AMGEN 20150291 CAPILANO - (dernière mise à jour : 24/01/2020)

http://archimaid.fr/index.php?action=show&id=857

Informations générales

Titre de l'étude : A Phase 2 Open-Label Study to Determine the Effect of Blinatumomab on Minimal Residual Disease in Subjects With High-risk Diffuse Large B-cell Lymphoma Post-autologous Hematopoietic Stem-cell Transplantation.

Traitement :

Type d'étude : Hors ciblage moléculaire

Phase : II **Stade** : NA **Ligne(s)** :

Schéma : This is a phase 2, multicenter, open-label, single arm estimation study in adult subjects with high-risk DLBCL in complete remission. The study will consist of up to a 28-day screening period, a run-in period of up to 24 months, a 12-week treatment period (8 weeks of blinatumomab treatment followed by a 4-week treatment free period), a 30-day safety follow-up visit after the last dose of blinatumomab, and a long-term follow-up period that begins after the safety follow-up visit is completed until 1 year from the first dose of blinatumomab. The study will enroll approximately 90 subjects in the screening period with biopsy proven, high-risk DLBCL that are positron emission tomography-computer tomography (PET-CT) negative 90 days (± 30 days) post aHSCT. During the run-in period subjects will be followed by clinic visits at regular interval for up to 24 months for monitoring of MRD status in plasma by a next generation sequencing (NGS)-based assay. It is estimated 30 subjects will be either MRD-positive at screening or become MRD-positive during the 24-month run-in period. The number of subjects enrolled may be altered in order to ensure that approximately 30 subjects are assigned to treatment with blinatumomab. Enrollment may be stopped, once approximately 30 subjects have been assigned to treatment with blinatumomab.

Drug: Blinatumomab will be supplied as 4 mL single-use sterile glass injection vials. Blinatumomab is administered as a continuous intravenous (IV) infusion.

Cycle 1 of blinatumomab treatment is 12 weeks (84 days) in duration and includes 8 weeks (56 days) of blinatumomab IV infusion followed by a 4-week (28-day) treatment-free interval. The initial dose of blinatumomab will be 9 ?g/day for the first 7 days of treatment. Blinatumomab dose will then be escalated (dose-step) to 28 ?g/day starting on day 8 (week 2) followed by a dose-step to 112 ?g/day starting on day 15 (week 3) and continuing until completion of therapy (day 57 of cycle 1).

Primary outcome:
Minimal residual disease [Time Frame: Cycle 1 is 12 weeks (84 days) in duration and includes 8 weeks (56 days) of blinatumomab IV infusion followed by a 4-week (28-day) treatment-free interval (day 57 to 84).]
To determine minimal residual disease (MRD) negative rate following blinatumomab treatment in high-risk Diffuse Large B-cell Lymphoma (DLBCL) subjects who are MRD-positive post-autologous hematopoietic stem cell transplantation (aHSCT).

Secondary outcomes:
- Progression-free survival [Time Frame: Cycle 1 is 12 weeks in duration, including 8 weeks (56 days) of blinatumomab IV infusion, followed by a 4-week (28 day) treatment-free interval (day 57 to 84). Follow up visits will then occur every 3 months for a maximum of 1 year from the first dose.]
- To describe the efficacy of blinatumomab in relation to progression-free survival
- Duration of MRD-negative status [Time Frame: Run in part 1 to determine MRD status can last up to 24 months]
- To describe the efficacy of blinatumomab in relation to MRD-negative status
- Overall Survival [Time Frame: Cycle 1 is 12 weeks in duration, including 8 weeks (56 days) of blinatumomab IV infusion, followed by a 4-week (28 day) treatment-free interval (day 57 to 84). Follow up visits will then occur every 3 months for a maximum of 1 year from the first dose.]
- To describe the efficacy of blinatumomab in relation to overall survival
- Adverse Events [Time Frame: Cycle 1 is 12 weeks in duration, including 8 weeks (56 days) of blinatumomab IV infusion, followed by a 4-week (28 day) treatment-free interval (day 57 to 84). Follow up visits will then occur every 3 months for a maximum of 1 year from the first dose.]
- Incidence, grade and severity of treatment emergent adverse events

Spécialités / Localisations

Spécialité n°1 : Tissus lymphoïde, hématopoïétique et apparentés

CIM10 - Localisation n°1 : **C85** - Lymphome non hodgkinien, de types autres et non précisés

