KURZPROTOKOLL
CLLRUmbrella1

Öffentlicher Titel	Phase II Studie zu Tirabrutinib, Idelalisib und Obinutuzumab bei CLL
Wissenschaftl. Titel	Eine prospektive, unverblindete, multizentrische Phase-II-Studie zur Evaluation der Sicherheit und Wirksamkeit der Kombination von Tirabrutinib (GS-4059) und Idelalisib mit und ohne Obinutuzumab bei Patienten mit chronischer lymphatischer Leukämie
Kurztitel	CLLRUmbrella1
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, offen/unverblindet, Pharma-Studie, zweiarmig
Studienphase	Phase II
Erkrankung	Blut: Non-Hodgkin-Lymphome (NHL), niedrig-maligne: Chronische lymphatische Leukämie (CLL) - rezidiviert/refraktär

Einschlusskriterien

- Documentation of relapsed or refractory CLL
- Requiring treatment per modified IWCLL 2008 criteria; subjects without radiographically mensurable disease (defined as >= 1 lesion > 1.5 cm in diameter as assessed by computed tomography (CT) or magnetic resonance imaging [MRI]) must have bone marrow evaluation at screening
- Adequate hematologic function: platelet count 50 × 10^9/L, neutrophil count >= 1 × 10^9/L, hemoglobin >= 8 g/dL unless lower values are directly attributable to documented bone marrow burden of CLL
- Creatinine clearance (CrCl) >= 50 mL/min
- Total bilirubin <= 1.5× institutional upper limit of normal (ULN) unless attributed to Gilbert's syndrome and aspartate transaminase (AST)/alanine transaminase (ALT) <= 2.5×ULN
- Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) <= 2
- Absence of active HIV, hepatitis B virus (HBV) infection, hepatitis C virus (HCV) infection, and cytomegalovirus (CMV) infection
- Satisfies the following criteria: a) For females of childbearing potential, willingness to abstain from sexual intercourse or use a protocol-specified method of contraception as described in the study protocol: b) Males of reproductive potential who engage in sexual intercourse must agree to use protocol-specified method(s) of contraception as described in the study protocol
- Able to comply with study procedures and restrictions including mandatory prophylaxis for Pneumocystis jirovecii pneumonia (PJP)

Ausschlusskriterien

- Known transformation of CLL (ie, Richter's transformation, prolymphocytic leukemia)
- Known central nervous system (CNS) involvement
- Progression on treatment with any inhibitor of Bruton's tyrosine kinase (BTK), spleen tyrosine kinase (SYK), phosphatidylinositol 3-kinase (PI3K), B-cell lymphoma 2 (BCL-2), or obinutuzumab. The treatment and disease response history of individuals with prior treatment with agents in these classes should be reviewed by the sponsor or the GCLLSG study office prior to enrollment to clarify sensitivity to these treatments.
- Any treatment for CLL other than corticosteroids for symptomatic management within 28 days of the start of study treatment
- Participation on a concurrent therapeutic clinical trial unless all treatment is complete with only ongoing surveillance
- Diagnosis of or concern for progressive multifocal leukoencephalopathy

	- History of myelodysplastic syndrome or another malignancy other than CLL, except for the following: any malignancy that has been in complete remission for 3 years, adequately treated local basal cell or squamous cell carcinoma of the skin, cervical carcinoma in situ, superficial bladder cancer, asymptomatic prostate cancer without known metastatic disease and with no requirement for therapy or requiring only hormonal therapy and with normal prostate-specific antigen for >=1 year prior to start of study therapy - Active infection requiring systemic therapy - Pregnant or nursing women (a negative pregnancy test is required for all women of childbearing potential within 7 days before start of treatment and monthly during therapy) - Active autoimmune disease or the need for higher than prednisone 10 mg daily unless for management of CLL symptoms - Treatment or prophylaxis for CMV within the past 28 days - History of stroke or intracranial hemorrhage within 12 months of randomization; subjects requiring therapeutic anticoagulation for any indication should be discussed with the German CLL Study Group (GCLLSG) cooperating physician and/or medical monitor prior to screening. - Use of a strong CYP3A4 or a strong P-gp inducer within 2 weeks of first dose of study treatment or anticipated chronic use while on study - Demonstration of corrected QT (QTc) interval > 450 milliseconds or requirement for ongoing treatment with concomitant medications that prolong the QT interval Note: Other protocol defined Inclusion/Exclusion criteria may apply.
Alter	18 Jahre und älter
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Sponsor	GILEAD
Registrierung in anderen Studienregistern	EudraCT 2015-003909-42 ClinicalTrials.gov NCT02968563