Trial record **1 of 1** for: ImbruVeRCHOP

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Ibrutinib, Bortezomib and Rituximab-CHOP for the Treatment of Elderly Patients With CD20+ DLBCL, IPI ≥ 2 (ImbruVeRCHOP)

This study is currently recruiting participants.

See **Contacts and Locations**

Verified April 2017 *by Prof. Dr. Clemens Schmitt, Charite University, Berlin, Germany*

Sponsor:
Prof. Dr. Clemens Schmitt

Collaborators:
Charite University, Berlin, Germany
Janssen-Cilag Ltd.

Information provided by (Responsible Party):
Prof. Dr. Clemens Schmitt, Charite University, Berlin, Germany

ClinicalTrials.gov Identifier:
NCT03129828

First received: April 20, 2017
Last updated: April 24, 2017
Last verified: April 2017
History of Changes

Full Text View | **Tabular View** | **No Study Results Posted** | Disclaimer

How to Read a Study Record

Purpose

The **ImbruVeRCHOP-**Trials is an Investigator-initiated, single-arm, multi-center, prospective, open phase I/II trial to evaluate the efficacy and feasibility of Ibrutinib and Bortezomib in the therapy of higher-risk DLBCL patients of different molecular subtypes and to correlate outcome with clinical, molecular and imaging-guided response parameters. The protocol includes a safety run-in phase, i.e.

the phase I part of the study, to uncover unexpected toxicities that may arise in the context of Ibrutinib and Bortezomib co-administered with the R-CHOP backbone. The safety run-in phase is followed by the phase II part of the trial. About 60 patients will be included over 3 years. Additional 8-11 German university centers will participate in this trial. The study treatment includes a pre-phase therapy with Prednisone and 6 cycles of a combined immuno-chemotherapy with the anti-CD20 antibody Rituximab together with 6 cycles of a chemotherapy consisting of Cyclophosphamide, Doxorubicin, Vincristine and Prednisone plus Bortezomib and Ibrutinib followed by two additional 3-week cycles of Rituximab. Secondary endpoints are the predictive power of subtypes (such as GCB/ABC-"cell-of-origin"), markers of minimal residual disease over time and during-the-study-determined markers (e.g. gene signatures) to identify patients who benefit from this treatment addition.

Condition	Intervention	Phase
Diffuse Large B Cell Lymphoma	Drug: Ibrutinib and Bortezomib + R-CHOP	Phase 1 Phase 2

Study Type: Interventional
Study Design: Intervention Model: Single Group Assignment
Masking: None (Open Label)
Primary Purpose: Treatment

Official Title: Ibrutinib (Imbruvica®), Bortezomib (Velcade®) s.c., Rituximab, CHOP for the Treatment of Elderly Patients (Age 61-80 Years) With CD20+ Diffuse Large B-cell Lymphoma, IPI ≥ 2

Resource links provided by NLM:

MedlinePlus related topics: Lymphoma

Drug Information available for: Rituximab Bortezomib Ibrutinib

Genetic and Rare Diseases Information Center resources: Lymphosarcoma B-cell Lymphoma Diffuse Large B-Cell Lymphoma

U.S. FDA Resources

Further study details as provided by Prof. Dr. Clemens Schmitt, Charite University, Berlin, Germany:

Primary Outcome Measures:

- 2-year progression-free survival [Time Frame: 2 years after completion of treatment]

  progression-free survival after 2 years after end of treatment

Secondary Outcome Measures:

- Number of participants with treatment-related adverse events as assessed by CTCAE v4.0 [Time Frame: through study completion, an average of 3 years]

- 1y- and 2y-PFS for patients based on cell-of-origin (COO, i.e. GCB vs. ABC subtype) [Time Frame: 1 and 2 years after end of treatment]
- number of patients with complete remission in all patients and based on cell-of-origin [Time Frame: 2 years after end of treatment]
- Predictive power of markers for Minimal Residual Disease (MRD) over time [Time Frame: 2 years after end of treatment]
- Objective Response Rate (ORR) in all patients and based on cell-of-origin [Time Frame: 2 years after end of treatment]

  Proportion of patients with reduction in tumor burden in all patients and based on cell-of-origin

- Disease-Free Survival in all patients and based on cell-of-origin [Time Frame: 2 years after end of treatment]

  number of patients with disease-free survival in all patients and based on cell-of-origin

- Overall survival in all patients and based on cell-of-origin [Time Frame: 2 years after end of treatment]

