KURZPROTOKOLL
BLU-285-1303

Öffentlicher Titel	Phase III Studie zu BLU-285 bei gastrointestinalem Stromatumor
Wissenschaftl. Titel	An International, Multicenter, Open-label, Randomized, Phase 3 Study of BLU-285 vs Regorafenib in Patients With Locally Advanced Unresectable or Metastatic Gastrointestinal Stromal Tumor (GIST)
Kurztitel	BLU-285-1303
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, offen/unverblindet, Pharma-Studie, zweiarmig
Studienphase	Phase III
Erkrankung	Verdauung: Gastrointestinale Stromatumoren (GIST): Zweitlinie oder höher Verdauung: Gastrointestinale Stromatumoren (GIST): Erstlinie
Einschlusskriterien	- Patients who are >= 18 years of age - Patients who have histologically confirmed metastatic or unresectable GIST. Unresectable GIST must be confirmed to be unresectable by a qualified surgeon - Patients who have received imatinib and 1 or 2 other TKIs for the treatment of GIST, including TKIs used for adjuvant therapy. Each different TKI is counted once regardless of how often it was used, and if 2 different TKIs are used in combination, both TKIs are counted. Patients must have disease progression prior to enrollment. Prior use of other systemic and local therapies is not restricted - Patients who have an ECOG PS of 0 to 1 - Patient, or legal guardian if permitted by local regulatory authorities, who provides informed consent to participate in the study
Ausschlusskriterien	- Patients who have received prior treatment with avapritinib or regorafenib - Patients who have previously received more than 3 different TKIs for the treatment of GIST, including TKIs used for adjuvant therapy. Each different TKI is counted once regardless of how often it was used, and if 2 different TKIs are used in combination, both TKIs are counted - Patients who are known to be both KIT and PDGRFalpha wild type - Patients who received any systemic anticancer therapy within 2 weeks before randomization. Prior radiotherapy (including stereotactic radiotherapy) to major organs within 2 weeks of randomization, or focal radiotherapy (including stereotactic radiotherapy), such as to bones, limbs, or other areas not involving major organs, within 3 days - Patients who have clinically significant, uncontrolled, cardiovascular disease, including congestive heart failure Grades II, III or IV according to the New York Heart Association classification, myocardial infarction or unstable angina within the previous 6 months, or uncontrolled hypertension - Patients who have experienced arterial thrombotic or embolic events such as cerebrovascular accident (including transient ischemic attacks) within 6 monthsbefore randomization, or venous thrombotic events such as pulmonary embolism or deep vein thrombosis within 14 days before randomization. Patients with venous thrombotic events such as pulmonary embolism or deep vein thrombosis >= 14 days before randomization are not excluded provided they are on stable doses of anticoagulation,or have completed the planned anti-coagulation regimen - Patients who have experienced any hemorrhage or bleeding event NCI CTCAE version 5.0 Grade 3 or higher within 4 weeks before randomization - Patients who have a known risk of intracranial bleeding, such as a brain aneurysm that has not been removed or repaired, or a history of intracranial bleeding within 1 year prior to randomization - Patients who have a non-healing wound, ulcer, gastrointestinal perforation, or bone fracture

- Patients who have poor organ function as defined by one or more of the following laboratory parameters:
- -> Persistent proteinuria of NCI-CTCAE version 5.0 Grade 3 or higher
- -> Alanine aminotransferase and AST > 3 x upper limit of normal (ULN) if no hepatic metastases are present; > 5 x ULN if hepatic metastases are present
- -> Total bilirubin >1.5 x ULN; and in presence of Gilbert's syndrome, total bilirubin > 3 x ULN or direct bilirubin > 1.5 x ULN
- -> Estimated (per institutional standard; eg, Cockcroft-Gault formula or Modification of Diet in Renal Disease equation) or measured creatinine clearance < 40 mL/min (if the estimated or measured creatinine clearance is >= 40 mL/min using any of these methods the patient is not excluded).
- -> Platelet count < 90 x 109/L and absolute neutrophil count (ANC) < 1.0 x 10^9/L
- -> Hemoglobin < 9 g/dL. Transfusion and erythropoietin may be used to reach atleast 9 g/dL, but must have been administered at least 2 weeks before randomization
- Patients who have received neutrophil growth factor support within 14 days of randomization
- Patients who require therapy with a concomitant medication that is a strong inhibitoror strong or moderate inducer of CYP3A4
- Patients who have had a major surgical procedure (minor surgical procedures such as central venous catheter placement, tumor needle biopsy, and feeding tube placement Patient has significant traumatic injury within 28 days before randomization
- Patients who have a history of another primary malignancy that has been diagnosed or required therapy within 3 years before randomization. (The following are exempt from the 3-year limit: completely resected basal cell and squamous cell skin cancer, curatively treated localized prostate cancer, and completely resected carcinoma in situ of any site.)
- Patients who have a history of a seizure disorder requiring anti-seizure medication
- Patients who have metastases to the brain
- Patients who are unwilling or unable to comply with scheduled visits, drug administration plan, laboratory tests, or other study procedures and study restrictions
- Patients who have a QT interval corrected using Fridericia's formula (QTcF) of > 450 msec
- Women who are unwilling, if not postmenopausal or surgically sterile, to abstain from sexual intercourse or employ highly effective contraception from the time of randomization and for at least 60 days after the last dose of study drug. Men who are unwilling, if not surgically sterile, to abstain from sexual intercourse or employ highly effective contraception from the time of randomization and for at least 90 days after the last dose of study drug. Refer to Section 9.6.1 for acceptable methods of contraception
- Women who are pregnant, as documented by a serum beta human chorionic gonadotropin (beta-hCG) pregnancy test consistent with pregnancy, obtained within 7 days before the randomization. Females with beta-hCG values that are within the range for pregnancy but are not pregnant (false-positives) may be enrolled with written consent of the Sponsor, after pregnancy has been ruled out. Females of nonchildbearing potential (postmenopausal for more than 1 year; bilateral tubal ligation; bilateral oophorectomy; hysterectomy) do not require a serum beta-hCG test
- Women who are breastfeeding

	- Patients who have prior or ongoing clinically significant illness, medical condition, surgical history, physical finding, or laboratory abnormality that, in the Investigator's opinion, could put the patient at an unacceptably high risk for toxicities, or alter the absorption, distribution, metabolism, or excretion of the study drug; or impair the assessment of study results - Patients with a known hypersensitivity to avapritinib, regorafenib, or the excipients in either study drug
Alter	18 Jahre und älter
Molekularer Marker	PDGFR
	KIT
Sponsor	Blueprint Medicines
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT03465722 (primäres Register) EudraCT 2017-003497-14