Kompetenznetz "Akute und chronische Leukämien"

KURZPROTOKOLL

TUD-RELAX1-070

Öffentlicher Titel	Phase-I/II Studie zu Venetoclax bei refraktärer AML
Wissenschaftl. Titel	Phase-I/II Studie für Patienten mit rezidivierter oder refraktärer Akuter Myeloischer Leukämie (AML) mit Venetoclax in Kombination mit Cytarabin und Mitoxantron
Kurztitel	TUD-RELAX1-070
Studiennummer KN/ELN	LN_SALAML_2020_695
Studiengruppe	SAL / AMLCG
Studienart	multizentrisch, einarmig, prospektiv, offen
Studienphase	Phase I/II
Erkrankung	Akute myeloische Leukämie (AML) - AML alle außer FAB M3
Leukämiestadium	rezidiviert/refraktär

Einschlusskriterien

- Ability to understand and the willingness to sign a written informed consent. A signed informed consent must be obtained before screening
- AML according to WHO-2016 criteria, excluding acute promyelocytic leukemia
- Relapsed from first or second CR after 1-2 cycles of standard induction chemotherapy (which must have included cytarabine with an anthracycline or anthracenedione), including relapse after allogeneic stem cell transplantation (dose escalation and expansion part)
- Age 18-75 years
- Fit for intensive chemotherapy, defined by • ECOG 0-2, life expectancy > 3months • Adequate hepatic function: ALAT/ASAT/Bilirubin <=2.5 x ULN* o unless considered due to leukemic organ involvement Note: Subjects with Gilbert's Syndrome may have a bilirubin > 2.5 × ULN per discussion between the investigator and Coordinating investigator. • Adequate renal function assessed by serum creatinine <= 1.5x ULN OR creatinine clearance (by Cockcroft Gault formula) >= 50 mL/min
- Patient is afebrile and hemodynamically stable for at least 72 hours at the time of study medication initiation
- Male subjects must agree to refrain from unprotected sex and sperm donation from time point of signing the informed consent until 30 days after the last dose of study drug
- Women must fulfill at least one of the following criteria in order to be eligible for trial inclusion: Post-menopausal (12 months of natural amenorrhea or 6 months of amenorrhea with Serum FSH > 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 - IUD) from time point of signing the informed consent until 30 days after the last dose of study drug. Note: At present, it is not known whether the effectiveness of hormonal contraceptives is reduced by venetoclax. For this reason, women should use a barrier method in addition to hormonal contraceptive methods
- Sexual abstinence
- Vasectomy of the sexual partner
- Inclusion criteria applying for expansion phase (Phase II) only: • Primary refractory after 1-2 cycles of standard induction chemotherapy (100 to 200 mg/m2 cytarabine over 7-10 days plus anthracycline or mitoxantrone over 3 days) or relapsed from first or second CR after 1-2 cycles of standard induction chemotherapy (which must have included cytarabine with an anthracycline or anthracenedione), including relapse after allogeneic stem cell transplantation

Ausschlusskriterien

- Acute promyelocytic leukemia (AML M3)
- CNS involvement or subjects with extramedullary disease only

- Known hypersensitivity to excipients of the preparation or any agent given in association with this study including cytarabine or mitoxantrone
- Intended hematopoietic stem cell transplantation planned as early conditioning from aplasia without previous blood count recovery
- Cumulative previous exposure to anthracyclines of >410 mg/m2 doxorubicin equivalents
- Acute GVHD >= grade 2, extensive chronic GVHD or requiring systemic immunosuppressive therapy within 2 weeks prior to start of study treatment
- HIV infection (due to potential drug-drug interactions between antiretroviral medications and venetoclax, as well as anticipated venetoclax mechanism-based lymphopenia that may potentially increase the risk of opportunistic infections)
- Inability to swallow oral medications
- Any malabsorption condition
- Treatment with strong and moderate CYP3A inhibitors (see Appendix 1) during screening
- Cardiovascular disability status of New York Heart Association (NYHA) Class >= 2. Class 2 is defined as cardiac disease in which patients are comfortable at rest but ordinary physical activity results in fatigue, palpitations, dyspnea, or anginal pain
- Chronic respiratory disease that requires continuous oxygen use
- White blood cell count > 25 × 109/L. Note: Hydroxyurea is permitted to meet this criterion
- AML relapse treatment with any investigational or commercial drug within 14 days before enrolment. Hydroxyurea is allowed until enrolment to control peripheral WBC counts. Toxic effects of previous investigational drug treatment have to recover to Grade <2
- Substance abuse, medical, psychological, or social conditions that may interfere with the subject's cooperation with the requirements of the trial or evaluation of the study results
- Pregnant or breastfeeding women. Breastfeeding has to be discontinued before onset of and during treatment and should be discontinued for at least 3 months after end of treatment
- History of active or chronic infectious 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 B core antibody) may be included if HBV DNA is undetectable, provided that they are willing to undergo monthly DNA testing. Patients who have protective titers of hepatitis B surface antibody after vaccination or prior but cured hepatitis B are eligible. Patients positive for hepatitis C virus antibody are eligible provided PCR is negative for HCV RNA)
- History of clinically significant liver cirrhosis (e.g., Child-Pugh class B and C)
- Live-virus vaccines given within 28 days prior to the initiation of study treatment

Alter	18 - 75 Jahre
Status	Aktiv
Beginn der Rekrutierung	06.05.2020
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Sponsoren	Technische Universität Dresden

Registrierung in anderen Studienregistern	ClinicalTrials.govNCT04330820 European Clinical Trials Database - EUDRACT2018-003025-28