BISCAY - (dernière mise à jour : 25/09/2017)

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Informations générales

Titre de l'étude : Etude de phase Ib, randomisée, en ouvert, multicentrique, multi-bras et utilisant plusieurs médicaments, portant sur la recherche des biomarqueurs chez des patients atteints de cancer de la vessie infiltrant le muscle vésical (CVIM) qui ont progressé après un traitement antérieur (BISCAY)

Traitement : Métastasique ou localement avancé

Type d'étude : Ciblage moléculaire / Innovation thérapeutique

Phase : Ib **Stade** : Métastatique **Ligne(s)** : 2, 3

Schéma : Objectif: Évaluer la sécurité et la tolérance des traitements à l'étude administrés à la sélection de patients atteints de cancer de la vessie invasif sur le plan musculaire ayant progressé suite à un traitement préalable, et confirmer la/les dose(s) pour une évaluation clinique plus approfondie

Experimental: Module A: AZD4547 Monotherapy
AZD4547 will be given orally twice daily until disease progression.
Patients who receive AZD4547 as monotherapy will have the option to cross over to durvalumab as monotherapy at the point of objective progression, as long as the following criteria are met:
1) The investigator believes it is in the patient's interest to receive durvalumab;
2) The patient consents to the continued treatment;
3) It is clinically appropriate for the patient to continue on durvalumab treatment;
4) The patient satisfies the key eligibility criteria for receiving durvalumab treatment

Experimental: Module A: Durvalumab + AZD4547
AZD4547 will be given orally twice daily until disease progression. Patients will also receive durvalumab by IV infusion once every 4 weeks

Experimental: Module B: Durvalumab + olaparib
Durvalumab will be given by IV infusion once every 4 weeks. Olaparib will be given orally twice daily

Experimental: Module C: Durvaluamb + AZD1775
Durvalumab will be given by IV infusion once every 4 weeks. AZD1775 will be given orally in approximate 12 hour intervals over 3 days (6 doses) on Days 1-3, 8-10, and 15-17 of 28 day cycles

Experimental: Module D: Durvalumab monotherapy
Durvalumab will be given by IV infusion once every 4 weeks

Experimental: Module E: Durvalumab + Vistusertib
Durvalumab will be given by IV infusion once every 4 weeks. Vistusertib will be given orally twice per day on an intermittent schedule (2 days on, 5 days off)

Spécialités / Localisations

Spécialité n°1 : Voies urinaires

CIM10 - Localisation n°1 : **C67** - Tumeur maligne de la vessie

Critères

Critères d'inclusion : Inclusion Criteria for all Modules:
- M/F >=18
- Metastatic MIBC
- 2nd/3rd line
- Failed adjuvant/neo-adjuvant chemotherapy <1 year
- 1 lesion >=10 mm at baseline in the longest diameter suitable for accurate repeated measurement
- WHO perf. status 0-1

Specific to Module A:
- M/F >=25
- Confirmation of FGFR3 mutation or FGFR fusion

Specific to Module B:
- Hgb >= 10 g/dL
- Deleterious mutation, deletion or truncation in any HRR genes

Specific to Module C:
- Tumour harbours a deletion or inactivating mutation of the CDKN2A or RB1 genes and/or amplification of CCNE1, MYC, MYCL or MYCN genes

Specific to Module E:
- Contraception must be sustained throughout treatment with vistusertib and 16 wks after last dose

