Kompetenznetz "Akute und chronische Leukämien"

KURZPROTOKOLL

BERGAMO

Öffentlicher Titel	Phase-II-Studie zu Bemcentinib bei Patienten mit MDS oder AML, die nicht auf die Standardtherapie ansprechen
Wissenschaftl. Titel	A phase II study evaluating the efficacy and safety of bemcentinib in patients with MDS or AML failing standard of care therapy
Kurztitel	BERGAMO
Studiennummer KN/ELN	LN_AMLINT_2019_639
Studiengruppe	AML-Intergroup
Studienart	einarmig, prospektiv
Studienphase	Phase II
Erkrankung	Myelodysplastisches Syndrom (MDS) - Intermediär II und Hochrisiko Akute myeloische Leukämie (AML) - AML alle außer FAB M3
Leukämiestadium	.
Einschlusskriterien	- Signed written informed consent - - Male and female 18 years at the first screening - - Must be able to adhere to the study visit schedule and other protocol requirements - - Initial diagnosis of AML or MDS according to WHO 2016 classification - - At least one cytopenia (ANC < 1800/µL or platelet count < 100,000/µL or hemoglobin < 10 g/dL) - - Failure to achieve complete or partial response or hematological improvement after at least six (azacitidine) or four (decitabine) 4-week treatment cycles administered during the past two years OR Relapse after initial complete or partial response or hematological improvement observed after at least six (azacitidine) or four (decitabine) 4-week treatment cycles administered during the past two years OR Intolerance to treatment with HMAs during the past two years - - Not eligible for allogeneic stem cell transplantation - - 5% bone marrow blasts at central morphology - - Off all other treatments for AML/MDS for at least four weeks; G-CSF and erythropoietin are allowed before and during the study as clinically indicated - - ECOG performance status of 0-2 - - Availability of blood counts and transfusion events for previous 2 months
Ausschlusskriterien	- - Prior intensive chemotherapy for MDS or AML - - Radiotherapy or chemotherapy within the 14 days prior to the first dose of Bemcentinib being administered (other than hydroxyurea) - - History of the following cardiac conditions: o Congestive cardiac failure of > Class II severity according to the NYHA (defined as symptomatic at less than ordinary levels of activity) o Ischemic cardiac event including myocardial infarction within 3 months prior to first dose o Uncontrolled cardiac disease, including unstable angina, uncontrolled hypertension (i.e. sustained systolic BP >140 mmHg or diastolic BP >90 mmHg), or need to change medication within 6 weeks of provision of consent due to lack of disease control o History or presence of sustained bradycardia (60 BPM), left bundle branch block, cardiac pacemaker or ventricular arrhythmia. Note: Patients with a supraventricular arrhythmia requiring medical treatment, but with a normal ventricular rate are eligible o Family history of long QTc syndrome; personal history of long QTc syndrome or previous drug-induced QTc prolongation of at least Grade 3 (QTc > 450 ms at baseline) - - Abnormal left ventricular ejection fraction on echocardiography or Multi Gated Acquisition Scan (MUGA) (less than the lower limit of normal for a patient of that age at the treating institution or < 45 %, whichever is lower)

- - Current treatment with any agent known to cause Torsades de Pointes which cannot be discontinued at least five half-lives or two weeks prior to the first dose of study treatment. Please see Appendix XI for list of relevant medications
- - Screening 12-lead ECG with a measurable QTc interval according to Fridericia's correction > 450 ms
- - Ongoing infection requiring systemic treatment. Patients who are on prophylactic antimicrobials or who have been afebrile for 48 hours following the initiation of antimicrobials are eligible
- - Inadequate liver function as demonstrated by serum bilirubin 1.5 times the upper limits of normal range (ULN) or alanine aminotransferase (ALT) or aspartate aminotransferase (AST) 2.5 times the ULN (or 5 times the ULN for AST or ALT in the presence of liver involvement by leukemia)
- - Inability to tolerate oral medication
- - Existing gastrointestinal disease affecting drug absorption such as celiac disease or Crohn's disease
- - Known lactose intolerance, congenital lactase deficiency, galactosemia, Glucose-galactose malabsorption
- - Treatment with any of the following: histamine receptor 2 inhibitors, proton pump inhibitors or antacids within 3 days or 5 half-lives of administration of BGB234, whichever is longer
- - Treatment with medications which are predominantly metabolized by CYP3A4 and have a narrow therapeutic index (examples of medication are in the appendix X15.10.2)
- - Previous bowel resection that would interfere with drug absorption
- - Impaired renal function as demonstrated by a creatinine clearance of < 30 mL/min determined by Cockcroft-Gault formula
- - Unresolved CTCAE > Grade 2 toxicity (other than stable toxicity) from previous anticancer therapy excluding alopecia
- - Any evidence of severe or uncontrolled systemic conditions (e.g., severe hepatic impairment) or current unstable or uncompensated respiratory or cardiac conditions which makes it undesirable for the patient to participate in the study or which could jeopardize compliance with the protocol
- - Known active, uncontrolled central nervous system (CNS) disease including CNS leukemia
- - Known active infection with human immunodeficiency virus (HIV), hepatitis B or C viruses - screening for viral infections is not required for entry to this study
- - Major surgery within 28 days prior to the start of Bemcentinib – excluding skin biopsies and procedures for insertion of central venous access devices
- - Patients who are unwilling to follow strict highly effective contraception requirements including combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, transdermal), progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, implantable), intrauterine device (IUD), intrauterine hormone-releasing system (IUS), bilateral tubal occlusion2, vasectomised partner, sexual abstinence, surgical sterilization)) before entry and throughout the studyFemale patients with reproductive potential who do not have a negative urine ß-HCG pregnancy test at screening and not more than 3 days prior to initiation of treatment
- - Female patients who are lactating
- - Exclusion periods from other studies or simultaneous participation in other clinical studies (excluding non-interventioneal studies/registries)

- - Criteria which in the opinion of the investigator precluded participation for scientific reasons, for reasons of compliance, or for reasons of the subject's safety
- - Close affiliation with the investigational site; e.g. a close relative of the investigator, dependent person (e.g. employee or student of the investigational site)
- - Subject is an employee of GWT-TUD GmbH or participating study groups

Alter	>= 18 Jahre
Status	Aktiv
Beginn der Rekrutierung	01.01.2019
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