Essai Clinique

Généré le 16 mai 2025 à partir de

Titre	A Phase 2 Study of Blinatumomab in Combination With Nivolumab, a Checkpoint Inhibitor of PD-1, in B-ALL Patients Aged ? 1 to < 31 Years Old With First Relapse
Protocole ID	COG-AALL1821
ClinicalTrials.gov ID	NCT04546399
Type(s) de cancer	Leucémie lymphoide aiguë (LLA)
Phase	Phase II
Type étude	Clinique
Médicament	Blinatumomab en association avec le nivolumab
Institution	CENTRE HOSPITALIER UNIVERSITAIRE SAINTE-JUSTINE
Ville	
Investigateur principal	Dr Yvan Samson
Coordonnateur	
Statut	Interruption temporaire
But étude	This phase II trial studies the effect of nivolumab in combination with blinatumomab compared to blinatumomab alone in treating patients with B-cell acute lymphoblastic leukemia (B-ALL) that has come back (relapsed). Down syndrome patients with relapsed B-ALL are included in this study. Blinatumomab is an antibody, which is a protein that identifies and targets specific molecules in the body. Blinatumomab searches for and attaches itself to the cancer cell. Once attached, an immune response occurs which may kill the cancer cell. Nivolumab is a medicine that may boost a patient's immune system. Giving nivolumab in combination with blinatumomab may cause the cancer to stop growing for a period of time, and for some patients, it may lessen the symptoms, such as pain, that are caused by the cancer.

Critères d'éligibilité	• Patients must be >= 1 and < 31 years at time of enrollment
	• Patients must have first relapse of CD19+ B-ALL (relapse blasts must express CD19) in one of the following categories:
	  • Isolated bone marrow relapse
	  • Isolated central nervous system (CNS) (excluding known optic nerve/retinal and CNS chloromas) and/or testicular relapse
	  • Combined bone marrow with extramedullary relapse in the CNS (excluding known optic nerve/retinal and CNS chloromas) and/or testes
	• Patients with Down syndrome (DS) are eligible in the following categories:
	  • Isolated bone marrow relapse
	  • Combined bone marrow with CNS (excluding known optic nerve/retinal and CNS chloromas) and/or testicular relapse
	• Patients must have a performance status corresponding to Eastern Cooperative Oncology Group (ECOG) scores of 0, 1 or 2. Use Karnofsky for patients > 16 years of age and Lansky for patients =< 16 years of age
	• Patients must have fully recovered from the acute toxic effects of all prior chemotherapy, immunotherapy, or radiotherapy prior to entering this study
	  • Patients with prior blinatumomab or CD19+ chimeric antigen receptor therapy in the upfront setting will be eligible, provided relapsed lymphoblasts retain CD19 expression
	  • Radiation therapy (RT): >= 3 months must have elapsed if prior RT. This includes any patient requiring urgent radiation to any sites of extramedullary disease prior to enrollment (e.g. retinal/optic nerve involvement)
	  • Hematopoietic stem cell transplant (HSCT): Patients must not have had a prior hematopoietic stem cell transplant
	  • A single intrathecal chemotherapy at the time of relapse will be allowed. If < 7 days

