Kompetenznetz "Akute und chronische Leukämien"

KURZPROTOKOLL

MOSAIC

Öffentlicher Titel	Phase-1/2-Studie zur Kombination Midostaurin und Gemtuzumab Ozogamicin als Erstlinientherapie für AML
Wissenschaftl. Titel	MidOStaurin + Gemtuzumab OzogAmIcin Combination in First-line Standard Therapy for Acute Myeloid Leukemia (MOSAIC)
Kurztitel	MOSAIC
Studiennummer KN/ELN	LN_SALAML_2020_716
Studiengruppe	SAL / AMLCG
Studienart	multizentrisch, randomisiert, mehrarmig, doppelblind
Studienphase	Phase I/II
Erkrankung	Akute myeloische Leukämie (AML) - AML alle außer FAB M3
Leukämiestadium	de novo/non-treated

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 -FLT3 wild-type Phase II Trial - MAGMA: -FLT3-ITD or -FLT3-TKD
- Male and female patients with age: -18 - 75 years in Phase I Trial - MODULE or Phase II Trial - MAGNOLIA -18 - 60 years in Phase II Trial - MAGMA
- 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 is permitted to meet this criterion.

Ausschlusskriterien

- Previous antineoplastic treatment for AML other than hydroxyurea
- 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 or active viral hepatitis

- 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/placebo, GO, cytarabine or daunorubicin.

Alter	18 - 75 Jahre
Status	Aktiv
Beginn der Rekrutierung	12.05.2020
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Sponsoren	Technische Universität Dresden (Hauptsponsor)
Registrierung in anderen Studienregistern	ClinicalTrials.govNCT04385290