KURZPROTOKOLL
CLL 13

Öffentlicher Titel	Phase-III-Studie für CLL-Patienten ohne del(17p) oder TP53 Mutationen, die eine von vier Kombinationstherapien zur Erstlinienbehandlung erhalten: Standardchemoimmuntherapie, Rituximimab + Venetoclax, Obinutuzumab + Venetoclax oder Obinutuzumab + Ibrutinib + Venetoclax
Wissenschaftl. Titel	A phase 3 multicenter, randomized, prospective, open-label trial of standard chemoimmunotherapy (FCR/BR) versus rituximab plus ve-netoclax (RVe) versus obinutuzumab (GA101) plus venetoclax (GVe) versus obinutuzumab plus ibrutinib plus venetoclax (GIVe) in fit pa-tients with previously untreated chronic lymphocytic leukemia (CLL) without del(17p) or TP53 mutation
Kurztitel	CLL 13
Studienart	multizentrisch, Therapiestudie, offen/unverblindet, mehrarmig
Studienphase	Phase III
Erkrankung	Blut: Non-Hodgkin-Lymphome (NHL), niedrig-maligne: Chronische lymphatische Leukämie (CLL) - neu diagnostiziert / de novo
Einschlusskriterien	- 1. Documented CLL requiring treatment according to iwCLL criteria12. - Age at least 18 years. - Life expectancy 6 months. - Ability and willingness to provide written informed consent and to ad-here to the study visit schedule and other protocol requirements. - Adequate bone marrow function indicated by a platelet count >30 x10^9/l (unless directly attributable to CLL infiltration of the bone marrow, proven by bone marrow biopsy) - Creatinine clearance 70ml/min directly measured with 24hr urine collection or calculated according to the modified formula of Cockcroft and Gault (for men: GFR ((140 - age) x bodyweight) / (72 x creatinine), for women x 0, 85). Dehydrated patients with an estimated creatinine clearance less than 70 ml/min may be eligible if a repeat estimate after adequate hydration is > 70 ml/min. - Adequate liver function as indicated by a total bilirubin 2 x, AST/ALT 2.5 x the institutional ULN value, unless directly attributable to the patient’s CLL or to Gilbert’s Syndrome. - Negative serological testing for hepatitis B (HBsAg negative and anti-HBc negative; patients positive for anti-HBc may be included if PCR for HBV DNA is negative and HBV-DNA PCR is performed every month until 12 months after last treatment cycle), negative testing for hepatitis C RNA within 6 weeks prior to registration. - Eastern Cooperative Oncology Group Performance Status (ECOG) performance status 0-2.
Ausschlusskriterien	- Any prior CLL-specific therapies (except corticosteroid treatment ad-ministered due to necessary immediate intervention; within the last 10 days before start of study treatment, only dose equivalents of 20 mg prednisolone are permitted). - Transformation of CLL (Richter transformation). - Decompensated hemolysis, defined as ongoing hemoglobin drop in spite of three more concurrent treatments being administered for he-molysis - Detected del(17p) or TP53 mutation. - Patients with a history of PML. - Any comorbidity or organ system impairment rated with a single CIRS (cumulative illness rating scale) score of 4 (excluding the eyes/ears/nose/throat/larynx organ system), a total CIRS score of more than 6 or any other life-threatening illness, medical condition or organ system dysfunction that, in the investigator´s opinion, could comprise the patients safety or interfere with the absorption or me-tabolism of the study drugs (e.g, inability to swallow tablets or im-paired resorption in the gastrointestinal tract).

- Urinary outflow obstruction.
- Malignancies other than CLL currently requiring systemic therapies, not being treated in curative intention before (unless the malignant disease is in a stable remission due to the discretion of the treating physician) or showing signs of progression after curative treatment.
- Uncontrolled or active infection.
- Patients with known infection with human immunodeficiency virus (HIV).
- Requirement of therapy with strong CYP3A4 and CYP3A5 inhibi-tors/inducers.
- Anticoagulant therapy with warfarin or phenoprocoumon, (rotation to alternative anticoagulation is allowed, but note that patients being treated with NOAKs can be included, but must be properly informed about the potential risk of bleeding under treatment with ibrutinib).
- History of stroke or intracranial hemorrhage within 6 months prior to registration.
- Use of investigational agents which might interfere with the study drug within 28 days prior to registration.
- Vaccination with live vaccines 28 days prior to registration.
- Major surgery less than 30 days before start of treatment.
- History of severe allergic or anaphylactic reactions to humanized or murine monoclonal antibodies, known sensitivity or allergy to murine products.
- Known hypersensitivity to any active substance or to any of the excipients of one of the drugs used in the trial.
- Pregnant women and nursing mothers (a negative pregnancy test is required for all women of childbearing potential within 7 days before start of treatment; further pregnancy testing will be performed regularly).
- Fertile men or women of childbearing potential unless: a. surgically sterile or 2 years after the onset of menopause b. willing to use two methods of reliable contraception including one highly effective contraceptive method (Pearl Index <1) and one additional effective (barrier) method during study treatment and for 18 months after the end of study treatment.
- Legal incapacity.
- Prisoners or subjects who are institutionalized by regulatory or court order.
- Persons who are in dependence to the sponsor or an investigator.

Alter	18 Jahre und älter
Fallzahl	920
Sponsor	Universität Köln
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT02950051 EudraCT 2015-004936-36