KURZPROTOKOLL
RAMTAS

Öffentlicher Titel	Phase II Studie zu Ramucirumab bei refraktärem Kolorektalkarzinom
Wissenschaftl. Titel	A Phase IIb Study of RAMucirumab in Combination with TAS102 vs. TAS102 Monotherapy in Chemotherapy Refractory Metastatic Colorectal Cancer Patients
Kurztitel	RAMTAS
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, offen/unverblindet, zweiarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase IIb
Erkrankung	Verdauung: Darmkrebs (Kolorektales Karzinom): Zweitlinie oder höher
Einschlusskriterien	- Metastatic and inoperable, colorectal cancer who has progressed on/after or did not tolerate: fluoropyrimidins, oxaliplatin, irinotecan, anti-angiogenic therapies (bevacizumab, aflibercept, regorafenib or ramucirumab) and if indicated anti-EGFR antibodies (cetuximab or panitumumab) Intolerance is defined as a permanent discontinuation of the respective treatment resulting from toxicity - Signed informed consent before start of specific protocol procedure - Histologically or cytologically documented diagnosis of adenocarcinoma of the colon or rectum - Presence of at least one measurable site of disease following RECIST 1.1 criteria - ECOG performance 0-1 - Known RAS and BRAF V600E mutational status - Life expectancy of at least 3 months - Adequate hematological, hepatic and renal function parameters: - a. Leukocytes >=3000/mm^3, platelets >=100,000/mm^3, neutrophil count (ANC) >=1500/MüL, hemoglobin >=9 g/dL (5.58 mmol/L) coagulation profile prior to first dose of protocol therapy - b. Serum creatinine <=1.5 x upper limit of normal - c. Urinary protein <=1+ on dipstick or routine urinalysis (UA; if urine dipstick or routine analysis is >=2+, a 24-hour urine collection for protein must demonstrate <1000 mg of protein in 24 hours to allow participation in this protocol) - d. Bilirubin <=1.5 x upper limit of normal, AST and ALT <=3.0 x upper limit of normal, <=5xULN if liver metastasis present, alkaline phosphatase <=6 x upper limit of normal - Patient able and willing to provide written informed consent and to comply with the study protocol - Female and male patients >=18. Patients in reproductive age must be willing to use adequate contraception during the study and for 7 months after the end of ramucirumab treatment (appropriate contraception is defined as surgical sterilization (e.g., bilateral tubal ligation, vasectomy) or hormonal contraception (implantable, patch, oral). Women who use a hormonal contraception method should use an additional barrier method like IUD, male or female condom with spermicidal gel, diaphragm, sponge, cervical cap). Female patients with childbearing potential need to have a negative pregnancy test within 7 days before study start
Ausschlusskriterien	- Known hypersensitivity against ramucirumab or TAS102 - Other known contraindications against ramucirumab, TAS102, or other anti-angiogenic therapies 3. Prior therapy with TAS102 - Drug-related severe adverse events upon pretreatment with anti-angiogenic drugs that would require permanent discontinuation and not allow re-challenge with the same class of drug (i.e. ramucirumab) such as noncontrollable severe hypertension or thromboembolic events (see Table 15 on p. 63 for additional examples) - Any antineoplastic treatment including irradiation within 28 days (42 days for mitomycin c) prior to start of therapy.

- Major surgery within 4 weeks of starting therapy within this study, or minor surgery/subcutaneous venous access device placement within 7 days prior to first dose of protocol therapy
- Symptomatic brain metastasis
- Clinically significant cardiovascular disease
- -> NYHA>II^0, myocardial infarction within 6 months prior study entry
- -> Known clinically significant valvular defect
- -> Uncontrolled or poorly-controlled hypertension (>160 mmHg systolic or >100 mmHg diastolic for >4 weeks) despite standard medical management
- -> Any arterial thromboembolic events, including but not limited to myocardial infarction, transient ischemic attack, cerebrovascular accident, or unstable angina, within 6 months prior to first dose of protocol therapy
- -> History of deep vein thrombosis (DVT), pulmonary embolism (PE), or any other significant thromboembolism (venous port or catheter thrombosis or superficial venous thrombosis are not considered “significant”) during the 3 months prior to first dose of protocol therapy
- Active clinically serious infections (> grade 2 NCI-CTC version 4.0)
- Chronic inflammatory bowel disease
- History of uncontrolled HIV infection or chronic hepatitis B or C 12. Patients with evidence of bleeding diathesis
- Grade 3-4 GI bleeding within 3 months prior to first dose of protocol therapy
- Receiving chronic antiplatelet therapy, including aspirin (once-daily aspirin use (maximum dose 325 mg/day) is permitted), nonsteroidal anti-inflammatory drugs (including ibuprofen, naproxen, and others), dipyridamole or clopidogrel, or similar agents
- History of gastrointestinal perforation or fistulae in past 6 months or risk factors for perforation
- Serious or nonhealing wound, ulcer, or bone fracture within 28 days prior to first dose of protocol therapy
- Past or current history of other malignancies not curatively treated and without evidence of disease for more than 5 years, except for curatively treated basal cell carcinoma of the skin and in situ carcinoma of the cervix or bladder, or low/intermediate risk prostate cancer (Gleason score <=7) with normal PSA levels
- Any condition that could jeopardize the safety of the patient and their compliance of the study
- Medical, psychological or social conditions that may interfere with the participation in the study
- Cirrhosis at a level of Child-Pugh B (or worse) or cirrhosis (any degree) and a history of hepatic encephalopathy or ascites. Clinically meaningful ascites is defined as ascites from cirrhosis requiring diuretics or paracentesis
- On-treatment participation in another clinical study or received investigational drug therapy in the period 30 days prior to inclusion and during the study
- Subject pregnant or breast feeding, or planning to become pregnant within 7 months after the end of treatment
- Patients in a closed institution according to an authority or court decision (AMG § 40, Abs. 1 No. 4)
- Any other concurrent antineoplastic treatment including irradiation

Alter 18 Jahre und älter

Status Aktiv

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Sponsor	IKF GmbH
Förderer	Lilly Deutschland GmbH
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT03520946 (primäres Register) EudraCT 2017-004162-99