ASCT After a Rituximab/Ibrutinib/Ara-c Containing iNduction in Generalized Mantle Cell Lymphoma

ClinicalTrials.gov Identifier: NCT02858258

Recruitment Status: Recruiting
First Posted: August 8, 2016
Last Update Posted: December 19, 2017

See Contacts and Locations

Sponsor:
Prof. Dr. M. Dreyling (co-chairman)

Collaborator:
Klinikum der Universitaet Muenchen

Information provided by (Responsible Party):
Prof. Dr. M. Dreyling (co-chairman), European Mantle Cell Lymphoma Network

Study Description

Go to

Brief Summary:
The primary objective of the the trial is to establish one of three study arms, as future standard based on the comparison of the investigator-assessed failure-free survival.

Condition or disease	Intervention/treatment	Phase
Mantle Cell Lymphoma	Drug: R-CHOP/R-DHAP Drug: Ibrutinib (Induction) Drug: **ASCT** conditioning Drug: Ibrutinib (Maintenance)	Phase 3

Show Detailed Description

Study Design

Go to

Study Type:	Interventional (Clinical Trial)
Estimated Enrollment:	870 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	Autologous Transplantation After a Rituximab/Ibrutinib/Ara-c Containing iNduction in Generalized Mantle Cell Lymphoma - a Randomized European Mcl Network Trial
Study Start Date:	July 2016
Estimated Primary Completion Date:	May 2021
Estimated Study Completion Date:	May 2026

Resource links provided by the National Library of Medicine

MedlinePlus related topics: Lymphoma

Drug Information available for: Cytarabine Rituximab Ibrutinib

Genetic and Rare Diseases Information Center resources: Lymphosarcoma Mantle Cell Lymphoma

U.S. FDA Resources

Arms and Interventions

Go to

Arm	Intervention/treatment
Active Comparator: Standard Arm A R-CHOP/R-DHAP: Alternating 3 cycles of R-CHOP in cycle 1,3,5 and 3 cyles of R-DHAP in cycle 2,4,6; each 21 day cycle Drug: R-CHOP/R-DHAP **ASCT** conditioning (**ASCT**: autologous stemm cell transplantation) Drug: THAM or BEAM	Drug: R-CHOP/R-DHAP Drug: R-CHOP/DHAP Alternating 3x R-CHOP (Rituximab , Cyclophosphamide ,Doxorubicine ,Vincristine , Prednisone) / 3x R-DHAP (Rituximab , Dexamethasone, Ara-C, Cisplatine, G-CSF) Other Name: rituximab, CHOP, DHAP Drug: **ASCT** conditioning **ASCT** conditioning THAM or BEAM, stratified per site before trial activation at site THAM (TBI (total body irradiation), Ara-C, Melphalan) or BEAM (BCNU, Etoposide, Cytarabine, Melphalan) Other Name: THAM or BEAM
Experimental: Experimental Arm A+I R-CHOP+Ibrutinib/R-DHAP: Alternating 3 cycles of R-CHOP + Ibrutinib at Days 1-19 in cycle 1,3,5 and 3 cyles of R-DHAP in cycle 2,4,6; each 21 day cycle	Drug: R-CHOP/R-DHAP Drug: R-CHOP/DHAP Alternating 3x R-CHOP (Rituximab , Cyclophosphamide ,Doxorubicine ,Vincristine , Prednisone) / 3x R-DHAP (Rituximab , Dexamethasone, Ara-C, Cisplatine, G-CSF)

