KURZPROTOKOLL
TEAM

Öffentlicher Titel	Phase II Studie zu Bortezomib auf eine epigenetisch bedingte Therapieresistenz bei rezidivierter/refraktärer AML
Wissenschaftl. Titel	TEAM-Trial: Targeting Epigenetic Therapy Resistance in AML With Bortezomib: A Multi-centre Matched Threshold Crossing Phase II Approach
Kurztitel	TEAM
Studienart	multizentrisch, prospektiv, Therapiestudie, offen/unverblindet, einarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase II
Erkrankung	Blut: Akute myeloische Leukämie (AML): Rezidiviert/refraktär
Einschlusskriterien	- Patients with confirmed diagnosis of AML according to WHO 2016 [27] (except acute promyelocytic leukemia) either de novo AML, AML after preceding myelodysplastic or myeloproliferative syndrome (MDS/MPD), and therapy related AML (t AML) after previous cytotoxic therapy or radiation are eligible either refractory (A) to first line chemotherapy or in first relapse (B), also after stem cell transplantation. FLT3 ITD status, cytogenetics (refractory and relapsed patients), in addition status of core binding factor as well as double mutant CEBPA in relapsed patients must be available. A) Refractory to induction therapy is defined as no CR, CRi, (according to standard criteria [4]) after 2 intensive induction cycles of at least 7 days of cytarabine 100 200 mg/m^2 continuously or an equivalent regimen with cytarabine with total dose not less than 700 mg/m^2 per cycle and 3 days of an anthracycline/antrachinone (e.g. daunorubicin, idarubicin). B) Relapsed after first line therapy is defined as relapsed AML after CR or CRi (according to standard criteria) after at least one intensive induction and consolidation (including intensive chemotherapy and/or hematopoietic cell transplantation) therapy - ECOG performance status <= 2 - Discontinuation of prior AML treatment before the start of study treatment (except hydroxyurea or other treatment to control hyperleukocytosis) for at least 10 days for cytotoxic agents and >= 5 half lives for non cytotoxic / investigational drug treatment preceding the first dose of trial medications - Age >= 18 years - Pregnancy and childbearing potential: • Non pregnant and non nursing women of childbearing potential must have a negative serum or urine ß HCG pregnancy test within a sensitivity of at least 25 mIU/mL within 72 hours prior to registration. (“Women of childbearing potential” is defined as a sexually active mature woman who has not undergone a hysterectomy or who has had menses at any time in the preceding 24 consecutive months). • Female patients of reproductive age must agree to avoid getting pregnant while on therapy. • Women of child bearing potential must either commit to continued abstinence from heterosexual intercourse or begin highly effective methods (referring to recommendation of the CTFG) of birth control during study and at least 7 months (women), after end of treatment. • Men must use a latex condom during any sexual contact with women of childbearing potential, even if they have undergone a successful vasectomy and must agree to avoid to father a child during study and until 6 months after end of treatment - Willingness of patients to adhere to protocol specific requirements and capacity to give written informed consent - Ability of patient to understand the character and individual consequences of clinical trial - Following receipt of verbal and written information about the study, the patient must provide signed informed consent before any study related activity is carried out
Ausschlusskriterien	- Acute promyelocytic leukemia (AML M3) - Akute myeloid leukemia previously treated with gemtuzumab ozogamicin

- Hyperleukocytosis (leukocytes > 30,000/l) at the time of study entry. These patients should be treated with hydroxyurea and / or receive leukocytapheresis treatment according to routine practice and are only allowed to enter into the study when leukocyte counts of 30,000/l or below are reached. If hydroxyurea is not sufficient to control hyperleukocytosis i.v. application of 100 mg cytarabine continuously over 24 hours may be discussed with the principle investigator or the scientific coordinator
- Known central nervous system manifestation of AML
- Uncontrolled or significant cardiovascular disease, including any of the following: • History of heart failure NYHA class 3 or 4 • Left ventricular ejection fraction (LVEF) <= 40% by echocardiogram ECHO) • History of uncontrolled angina pectoris or myocardial infarction within 12 months prior to screening • History of second (Mobitz II) or third degree heart block or any cardiac arrhythmias requiring anti arrhythmic therapy (beta blockers or digoxin are permitted)
- Pregnant or nursing women
- Chronically impaired renal function (creatinine clearance < 30 ml / min)
- Inadequate liver function (ALT and AST >= 2 x ULN), total bilirubin >= 1.5 x ULN
- Known liver cirrhosis or history of veno occlusive disease (VOD)
- HIV infection and/or active hepatitis B or C infection (active hepatitis B defined by HBs Ag positivity, active hepatitis C defined by positive virus load)
- Evidence or history of severe non leukemia associated bleeding diathesis or coagulopathy
- Uncontrolled active infection
- Concurrent malignancies other than AML with an estimated life expectancy of less than two years
- Known hypersensitivity to cytarabine (AraC) (not including drug fever, conjunctivitis or exanthema)
- Known hypersensitivity to bortezomib, boron or mannitol
- Isolated extramedullary manifestation of AML
- Patients within 100 days after allogeneic stem cell transplantation at the time of screening
- Patients with clinically relevant Graft versus Host Disease (GvHD) requiring initiation of treatment or treatment escalation within 21 days prior to screening
- Patients with pre existing severe neuropathy
- Acute diffuse infiltrative pulmonary disease
- Pericardial disease
- Expected uncompliance of patient

Alter 18 Jahre und älter

Status Aktiv

Prüfzentren

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Förderer	Pfizer
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Links	Studiendokumente zum Download