A Multicenter, Single arm, Open Label Clinical Trial to Evaluate the Safety and Health-Related Quality of Life of Aflibercept in Patients with Metastatic Colorectal Cancer (mCRC) Previously Treated with an Oxaliplatin-Containing Regimen

Published: 13-06-2012
Last updated: 26-04-2024

Primary: To provide metastatic colorectal cancer patients with access to aflibercept and todocument the overall safety in these patientsSecondary: To document the Health-Related Quality of Life of aflibercept in this patientpopulation

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON37124

Source
ToetsingOnline

Brief title
Safety and Quality of Life study: Aflibercept in patients with mCRC

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

Synonym
metastatic colorectal cancer; colorectal cancer.

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi-aventis
Source(s) of monetary or material Support: sponsor/opdrachtgever

Intervention

Keyword: Aflibercept, Colorectal cancer, Quality of life, Safety

Outcome measures

Primary outcome

- Number of patients reporting adverse events up to 30 days after the end of treatment.

- Number of patients reporting laboratory abnormalities up to 30 days after the end of treatment.

Secondary outcome

Health-Related Quality of Life (HRQL) assessed by using changes from baseline in scores derived from the 3 HRQL questionnaires (EQ-5D, EORTC QLQ-C30 and EORTC QLQ-CR-29), every 4 weeks.

Study description

Background summary

Aflibercept is a man-made novel anti-cancer agent of the antiangiogenic class (i.e. that causes decreased blood vessel formation). This is a protein and, like agents of the same category, has a different mechanism of action than the chemotherapy that will be given with it. Therefore, when added to the chemotherapy, it is hypothesised that it might expand the benefit of the chemotherapy itself.
So far more than 3700 patients have received aflibercept alone or in combination with different chemotherapies including irinotecan and 5-FU/LV, in

several clinical studies.
In the phase III/IV trial conducted in metastatic colorectal cancer patients, previously treated with an oxaliplatin containing chemotherapy, the combination of aflibercept (AVE0005) with irinotecan, 5-fluorouracil and leucovorin (FOLFIRI) has demonstrated a statistically significant and clinically meaningful improvement in patient survival and delaying the progression of the disease. Overall, the side effects noted when aflibercept and FOLFIRI were combined, were more frequent than ones observed with FOLFIRI alone however, the toxicities observed were consistent with the type of side effects observed with the chemotherapy and with agents belonging to the same class as aflibercept (antiangiogenic compounds).

This study aims to provide access for patients to aflibercept (given in combination with FOLFIRI) and will permit gathering information about its safety and tolerability and about the quality of life while treated.

Study objective

Primary: To provide metastatic colorectal cancer patients with access to aflibercept and to
document the overall safety in these patients
Secondary: To document the Health-Related Quality of Life of aflibercept in this patient
population

Study design

This is a prospective, phase IIIb/IV, International, Multicenter, Single Arm, Open-label Study.
Each patient will be treated until disease progression, unacceptable toxicity, death, Investigator*s decision or
patient*s refusal for further treatment (whichever come first).
Patients will be followed-up during treatment and for at least 30 days after last treatment (either aflibercept or FOLFIRI)
administration (for safety assessment).

Intervention

Aflibercept one (1) hour intravenous infusion every two (2) weeks in combination with FOLFIRI (ironotecan, 5-Fluorouracil and leucovorin) regimen.

Study burden and risks

Risks are related to blood sampling and possible site effects of the study drug.
Potential benefits include possible shrinkage of the patient's tumor, delaying

in progression of the disease and/or prolongation of the patient's overall survival.

Contacts

Public
Sanofi-aventis

Kampenringweg 45
GOUDA 2803 PE
NL
Scientific
Sanofi-aventis

Kampenringweg 45
GOUDA 2803 PE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Histologically or cytologically proven adenocarcinoma of the colon or rectum.
Metastatic disease.
Eastern Cooperative Oncology Group performance status 0-1.
One and only one prior chemotherapeutic regimen for metastatic disease. This prior chemotherapy must be an oxaliplatin containing regimen. Patients must have progressed during or after the oxaliplatin based chemotherapy. Patients relapsed within 6 months of completion of oxaliplatin adjuvant chemotherapy are

eligible.

Exclusion criteria

Prior therapy with irinotecan,
Inadequate bone marrow, liver and renal function: neutrophils < 1.5x109/L platelets < 100x109/L, hemoglobin < 9.0 g/dL, total bilirubin >1.5 x upper normal limit (ULN), transaminases >3 x ULN (unless liver metastasis are present), alkaline phosphatase >3 x ULN (unless liver metastasis are present), serum creatinine > 1.5 x ULN.
Less than 4 weeks from prior radiotherapy, prior chemotherapy, prior major surgery (or until the surgical wound is fully healed).
Treatment with any investigational drug within the prior 30 days.
Treatment with concomitant anticonvulsivant agents that are CYP3A4 inducers (phenytoin, phenobarbital, carbamazepine), unless discontinued >7 days.
History of brain metastases, uncontrolled spinal cord compression carcinomatous meningitis or new evidence of brain or leptomeningeal disease,
Prior malignancy (other than colorectal) including prior malignancy from which the patient has been disease free for < 5 years (except adequately treated basal or squamous cell skin cancer or carcinoma in situ of the cervix).
Any of the following within 6 months prior to study inclusion: myocardial infarction, severe/unstable angina pectoris, coronary/peripheral artery bypass graft, severe congestive heart failure, stroke or transient ischemic attack.
Any of the following within 3 months prior study inclusion: severe gastrointestinal bleeding/hemorrhage, treatment resistant peptic ulcer disease, erosive oesophagitis or gastritis, infectious or inflammatory bowel disease, diverticulitis, pulmonary embolism or other uncontrolled thromboembolic event.
Occurrence of deep vein thrombosis within 4 weeks, prior to study inclusion.
Known dihydropyrimidine dehydrogenase deficiency.
Predisposing colonic or small bowel disorders in which the symptoms were uncontrolled.
Prior history of chronic enteropathy, inflammatory enteropathy, chronic diarrhea, unresolved bowel obstruction/sub-obstruction, more than hemicolectomy, extensive small intestine resection with chronic diarrhea.
Known Gilbert*s syndrome.
Unresolved or unstable toxicity from any prior anti cancer therapy at the time of inclusion.
History of anaphylaxis or known intolerance to atropine sulphate or loperamide or appropriate antiemetics to be administered in conjunction with FOLFIRI (irinotecan, 5-Fluorouracil, leucovorin).
Severe acute or chronic medical condition, which could impair the ability of the patient to participate to the study.
Urine protein-creatinine ratio (UPCR) >1 on morning spot urinalysis or proteinuria > 500 mg/24-h.
Uncontrolled hypertension within 3 months prior to study inclusion.

Patients on anticoagulant therapy with unstable dose of warfarin and/or having an out-of-therapeutic range INR within the 4 weeks prior to study inclusion.
Evidence of clinically significant bleeding predisposition or underlying coagulopathy, non-healing wound.
Pregnant or breast-feeding women.
Patients with reproductive potential who do not agree to use an accepted effective method of contraception.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-11-2012
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	5 Fluorouracil
Generic name:	5 Fluorouracil
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Irinotecan
Generic name:	Irinotecan
Registration:	Yes - NL intended use
Product type:	Medicine

Brand name:	Leucovorin
Generic name:	Leucovorin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Zaltrap
Generic name:	Aflibercept

Ethics review

Approved WMO Date:	13-06-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-08-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2011-005724-17-NL
ClinicalTrials.gov	NCT01571284

Register	ID
CCMO	NL40690.060.12