Kompetenznetz "Akute und chronische Leukämien"

KURZPROTOKOLL

GMALL-MOLACT2-PONA

Öffentlicher Titel	Phase II Studie zu Ponatinib bei erwachsenen Patienten mit minimaler Resterkrankung (MRD) einer Philadelphia-Chromosom-positiven ALL
Wissenschaftl. Titel	A confirmatory multicenter, single-arm study to assess the efficacy, safety, and tolerability of ponatinib (Iclusig®) in adult patients with minimal residual disease (MRD) in Philadelphia-Chromosome positive acute lymphoblastic leukemia
Kurztitel	GMALL-MOLACT2-PONA
Studiennummer KN/ELN	LN_GMALL_2021_713
Studiengruppe	GMALL
Studienart	multizentrisch, einarmig, prospektiv, offen
Studienphase	Phase II
Erkrankung	Akute lymphatische Leukämie (ALL) - Ph/BCR ABL +
Leukämiestadium	MRD positiv
Molekularer Marker	BCR-ABL

Einschlusskriterien

- Patients with Philadelphia-Chromosome/BCR-ABL1 positive ALL in complete hematological remission defined as less than 5% blasts in bone marrow after at least three intense chemotherapy blocks (e.g., GMALL induction I-II/consolidation I for patients < 55 years or after consolidation II for patients > 55 years) who received treatment with at least one tyrosine kinase inhibitor
- Presence of minimal residual disease (MRD) in molecular failure or with molecular relapse documented after an interval of at least 2 weeks from last systemic chemotherapy (Definition of Molecular failure/Mo-lecular Relapse: BCR-ABL1/ABL1>10E-04 and BCR-ABL1 copies > 10)
- Molecular evaluation for BCR-ABL1 performed
- Bone marrow function as defined below: ANC (Neutrophils) 1,000/L Platelets 50,000/L (transfusion permitted) HB level 9g/dl (transfusion permitted)
- ECOG performance status 2
- Normal QTcF interval 450 ms for males and 470 ms for females
- Normal serum levels > LLN (lower limit of normal) of potassium and magnesium, or corrected to within normal limits with supplements, prior to the first dose of study medication
- Adequate renal, hepatic and pancreatic function
- Minimum life expectancy of 3 months
- Negative pregnancy test and agree to use effective form of contraception (as applicable)
- Age 18 years
- Ability to understand and willingness to sign a written informed consent
- Signed and dated written informed consent is available
- Participation in the registry of the German Multicenter Study Group for Adult ALL (GMALL)

Ausschlusskriterien

- Ph-negative ALL
- Presence of circulating blasts or current extramedullary involvement by ALL
- Current detection of ALL blast cells in cerebro-spinal fluid
- Any cancer chemotherapy or immunotherapy after sampling for the MRD test which leads to study inclu-sion (except for intrathecal prophylaxis and continued tyrosine kinase inhibitor)
- Autologous hematopoietic stem cell transplantation (SCT) or allogeneic SCT

- Treatment with any investigational product within four weeks prior to study treatment or within five terminal elimination half-lives of a preceding investigational medicinal product or of its relevant me-tabolite. The longer period of time will apply
- History of malignancy other than ALL diagnosed within 5 years prior to start of protocol-specified ther-apy with the exception of: a. Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease b. Adequately treated cervical carcinoma in situ without evidence of disease c. Adequately treated breast ductal carcinoma in situ without evidence of disease d. Prostatic intraepithelial neoplasia without evidence of prostate cancer
- Active infection, any other concurrent disease or medical condition that are deemed to interfere with the conduct of the study as judged by the investigator
- Pregnant and nursing women
- Woman of childbearing potential and is not willing to use highly effective methods (as defined in the pro-tocol) of contraception while receiving study treatment and for an additional 3 months after the last dose of study treatment (Pearl-Index <1%). Women of childbearing potential are defined as mature women without hysterectomie or surgical sterilization or women without menopause. Menopause means without menstruation for natural reasons for one year
- Male who has a female partner of childbearing potential, and is not willing to use highly effective forms (as defined in the protocol) of contraception while receiving study treatment and for at least an additional 3 months after the last dose of study treatment (Pearl-Index <1%)
- Tyrosine kinase inhibitor (TKI) treatment within 3 days prior to receiving the first dose of ponatinib
- Treatment with medications that are known to be associated with torsades de pointes
- Prior treatment with ponatinib
- History or presence of clinically significant bleeding or coagulation disorder unrelated to completed ALL treatment elements, e.g asparaginase treatment
- History of pancreatitis within 1 year of study start or history of chronic pancreatitis, serum lipase and amylase 1.5 x ULN
- Known impaired cardiac function, including any of the following: a. LVEF < 40% b. Complete left bundle branch block c. Right bundle branch block plus left anterior hemiblock, bifascicular block d. History of or presence of clinically significant ventricular or atrial tachyarrhythmias e. Clinically significant resting bradycardia (< 50 beats per minute) f. Congenital long QT syndrome or QTcF >470 msec on screening ECG. If QTc > 470 msec and electrolytes are not within normal ranges before ponatinib dosing, electrolytes should be cor-rected and then the patient rescreened for QTcF criterion. g. Previous myocardial infarction h. Other clinically significant heart disease (e.g. unstable angina, congestive heart failure, uncontrolled hypertension) i. History of or presence of clinically relevant peripheral vascular disease or other vascular ste-nosis or occlusion, j. Any history of ischemic stroke or transient ischemic attacks (TIAs)
- Inadequate hepatic functions defined as ASAT or ALAT > 2.5 times the institutional upper limit of normal (ULN) or > 5 times ULN if considered due to leukemia
- Total bilirubin >1.5 fold the institutional ULN unless considered to be due to organ involvement by the leukemia or to M. Gilbert / M. Meulengracht
- Concurrent severe diseases which exclude the administra-tion of therapy
- Uncontrolled hypertriglyceridemia (triglycerides >450 mg/dL)
- Major surgery within 14 days prior to first dose of ponatinib
- Ongoing or active infection

	- Malabsorption syndrome or other gastrointestinal illness that could affect absorption of ponatinib - Any other condition or illness that would compromise safety
Alter	>= 18 Jahre
Status	Aktiv
Beginn der Rekrutierung	18.03.2021
Studienleiter/in	Pfeifer, Dr. med., Heike Universitätsklinikum Frankfurt Medizinische Klinik II Theodor-Stern Kai 7 60590 Frankfurt / Main Tel: +49 (0)69 6301-83044 Fax: +49 (0)69 6301-83046 E-Mail: h.pfeifer@em.uni-frankfurt.de
Sponsoren	Universitätsklinikum Frankfurt (Hauptsponsor)
Förderer	Incyte Corporation
Registrierung in anderen Studienregistern	European Clinical Trials Database - EUDRACT2019-004491-19 (primäres Register)