Estimated Enrollment:	60
Actual Study Start Date:	March 17, 2017
Estimated Study Completion Date:	March 31, 2022
Estimated Primary Completion Date:	March 31, 2022 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Ibrutinib and Bortezomib + R-CHOP A pre-phase therapy with Prednisone 100 mg p.o. is mandatory from d-4 until d0. Patients receive 6 cycles of a combined immunochemotherapy with the anti-CD20 antibody Rituximab (375 mg/m2 d0 or d1) together with 6 cycles of a chemotherapy consisting of Cyclophosphamide (750 mg/m2 d1), Doxorubicin (50 mg/m2 d1), Vincristine 1 mg absolute d1), Prednisone (100 mg absolute p.o. d1-5) and Bortezomib s.c. (1.3 mg/m2 C1 on d3 and 8, other cycles d1 and d8), in 21-day intervals and Ibrutinib 560 mg p.o. (from d6 of C1 until d21 of C6), followed by two additional 3-week cycles of Rituximab (375 mg/m2).	Drug: Ibrutinib and Bortezomib + R-CHOP A pre-phase therapy with Prednisone 100 mg p.o. is mandatory from d-4 until d0. Patients receive 6 cycles of a combined immunochemotherapy with the anti-CD20 antibody Rituximab (375 mg/m2 d0 or d1) together with 6 cycles of a chemotherapy consisting of Cyclophosphamide (750 mg/m2 d1), Doxorubicin (50 mg/m2 d1), Vincristine 1 mg absolute d1), Prednisone (100 mg absolute p.o. d1-5) and Bortezomib s.c. (1.3 mg/m2 C1 on d3 and 8, other cycles d1 and d8), in 21-day intervals and Ibrutinib 560 mg p.o. (from d6 of C1 until d21 of C6), followed by two additional 3-week cycles of Rituximab (375 mg/m2). Other Name: Ibrutinib (Imbruvica®), Bortezomib (Velcade®)

Detailed Description:

Cycle 1 (C1): At C1/day d2, there will be a CT- or ultrasound-guided re-biopsy of a lymphoma lesion that is accessible for biopsy without considerable risk for the patient.

Cycle 2 (C2): After C2, a post-Interim CT will be performed (eventually FDG and FLT PET-CT imaging added to the protocol by amendment).

Cycle 3 (C3): At C3/d0 (prior to therapy), there will also be another bone marrow aspirate for MRD follow-up. At C3/d2, there will be a re-biopsy of a lymphoma site in case of a residual lesion by CT that is accessible for biopsy without considerable risk for the patient. Biopsies can be obtained CT- or ultrasound-guided.

End of treatment/post-therapy: The end-of-treatment visit is required for all subjects, irrespective of a completion of all 8 cycles of therapy or exit of the study protocol. It has to be scheduled approximately 4 to 6 weeks after the last cycle. A total of 7 Follow up visits is planned over 30 months of follow up.

Eligibility

Ages Eligible for Study:	61 Years to 80 Years (Adult, Senior)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Written informed consent indicating that they understand the purpose of and procedures required for the study, including biomarkers and are willing to participate in the study
- Age ≥ 61 years and ≤ 80 years
- CD20-positive diffuse large B-cell lymphoma (DLBCL); including T-cell-rich large B-cell lymphoma, anaplastic large B-cell lymphoma, plasmablastic lymphoma; follicular lymphoma grade 3b or primary transformed follicular lymphoma at initial diagnosis
- Lymphoma biopsy native, fresh-frozen for genome-wide transcriptome array or RNA-Seq analyses (gene expression profiling [GEP]) for molecular subtype diagnosis
- Willingness to consent to a re-biopsy in C1/day d2, and - in case of a residual lesion by interim CT - in C3/d2 if it can be obtained without inadequate risk
- Unfavorable risk profile according to the IPI score (IPI ≥ 2)
- Performance status (ECOG) 0-2
- Bi-dimensionally measurable disease (measurable by CT scan or MRI)
- Cardiac ejection fraction ≥ 50 % without clinically significant abnormalities
- Adequate hematological function: hemoglobin ≥ 9 g/dL absolute neutrophil count ≥ 1,00/µL independent of growth factor support and platelet count ≥ 100,000/µL or ≥ 50,000/µL if bone marrow involvement independent of transfusion support in either situation
- Adequate renal function as documented by serum creatinine level < 2 x ULN or estimated GFR ≥ 40 ml/min/1,73m²
- Adequate hepatic function (total bilirubin ≤ 1,5 x ULN unless bilirubin rise is due to Gilbert's syndrome or of non-hepatic origin, alanine aminotransferase ALT and aspartate aminotransferase AST ≤ 3 x ULN)
- Life expectancy > 6 months
- Women of childbearing potential must have a negative serum (beta-human chorionic gonadotropin [ß-hCG]) or urine pregnancy test at screening. Women who are pregnant or breastfeeding are ineligible for this study.

- Women of childbearing potential and men who are sexually active must be practicing a highly effective method of birth control during and after the study consistent with local regulations regarding the use of birth control methods for subjects participating in clinical trials. Men must agree to not donate sperm during and after the study. For females, These restrictions apply for 1 month after the last dose of study drug. For males, these restrictions apply for 3 month after the last dose of study drug.