Drug: R-CHOP/R-DHAP Drug: Ibrutinib (Induction) **ASCT** conditioning (**ASCT**: autologous stemm cell transplantation) Drug: THAM or BEAM 2 years Ibrutinib Maintenance Drug: Ibrutinib (Maintenace)	Other Name: rituximab, CHOP, DHAP Drug: Ibrutinib (Induction) Ibrutinib: only in cycle 1,3,5 on Day 1-19 Other Name: Imbruvica Drug: **ASCT** conditioning **ASCT** conditioning THAM or BEAM, stratified per site before trial activation at site THAM (TBI (total body irradiation), Ara-C, Melphalan) or BEAM (BCNU, Etoposide, Cytarabine, Melphalan) Other Name: THAM or BEAM Drug: Ibrutinib (Maintenance) Ibrutinib (Maintenance), daily 560 mg for 2 years; Other Name: Imbruvica
Experimental: Experimental Arm I R-CHOP+Ibrutinib / R-DHAP: Alternating 3 cycles of R-CHOP + Ibrutinib at Days1-19 in cycle 1,3,5 and 3 cyles of R-DHAP in cycle 2,4,6; each 21 day cycle Drug: R-CHOP/R-DHAP Drug: Ibrutinib (Induction) 2 years Ibrutinib Maintenance Drug: Ibrutinib (Maintenance)	Drug: R-CHOP/R-DHAP Drug: R-CHOP/DHAP Alternating 3x R-CHOP (Rituximab , Cyclophosphamide ,Doxorubicine ,Vincristine , Prednisone) / 3x R-DHAP (Rituximab , Dexamethasone, Ara-C, Cisplatine, G-CSF) Other Name: rituximab, CHOP, DHAP Drug: Ibrutinib (Induction) Ibrutinib: only in cycle 1,3,5 on Day 1-19 Other Name: Imbruvica Drug: Ibrutinib (Maintenance) Ibrutinib (Maintenance), daily 560 mg for 2 years; Other Name: Imbruvica

Outcome Measures

Go to

Primary Outcome Measures :

1. Failure Free Survival [Time Frame: From start of treatment until stable disease at end of immuno-chemotherapy, progressive disease, or death from any cause, whichever comes first, assessed up to 120 months.]

Secondary Outcome Measures :

1. Overall Survival [Time Frame: From start of treatment until the date of first documented progression, assessed up to 120 months.]
2. Number of participants with treatment-related adverse events as assessed by CTC Version 4.03 [Time Frame: From start of Ibrutinib treatment during induction immuno-chemotherapy and during

maintenance and to compare the safety profile of the three treatment arms in terms of secondary toxicity endpoints. Through study conduction, an average of up to 30 months.]

Safety and tolerability

3. Progression-free survival (PFS) [Time Frame: PFS is the time to progression or death from any cause. Assed up to 120 months.]
4. Number of Secondary Primary Malignancies [Time Frame: From start of treatment through the study conduction, up to 120 months.]

   Toxicity Endpoints

5. Number of Adverse Events by CTC grade (Version 4.03) [Time Frame: From start of treatment through the study conduction, up to 120 months.]

   Toxicity Endpoints

Eligibility Criteria

Go to

Information from the National Library of Medicine

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, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years to 65 Years (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

All patients must meet the following criteria:

- Histologically confirmed diagnosis of MCL according to WHO classification
- suitable for high-dose treatment including high-dose Ara-C
- Stage II-IV (Ann Arbor)
- Age ≥ 18 years and ≤ 65 years
- Previously untreated MCL
- At least 1 measurable lesion; in case of bone marrow infiltration only, bone marrow aspiration and biopsy is mandatory for all staging evaluations.
- ECOG/WHO performance status ≤ 2
- The following laboratory values at screening (unless related to MCL):
  - Absolute neutrophil count (ANC) ≥1000 cells/µL
  - Platelets ≥100,000 cells/µL
  - Transaminases (AST and ALT) ≤3 x upper limit of normal (ULN)

- Total bilirubin ≤2 x ULN unless due to known Morbus Meulengracht [Gilbert-Meulengracht-Syndrome])
- Creatinine ≤2 mg/dL or calculated creatinine clearance ≥ 50 mL/min

- Written informed consent form according to ICH/EU GCP and national regulations
- Sexually active men and women of child-bearing potential must agree to use highly effective contraceptives (eg, condoms, implants, injectables, combined oral contraceptives, intrauterine devices, sexual abstinence, or sterilized partner) while on study; this should be maintained for 90 days after the last dose of study drug.

Exclusion Criteria:

Any potential subject who meets any of the following criteria will be excluded from participating in the study.

