Efficacy of Rituximab - Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (R-CHOP) Versus R-CHOP/R-DHAP in Patients With Untreated Mantle Cell Lymphoma

The recruitment status of this study is unknown because the information has not been verified recently.

Verified July 2009 by European Mantle Cell Lymphoma Network. Recruitment status was Recruiting.

First Received on September 13, 2005. Last Updated on July 16, 2009

Purpose

The aim of this study is to determine whether alternating courses of cyclophosphamide, doxorubicin, vincristine, prednisone/dexamethasone, cytarabine, cisplatin (CHOP/DHAP) plus rituximab followed by total body irradiation [TBI]/high dose cytarabine [ARA-C]/melphalan-peripheral blood stem cell transplantation (TAM-PBSCT) can improve the time to treatment failure compared to CHOP plus rituximab followed by standard PBSCT (dexamethasone, carmustine, cytarabine, etoposide, and melphalan [Dexa-BEAM]/TBI/high dose cyclophosphamide) in patients with untreated mantle cell lymphoma.

Condition | Intervention | Phase
---|---|---
Study Type: Intervventional  
Study Design: Allocation: Randomized  
  Endpoint Classification: Efficacy Study  
  Intervention Model: Parallel Assignment  
  Masking: Open Label  
  Primary Purpose: Treatment  

Official Title: Efficacy of 6x R-CHOP Followed by Myeloablative Radiochemotherapy and Autologous Stem Cell Transplantation vs. 3 x (R-CHOP/R-DHAP) Followed by a High Dose ARA-C Containing Myeloablative Regimen and Autologous Stem Cell Transplantation  

Resource links provided by NLM:  
  MedlinePlus related topics: Lymphoma  
  Drug Information available for: Dexamethasone Cyclophosphamide Prednisone Cytarabine Melphalan Dexamethasone acetate Vincristine sulfate Dexamethasone Sodium Phosphate Melphalan hydrochloride Cisplatin Doxorubicin Doxorubicin hydrochloride Etoposide Etoposide phosphate Rituximab  
  U.S. FDA Resources  

Further study details as provided by European Mantle Cell Lymphoma Network:  

Primary Outcome Measures:  
- time to treatment failure after start of therapy  

Secondary Outcome Measures:  
- complete remission (CR) rate  
- overall survival  
- progression-free survival  
- adverse events  
- serious infectious complications  

Estimated Enrollment: 360  
Study Start Date: July 2004  
Estimated Study Completion Date: June 2010  
Estimated Primary Completion Date: January 2010 (Final data collection date for primary outcome measure)  

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
<th></th>
</tr>
</thead>
</table>
| Active Comparator: 1  
  induction: R-CHOP consolidation: TBI/Cyclo | Drug: Rituximab  
  antibody  
  Drug: Cyclophosphamide chemotherapy  
  Drug: Doxorubicin chemotherapy  
  Drug: Vincristine chemotherapy  
  Drug: Prednisone corticosteroid  
  Drug: BCNU |  

Detailed Description:
Recently, a prospective randomized intergroup trial of the European MCL Network has shown that a myeloablative radio-chemotherapy followed by autologous stem cell transplantation (PBSCT) improves event-free survival (EFS) when compared to an interferon alpha maintenance therapy after a CHOP-like induction. However, the CR rate after the CHOP induction was still low (<20%). Thus, several studies have been conducted to increase the CR rate of induction therapy to further improve event-free and overall survival. Two recent phase II trials suggest that
induction regimens containing high dose Ara-C may significantly improve the CR rate up to 80%. In addition, a number of studies provide evidence that the humanized anti-CD20 antibody Rituximab may induce significant responses in relapsed MCL. A prospective randomized study of the GLSG demonstrated that a combined immuno-chemotherapy (CHOP plus Rituximab) induces a significantly higher response rate than CHOP alone.

The aim of this study is the comparison of the current standard (R-CHOP followed by myeloablative radio-chemotherapy and subsequent blood stem cell transplantation) to a new alternating induction regimen containing high dose Ara-C (R-CHOP/DHAP) followed by a high dose ARA-C containing myeloablative radio-chemotherapy and PBSCT.

This study will be performed as a prospective, randomized, open-label multicenter phase III trial. All patients will be initially randomized for standard treatment versus experimental treatment.

