KURZPROTOKOLL
GMALL-Isatuximab

Öffentlicher Titel	Phase-2-Studie zu Isatuximab bei rezidivierter/refrektärer akuter lymphoblastischer Leukämie
Wissenschaftl. Titel	A multicenter, single-arm phase II study to assess the safety, tolerability, and efficacy of Isatuximab in adult patients with cytologic or molecular relapsed/refractory CD38 positive T-cell acute lymphoblastic leukemia
Kurztitel	GMALL-Isatuximab
Studienart	multizentrisch, prospektiv, Therapiestudie, einarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase II
Erkrankung	Blut: Akute lymphatische Leukämie (ALL): Rezidiviert/refraktär
Einschlusskriterien	- Patients with CD38 positive T-ALL fitting either to the definitions for cohort 1 or cohort 2 - Adequate renal function defined as follows: - Serum creatinine 2 x ULN; - Any serum creatinine level associated with a calculated creatinine clearance >= 40 mL/min - Negative pregnancy test in women of childbearing potential (WOCBP) - WOCBP must commit to either abstain continuously from heterosexual sexual intercourse or to use 2 methods of reliable birth control simultaneously - Men who are sexually active with a WOCBP must agree to use a barrier method of contraception - Participation in the registry of the German Multicenter Study Group for Adult ALL (GMALL) - Cohort 1: In relapse or with primary refractory disease defined as 5% blasts in bone marrow after at least three chemotherapy cycles (induction I-II, consolidation I) with the following additional specifications: • early relapse within 12 months from first achievement of CR or • late relapse later than 12 months from first achievement of CR or • primary refractory disease without any CR or • any relapse after stem cell transplantation or • any refractory relapse, defined as no response to at least one salvage therapy or • any second or later relapse and • Availability of patient material with blast cells (bone marrow or peripheral blood) for central MRD assessment - Cohort 2: In complete hematological remission (defined as less than 5% blasts in bone marrow and no evidence of extramedullary disease) after at least three chemotherapy cycles (induction I-II, consolidation I) - Cohort 2: Detection of quantifiable MRD at a level of 10-4, either as molecular failure without prior achievement of molecular remission or molecular relapse after prior achievement of molecular remission - Cohort 2: MRD assay at the central reference lab with at least one marker a minimum sensitivity of 10-4 - Cohort 2: MRD detection for study inclusion after an interval of at least 2 weeks from last systemic chemotherapy including antibody therapy - Cohort 2: In patients without clonal molecular MRD marker, MRD testing can be based on flow-cytometry established in reference laboratory - ECOG status: • Cohort 1: 0-2 • Cohort 2: 0-1 - Evidence of a personally signed and dated informed consent indication that the patient has been informed of all pertinent aspects of the study - Patient must be willing and able to comply with scheduled visits, treatment plan, laboratory tests and other study procedures - Regeneration from last chemotherapy defined as follows: • Cohort 1: -Platelets >=10.000/µL (platelet transfusion allowed); - Hemoglobin >=7.5 g/dL (red blood cell transfusion allowed) • Cohort 2: -Neutrophils >=1.000/µL; -Platelets >=50.000/µL; - Hemoglobin >=9 g/dL

- Adequate liver function defined as follows: - Bilirubin 1.5 ULN (unless Gilbert Meulengracht disease or classified as result of liver infiltration by investigator); - AST and ALT 2.5 x ULN (unless classified as result of liver infiltration by investigator)

Ausschlusskriterien

- Extramedullary involvement except for non-bulky (<7.5 cm) lymph node involvement, splenomegaly, or hepatomegaly
- Treatment with an investigational agent within 4 weeks from start of study treatment (safety follow-up period of respective study)
- Concurrent active malignancy other than non-melanoma skin cancer, carcinoma in situ of the cervix, or localized prostate cancer that has been treated with radiation or surgery; patients with previous malignancies are eligible if they have been disease free for >= 2 years and do not require any antitumor therapy
- Evidence of uncontrolled current serious active infection or recent history (within 4 months) of deep tissue infections such as fasciitis or osteomyelitis
- Known allergies, hypersensitivity, or intolerance to Boron or Mannitol, corticosteroids, mAb (including Isatuximab) or human proteins, or their excipients (refer to respective Summary of Product Characteristics), or known sensitivity to mammalian-derived products
- 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 or breastfeeding females
- Vaccination with live attenuated vaccines within 4 weeks of first study agent administration
- Other severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results and, in the judgement of the investigator, would make the patient inappropriate for entry into this study
- Patients who have received prior antileukemic immunotherapy within 2 weeks prior to start of Isatuximab treatment
- Patients who have received treatment for leukemia with chemotherapy as follows: • Cohort 1: Patients who have received treatment for leukemia with chemotherapy within 2 weeks prior to start of Isatuximab treatment (exception: pre-phase therapy with 5-7 days of Dexamethasone, 3 days of Cyclophosphamide; intrathecal prophylaxis); • Cohort 2: Any chemotherapy or antibody therapy after the MRD assay leading to study inclusion (exception: intrathecal prophylaxis)
- Patients must have recovered from acute non-hematologic toxicity form previous therapies to grade I unless signs or symptoms are correlated to leukaemia involvement
- Prior SCT 3 months from start of study treatment
- Acute GvHD >= grade II or active chronic GvHD requiring systemic treatment
- Any systemic GvHD prophylaxis or treatment within 2 weeks from start of study treatment
- Known HIV positivity, known hepatitis B surface antigen positivity or known history of hepatitis C
- Unstable or severe uncontrolled medical condition e.g. unstable cardiac function or unstable pulmonary condition

Alter

18 Jahre und älter

Prüfzentren	**Innere Medizin 2** (Aktiv) Hämatologie / Medizinische Onkologie Theodor-Stern-Kai 7 60590 Frankfurt am Main Marieke Brinkmann Tel: 069 6301-86389
Sponsor	Goethe-Universität Frankfurt
Förderer	Sanofi Aventis GmbH
Registrierung in anderen Studienregistern	EUCT 2023-507899-47-00
Links	Weiterführende Informationen Studiendokumente zum Download (roXtra)