Critères

Critères d'inclusion : Inclusion Criteria - Part 1:
- Subject has provided informed consent prior to initiation of any study-specific activities/procedures or subject's legally acceptable representative has provided informed consent prior to any study-specific activities/procedures being initiated when the subject has any kind of condition that, in the opinion of the investigator, may compromise the ability of the subject to give written informed consent.
- Age >= 18 at time of informed consent
- Biopsy-proven DLBCL excluding DLBCL that represents transformation of indolent NHL Note: Lymphoblastic Lymphoma and Burkitt Lymphoma histology are not eligible
* Subject has >= 1 characteristic feature of high-risk DLBCL:
* High-risk first complete remission (defined as interim PET-CT positive or < complete remission to frontline chemotherapy AND achieved complete remission to platinum-containing salvage)
* Relapse within 1 year of diagnosis
* Secondary aaIPI > 1
* Partial response/partial metabolic response after minimum of 2 cycles of platinum-containing salvage chemotherapy
* C-myc rearrangement
- aHSCT with high-dose chemotherapy following first (or later) salvage treatment.
- PET-CT negative (Deauville score <= 3) 90 days (± 30 days) post aHSCT
- Available relapsed and/or diagnostic pathology formalin-fixed paraffin-embedded (FFPE) tumor block or slide samples at the time of enrollment including the successful identification of malignant clone sequences by the central laboratory.
- MRD plasma sample collected <= 3 weeks after the post aHSCT PET-CT scan
- Eastern Cooperative Oncology Group (ECOG) performance status <= 2.
- Adequate organ function determined <= 3 weeks prior to enrollment defined as follows:
* Hematological: Absolute neutrophil count (ANC) >= 1.0 x 109/L Platelet count >= 75 x 109/L Hemoglobin >= 8 g/dL
* Renal: Creatinine clearance >= 50 mL/min Cockcroft-Gault equation
* Hepatic: Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) < 3 x upper limit of normal (ULN) Total bilirubin < 2 x ULN (unless Gilbert's Disease or if liver involvement with lymphoma)
- Subject will be available to complete all protocol-required study visits or procedures, and/or to comply with all required study procedures to the best of the subject's and investigator's knowledge including but not limited to:
- Completion of up to a 24-month run-in period
- Completion of all regularly scheduled study visits including blood draws for MRD assessment, clinical disease state assessment, PET-CT scans (ie, at time of MRD positivity or relapse), assignment to treatment with blinatumomab

Inclusion Criteria - Part 2:
- MRD-positive assessment (by NGS analysis) at enrollment or at any time during the run-in 1 period
- PET-CT negative (defined by Deauville criteria <= 3) at run-in 2 performed <= 3 weeks from MRD test result available to the site at run-in 1. Historical PET-CT are allowed if performed <= 6 weeks from day 1 (first dose of blinatumomab) and subject has no clinical signs or symptoms suggestive of disease progression (eg, increase in lactate dehydrogenase [LDH] not otherwise explained)
- Adequate organ function determined <= 7 days prior to treatment assignment with blinatumomab as follows:
* Hematological:ANC >= 1.0 x 109/L Hemoglobin >= 8 g/L Platelet count >= 75 x 109/L
* Renal: Creatinine clearance >= 50 mL/min Cockcroft-Gault equation
* Hepatic: AST and ALT < 3 x ULN Total bilirubin < 2 x ULN (unless Gilbert's Disease or if liver involvement with lymphoma)

Critères de non-inclusion : Exclusion Criteria - Part 1:
- Clinically relevant CNS pathology such as epilepsy, seizure, paresis, aphasia,stroke, severe brain injury, dementia, Parkinson's disease, cerebellar disease, organic brain syndrome, and psychosis
- Evidence of CNS involvement with DLBCL at disease evaluation obtained prior to starting blinatumomab

- Current autoimmune disease or history of autoimmune disease with potential of CNS involvement
- Prior anti-CD19 directed therapies
- Prior alloHSCT
- Received radiation <= 2 weeks prior to enrollment
- Infection with human immunodeficiency virus or chronic infection with hepatitis B virus (hepatitis B surface antigen positive) or hepatitis C virus (anti-hepatitis C virus positive)
- History of malignancy other than DLBCL within the past 3 years with the following exceptions:
* Malignancy treated with curative intent and with no known active disease present for >= 3 years before enrollment and felt to be at low risk for recurrence by the treating physician
* Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease
* Adequately treated cervical carcinoma in situ without evidence of disease
* Adequately treated breast ductal carcinoma in situ without evidence of disease
* Prostatic intraepithelial neoplasia without evidence of prostate cancer
* Adequately treated urothelial papillary noninvasive carcinoma or carcinoma in situ
-Subject has known hypersensitivity to immunoglobulins or any of the products or components to be administered during dosing.
- History or evidence of any other clinically significant disorder, condition or disease (with the exception of those outlined above) that, in the opinion of the investigator or Amgen physician, if consulted, would pose a risk to subject safety or interfere with the study evaluation, procedures or completion.
- Women who are pregnant or breastfeeding or planning to become pregnant or breastfeed while receiving blinatumomab and for an additional 48 hours after the last treatment dose of blinatumomab. (Females of child bearing potential should only be included after a negative highly sensitive urine or serum pregnancy test.)
- Women of childbearing potential unwilling to use an acceptable method of effective contraception while receiving blinatumomab and for an additional 48 hours after last dose of blinatumomab. Note: The pregnancy, breastfeeding and contraceptive requirements are specific to blinatumomab. The investigator is responsible for providing the subject (male and female) with pregnancy and breastfeeding (female only) avoidance requirements for other medications given during the study.
- Currently receiving treatment in another investigational device or drug study or less than 30 days since ending treatment on another investigational device or drug study. Other investigational procedures while participating in this study are excluded.

Exclusion Criteria - Part 2:
- Subject has active infection requiring systemic therapy
- Any change in the part 1 eligibility criteria during the run-in period.

Informations promoteur

Nom du promoteur : AMGEN

Type de promoteur : Industriel

Adresse : Arcs de Seine 18-20 Quai du Point du Jour - 92100 BOULOGNE BILLANCOURT

Coordonnateur : - *Mail :* - *Tél :*

Informations centre investigateur n°1

Nom du centre : Centre Henri Becquerel

Adresse : Rue d'Amiens CS 11516 76000 ROUEN

Investigateur : Hervé TILLY

TEC / ARC / IDE : Laure Gaillon - *Mail :* laure.ditullio-gaillon@chb.unicancer.fr - *Tél :* 07.67.02.99.39

Statut de l'essai : CLOS

Liens utiles

ClinicalTrials (anglais) : https://clinicaltrials.gov/ct2/show/record/NCT03298412?term=NCT03298412&cntry=FR&rank=1