REFERENCE ARM:
The induction therapy consists of 6 cycles of a CHOP chemotherapy in combination with Rituximab. If the mantle cell lymphoma is progressive after 4 cycles of chemotherapy, patients will be taken off study. Patients achieving at least a partial remission after 6 cycles R-CHOP will proceed to intensified consolidation (Dexa-BEAM) with stem cell collection and subsequent myeloablative radio-chemotherapy (TBI/High Dose Cyclophosphamide) with autologous stem cells transplantation.

EXPERIMENTAL ARM:
Initial cytoreductive chemotherapy comprises of alternating cycles of 3xCHOP and 3x DHAP plus Rituximab. Patients with progressive disease after 2 treatment cycles R-CHOP and 2x R-DHAP will be off study. Patients achieving at least a partial remission after 3x CHOP and 3x DHAP plus Rituximab will proceed to with stem cell collection. The subsequent myeloablative radio-chemotherapy with stem cell transplantation consists of a radiotherapy (TBI), high dose Ara-C and Melphalan.

The primary end point in this study is the time to treatment failure. The time to treatment failure will be defined as time from start of initial therapy until first failure. A failure will be defined as failure of initial therapy or progression of the lymphoma or death of the patient.

Using the data of the PBSCT group in the former European mantle cell study as baseline in a proportional hazard model, the improvement for the time to treatment failure expected by the new strategy can be expressed by reduction of relative risk (rr). A risk reduction to 52% which would correspond to a improvement of 20% in failure free survival after 3 years seems to be a clinical relevant improvement. For a working significance level alpha=0.05 and a power of 95% the number of events necessary for a one sided fixed sample trial is about 105. During this study the time to treatment failure will be monitored using an equivalent one-sided triangular sequential test.

In order to evaluate the impact of therapy on overall survival in this patients, a total follow up of about 12 years for this study is expected.

### Eligibility

- **Ages Eligible for Study:** 18 Years to 65 Years
- **Genders Eligible for Study:** Both
- **Accepts Healthy Volunteers:** No

### Criteria

**Inclusion Criteria:**
- Histologically proven diagnosis of mantle cell lymphoma (World Health Organization [WHO] classification)
- Clinical stage II - IV (Ann Arbor)
- Previously untreated patients
- Age 18 - 65 years
- WHO performance < 2
- Measurable disease (also: patients with isolated bone marrow involvement)
- Informed consent according to International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use/European Union Good Clinical Practice (ICH/EU GCP) and national/local regulations
Exclusion Criteria:

- Age > 65 years
- WHO performance status > 2
- Known anti-murine antibody (HAMA) reactivity or known hypersensitivity to murine antibodies
- Previous lymphoma therapy with radiation, cytostatic drugs, anti-CD20 antibody or interferon
- Serious disease interfering with a regular therapy according to the study protocol:
  - cardiac (e.g. manifest heart failure, coronary heart disease, uncontrolled hypertension)
  - pulmonary (e.g. chronic lung disease with hypoxemia)
  - endocrine (e.g. severe, not sufficiently controlled diabetes mellitus)
  - renal insufficiency (unless caused by the lymphoma): creatinine > 2x normal value and/or creatinine clearance < 50 ml/min
  - impairment of liver function (unless caused by the lymphoma): transaminases > 3x normal or bilirubin > 2,0 mg/dl
- Patients with unresolved hepatitis B or C infection or known HIV infection
- Prior organ, bone marrow or peripheral blood stem cell transplantation
- Concomitant or previous malignancies within the last 5 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

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT00209222

Contacts

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Locations

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Sponsors and Collaborators

Efficacy of Rituximab - Cyclophosphamide, Doxorubicin, Vincristine, a...
European Mantle Cell Lymphoma Network
German Low Grade Lymphoma Study Group
Lymphoma Study Association

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Study Chair: Wolfgang Hiddemann, PhD University Hospital Großhadern/LMU, Dept. of Medicine

More Information

Publications:


Additional publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

<table>
<thead>
<tr>
<th>Immunoproliferative Disorders</th>
<th>BB 1101</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune System Diseases</td>
<td>Antineoplastic Agents</td>
</tr>
<tr>
<td>Lymphoma, Non-Hodgkin</td>
<td>Therapeutic Uses</td>
</tr>
<tr>
<td>Rituximab</td>
<td>Pharmacologic Actions</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>Radiation-Sensitizing Agents</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Physiological Effects of Drugs</td>
</tr>
<tr>
<td>Cytarabine</td>
<td>Immunosuppressive Agents</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>Immunologic Factors</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>Antirheumatic Agents</td>
</tr>
</tbody>
</table>

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