Essai Clinique

Généré le 29 avr. 2024 à partir de

Titre	An Open-label, Phase 1, First-in-human, Dose Escalation and Expansion Study to Evaluate the Safety, Tolerability, Maximum Tolerated or Administered Dose, Pharmacokinetics, Pharmacodynamics and Tumor Response Profile of the Aryl Hydrocarbon Receptor Inhibitor (AhRi) BAY 2416964 in Participants With Advanced Solid Tumors
Protocole ID	20201
ClinicalTrials.gov ID	NCT04069026
Type(s) de cancer	Tumeurs solides
Phase	Phase I
Stade	Maladie avancée ou métastatique
Type étude	Clinique
Médicament	BAY 2416964
Institution	CHU DE QUEBEC – UNIVERSITE LAVAL L'HOTEL-DIEU DE QUEBEC ET CRCEO 11 Côte du Palais, Québec, QC, G1R 2J6
Ville	
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But étude	In this study researchers want to gather relevant information regarding the safety of BAY2416964 and how well the drug works in participants with a type of solid tumors that cannot be cured by currently available drugs. Researchers want to find the highest dose of BAY2416964 that participants could take without having too many side effects, how the drug is tolerated and the way the body absorbs, distributes and gets rid of the study dug. BAY2416964 is a small molecule which blocks the Aryl Hydrocarbon Receptor (a protein involved in immune cell reaction to tumor cells) allowing the body to use its immune response against the tumor cells.

Critères d'éligibilité	• Participants must be ≥18 years of age inclusive, at the time of signing the informed consent.
	• Participants with following histologically or cytologically confirmed advanced solid tumors that have progressed after treatment with all available therapies for metastatic disease that are known to confer clinical benefit, or are intolerant to treatment, or refuse standard treatment. Note: there is no limit to the number of prior treatment regimens. Immune checkpoint inhibitors are also allowed in pretreatment.
	  • Dose Escalation: all solid tumor types
	  • Tumor type-specific high-dose (MTD or MAD) Expansion cohorts: Will be grouped by tumor type, but no specific biomarker selection will be applied:
	  • NSCLC
	  • HNSCC
	  • Colorectal cancer MSS
	  • Urothelial cancer
	  • Tumor type-specific low-dose Expansion cohort: Any tumor type based on data from dose escalation and expansion indicating pharmacodynamics effect and/or clinical response from the tumor type-specific high-dose(MTD or MAD) expansion.
	• Have measurable disease per RECIST 1.1 as assessed by CT/MRI. At least one measurable lesion by RECIST 1.1 is required. Lesions situated in a previously irradiated area, or in an area subjected to other loco-regional therapy, are considered measurable if progression has been

	demonstrated in such lesions. • Life expectancy at least 12 weeks. • Eastern Cooperative Oncology Group (ECOG)performance status of 0 to 1. • Adequate bone marrow and organ function as assessed by the following laboratory tests performed within 7 days before treatment initiation. • Bone marrow reserve: • Absolute neutrophil count (ANC) ≥ 1.5 x 109/L • Hemoglobin (Hb) ≥ 9.0g/dL, without erythropoietin dependency and without packed red blood cell (pRBC) transfusion within last 2 weeks. • Platelet count ≥ 100 x 109/L. Transfusion to meet the inclusion criteria will not be allowed. • Hepatic: • Total bilirubin ≤ 1.5 x the upper limit of normal range (ULN). Known Gilbert syndrome is allowed if total bilirubin is ≤ 3 x ULN. • Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≤ 2.5 x ULN (≤ 5 x ULN for participants with liver metastases). • Albumin > 25 g/L. • Renal: --- eGFR ≥ 60 mL/min as calculated using the MDRD equation or creatinine level ≤ 1.5x ULN. • Lipase and amylase ≤ 1.5 x ULN. • Coagulation: • International normalized ratio (INR) OR prothrombin time (PT) AND activated partial thromboplastin time (aPTT) ≤ 1.5 x ULN unless the participant is receiving anticoagulant therapy as long as PT or aPTT is within therapeutic range of intended use of anticoagulants. • Adequate cardiac function, measured by echocardiography within 28 days before start of study intervention (left ventricular ejection fraction within institutional normal range for age and gender).
Critères d'exclusion	• Severe (CTCAE v.5 Grade ≥ 3) infections within 4 weeks before the first BAY2416964 administration, including but not limited to hospitalization for complications of infection, bacteremia, or severe pneumonia. Clinically active infections (CTCAE v.5 > Grade 1) within 2 weeks before the first BAY2416964 administration. • 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) is not considered a form of systemic treatment and is allowed. • Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy (in dosing exceeding 10 mg daily of prednisone or equivalent) or any other form of immunosuppressive therapy within 7 days prior the first dose of study intervention. • Congestive heart failure New York Heart Association (NYHA) greater than Class I or cardiac arrhythmias requiring anti-arrhythmic therapy other than beta blockers or calcium channel blockers. • Has known active central nervous system (CNS) metastases and/or carcinomatous meningitis. Participants with previously treated brain metastases may participate provided they are radiologically stable, i.e., without evidence of progression for at least 4 weeks by repeat imaging (note that repeat imaging should be performed during study screening), clinically stable and without requirement of steroid treatment for at least 14 days prior to first dose of study intervention. • Interstitial lung disease or chronic obstructive pulmonary disease (COPD) with ongoing signs and symptoms at the time of screening. Has a history of (non-infectious) pneumonitis that required steroids or has current pneumonitis. • Significant acute gastrointestinal disorders with diarrhea as a major symptom, e.g. Crohn's disease, malabsorption, or ≥ NCI-CTCAE v. 5.0 Grade 2 diarrhea of any etiology. • History of organ allograft transplantation, including allogeneic bone marrow transplantation. • Has received prior radiotherapy within 2 weeks before start of BAY2416964 or received radiation therapy to the lung that is > 30 Gy within 6 months before start of study intervention. Participants must have recovered from all radiation-related toxicities, not require corticosteroids, and not have had radiation pneumonitis. A 1-week washout is permitted for palliative radiation (≤2 weeks of radiotherapy) to non-CNS disease. • Treatment with systemic immunosuppressant medications (including but not limited to doses > 10 mg/day prednisone or equivalent, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor [anti-TNF] agents) within 2 weeks before the first BAY2416964 administration. The use of inhaled corticosteroids, or low doses of glucocorticoids (no more than 10 mg/day prednisone or equivalent; if a higher dose would be needed to maintain adrenal function investigator must obtain approval from sponsor), and mineralocorticoids (e.g. fludrocortisone for adrenal insufficiency) is allowed.