	have elapsed between this intrathecal therapy (IT) and the start of protocol therapy, then the day 1 intrathecal chemotherapy (i.e. methotrexate, cytarabine, or triple intrathecal) may be omitted • In the 28 days prior to enrollment, up to five days of post-relapse, pre-enrollment therapy (steroid and/or hydroxyurea only) is permissible • Group 1 and Down syndrome patients who received pre-enrollment therapy and have a white blood count (WBC) >= 30,000/ul at the time of enrollment must receive protocol specified cytoreductive therapy with vincristine and dexamethasone, and no "washout" is required • Group 1 and Down syndrome patients who received pre-enrollment therapy and have a WBC < 30,000/ul at the time of enrollment must be given a 24 hour "washout" before starting immunotherapy • Note: There is no waiting period or "washout" for patients who relapse while receiving upfront therapy • Creatinine clearance or radioisotope glomerular filtration rate (GFR) >= 70 mL/min/1.73 m^2 OR a serum creatinine based on age/gender as follows (within 5 calendar days prior to enrollment): • Age: Maximum serum creatinine (mg/dL) • 1 to < 2 years: 0.6 (male), 0.6 (female) • 2 to < 6 years: 0.8 (male), 0.8 (female) • 6 to < 10 years: 1 (male), 1 (female) • 10 to < 13 years: 1.2 (male), 1.2 (female) • 13 to < 16 years: 1.5 (male), 1.4 (female) • >= 16 years: 1.7 (male), 1.4 (female) • Shortening fraction of >= 27% by echocardiogram, or ejection fraction of >= 50% by echocardiogram, cardiac magnetic resonance imaging (MRI) or radionuclide angiogram • No evidence of dyspnea at rest, no exercise intolerance, and a pulse oximetry > 94% if there is clinical indication for determination. • All patients and/or their parents or legal guardians must sign a written informed consent • All institutional, Food and Drug Administration (FDA), and National Cancer Institute (NCI) requirements for human studies must be met
Critères d'exclusion	• Patients with B-lymphoblastic lymphoma (B-LLy) • Patients with Burkitt leukemia/lymphoma or mature B-cell leukemia • Patients with Philadelphia chromosome positive (Ph+) B-ALL • Patients with mixed phenotype acute leukemia (MPAL) • Patients with known Charcot-Marie-Tooth disease • Patients with known MYC translocation associated with mature (Burkitt) B-cell ALL, regardless of blast immunophenotype • Patients with active, uncontrolled infection defined as: • Positive bacterial blood culture within 48 hours of study enrollment • Receiving IV or PO antibiotics for an infection with continued signs or symptoms. Note: Patients may be receiving IV or oral antibiotics to complete a course of therapy for a prior documented infection as long as cultures have been negative for at least 48 hours and signs or symptoms of active infection have resolved. For patients with clostridium (C.) difficile diarrhea, at least 72 hours of antibacterial therapy must have elapsed and stools must have normalized to baseline. • Fever above 38.2 degrees Celsius (C) within 48 hours of study enrollment with clinical signs of infection. Fever without clinical signs of infection that is attributed to tumor burden is allowed as long as blood cultures are negative for > 48 hours • A positive fungal culture within 30 days of study enrollment or active therapy for presumed invasive fungal infection • Active viral or protozoal infection requiring IV treatment • Patients known to have one of the following concomitant genetic syndromes: Bloom syndrome, ataxia-telangiectasia, Fanconi anemia, Kostmann syndrome, Shwachman syndrome or any other known bone marrow failure syndrome are not eligible. Of note, patients with known human immunodeficiency virus (HIV) infection on effective anti-retroviral therapy with undetectable viral load for at least the last 6 months prior to enrollment are eligible. Similarly, hepatitis B and hepatitis C positive patients who have been treated and have no viral detectable burden are also eligible • Patients with significant central nervous system pathology that would preclude treatment with blinatumomab, including history of severe neurologic disorder or autoimmune disease with CNS involvement • Note: Patients with a history of seizures that are well controlled on stable doses of anti-epileptic drugs are eligible Patients with a history of cerebrovascular ischemia/hemorrhage with residual deficits are not eligible. Patients with a history of cerebrovascular ischemia/hemorrhage remain eligible provided all neurologic deficits have resolved • Patients with an active known/suspected autoimmune disease are not eligible. However, patients with type I diabetes mellitus, hypothyroidism only requiring hormone replacement, skin disorders (such as vitiligo, psoriasis, or alopecia) not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger are permitted to enroll • Group 1 and DS patients with known non-hematopoietic, non-CNS/testicular extramedullary disease (i.e., chloromatous disease) are not eligible • Note: Group 2 and 3 patients with known non-hematopoietic, non-CNS/testicular extramedullary disease (i.e., chloromatous disease) are eligible provided that this is

NOT the only site of relapsed disease

- Female patients of childbearing potential are not eligible unless a negative pregnancy test result has been obtained within 7 days prior to enrollment. Patients who are sexually active and of reproductive potential are not eligible unless they agree to use an effective contraceptive method for the duration of this study. Men with female partners of childbearing potential should use effective contraception during the duration of their treatment. The effect of blinatumomab on fertility has not been evaluated. Blinatumomab is not recommended for pregnant women or women of childbearing potential (WOCBP) not using contraception. Females of reproductive potential must use effective contraception during treatment and for at least 48 hours after the last dose of blinatumomab. Studies in animal models have shown that nivolumab can adversely impair pregnancy. Thus, nivolumab is expected to cause fetal harm during pregnancy. WOCBP receiving nivolumab must continue contraception for a period of at least 5 months after the last dose of nivolumab. It is unknown whether nivolumab is present in breast milk, thus breastfeeding should be discontinued while a patient is receiving nivolumab. Men receiving nivolumab and who are sexually active with WOCBP must continue contraception for 7 months after the last dose of nivolumab
- Lactating females are not eligible unless they agree not to breastfeed their infants. It is unknown whether blinatumomab or its metabolites are excreted in human breast milk. Women are not permitted to breastfeed while receiving blinatumomab and for the last 48 hours after the last blinatumomab dose. Due to the potential for serious adverse reactions in the breastfed infant, women are not permitted to breastfeed during treatment and for 5 months after the last nivolumab dose