: contrast dye allergy) or for treatment of non-autoimmune conditions (for example: nausea, delayed-type hypersensitivity reaction caused by a contact allergen) is permitted
- No uncontrolled adrenal insufficiency
- No known chronic active liver disease or evidence of acute or chronic hepatitis B virus (HBV) or hepatitis C virus (HCV)
- No serious intercurrent illness, including ongoing or active infection requiring parenteral antibodies
- No known evidence of human immunodeficiency virus (HIV) infection, since the effects of nivolumab on anti-retroviral therapy have not been studied
- No known medical condition (e.g. a condition associated with uncontrolled diarrhea such as ulcerative colitis or acute diverticulitis) that, in the investigator's opinion, would increase the risk associated with study participation or interfere with the interpretation of safety results
- No major surgery within 28 days prior to randomization
- No patients currently enrolled in other clinical trials testing a therapeutic intervention
- No history of severe hypersensitivity to a monoclonal antibody
- Ability to understand and the willingness to sign a written informed consent document

ELIGIBILITY CRITERIA FOR RANDOMIZATION (STEP 1):

- Patients must meet all Step 0 eligibility criteria at the time of their registration to Step 1
- In patients randomized to Arm H, core tumor biopsy must demonstrate RCC of any histology, including sarcomatoid, unclassified, or "unknown histology" (if preoperative biopsy was uninformative)
- NOTE: A non-diagnostic biopsy is considered a good faith effort and does not need to be repeated unless deemed clinically necessary by the treating investigator
- Women must not be pregnant or breast-feeding, as the effects of nivolumab on the developing human fetus or in the nursing infant are unknown; all females of childbearing potential must have a blood test or urine study within 2 weeks prior to registration to rule out pregnancy; a female of childbearing potential is any woman, regardless of sexual orientation or whether they

	have undergone tubal ligation, who meets the following criteria: 1) has achieved menarche at some point 2) has not undergone a hysterectomy or bilateral oophorectomy; or 2) has not been naturally postmenopausal for at least 24 consecutive months (i.e., has had menses at any time in the preceding 24 consecutive months) • Women of childbearing potential (WOCBP) and males who are sexually active with WOCBP must use accepted and effective method(s) of contraception, or to abstain from sexual intercourse for the duration of their participation in the study; women of childbearing potential must use adequate methods to avoid pregnancy for 23 weeks after the last dose of nivolumab; sexually active males must use adequate methods to avoid pregnancy for 31 weeks after the last dose of nivolumab • White blood cells >= 2000/uL (within 8 weeks of registration) • Absolute neutrophil count (ANC) >= 1,500/mm^3 (within 8 weeks of registration) • Platelet count >= 100,000/mm^3 (within 8 weeks of registration) • Hemoglobin >= 9.0 g/dL (within 8 weeks of registration) • Serum creatinine =< 1.5 x upper limit of normal (ULN) (except subjects with Gilbert syndrome, who can have total bilirubin < 3.0 x ULN) (within 8 weeks of registration) • Total bilirubin =< 1.5 x ULN (except subjects with Gilbert syndrome, who can have total bilirubin < 3.0 x ULN) (within 8 weeks of registration) • Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) =< 2.5 x ULN (within 8 weeks of registration)
Critères d'exclusion	