- Major surgery within 4 weeks prior to randomization.
- Requires anticoagulation with warfarin or equivalent vitamin K antagonists (eg phenprocoumon).
- History of stroke or intracranial hemorrhage within 6 months prior to randomization.
- Requires treatment with strong CYP3A4/5 inhibitors.
- Any life-threatening illness, medical condition, or organ system dysfunction which, in the investigator's opinion, could compromise the subject's safety, interfere with the absorption or metabolism of ibrutinib capsules, or put the study outcomes at undue risk.
- Vaccinated with live, attenuated vaccines within 4 weeks prior to randomization.
- Known CNS involvement of MCL
- Clinically significant hypersensitivity (eg, anaphylactic or anaphylactoid reactions to the compound of ibrutinib itself or to the excipients in its formulation)
- Known anti-murine antibody (HAMA) reactivity or known hypersensitivity to murine antibodies
- Previous lymphoma therapy with radiation, cytostatic drugs, anti-CD20 antibody or interferon except prephase therapy according to trial protocol
- Serious concomitant disease interfering with a regular therapy according to the study protocol:
  - Cardiac (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 (moderate) or Class 4 (severe) cardiac disease as defined by the New York Heart Association Functional Classification or LVEF below LLN)
  - Pulmonary (e.g. chronic lung disease with hypoxemia)
  - Endocrinological (e.g. severe, not sufficiently controlled diabetes mellitus)
  - Renal insufficiency (unless caused by the lymphoma): creatinine > 2x normal value and/or creatinin clearance < 50 ml/min)
  - Impairment of liver function (unless caused by the lymphoma): transaminases > 3x normal or bilirubin > 2,0 mg/dl unless due to morbus Meulengracht (Gilbert-Meulengracht-Syndrome)
- Patients with unresolved hepatitis B or C infection or known HIV positive infection (mandatory test)
- Prior organ, bone marrow or peripheral blood stem cell transplantation
- Concomitant or previous malignancies within the last 3 years other than basal cell skin cancer or in situ uterine cervix cancer
- Pregnancy or lactation
- Any psychological, familiar, sociological, or geographical condition potentially hampering compliance with the study protocol and follow up schedule
- Subjects not able to give consent
- Subjects without legal capacity who are unable to understand the nature, scope, significance and consequences of this clinical trial
- Participation in another clinical trial within 30 days before randomization in this study.

Contacts and Locations

Go to

Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT02858258***

Contacts

Contact: Döndü Gözel	+49 89 4400 ext 77906	Doendue.Goezel@med.uni-muenchen.de
Contact: Christian Schmidt, Dr.	+49 89 4400 ext 74900	Christian_Schmidt@med.uni-muenchen.de

Show 112 Study Locations

Sponsors and Collaborators

Prof. Dr. M. Dreyling (co-chairman)

Klinikum der Universitaet Muenchen

Investigators

Principal Investigator: Martin Dreyling, Prof. Klinikum der Universität München

More Information

Go to

Responsible Party:	Prof. Dr. M. Dreyling (co-chairman), Sponsor Delegated Person / Coordinating Prinicipal Investigator, European Mantle Cell Lymphoma Network
ClinicalTrials.gov Identifier:	NCT02858258 History of Changes
Other Study ID Numbers:	**TRIANGLE**
First Posted:	August 8, 2016 Key Record Dates
Last Update Posted:	December 19, 2017
Last Verified:	December 2017

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: No

Keywords provided by Prof. Dr. M. Dreyling (co-chairman), European Mantle Cell Lymphoma Network:
MCL

Additional relevant MeSH terms:

Lymphoma
Lymphoma, Mantle-Cell
Neoplasms by Histologic Type
Neoplasms
Lymphoproliferative Disorders
Lymphatic Diseases
Immunoproliferative Disorders
Immune System Diseases
Lymphoma, Non-Hodgkin

Antineoplastic Agents
Immunologic Factors
Physiological Effects of Drugs
Antirheumatic Agents
Antimetabolites, Antineoplastic
Antimetabolites
Molecular Mechanisms of Pharmacological Action
Antiviral Agents
Anti-Infective Agents

Rituximab

Immunosuppressive Agents

Cytarabine