KURZPROTOKOLL
ZUMA-3

Öffentlicher Titel	Phase I/II Studie einer T-Zelltherapie bei rezidivierter oder refraktärer B-Vorläufer ALL
Wissenschaftl. Titel	A Phase 1/2 Multi-Center Study Evaluating the Safety and Efficacy of KTE-X19 in Adult Subjects with Relapsed/Refractory B-precursor Acute Lymphoblastic Leukemia (r/r ALL)
Kurztitel	ZUMA-3
Studienart	multizentrisch, prospektiv, Therapiestudie, offen/unverblindet, einarmig, Pharma-Studie
Studienphase	Phase I/II
Erkrankung	Blut: Akute lymphatische Leukämie (ALL): Rezidiviert/refraktär

Einschlusskriterien

- Relapsed or refractory B-precursor ALL defined as one of the following:
- -> Primary refractory disease
- -> Relapsed or refractory disease after 2 or more lines of systemic therapy
- -> First relapse if first remission <= 12 months
- -> Relapsed or refractory disease after allogeneic transplant provided individuals is at least 100 days from stem cell transplant at the time of enrollment
- Morphological disease in the bone marrow (>= 5% blasts)
- Individuals with Ph+ disease are eligible if they are intolerant to tyrosine kinase inhibitor (TKI) therapy, or if they have relapsed/refractory disease despite treatment with at least 2 different TKIs
- Age 18 or older
- Eastern cooperative oncology group (ECOG) performance status of 0 or 1
- Adequate renal, hepatic, pulmonary and cardiac function defined as:
- -> Creatinine clearance (as estimated by Cockcroft Gault) >= 60 cc/min
- -> Serum alanine aminotransferase (ALT)/aspartate aminotransferase (AST) <= 2.5 x upper limit of normal (ULN)
- -> Total bilirubin <= 1.5 mg/dl, except in individuals with Gilbert's syndrome
- -> Cardiac ejection fraction >= 50%, no evidence of pericardial effusion, and no clinically significant arrhythmias
- -> Baseline oxygen saturation > 92% on room air
- In individuals previously treated with blinatumomab, CD19 tumor expression in bone marrow or peripheral blood.

Ausschlusskriterien

- Diagnosis of Burkitt's leukemia/lymphoma according to World Health Organization (WHO) classification or chronic myelogenous leukemia lymphoid blast crisis
- History of malignancy other than non-melanoma skin cancer or carcinoma in situ (e.g. cervix, bladder, breast) unless disease free for at least 3 years
- Isolated extramedullary disease
- Central nervous system (CNS) abnormalities
- -> Presence of CNS-3 disease or CNS-2 disease with neurological changes
- -> History or presence of any CNS disorder such as a seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, or any autoimmune disease with CNS involvement
- History of concomitant genetic syndrome such as Fanconi anemia, Kostmann syndrome, Shwachman-Diamond syndrome or any other known bone marrow failure syndrome
- History of myocardial infarction, cardiac angioplasty or stenting, unstable angina, or other clinically significant cardiac disease within 12 months of enrollment
- History of symptomatic deep vein thrombosis or pulmonary embolism within 6 months of enrollment.
- Primary immunodeficiency

- Known infection with HIV, hepatitis B (HBsAg positive) or hepatitis C virus (anti-HCV positive).
- Presence of fungal, bacterial, viral, or other infection that is uncontrolled or requiring IV antimicrobials for management.
- Prior medication:
- -> Salvage chemotherapy including TKIs for Ph+ ALL within 1 week prior to enrollment
- -> Prior CD19 directed therapy other than blinatumomab
- -> Treatment with alemtuzumab within 6 months prior to leukapheresis, or treatment with clofarabine or cladribine within 3 months prior to leukapheresis
- -> Donor lymphocyte infusion (DLI) within 28 days prior to enrollment
- -> Any drug used for graft-versus-host disease (GVHD) within 4 weeks prior to enrollment
- -> At least 3 half-lives must have elapsed from any prior systemic inhibitory/stimulatory immune checkpoint molecule therapy prior to enrollment
- -> Corticosteroid therapy for 7 days prior to enrollment
- Presence of any indwelling line or drain (e.g., percutaneous nephrostomy tube, indwelling Foley catheter, biliary drain, or pleural/peritoneal/pericardial catheter). Ommaya reservoirs and dedicated central venous access catheters such as a Port-a-Cath or Hickman catheter are permitted
- Acute GVHD grade II-IV by Glucksberg criteria or severity B-D by IBMTR index; acute or chronic GVHD requiring systemic treatment within 4 weeks prior to enrollment
- Live vaccine <= 4 weeks prior to enrollment
- Women of child-bearing potential who are pregnant or breastfeeding because of the potentially dangerous effects of the preparative chemotherapy on the fetus or infant. Females who have undergone surgical sterilization or who have been postmenopausal for at least 2 years are not considered to be of childbearing potential
- Individuals of both genders of child-bearing potential who are not willing to practice birth control from the time of consent through 6 months after the completion of KTE-X19
- In the investigators judgment, the individuals is unlikely to complete all protocol-required study visits or procedures, including follow-up visits, or comply with the study requirements for participation
- History of autoimmune disease (e.g. Crohns, rheumatoid arthritis, systemic lupus) resulting in end organ injury or requiring systemic immunosuppression/systemic disease modifying agents within the last 2 years

Alter	18 Jahre und älter
Molekularer Marker	CD19
Prüfzentren	**Universitätsklinikum Frankfurt** (Geschlossen) Medizinische Klinik II, Hämatologie/Onkologie Theodor-Stern-Kai 7 60590 Frankfurt am Main Silvia Koss Tel: 069 6301-80429 Fax: 069 6301-83655 silvia.koss@unimedizin-ffm.de
Sponsor	Kite Pharma Inc.
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT02614066 (primäres Register) EudraCT 2015-005009-35

Links Studiendokumente zum Download (roXtra)