# *KURZPROTOKOLL*
# *FLOT7*

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| **Öffentlicher Titel** | Phase II/III Studie zu Ramucirumab mit FLOT oder FLOT allein bei resektablem ösophagogastrischem Adenokarzinom |
| **Wissenschaftl. Titel** | Perioperative RAMucirumab in combination with FLOT versus FLOT alone for reSEctable eSophagogastric adenocarcinoma – RAMSES - a phase II/III trial of the AIO |
| **Kurztitel** | FLOT7 |
| **Studienart** | prospektiv, randomisiert, offen/unverblindet, zweiarmig, Investigator Initiated Trial (IIT) |
| **Studienphase** | Phase II/III |
| **Erkrankung** | Verdauung: Magen-/Speiseröhrenkrebs (Magen-/Ösophaguskarzinom): neoadjuvant |
| **Einschlusskriterien** | - Histologically confirmed, resectable adenocarcinoma of the gastroesophageal junction (AEG I-III) or the stomach (uT2, uT3, uT4, any N category, M0), or any T N+ M0 patient, with the following specifications:<br>- Medical and technical operability<br>- Participating sites in PETRARCA study: Negative HER-2 detection (score IHC HER-2 0 or IHC HER-2 1+ ); IHC HER-2 2+ and negative by FISH, SISH or CISH<br>- No preceding cytotoxic or targeted therapy<br>- No prior partial or complete tumor resection<br>- Female and male patients  18 and  70 years. 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), hormonal contraception (implantable, patch, oral), and double-barrier methods (any double combination of: 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.<br>- ECOG <= 1<br>- Exclusion of distant metastasis by CT or MRI of abdomen, pelvis, and thorax, bone scan or MRI (if bone metastases are suspected due to clinical signs). Exclusion of the infiltration of any adjacent organs or structures by CT or MRI.<br>- Laparoscopic exclusion of peritoneal carcinomatosis, in case of ascites, peritoneal masses, or if otherwise suspected clinically<br>- Adequate hematological, hepatic and renal function parameters:<br>- Leukocytes  3000/mm³, platelets  100,000/mm³, neutrophil count (ANC) 1000/µL, hemoglobin 9 g/dL (5.58 mmol/L),<br>- Adequate coagulation function as defined by International Normalized Ratio (INR) 1.5, and a partial thromboplastin time (PTT)  5 seconds above the ULN (unless receiving anticoagulation therapy). Patients receiving warfarin/phenprocoumon must be switched to low molecular weight heparin and have achieved stable coagulation profile prior to randomization.<br>- Serum creatinine  1.5 x upper limit of normal<br>- 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).<br>- Bilirubin  1.5 x upper limit of normal, AST and ALT  3.0 x upper limit of normal, alkaline phosphatase  6 x upper limit of normal<br>- Patient able and willing to provide written informed consent and to comply with the study protocol and with the planned surgical procedures |
| **Ausschlusskriterien** | - Known hypersensitivity against ramucirumab, 5-FU, leucovorin, oxaliplatin, or docetaxel<br>- Other known contraindications against ramucirumab, 5-FU, leucovorin, oxaliplatin, or docetaxel |

- Clinically significant active coronary heart disease, cardiomyopathy or congestive heart failure, NYHA III-IV
- Any arterial thromboembolic events, including but not limited to myocardial infarction, transient ischemic attack, cerebrovascular accident, or unstable angina, within 6 months prior to enrollment.
- Uncontrolled or poorly-controlled hypertension (>160 mmHg systolic or > 100 mmHg diastolic for >4 weeks) despite standard medical management.
- Clinically significant valvular defect
- 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
- Criteria of unresectability, e.g.:
- Radiologically documented evidence of major blood vessel invasion or encasement by cancer.
- Patients with involved retroperitoneal (e.g. para-aortal, paracaval or interaortocaval lymph nodes) or mesenterial lymph nodes (distant metastases!)
- Known brain metastases
- Other severe internal disease or acute infection
- Peripheral polyneuropathy  NCI Grade II
- Chronic inflammatory bowel disease
- Grade 3-4 GI bleeding within 3 months prior to enrollment.
- History of gastric perforation or fistulae in past 6 months
- Serious or nonhealing wound, ulcer, or bone fracture within 28 days prior to enrollment.
- The patient has undergone major surgery within 28 days prior to enrollment except staging laparoscopy.
- 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 deep vein thrombosis, pulmonary embolism, or any other significant thromboembolism (venous port or catheter thrombosis or superficial venous thrombosis are not considered "significant") during the 3 months prior to randomization.
- Cirrhosis at a level of Child-Pugh B (or worse) or cirrhosis (any degree) and a history of hepatic encephalopathy or ascites.
- On-treatment participation in another clinical study 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

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| **Alter** | 18 - 70 Jahre |
| **Molekularer Marker** | HER2/neu neg. |
| **Fallzahl** | 908 |
| **Sponsor** | IKF GmbH |
| **Förderer** | Eli Lilly and Company |

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| **Registrierung in anderen Studienregistern** | EudraCT 2015-003118-26<br>ClinicalTrials.gov NCT02661971 |
| **Links** | Zu den Ein- und Ausschlusskriterien |