# *KURZPROTOKOLL*
# *I4T-MC-JVBB*

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| **Öffentlicher Titel** | Folfiri plus Ramucirumab bei metastasierten kolorektalem Karzinom |
| **Wissenschaftl. Titel** | A Randomized, Double-blind, Multicenter Phase 3 Study of Irinotecan, Folinic Acid, and 5-Fluorouracil (FOLFIRI) Plus Ramucirumab or Placebo in Patients With Metastatic Colorectal Carcinoma Progressive During or Following First-Line Combination Therapy With Bevacizumab, Oxaliplatin, and a Fluoropyrimidine |
| **Kurztitel** | I4T-MC-JVBB |
| **Studienart** | prospektiv, Therapiestudie, randomisiert, Pharma-Studie, doppelblind, zweiarmig |
| **Studienphase** | Phase III |
| **Erkrankung** | Verdauung: Darmkrebs (Kolorektales Karzinom): Zweitlinie oder höher |
| **Ziele** | - Overall Survival<br>- Progression-free survival time<br>- Proportion of patients achieving an objective response (objective response rate)<br>- Change in European Organisation for Research and Treatment of Cancer [EORTC] QLQ-C30<br>- Incidence of anti-ramucirumab antibodies<br>- Cmax and Cmin of ramucirumab<br>- Change in EuroQol EQ-5D |
| **Einschlusskriterien** | - Histologically or cytologically confirmed colorectal cancer, excluding primary tumors of appendiceal origin (participants are eligible to enroll irrespective of KRAS mutation status)<br>- Confirmed metastatic colorectal cancer (Stage IV)<br>- The participant has received first-line combination therapy of bevacizumab, oxaliplatin, and a fluoropyrimidine for metastatic disease and a) Experienced radiographic disease progression during first-line therapy, or b) Experienced radiographic disease progression  6 months after the last dose of first-line therapy, or c) Discontinued part or all of first-line therapy due to toxicity and experienced radiographic disease progression  6 months after the last dose of first-line therapy; Note that a participant must have received a minimum of 2 doses of bevacizumab as part of a first-line regimen containing chemotherapy; in addition, a participant must have received at least 1 cycle of first-line therapy that included bevacizumab, oxaliplatin and a fluoropyrimidine in the same cycle; Note that a participant must not have received more than 2 different fluoropyrimidines as part of a first-line regimen; disease progression is not an acceptable reason for discontinuing one fluoropyrimidine and starting a second fluoropyrimidine<br>- Receipt of no more than 2 prior systemic chemotherapy regimens in any setting (only 1 prior regimen for metastatic disease is permitted); For participants with rectal cancer, sequential neoadjuvant and adjuvant therapy will count as a single systemic regimen; Note that rechallenge with oxaliplatin is permitted and will be considered part of the first-line regimen for metastatic disease, both initial oxaliplatin treatment and subsequent rechallenge are considered as 1 regimen<br>- Measurable or nonmeasurable disease based on the Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST v. 1.1)<br>- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1<br>- Adequate hematologic, renal and hepatic function<br>- Adequate coagulation function (International Normalized Ratio [INR] <=1.5 and Partial Thromboplastin Time [PTT] or activated PTT [aPTT] <=1.5 X upper limit of normal [ULN]). Participants on full-dose anticoagulation must be on a stable dose of anticoagulant therapy and if on oral anticoagulation, must have an INR 3 and have no clinically significant active bleeding or pathological condition that carries a hish risk of bleeding |

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| | - Consent to provide a historical colorectal cancer tissue sample for assessment of biomarkers and the tumor tissue sample is available<br>- Ability to provide signed informed consent |
| **Ausschlusskriterien** | - Receipt of bevacizumab <= 28 days prior to randomization<br>- Receipt of any investigational therapy for non-oncology clinical indication <= 28 days prior to randomization<br>- Receipt of any previous systemic therapy, other than a combination of bevacizumab, oxaliplatin, and a fluoropyrimidine, for first-line treatment of metastatic colorectal cancer<br>- Known leptomeningeal disease or brain metastases or uncontrolled spinal cord compression (currently or in the past)<br>- Experience of any arterial thrombotic or arterial thromboembolic events, including, but not limited to myocardial infarction, transient ischemic attack, or cerebrovascular accident, <= 12 months prior to randomization<br>- Pregnant (confirmed by serum beta human chorionic gonadotropin [beta-HCG] test <= 7 days prior to randomization) or lactating<br>- History of inflammatory bowel disease or Crohn's disease requiring medical intervention (immunomodulatory or immunosuppressive medications or surgery) <= 12 months prior to randomization<br>- Acute or subacute bowel obstruction or history of chronic diarrhea which is considered clinically significant in the opinion of the investigator<br>- Grade 3 or higher bleeding event <= 3 months prior to randomization<br>- Experience of any of the following during first-line therapy with a bevacizumab-containing regimen: an arterial thrombotic/thromboembolic event, Grade 4 hypertension, Grade 3 proteinuria, a Grade 3-4 bleeding event, or bowel perforation Known history or clinical evidence of Gilbert's Syndrome, or is known to have any of the following genotypes: UGT1A1*6/*6, UGT1A1*28/*28, or UGT1A1*6/*28<br>- Known allergy to any of the study treatment components, including any components used in the preparation of ramucirumab, or other contraindication to receive the study treatments<br>- Cirrhosis at a level of Child-Pugh B (or worse) or cirrhosis (any degree) and a history of hepatic encephalopathy or clinical meaningful ascites resulting from cirrhosis; Clinically meaningful ascites is defined as ascites resulting from cirrhosis and requiring ongoing treatment with diuretics and/or paracentesis |
| **Alter** | 18 Jahre und älter |
| **Molekularer Marker** | KRAS wt |
| | KRAS |
| **Status** | Geschlossen |
| **Fallzahl** | 1050 |
| **Sponsor** | Eli Lilly and Company |
| **Förderer** | Eli Lilly and Company |
| **Registrierung in anderen Studienregistern** | ClinicalTrials.gov NCT01183780 (primäres Register)<br>EudraCT 2010-021037-32 |
| **Therapie** | FOLFIRI + Ramucirumab FOLFIRI + Placebo |