KURZPROTOKOLL
GMALL-BLIVEN

Öffentlicher Titel	Phase I/II Studie zu Venetoclax und Blinatumomab bei rezidivierter/refraktärer oder MRD -positiver ALL
Wissenschaftl. Titel	An open label, phase I/II study of Venetoclax in addition to Blinatumomab immunotherapy in adult patients with relapsed/refractory B cell precursor acute lymphoblastic leukemia (BCP-ALL)
Kurztitel	GMALL-BLIVEN
Studienart	multizentrisch, prospektiv, Therapiestudie, offen/unverblindet, Investigator Initiated Trial (IIT)
Studienphase	Phase I/II
Erkrankung	Blut: Akute lymphatische Leukämie (ALL): Rezidiviert/refraktär
Einschlusskriterien	- 1. Written informed consent in accordance with federal, local, and institutional guidelines. The patient must provide informed consent prior to the first screening procedure - 2. Age >= 18 years - 3. Eastern Cooperative Oncology Group (ECOG) performance status of <= 2 - 4. Availability of patient-specific molecular MRD markers of immunoglobulin/T-cell receptor gene rearrangementsas assessed by PCR with a sensitivity of at least 10E-04 - 5. Diagnosis of Philadelphia negative, CD19-positive B-precursor acute lymphoblastic leukemia according to WHO classification: a) Refractory BCP-ALL to primary induction therapy, including at least three cycles of standard chemotherapy; b) Untreated first relapse of BCP-ALL with first remission duration < 12 months or c)Second or greater relapse of BCP-ALL or refractory relapse or d) Relapse of BCP-ALL any time after allogeneic HSCT or - 6. Positivity of MRD marker of immunoglobulin/T-cell receptor gene rearrangements of greater than 0.1% if in first or second remission of BCP-ALL - 7. Negative pregnancy test in women of childbearing potential - 8. Ability to understand and willingness to sign a written informed consent - 9. Willingness to participate in the registry of the German Multicenter Study Group for Adult ALL (GMALL)
Ausschlusskriterien	- 1. Patients with diagnosis of Philadelphia positive BCP-ALL - 2. Patients with diagnosis of Burkitt's Leukemia - 3. Patients with extramedullary relapse - 4. Patients with CNS involvement at relapse - 5. Patients with suspected or histologically confirmed testicular involvement at relapse - 6. Current autoimmune disease of any kind or history of autoimmune disease with potential CNS involvement - 7. Patients with Philadelphia-positive BCP-ALL still receiving TKI - 8. Prior or concomitant therapy with BH3 mimetics - 9. Prior therapy with anti CD19 therapy, unless administered in MRD-positive setting - 10. Treatment with any of the following within 7 days prior to the first dose of study drug: strong cytochrome P450 3A (CYP3A) inhibitors, moderate or strong CYP3A inducers - 11. Intake of any of the following within 3 days prior to the first dose of study drug: grapefruit, grapefruit products, Seville oranges or star fruit - 12. Presence of GvHD and/or on immunosuppressant medication within 2 weeks before start of protocol-specified therapy

- 13. Radiation, chemotherapy (with the exception of prephase therapy), or immunotherapy or any other anticancer therapy <= 2 weeks prior to Cycle 1 Day 1 or radio-immunotherapy 4 weeks prior to Cycle 1 Day 1
- 14. Major surgery within 2 weeks of first dose of study drug
- 15. Patients who are pregnant or lactating
- 16. Any life-threatening illness, medical condition or organ system dysfunction which, in the investigator's opinion, could compromise the patient's safety
- 17. Unstable cardiovascular function: a) Symptomatic ischemia, or b) Uncontrolled clinically significant conduction abnormalities, or c) CHF of NYHA Class >= 3, or d) MI within 3 months
- 18. Evidence of clinically significant uncontrolled condition(s) including, but not limited to: Uncontrolled and/or active systemic infection (viral, bacterial or fungal), chronic HBV or HCV requiring treatment
- 19. Known HIV infection
- 20. Patients unable to swallow tablets, patients with malabsorption syndrome, or any other GI disease or GI dysfunction that could interfere with absorption of study treatment
- 21. Adequate hepatic function per local laboratory reference range as follows: AST and ALT < 3.0X ULN, Bilirubin <= 1.5 x ULN (unless bilirubin rise is due to Gilbert's syndrome or of non-hepatic origin)
- 22. Severe renal dysfunction: estimated creatinine clearance of < 20 mL/min, measured in 24 hour urine or calculated using the formula of Cockroft and Gault
- 23. History or presence of clinically relevant CNS pathology such as epilepsy, childhood or adult seizure, paresis, aphasia, stroke, severe brain injuries, dementia, Parkinson's disease, cerebellar disease, organic brain syndrome, or psychosis
- 24. History of malignancy other than ALL within 5 years prior to start of protocol-specified therapy with the exception of: a) Malignancy treated with curative intent and with no known active disease present for 2 years before enrollment and felt to be at low risk for recurrence by the treating physician including; b) Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease; c) Adequately treated cervical carcinoma in situ without evidence of disease; d) Adequately treated breast ductal carcinoma in situ without evidence of disease; e) Prostatic intraepithelial neoplasia without evidence of prostate cancer
- 25. Current autoimmune disease or history of autoimmune disease with potential CNS involvement
- 26. Live vaccination within 2 weeks before the start of study treatment
- 27. Known hypersensitivity to immunoglobulins or to any other component of the study drug formulation
- 28. Subject has known sensitivity to immunoglobulins or any of the products or components to be administered during dosing
- 29. Currently receiving treatment in another investigational device or drug study or less than 30 days since ending treatment on another investigational device or drug study(s). Thirty days is calculated from day 1 of protocol-specified therapy
- 30. Subject likely to not be available to complete all protocol-required study visits or procedures, including follow-up visits, and/or to comply with all required study procedures to the best of the subject's and Investigator's knowledge
- 31. History or evidence of any other clinically significant disorder, condition or disease (with the exception of those outlined above) that, in the opinion of the investigator would pose a risk to subject safety or interfere with the study evaluation, procedures or completion

	- 32. Woman of childbearing potential and is not willing to use a highly effective method of contraception while receiving study treatment and for an additional 3 months after the last dose of study treatment - 33. Male who has a female partner of childbearing potential, and is not willing to use 2 highly effective forms of contraception while receiving protocol-specified therapy and for at least an additional 3 months after the last dose of protocol-specified therapy
Alter	18 Jahre und älter
Molekularer Marker	CD19
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Sponsor	Goethe-Universität Frankfurt
Förderer	AbbVie
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT05182385 EudraCT 2021-001384-25 (primäres Register)
Links	Zu den Ein- und Ausschlusskriterien Studiendokumente zum Download (roXtra)