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Panitumumab After Resection of Liver Metastases From Colorectal Cancer in KRAS Wild-type Patients

This study is not yet open for participant recruitment.

Verified on May 2011 by Ludwig-Maximilians - University of Munich

First Received on May 2, 2011. Last Updated on June 28, 2011 [History of Changes](#)

Sponsor:	Ludwig-Maximilians - University of Munich
Collaborator:	Amgen
Information provided by:	Ludwig-Maximilians - University of Munich
ClinicalTrials.gov Identifier:	NCT01384994

► Purpose

Up to 50% of patients with colorectal cancer (CRC) develop liver metastasis during the course of their disease. In 30-40% of patients metastasis is confined to the liver. In these patients R0-resection of metastases may contribute to marked improvement of overall survival. Primary resection of liver metastasis is possible in about 15-20% of patients (Scheele 2005, Petrelli 2005). Recent studies indicate that perioperative chemotherapy may improve survival after resection of liver metastases (Portier 2007, Nordlinger 2007). Nevertheless, there is evidence that 70-80% of patients have recurrent disease after resection of liver metastasis. Stratification for the risk of recurrence may be performed using the FONG-score (Fong 1999).

This study is designed to investigate the efficacy of postoperative chemotherapy combined with an anti-EGFR treatment using panitumumab.

The majority of patients present to the surgeon after chemotherapeutic pretreatment with various not necessarily standardized regimens. Also postoperative therapy after resection of liver metastasis is not a clearly defined standard of care in Germany.

Based on the study by Nordlinger et al. an oxaliplatin-based regimen is chosen for postoperative therapy (Nordlinger 2008). For reasons of practicability mFOLFOX6 was selected as the chemotherapy backbone for additive treatment (Allegra 2010).

Also, there is evidence that the combination of FOLFOX with panitumumab is associated with enhanced antitumor activity (Douillard et al. ESMO 2009). The experimental treatment arm will therefore evaluate the combination of FOLFOX plus panitumumab. Since in colorectal cancer monoclonal antibodies directed against the EGFR are not active in KRAS mutant patients, the experimental arm including panitumumab will only be performed in KRAS wild-type patients (Amado 2008).

The planned study aims to assess the efficacy of postoperative therapy with FOLFOX plus panitumumab followed by maintenance with panitumumab for 3 months in KRAS wild-type patients, compared to the historical data for standard FOLFOX chemotherapy alone, which are verified by a randomised control group without the antibody. (Figure 1: Study Design).

The study will allow preoperative treatment with regimens such as FOLFIRI, XELIRI, FOLFOX or XELOX +/- bevacizumab or +/- cetuximab. However, only those patients will be considered eligible who did not progress during preoperative therapy.

After surgery, a treatment-free interval of at least 4 weeks, but no longer than 8 weeks will be granted.

KRAS-wild-type patients (60% of all pts) will then be randomized in a 2:1 ratio to an experimental arm with FOLFOX + panitumumab or to a reference arm with FOLFOX alone. Combination treatment will be performed for a duration of 3 months, after which patients in the experimental arm will receive maintenance therapy with panitumumab for further 3 months. In the reference arm, treatment will, however, be ended after 3 months.

Condition	Intervention	Phase
Colorectal Cancer KRAS Wildtype After Resection of Liver Metastases	Drug: Folic Acid Drug: 5-FU Drug: Oxaliplatin Drug: Panitumumab	Phase II

Study Type: Interventional
 Study Design: Allocation: Randomized
 Endpoint Classification: Efficacy Study
 Intervention Model: Parallel Assignment
 Masking: Open Label
 Primary Purpose: Treatment

Resource links provided by NLM:

[MedlinePlus](#) related topics: [Cancer](#) [Colorectal Cancer](#)

[Drug Information](#) available for: [Fluorouracil](#) [Folic acid](#) [Oxaliplatin](#) [Panitumumab](#)

[U.S. FDA Resources](#)

Further study details as provided by Ludwig-Maximilians - University of Munich:

Primary Outcome Measures:

- Progression Free Survival [Time Frame: 2 years after randomisation]
[Designated as safety issue: No]

Secondary Outcome Measures:

- Tolerability and side effects [Time Frame: approximate 6 months after randomisation]
[Designated as safety issue: Yes]
- Overall Survival [Time Frame: 2 years after randomisation]
[Designated as safety issue: No]

Estimated Enrollment: 111
 Study Start Date: August 2011
 Estimated Study Completion Date: August 2014
 Estimated Primary Completion Date: August 2013 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
FOLFOX + Panitumumab: Experimental Interventions: <ul style="list-style-type: none"> • Drug: Folic Acid • Drug: 5-FU • Drug: 5-FU • Drug: Oxaliplatin • Drug: Panitumumab • Drug: Panitumumab 	Drug: Folic Acid 400 mg/m2, 2h infusion, d1, q2w Drug: 5-FU 400 mg/m2 bolus iv, d1, q2w Drug: 5-FU 2400 mg/m2 46-h infusion, d1-2, q2w Drug: Oxaliplatin 85 mg/m2 d1, q2w Drug: Panitumumab 6 mg/kg BW every 2 weeks Drug: Panitumumab Panitumumab maintenance phase (3 months) 9mg/kg BW every 3 weeks
FOLFOX: Active Comparator Interventions: <ul style="list-style-type: none"> • Drug: Folic Acid 	Drug: Folic Acid 400 mg/m2, 2-h infusion, d1, q2w Drug: 5-FU

