MEDIOLA - BRCAm ovarian cancer expansion cohort (dernière mise à jour : 06/08/2019)

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Informations générales

Titre de l'étude : A Phase I/II Study of MEDI4736 (Anti-PD-L1 Antibody) in Combination with Olaparib (PARP inhibitor) in Patients with Advanced Solid Tumors

Traitement : Métastasique ou localement avancé

Type d'étude : Ciblage moléculaire / Innovation thérapeutique

Phase : I/II **Stade** : Localement avancé à Métastatique **Ligne(s)** : 2, 3

Schéma : This is a phase I/II open-label, multicenter study to evaluate the safety, tolerability, pharmacokinetics (PK) and antitumor activity of MEDI4736 in combination with olaparib in patients with advanced solid tumors, selected based on a rationale for response to olaparib.

Patients will be poly (adenosine diphosphate-ribose) polymerase (PARP)-inhibitor and immunotherapy (IMT)-naïve (defined as no prior exposure to PARP inhibitors or IMT, including, but not limited to, other anti-cytotoxic T-lymphocyte-associated protein 4 [CTLA-4], anti-programmed cell death 1 [PD-1], anti-programmed death-ligand 1 [PD-L1] monoclonal antibodies, or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways).

The 4 initial stage cohorts (Modules 1 to 4) include patients with relapsed small cell lung cancer (SCLC), germline BRCA mutated (gBRCAm) metastatic human epidermal growth factor receptor 2 (HER2)-negative breast cancer, gBRCAm platinum-sensitive relapsed ovarian cancer, and gastric cancer. Enrollment for these cohorts has been completed.

Second stage cohorts (Modules 5 to 7) will include patients with relapsed BRCAm platinum-sensitive relapsed ovarian cancer and non BRCAm platinum-sensitive relapsed ovarian cancer.

Spécialités / Localisations

Spécialité n°1 : Seins, organes génitaux de la femme

CIM10 - Localisation n°1 : **C56** - Tumeur maligne de l'ovaire

Critères

Critères d'inclusion : - Patients must have histologically or cytologically confirmed progressive advanced or metastatic gBRCAm ovarian cancer
- At least one measurable lesion that can be accurately assessed at baseline by computed tomography (CT) (or magnetic resonance imaging [MRI] suitable for assessment as per RECIST 1.1. The baseline scan must be obtained within 28 days prior to the first dose of olaparib.
- Male or female patients, age >=18 years (>=19 years for South Korea)
- Eastern Cooperative Oncology Group (ECOG) performance status 0-1
- Life expectancy >=12 weeks
- Adequate organ and marrow function
- Ability to swallow oral medications (capsules and tablets) without chewing, breaking, crushing, opening or otherwise altering

the product formulation. Patients should not have gastrointestinal illnesses that would preclude the absorption of olaparib, which is an oral agent. For the gastric cancer cohort, patients with a full or partial gastrectomy will be permitted.
- Ability of patient to understand and the willingness to sign a written informed consent document prior to any protocol related procedures, including screening evaluations.
- Female patients must either:
-> Be of non-reproductive potential OR
-> Have a negative serum pregnancy test within 28 days of study treatment and confirmed prior to treatment on Day 1, and agree to use contraception if they or their partner are of reproductive potential

Critères de non-inclusion : - Prior chemotherapy or other systemic anticancer therapy within 4 weeks prior to start of olaparib treatment, 6 weeks for nitrosoureas or mitomycin. Exceptions include: Anti-hormonal treatment for ER positive or PR positive breast cancer is allowed until 7 days prior to treatment with olaparib, exposure to an investigational agent within 30 days or 5 half-lives (whichever is the longer) prior to start of olaparib treatment is not allowed, prior receipt of biologics targeting T cell co-regulatory proteins and/or immune checkpoints is not allowed. Examples include MEDI4736 or other PD1 or PD-L1 or PD-L2 inhibitors or anti-CTLA4 therapy, previous treatment with a PARP inhibitor, is not allowed.
- Radiation therapy within 4 weeks prior to start of olaparib treatment (includes radiation targeting bone metastases) or radionuclide treatment within 6 weeks of treatment start.
- Current dependency on total parenteral nutrition or IV fluid hydration.
- Concomitant use of known strong cytochrome P450 (CYP) 3A (CYP3A) inhibitors or moderate CYP3A inhibitors. Concomitant use of known strong or moderate CYP3A inducers.
- Concomitant therapy with any other anticancer therapy or chronic use of systemic corticosteroids.
- Previous allogenic bone marrow transplant or double umbilical cord blood transplantation
- Whole blood transfusions in the last 120 days
- Known brain metastases or spinal cord compression
- Patients being considered at poor medical risk due to a serious, uncontrolled medical disorder or non-malignant systemic disease.
- Any psychiatric disorder that prohibits obtaining informed consent
- Major surgery or significant traumatic injury within 2 weeks of run-in
- Immunocompromised patients
- QTc prolongation >470 msec or other significant ECG abnormality noted within 14 days of treatment
- Pregnant and breastfeeding women are excluded.
- Involvement in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff at the study site)
- Previous enrolment in the present study
- Participation in a clinical study within 28 days or 5 half-lives of the drug, whichever is longer.

Informations promoteur

Nom du promoteur : AstraZeneca

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Ouverture de l'essai : OUVERT

Liens utiles

ClinicalTrials : https://clinicaltrials.gov/ct2/show/NCT02734004?titles=mediola&cntry=FR&rank=1