Kompetenznetz "Akute und chronische Leukämien"

KURZPROTOKOLL

R1979-ONC-1504

Öffentlicher Titel	Phase I Studie zum anti-CD20 und anti-CD3 bispezifischen Antikörper REGN1979 und dem PD-1 Antikörper REGN2810 bei Patienten mit B-Zell-Leukämien
Wissenschaftl. Titel	A Phase 1 Study to Assess Safety and Tolerability of REGN1979, an anti-CD20 x anti-CD3 bispecific monoclonal antibody, and REGN2810, an anti-programmed death-1 (PD-1) monoclonal antibody, in Patients with B-cell Malignancies
Kurztitel	R1979-ONC-1504
Studiennummer KN/ELN	LN_NN_2016_587
Studiengruppe	NN
Studienart	mehrarmig
Studienphase	Phase I
Erkrankung	Akute lymphatische Leukämie (ALL) - Ph/BCR ABL + Akute lymphatische Leukämie (ALL) - B-Vorläufer ALL Akute lymphatische Leukämie (ALL) - Reife B-ALL/NHL
Leukämiestadium	rezidiviert/refraktär
Molekularer Marker	CD20 BCR-ABL
Ziele	- To assess safety, tolerability and dose limiting toxicity (DLT) of: o Single agent REGN2810 in patients with B-cell malignancies including HL o Single agent REGN1979 in patients with ALL o Combination REGN1979 and REGN2810 in patients with B-cell NHL o Combination REGN1979 and REGN2810 in patients with ALL - To determine a recommended dose for: o REGN2810 as a single-agent in patients with lymphoma (B-NHL and HL) o REGN1979 as a single agent in patients with ALL o REGN1979 and REGN2810 administered in combination in patients with B-NHL. o REGN1979 and REGN2810 administered in combination in patients with ALL - To characterize the PK profile of REGN1979 and REGN2810 when administered as single agent and in combination - To assess the immunogenicity of REGN1979 and REGN2810 when administered as single agent and in combination - To study the preliminary antitumor activity of REGN1979 and REGN2810 when administered as single agents in specific indications and in combination as measured by overall response rate (ORR), minimal residual disease (MRD) in patients with bone marrow disease at baseline, duration of response, progression-free survival, median, and rate at 6 and 12 months
Einschlusskriterien	- Principal Inclusion Criteria for Acute Lymphoblastic Leumkemia (ALL) Study Arms: - Documented relapsed or refractory CD20+ (defined as CD20 expression by flow cytometry on 20% of leukemic lymphoblasts) B-lineage ALL after at least induction and 1 cycle of consolidation chemotherapy o Patients with Philadelphia chromosome positive ALL are required to have failed or be intolerant to at least 1 tyrosine-kinase inhibitor - ECOG performance status 2 - CNS negative disease, confirmed by lumbar puncture, within 28 days of starting study drug. - Adequate bone marrow function documented by: o Platelet counts 10 x 109/L o Hb level 7 g/dL o Absolute phagocyte count 0.5 x 109/L (phagocytes: neutrophils, bands and monocytes) - Adequate hepatic function: o Total bilirubin 1.5 x ULN (3 x ULN if liver involvement) o Transaminases 2.5 x ULN (5 x ULN if liver involvement) o Alkaline phosphatase 2.5 x ULN (5 x ULN if liver involvement) - Principal Inclusion Criteria for for B-NHL and HL Treatment Arms:

- Hematologic malignancy defined by either: a. NHL: Documented CD20+ B-cell malignancy, with active disease that is either refractory to or relapsed after most recent prior therapy, for whom no standard of care options exist, and for whom treatment with an anti-CD20 antibody may be appropriate (i. B-NHL per WHO 2008 criteria (Campo 2011)) b. Documented HL, per WHO 2008 criteria (Campo 2011), with active disease not responsive to prior therapy or relapsed after prior therapy for whom no standard of care options exist (REGN2810 single-agent therapy cohorts ONLY)
- All patients must have at least one bi-dimensionally measurable lesion (1.5 cm) documented by diagnostic imaging (CT, PET-CT or MRI)
- Adequate bone marrow function documented by: a. Platelet counts 75 x 109/L b. Hb level 9 g/dL c. ANC 1 x 109/L
- Adequate hepatic function: a. Total bilirubin 1.5 x ULN (3 x ULN if liver involvement) b. Transaminases 2.5 x ULN (5 x ULN if liver involvement) c. Alkaline phosphatase (ALP) 2.5 x ULN (5 x ULN if liver involvement)

Ausschlusskriterien

- Principal Exclusion Criteria for Acute Lymphoblastic Leumkemia (ALL) Study Arms:
- History of or current relevant CNS pathology
- Ongoing or recent (within 2 years) evidence of significant autoimmune disease (with the exception of GvHD) that required treatment with systemic immunosuppressive treatments
- Standard or investigational anti-neoplastic therapy (nonbiologic) within 5-times the half-life or within 14 days, whichever is shorter, prior to first administration of study drug
- Treatment with rituximab, immune-modulating agents or other investigational or commercial biologic agent less than 14 days prior to first administration of study drug(s)
- Treatment with alemtuzumab, within 12 weeks
- Prior Allogeneic stem cell transplantation within 3 months of treatment
- Principal Exclusion Criteria for for B-NHL and HL Treatment Arms:
- Primary central nervous system (CNS) lymphoma, or known or suspected CNS involvement by non-primary CNS NHL
- History of or current relevant CNS pathology
- Ongoing or recent (within 2 years) evidence of significant autoimmune disease that required treatment with systemic immunosuppressive treatments
- Standard or investigational anti-neoplastic therapy (nonbiologic) within 5-times the half-life or within 28 days, whichever is shorter, prior to first administration of study drug
- Treatment with rituximab, immune-modulating agents or other investigational or commercial biologic agent less than 28 days prior to first administration of study drug(s)
- Prior Allogeneic stem cell transplantation
- Prior treatment with an agent that blocks the PD-1/PD-L1 pathway, unless the patient demonstrated benefit (applicable only for patients in single-agent REGN2810 therapy)

Alter	>= 18 Jahre
Status	Rekrutierung beendet
Beginn der Rekrutierung	01.03.2016
Fallzahl	160

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Sponsoren	Regeneron
Registrierung in anderen Studienregistern	European Clinical Trials Database - EUDRACT2015-001697-17