Exclusion Criteria:

- Unable to sign informed consent
- Secondary transformed B-NHL or types of NHL other than DLBCL and its subtypes according to WHO classification
- Prior therapy for DLBCL
- Known central nervous system lymphoma
- CNS involvement by lymphoma or any evidence of spinal cord compression. Brain CT/MRI is only mandatory (within 4 weeks prior to study entrance) in case of clinical suspicion of CNS involvement by lymphoma
- Major surgery within 4 weeks of study entrance
- History of stroke or intracranial hemorrhage within 6 months prior to study entrance
- Anticoagulation with Warfarin or equivalent vitamin K antagonists (e.g, Phenprocoumon)
- Clinically significant cardiovascular disease such as uncontrolled or symptomatic arrhythmias, congestive heart failure or myocardial infarction within 6 months of Screening or any class 3 or 4 cardiac disease as defined by NYHA
- treatment with strong CYP3A inhibitors
- Known history of human immunodeficiency virus HIV or active Hepatitis C virus or active Hepatitis B virus infection or any uncontrolled active systemic infection requiring intravenous iv antibiotics
- Vaccination with live, attenuated vaccines within 3 weeks of study entrance
- History of solid organ transplantation
- Pregnant or nursing females
- Prior malignancy (except adequately treated basal cell carcinoma and squamous cell carcinoma of the skin, cervical cancer in situ, or any other cancer for which the patient has been in remission for at least 5 years)
- Known hypersensitivity or contraindication to any of the study drugs, its ingredients or recombinant human antibodies and contrast agents
- Pre-existing polyneuropathy of any kind > grade I
- Severe chronic obstructive pulmonary disease with hypoxemia
- Current or recent (within the last 30 days prior to enrollment) treatment with another investigational drug or participation in another clinical trial
- Evidence of any other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates use of an investigational drug, or patient at high risk from treatment complications
- Any life-threatening illness, medical condition, or organ system dysfunction which, in the investigators opinion, could compromise the subjects safety, interfere with the absorption or metabolism of ibrutinib capsules or put the study outcomes at undue risk

- Any co-existing medical or psychological condition that would compromise the ability to give informed consent
- Subjects who are legally detained in an official institution
- Subjects who may be dependent on the sponsor, the investigator or the trial sites, have to be exclude from the trial
- Lack of willingness to storage and disclosure of pseudonymous disease data in the context of the clinical trial

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT03129828

Contacts

Contact: Clemens Schmitt, Prof. Dr. 004930 450 553896 clemens.schmitt@charite.de

Contact: Sophy Denker, Dr. 004930 450 653569 sophy.denker@charite.de

Locations

Germany

Charité - Universitätsmedizin Berlin, Hematology, Oncology and Tumor Immunology, Campus Virc
Berlin, Germany, 13353
Contact: Clemens Schmitt, Prof. Dr. +49-30-450 553 896 clemens.schmitt@charite.de
Contact: Sophy Denker, Dr. +49-30-450 653 569 sophy.denker@charite.de
Principal Investigator: Clemens Schmitt, Prof. Dr.

Sponsors and Collaborators

Prof. Dr. Clemens Schmitt

Charite University, Berlin, Germany

Janssen-Cilag Ltd.

Investigators

Principal Investigator: Clemens Schmitt, Prof. Dr. Representative of the Sponsor, National Coordina

More Information

Responsible Party:	Prof. Dr. Clemens Schmitt, Principal Investigator, Representative of the Sponsor, National Coordinator, Charite University, Berlin, Germany
ClinicalTrials.gov Identifier:	NCT03129828 History of Changes

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Individual Participant Data (IPD) Sharing Statement:
Plan to Share IPD: No

Studies a U.S. FDA-regulated Drug Product: No
Studies a U.S. FDA-regulated Device Product: No
Product Manufactured in and Exported from the U.S.: No

Keywords provided by Prof. Dr. Clemens Schmitt, Charite University, Berlin, Germany:
Diffuse Large B Cell Lymphoma
Ibrutinib
Bortezomib

Additional relevant MeSH terms:

Lymphoma
Lymphoma, B-Cell
Lymphoma, Large B-Cell, Diffuse
Neoplasms by Histologic Type
Neoplasms
Lymphoproliferative Disorders
Lymphatic Diseases
Immunoproliferative Disorders
Immune System Diseases
Lymphoma, Non-Hodgkin
Rituximab
Prednisone
Bortezomib
Antineoplastic Agents
Immunologic Factors
Physiological Effects of Drugs
Antirheumatic Agents
Anti-Inflammatory Agents
Glucocorticoids
Hormones
Hormones, Hormone Substitutes, and Hormone Antagonists
Antineoplastic Agents, Hormonal

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