PRODIGE 58 - UCGI 35 - REGIRI (dernière mise à jour : 22/11/2019)

http://archimaid.fr/index.php?action=show&id=973

Informations générales

Titre de l'étude : Essai de phase II randomisé évaluant l'association du REGorafenib et de l'IRInotecan en deuxième ligne de traitement des patients atteints d'un adénocarcinome œsogastrique métastatique.

Traitement : Métastatique ou localement avancé

Type d'étude : Hors ciblage moléculaire

Phase : II **Stade** : Métastasique **Ligne(s)** : 2

Schéma : L' étude REGIRI est un essai PRODIGE de phase II randomisé dont l'objectif principal est de montrer un bénéfice de l'association régorafénib+irinotecan sur la survie globale(6 à 10 mois de survie : HR = 0,60) par rapport à l'irinotecan en monothérapie, des patients traités en seconde ligne d'un adénocarcinome oesogastrique métastatique. Les objectifs secondaires sont la survie sans progression, le taux de contrôle de la maladie, le taux de réponse objective ainsi que la tolérance et la qualité de vie.Actuellement après échec d'une chimiothérapie à base de 5FU et sels de platine les options thérapeutiques comprennent l'irinotecan (monothérapie ou FOLFIRI), le paclitaxel seul ou combiné au ramucirumab (mais le ramucirumab est non remboursé en France). Le Régorafénib, inhibiteur de multiples protéines kinases a déjà été évalué en monothérapie en 2ème ligne ou plus dans les cancers gastriques métastatiques avec des résultats prometteurs (essai INTEGRATE) et un essai de phase III est en cours (INTEGRATE II). Cent cinquante-quatre patients sont prévus au total ayant un adénocarcinome gastrique ou de la jonction œsogastrique, métastatique, asymptomatique, ECOG 0-1, ayant progressé après une première ligne de traitement à base de 5FU et platine.Les patients traités en 1ère ligne dans GASTFOX (FOLFOX vs TFOX) sont donc éligibles dans REGIRI à progression.

Spécialités / Localisations

Spécialité n°1 : Organes digestifs

CIM10 - Localisation n°1 : **C15** - Tumeur maligne de l'oesophage

Spécialité n°2 : Organes digestifs

CIM10 - Localisation n°2 : **C16** - Tumeur maligne de l'estomac

Critères

Critères d'inclusion : 1. Patient must have signed a written informed consent form prior to any study specific procedures
2. Patients aged >=18 years old
3. Histologically confirmed diagnosis of gastro-oesophageal adenocarcinomas: gastroesophageal junction (Siewert II and III) and gastric adenocarcinomas
4. Asymptomatic primary tumour
5. Metastatic disease
6. At least one target lesion (according to RECIST v1.1):
Unidimensionally measurable on cross-sectional imaging
In an area not previously irradiated
7. Disease progression after a fluoropyrimidine and platinum agent-based chemotherapy (5-fluorouracil or 5-fluorouracil prodrugs combined with cisplatin or oxaliplatin). For example, docetaxel combined with FOLFOX, PD-L1/PD-1 inhibitors

combined with FOLFOX, LV5-FU2-cisplatin or 5-fluorouracilcisplatin are acceptable prior therapies.
8. Eastern Cooperative Oncology Group (ECOG) performance status <=1
9. Life expectancy >3 months
10. Amylase <=1.5 x upper limit of normal (ULN) and lipase <=1.5 xULN
11. Adequate liver function:
Total bilirubin <=1.5 x ULN
Alanine aminotransferase (ALT) and aspartate
aminotransferase (AST) <=3.0 x ULN (<=5 x ULN for patients with liver metastasis)
Alkaline phosphatase (ALP) <=2.5 x ULN (<=5.0 x ULN for patients with liver or bone metastases)
12. Platelet count >=100,000/mm³; haemoglobin (Hb) >=9 g/dL; absolute neutrophil count (ANC) >=1,500/mm³. The use of blood transfusion(s) to meet the inclusion criteria will not be allowed
13. International normalised ratio (INR) <=1.5 x ULN and partial thromboplastin time (PTT) or activated partial thromboplastin time (aPTT) <=1.5 x ULN unless receiving treatment with therapeutic anticoagulation. Patients being treated with anticoagulant, e.g., heparin, are eligible if there is no evidence of an underlying abnormality with these parameters and if a close monitoring of at least weekly evaluations was performed until INR and PTT are stable based on a pre-dose measurement as defined by the local standard of care
14. Creatinine clearance (CLcr) >=50 mL/min estimated by CockcroftGault equation
15. Women of childbearing potential and men must agree to use adequate contraception during the study and for at least 3 months after the last study drug administration
16. Patients affiliated to the social security system