Critères de non-inclusion : Exclusion Criteria for all Modules:
- Immunotherapy, chemotherapy, anticancer agents, radiotherapy <4 wks, or radiotherapy for palliation <2 wks, any study drugs <30 days.
- Major surgery <4 wk
- Unresolved toxicities from prior therapy
- Concurrent chemotherapy, immunotherapy, biologic or hormonal therapy
- Immunosuppressive drugs <28 days
- Any of the following:
1) Autoimmune disease <=2 yr
2) IBD
3) Primary immunodeficiency
4) Organ transplant requiring immunosuppressives
- Spinal cord compression or brain metastases, treated and stable & not requiring steroids for at least 4 weeks
- Severe or uncontrolled systemic disease
- Any of the following:
1) Mean QTc >=470 ms
2) Abnormalities in resting ECG
3) Factors that increase the risk of QTc prolongation or arrhythmia
4) Uncontrolled hypertension or hypotension
5) LVEF <55%
6) Atrial fibrillation
7) NYHA Grade II-IV
8) Severe valvular disease
9) Uncontrolled angina
10) Stroke/TIA <6 months
11) Acute coronary syndrome <6 months
- Any of the following laboratory values:
1) ANC <1.5x10(exp9)/L
2) Platelets <100x10(exp9)/L
3) Hgb <9.0 g/dL
4) ALT >2.5xULN or >5xULN with liver mets
5) Total bilirubin >1.5 times ULN or with Gilbert's disease >=2×ULN
6) Creatinine >1.5xULN concurrent with creatinine clearance <50 mL/min
7) Corrected CA >ULN

8) PO4 >ULN
- History of tuberculosis
- Live attenuated vaccination <30 days

For Module A:
- Prior exposure to:
1) Nitrosourea or mitomycin C <6 weeks
2) Agent with FGFR inhibition as its primary pharmacology
3)AZD4547
4) Potent inhibitors/inducers of CYP3A4, inhibitors of CYP2D6 or substrates of CYP3A4 <2 wks
- Ophthalmological criteria:
1) RPED
2) Laser treatment or intra-ocular injection for macular degeneration
3) Age-related macular degeneration
4) Retinal vein occlusion
5) Retinal degenerative disease
6) Any other clinically relevant chorioretinal defect
- Refractory nausea/vomiting, chronic GI diseases, or previous bowel resection

For Module B:
- Transfusion <120 days
- Concurrent medications that are strong inhibitors of cytochrome P450 (CYP) 3A (CYP3A) or strong inducers of CYP3A4.
- Previous treatment with PARP inhibitor, including olaparib
- Patients with history of MDS or AML

For Module C:
- Prior exposure to any of the following:
1) Nitrosourea or mitomycin C <6 wks
2) Any agent with Wee1 inhibition as its primary pharmacology
3) Prior treatment with AZD1775
- Any drugs or products known to be sensitive to CYP3A4 substrates or CYP3A4 substrates with narrow therapeutic index, or moderate to strong inhibitors/inducers of CYP3A4
- Herbal preparations
- Refractory nausea and vomiting or chronic GI diseases
- Cardiac disease <6 months

For Module E:
- Minor surgery <14 days of first dose
- Exposure to specific substrates of OATP1B1, OATP1B3, MATE1 and MATE2K <5x half-life) before treatment. Exposure to strong/moderate inhibitors of inducers of CYP3A4/5, Pgp (MDR1) and BRCP if taken within washout periods before the first dose
- Haemopoietic growth factors (filgrastim, sargramostim, GM-CSF) <14 days prior to receiving treatment
- Other mTOR inhibitors
- Renal disease or renal tubular acidosis
- Uncontrolled Type 1 or 2 diabetes

Informations promoteur

Nom du promoteur : AstraZeneca

Type de promoteur : Industriel

Adresse : - 00000 HORS FRANCE

Coordonnateur : - *Mail :* - *Tél :*

Informations centre investigateur n°1

Nom du centre : Centre François BACLESSE

Adresse : 3 avenue du Général Harris 14000 CAEN

Investigateur : Florence JOLY

TEC / ARC / IDE : Astrid LETIEMBRE - *Mail :* a.letiembre@baclesse.unicancer.fr - *Tél :*

Ouverture de l'essai : CLOS

Liens utiles

Clinicaltrials : https://clinicaltrials.gov/ct2/show/NCT02546661?titles=biscay&cntry1=EU%3AFR&phase=0&rank=1