KURZPROTOKOLL
PaFLO

Öffentlicher Titel	FLO +/- Pazopanib als First-line Therapie von fortgeschrittenem Magenkrebs
Kurztitel	PaFLO
Studienart	multizentrisch, prospektiv, randomisiert, offen/unverblindet, zweiarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase II
Erkrankung	Verdauung: Magen-/Speiseröhrenkrebs (Magen-/Ösophaguskarzinom): Erstlinie
Ziele	- Progression free survival rate at 6 months - progression free survival rate at 9 and 12 months median progression free survival response rate duration of response toxicity tolerability overall survival time to treatment failure evaluation of the predictive and prognostic relevance of biomarkers
Einschlusskriterien	- Subjects must provide written informed consent prior to performance of study-specific procedures or assessments, and must be willing to comply with treatment and follow up. - Age 18 years or legal age of consent if greater than 18 years. - Histologically confirmed adenocarcinoma of the stomach or the gastroesophageal junction with either metastatic or locally advanced disease, incurable by operation. - Eastern Cooperative Oncology Group (ECOG) performance status of < or = 2 - At least one unidimensional, measurable tumour parameter according to RECIST 1.1) - No preceding cytotoxic therapy (neoadjuvant or adjuvant treatment allowed if finished > 6 months before inclusion) - Adequate organ system function. - Men and women must perform an adequate contraception. - Female subjects who are lactating should discontinue nursing prior to the first dose of study drug and should refrain from nursing throughout the treatment period and for 14 days following the last dose of study drug
Ausschlusskriterien	- Prior malignancy, except for curatively treated basal cell carcinoma of the skin and in situ carcinoma of the cervix. - Overexpression of HER-2, defined as IHC 3+ or IHC 2+ and FISH positive. - Known hypersensitivity against 5-FU, leukovorin,oxaliplatin or other platinum compounds or pazopanib. - History or clinical evidence of central nervous system (CNS) metastases or leptomeningeal carcinomatosis. - Clinically significant gastrointestinal abnormalities that may increase the risk for gastrointestinal bleeding including, but not limited to: active peptic ulcer disease, known intraluminal metastatic lesion/s with risk of bleeding, inflammatory bowel disease (e.g. ulcerative colitis, Chrohn's disease), or other gastrointestinal conditions with increased risk of perforation, history of abdominal fistula, gastrointestinal perforation, or intra abdominal abscess within 28 days prior to beginning study treatment. - Clinically significant gastrointestinal abnormalities that may affect absorption of investigational product including, but not limited to: malabsorption syndrome, bowel obstruction within the last 30 days prior to study initiation, upper GI obstruction making the swallowing of tablets impossible. - Presence of uncontrolled infection - Corrected QT interval (QTc) > 480 msecs using Bazett's formula.

- History of any one or more of the following cardiovascular conditions within the past 6 months: cardiac angioplasty or stenting, myocardial infarction, unstable angina, coronary artery bypass graft surgery, symptomatic peripheral vascular disease, class III or IV congestive heart failure, as defined by the New York Heart Association (NYHA).
- Poorly controlled hypertension [defined as systolic blood pressure (SBP) of 140 mmHg or diastolic blood pressure (DBP) of 90mmHg].
- History of cerebrovascular accident including transient ischemic attack (TIA), pulmonary embolism or untreated deep venous thrombosis (DVT) within the past 6 months.
- Prior major surgery or trauma within 28 days prior to first dose of study drug and/or presence of any non-healing wound, fracture, or ulcer (procedures such as catheter placement, port implantation and laparoskopy not considered to be major).
- Evidence of active bleeding or bleeding diathesis.
- Known endobronchial lesions and/or lesions infiltrating major pulmonary vessels.
- Hemoptysis in excess of 2.5 mL (or one half teaspoon) within 8 weeks of first dose of study drug.
- Any serious and/or unstable pre-existing medical, psychiatric, or other condition that could interfere with subject's safety, provision of informed consent, or compliance to study procedures.
- Unable or unwilling to discontinue use of prohibited medications for at least 14 days or five half-lives of a drug (whichever is longer) prior to the first dose of study drug and for the duration of the study.
- Treatment with any of the following anti-cancer therapies: radiation therapy, surgery or tumor embolization within 14 days prior to the first dose of pazopanib OR chemotherapy, immunotherapy, biologic therapy, investigational therapy or hormonal therapy within 14 days or five half-lives of a drug (whichever is longer) prior to the first dose of pazopanib.
- A neoadjuvant or adjuvant chemotherapy must be finished at least 6 month before study entry.
- Any ongoing toxicity from prior anti-cancer therapy that is >Grade 1 and/or that is progressing in severity, except alopecia.
- Grade 3 or 4 diarrhea.
- Peripheral polyneuropathy > NCI Grade.
- Pregnant or lactating women.
- Men or woman who are planning a pregnancy within the next six months.
- Participation in another clinical trial with investigational agents within the last 30 days prior to study start.
- The patient is a colleague or employed by the study investigator or by an involved institution including the sponsor of the study.
- Patient is detained in a psychiatric unit or inprisoned.

Alter	18 Jahre und älter
Molekularer Marker	HER2/neu neg.
Sponsor	Universitätsmedizin Berlin, Charite (Hauptsponsor)
Förderer	Universitätsmedizin Berlin, Charite
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT01503372 (primäres Register) EudraCT 2010-024379-15
Therapie	Pazopanib 5-FU, Oxaliplatin, Leukovorin (FLO)