Critères de non-inclusion : 1. Symptomatic brain metastases or carcinomatous meningitis
2. Bone-only metastasis
3. Known and documented UGT1A1 deficiency
4. History of Gilbert's syndrome
5. Previous or concurrent cancer with a distinct primary site, other than gastro-oesophageal cancer, within 5 years prior to randomisation (except for curatively treated cervical cancer in situ, non-melanoma skin cancer, and superficial bladder tumours)
6. Persistent proteinuria >3.5 g/24 h measured by urine proteincreatinine ratio from a random urine sample (grade >=3, NCICTCAE v 5.0)
7. Interstitial lung disease with ongoing signs and symptoms at inclusion
8. Known hypersensitivity to any of the study drugs, study drug classes, or excipients
9. Non-healing wound, non-healing ulcer, or non-healing bone fracture
10. Patients with evidence or history of any bleeding diathesis, irrespective of severity
11. Any haemorrhage or bleeding event grade >=3 (NCI-CTCAE v.5.0) within 4 weeks before starting of the study treatment
12. Arterial or venous thrombotic or embolic events such as cerebrovascular accident (including transient ischemic attacks), deep vein thrombosis or pulmonary embolism within 6 month before starting the study treatment (except for adequately treated catheter-related venous thrombosis occurring more than one month before the start of study medication)
13. Previous major surgical procedure, significant traumatic injury, or radiotherapy within the 4 weeks before inclusion
14. Uncontrolled hypertension (systolic blood pressure >140 mmHg or diastolic pressure >90 mmHg) despite optimal medical management. Congestive heart failure: New York Heart Association (NYHA) >= class 2
15. Unstable angina (angina symptoms at rest), new-onset angina
(that started within the last 3 months)
16. Myocardial infarction less than 6 months before starting the study treatment
17. Uncontrolled cardiac arrhythmias
18. History of epileptic seizures requiring long-term anticonvulsant therapy
19. History of organ transplantation with use of immunosuppression therapy
20. Ongoing bacterial or fungal infection (grade >2 by NCI-CTCAE v.5.0)
21. Known history of human immunodeficiency virus (HIV) infection
22. Active hepatitis B or C, or chronic hepatitis B or C requiring treatment with antiviral therapy
23. Use of CYP3A4 inducers or inhibitors
24. Pregnant or breast-feeding women
25. Bowel malabsorption or extended bowel resection that could affect the absorption of regorafenib, occlusive syndrome, inability to take oral medications
26. Inflammatory bowel disease with chronic diarrhoea
27. Participation in another clinical trial within the 30 days before inclusion
28. Concurrent treatment with another investigational product or anticancer therapy (other than irinotecan or regorafenib)
29. Concomitant treatment with hypericum or live attenuated vaccines
30. Gastro-intestinal fistula or perforation
31. Person kept in detention or incapable of giving consent
32. Patient unwilling or unable to comply with the medical follow-up required by the study because of geographic, social, or psychological reasons

Informations promoteur

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Statut de l'essai : À VENIR

Liens utiles

FFCD : http://www.ffcd.fr/DOC/LETTRE/Lettre_Avril2019.pdf

ClinicalTrials.gov (anglais) : https://clinicaltrials.gov/ct2/show/NCT03722108