<ul style="list-style-type: none"> • Drug: 5-FU • Drug: 5-FU • Drug: Oxaliplatin 	<p>400 mg/m² bolus iv, d1, q2w</p> <p>Drug: 5-FU</p> <p>2400 mg/m² 46-h infusion, d1-2, q2w</p> <p>Drug: Oxaliplatin</p> <p>85 mg/m² d1, q2w</p>
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► Eligibility

Ages Eligible for Study: 18 Years and older
 Genders Eligible for Study: Both
 Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Patient has provided written informed consent.
- R0-resection of liver metastasis, at least four weeks but not longer than 8 weeks ago.
- Histologically confirmed diagnosis of metastatic colorectal cancer confined to the liver
- KRAS-wildtype of the tumor
- Age 18 years or older
- ECOG performance status 0-1
- Females with child-bearing potential must use adequate contraceptive measures
- Exclusion of pregnancy
- Relevant toxicities of previous treatments must have subsided
- Magnesium \geq lower limit of normal; Calcium \geq lower limit of normal
- Normal cardiac function demonstrated by ECG and echocardiogram (LVEF \geq 55%)
 - No symptomatic congestive heart failure
 - No unstable angina pectoris
 - No cardiac arrhythmia
- Adequate organ function as defined by Table 1:
 - Hematologic: ANC (absolute neutrophil count) \geq 1.5 G/L, Leucocytes $>$ 3.0 G/L, Hemoglobin \geq 9 g/dL, Platelets \geq 100 G/L
 - Hepatic: Albumin \geq 2.5 g/dL, Serum bilirubin \leq 2 mg/dL, AST and ALT \leq 3 x ULN
 - Renal: Serum Creatinine \leq 1.5 mg/dL

Exclusion Criteria:

- Known manifestations of metastatic disease
- Progression during preoperative treatment
- Missing KRAS mutation status of the tumor
- Contraindication against therapy with 5-fluorouracil/ folinic acid or oxaliplatin
- Known intolerance of panitumumab
- Known DPD deficiency
- Polyneuropathy $>$ grade 1 (NCI-CTCv4) which precludes the use of oxaliplatin
- Evidence of ascites or cirrhosis
- Patient is pregnant or lactating or planning to become pregnant within 6 months after end of treatment
- Subject (male or female) is not willing to use highly effective methods of contraception (per institutional standard) during treatment and for 6 months (male or female) after the end of treatment
- Has had a major surgical procedure, open biopsy, or significant traumatic injury within 28 days prior to study enrolment, or there is an anticipated need for major surgical procedure during the course of the study
- Clinically significant cardiovascular disease (including myocardial infarction, unstable angina, symptomatic congestive heart failure, serious uncontrolled cardiac arrhythmia) \leq 1 year

before enrolment/randomization

- History of interstitial lung disease e.g. pneumonitis or pulmonary fibrosis or evidence of interstitial lung disease on baseline chest CT scan
- Has a concurrent disease or condition that would make the subject inappropriate for study participation or would interfere with the subject's safety.
- Has any psychological, familial, sociological, or geographical conditions that do not permit compliance with the protocol.
- Requires concurrent cancer therapy (chemotherapy, radiation therapy, biologic therapy, immunotherapy, or hormonal therapy) while on study.
- Requires concurrent treatment with an investigational agent, participation in another clinical trial, or any specifically prohibited medication while on study.
- Has a known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to 5-fluorouracil, folinic acid, oxaliplatin, or panitumumab.
- Other active malignancy
- Known alcohol abuse or drug addiction
- Incapability to give informed consent

▶ Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01384994

Contacts

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▶ More Information

Additional Information:

[Darmkrebsstudien](#) 

No publications provided

Responsible Party: Prof. Dr. Volker Heinemann, Ludwig-Maximilians - University of Munich
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Keywords provided by Ludwig-Maximilians - University of Munich:

Colorectal Cancer
PARLIM
KRAS Wildtype
Liver metastases

Additional relevant MeSH terms:

Colorectal Neoplasms	Liver Diseases
Neoplasm Metastasis	Fluorouracil
Liver Neoplasms	Oxaliplatin
Intestinal Neoplasms	Antibodies, Monoclonal
Gastrointestinal Neoplasms	Folic Acid
Digestive System Neoplasms	Hematinics
Neoplasms by Site	Antimetabolites
Neoplasms	Molecular Mechanisms of Pharmacological Action
Digestive System Diseases	Pharmacologic Actions
Gastrointestinal Diseases	Antimetabolites, Antineoplastic
Colonic Diseases	Antineoplastic Agents
Intestinal Diseases	Therapeutic Uses
Rectal Diseases	Immunosuppressive Agents
Neoplastic Processes	Immunologic Factors
Pathologic Processes	Physiological Effects of Drugs

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