KURZPROTOKOLL
TUD-MOSAIC

Öffentlicher Titel	Phase I/II Studie zu Midostaurin und Gemtuzumab Ozogamicin bei neu diagnostizierter akuter myeloischer Leukämie
Wissenschaftl. Titel	MidOStaurin + Gemtuzumab OzogAmIcin Combination in Firstline Standard Therapy for Acute Myeloid Leukemia
Kurztitel	TUD-MOSAIC
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, doppelblind, Investigator Initiated Trial (IIT), mehrarmig
Studienphase	Phase II
Erkrankung	Blut: Akute myeloische Leukämie (AML): Neu diagnostiziert / de novo

Einschlusskriterien

- Written informed consent
- Newly diagnosed AML according to the criteria of the World Health Organisation plus the following molecular or cytogenetic specifications: Phase I Trial - MODULE: t(8;21)/RUNX1-RUNX1T1 or inv(16) or t(16;16)/CBFB-MYH11 or FLT3-ITD or FLT3-tyrosine kinase domain (FLT3-TKD) Phase II Trial - MAGNOLIA t(8;21)/RUNX1-RUNX1T1 or inv(16) or t(16;16)/CBFB-MYH11 Phase II Trial - MAGMA FLT3-ITD or FLT3-TKD Absence of mutations in CBF genes (i.e. t(8;21)/RUNX1-RUNX1T1 or inv(16) or t(16;16)/CBFB-MYH11)
- 18 - 75 years in Phase I Trial - MODULE
- 18 - 70 years in Phase II Trials - MAGMA and MAGNOLIA
- Eastern Cooperative Oncology Group (ECOG) Score of 0-2
- Life expectancy > 14 days
- Adequate hepatic and renal function
- alanine aminotransferase / aspartate transaminase 2.5 x ULN
- Bilirubin < 2 x upper limits of normal
- Creatinine < 1.5 x upper limits of normal or Creatinine clearance > 40 ml/min
- White blood cell count < 30 × 10^9/L. Note: Hydroxyurea and/or a dose of 100-200 mg/m^2 cytarabine per day for up to 3 days (for emergency use for clinical stabilization) is permitted to meet this criterion.

Ausschlusskriterien

- Previous antineoplastic treatment for AML other than hydroxyurea and/or cytarabine for emergency use (100-200 mg/m^2 per day on maximal 3 days)
- Previous treatment with anthracyclines
- central nervous system involvement
- Isolated extramedullary AML
- Uncontrolled infection
- AML after antecedent myelodysplasia (MDS) with prior cytotoxic treatment (e.g., azacytidine or decitabine)
- Any investigational agent within 30 days or 5 half-lives, whichever is greater, prior to day 1. An investigational agent is defined as an agent with no approved medical use in adults or in pediatric patients
- Prior treatment with a FLT3 inhibitor (e.g., midostaurin, quizartinib, sorafenib)
- Strong CYP3A4/5 enzyme inducing drugs unless they can be discontinued or replaced prior to enrollment
- Any other known disease or concurrent severe and/or uncontrolled medical condition (e.g., cardiovascular disease including congestive heart failure or active uncontrolled infection) that could compromise participation in the study
- Impairment of gastrointestinal (GI) function or GI disease that might alter significantly the absorption of midostaurin
- Confirmed diagnosis of HIV infection

- Active viral hepatitis unless serology demonstrates clearance of infection. Occult or prior hepatitis B virus (HBV) infection, defined as negative hepatitis B surface antigen and positive total hepatitis core antibodies, may be included if HBV DNA is undetectable, provided that patients are willing to undergo monthly DNA testing. Patients who have protective titers of hepatitis B surface antibody after vaccination or prior cured hepatitis B are eligible. Patients for hepatitis C virus (HCV) antibody are eligible provided PCR is negative for HCV RNA.
- Cardiovascular abnormalities, including any of the following: History of myocardial infarction, angina pectoris, Coronary Artery Bypass Grafting within 6 months prior to starting study treatment Clinically uncontrolled cardiac arrhythmias (e.g., ventricular tachycardia), complete left bundle branch block, high-grade atrioventricular block (e.g., bifascicular block, Mobitz type II and third degree atrioventricular block) Uncontrolled congestive heart failure Left ventricular ejection fraction of < 50% Poorly controlled arterial hypertension
- Pregnant or nursing (lactating) women
- Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they fulfill at least one of the following criteria: Post-menopausal (12 months of natural amenorrhea or 6 months of amenorrhea with serum follicule stimulating hormone > 40 U/ml) Postoperative (i.e. 6 weeks) after bilateral ovariectomy with or without hysterectomy Women of childbearing potential must have a negative serum pregnancy test performed within 7 days before the first dose of study drug Continuous and correct application of a contraception method with a Pearl Index of < 1% (e.g. implants, depots, oral contraceptives, intrauterine device) from initial study drug administration until at least 7 months after the last dose of gemtuzumab ozogamicin and at least 4 months after the last dose of midostaurin, whichever period is longer. A hormonal contraception method must always be combined with a barrier method (e.g. condom) Sexual abstinence Vasectomy of the sexual partner
- Sexually active males unless they use a condom during intercourse while taking the drug during treatment, and for at least 4 months after stopping treatment and should not father a child in this period. A condom is required to be used also by vasectomized men as well as during intercourse with a male partner in order to prevent delivery of the drug via semen
- Unwillingness or inability to comply with the protocol
- Known hypersensitivity to midostaurin, GO, cytarabine or daunorubicin or to any of the excipients of midostaurin, GO, cytarabine or daunorubicin.

Alter 18 - 75 Jahre

Prüfzentren

Innere Medizin 2 (Aktiv)
Theodor-Stern-Kai 7
60590 Frankfurt am Main
Kathrin Behnke
Tel: 069 6301-84497
Fax: 069 6301-5744
Kathrin.Behnke@unimedizin-ffm.de

Universitätsmedizin Frankfurt (Aktiv)
Medizinische Klinik II, Hämatologie/Onkologie
Theodor-Stern-Kai 7
60590 Frankfurt am Main
Kathrin Behnke
Tel: 069 6301-84497
Fax: 069 6301-5744
Kathrin.Behnke@unimedizin-ffm.de

Sponsor Universitätsklinikum Dresden

Förderer Novartis Pharma

	Pfizer
Registrierung in anderen Studienregistern	EudraCT 2019-003863-23 (primäres Register)
Links	Studiendokumente zum Download (roXtra)
	Zu den Ein- und Ausschlusskriterien