**Purpose**

RATIONALE: Monoclonal antibodies, such as rituximab, can block cancer growth in different ways. Some find cancer cells and kill them or carry cancer-killing substances to them. Others interfere with the ability of cancer cells to grow and spread. Drugs used in chemotherapy, such as cyclophosphamide, doxorubicin, vincristine, and prednisone, work in different ways to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing. Giving rituximab together with combination chemotherapy may kill more cancer cells. It is not yet known which schedule of rituximab and combination chemotherapy is more effective in treating non-Hodgkin's lymphoma.

PURPOSE: This randomized phase III trial is studying two different schedules of rituximab and combination chemotherapy to compare how well they work in treating patients with aggressive B-cell non-Hodgkin's lymphoma.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoma</td>
<td>Biological: rituximab</td>
<td>Phase III</td>
</tr>
<tr>
<td></td>
<td>Drug: cyclophosphamide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Drug: doxorubicin hydrochloride</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Drug: prednisone</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Drug: vincristine sulfate</td>
<td></td>
</tr>
</tbody>
</table>

Study Type: Interventional  
Study Design: Allocation: Randomized  
Masking: Open Label  
Primary Purpose: Treatment

Official Title: Randomized Study Comparing 4 and 6 Cycles of Chemotherapy With CHOP (Cyclophosphamide, Doxorubicin, Vincristine and Prednisone) at 21-day Intervals, Both With 6 Cycles of Immunotherapy With the Monoclonal Anti-CD20-Positive B-Cell Lymphoma Aged 18-60 Years Having no Risk Factor (Age-Adjusted IPI=0) and No Large Tumor Mass (Diameter <7.5cm) [FLYER 6-6-6-4 Study]

Resource links provided by NLM:

- MedlinePlus related topics: [Cancer](http://clinicaltrials.gov/show/NCT00278421) [Lymphoma](http://clinicaltrials.gov/show/NCT00278421)
- Drug Information available for: [Cyclophosphamide](http://clinicaltrials.gov/show/NCT00278421) [Prednisone](http://clinicaltrials.gov/show/NCT00278421) [Vincristine sulfate](http://clinicaltrials.gov/show/NCT00278421) [Doxorubicin](http://clinicaltrials.gov/show/NCT00278421) [Doxorubicin hydrochloride](http://clinicaltrials.gov/show/NCT00278421) [Rituximab](http://clinicaltrials.gov/show/NCT00278421)
- U.S. FDA Resources

Further study details as provided by National Cancer Institute (NCI):

Primary Outcome Measures:
Time to treatment failure (TTF) measured from day 1 of course 1 of Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (CHOP) therapy up to 3 years on study with life-long follow-up [Designated as safety issue: No]

Secondary Outcome Measures:
- Complete response (CR) rate duration until first relapse [Designated as safety issue: No]
- Progression rate during treatment [Designated as safety issue: No]
- Survival [Designated as safety issue: No]
- Tumor control measured from day 1 of course 1 of CHOP therapy (non-tumor related events are censored) [Designated as safety issue: No]
- Disease-free survival measured from day 1 of course 1 of CHOP therapy [Designated as safety issue: No]
- Safety (adverse events, serious adverse events) assessed at 3 months after treatment [Designated as safety issue: Yes]

Estimated Enrollment: 622
Study Start Date: November 2005
Estimated Primary Completion Date: April 2015 (Final data collection date for primary outcome measure)

Objective:
Primary
- Compare the efficacy of 2 different schedules of immunochemotherapy comprising rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine, and prednisone in patients with previously untreated, low-risk, aggressive B-cell non-Hodgkin's lymphoma.
- Compare acute and chronic side effects in patients treated with these regimens.
- Compare time to treatment failure in patients treated with these regimens.

Secondary
- Compare the time to progression in patients treated with these regimens.
- Compare the overall and disease-free/relapse-free survival of patients treated with these regimens.
- Compare the complete response rate in patients treated with these regimens.
- Compare the tumor control in patients treated with these regimens.
- Compare the safety of these regimens in these patients.
- Compare the pharmacoeconomics of these regimens.
- Compare patient adherence to these regimens.

Outline: This is an open-label, randomized, multicenter study. Patients are stratified according to participating center. Patients are randomized to 1 of 2 treatment arms.

All patients are given the option of receiving a 1-week course of pretreatment therapy comprising vincristine IV once on day -6 and oral prednisone once daily on days -6 to 0.

- Arm I: Patients receive R-CHOP immunochemotherapy comprising rituximab IV, cyclophosphamide IV over 15 minutes, doxorubicin hydrochloride IV, and vincristine IV on day 1 and oral prednisone once daily on days 1-5. Treatment repeats every 21 days for 3 courses in the absence of disease progression or unacceptable toxicity. Patients then undergo restaging of their disease. Patients with disease progression proceed to salvage therapy off study. All other patients receive 3 more courses of R-CHOP.
- Arm II: Patients receive R-CHOP as in arm I. Treatment repeats every 21 days for 3 courses in the absence of disease progression or unacceptable toxicity. Patients then undergo restaging of their disease. Patients with disease progression proceed to salvage therapy off study. All other patients receive 1 more course of R-CHOP followed by 2 courses of rituximab alone.

All patients undergo final restaging after 6 courses of rituximab. Patients with disease progression, stable disease, or partial response proceed to salvage therapy off study.

After completion of study treatment, patients are followed periodically for 5 years and then annually thereafter.

Projected accrual: A total of 622 patients will be accrued for this study.

Eligibility

http://clinicaltrials.gov/show/NCT00278421

17.04.2012
DISEASE CHARACTERISTICS:
- Histologically confirmed aggressive B-cell non-Hodgkin's lymphoma, including the following subtypes:
  - Grade 3 follicular lymphoma
  - Diffuse B-cell lymphoma, including diffuse large cell lymphoma with any of the following variants:
    - Centroblastic
    - Immunoblastic
    - Plasmablastic
    - Anaplastic large cell
    - T-cell-rich B-cell lymphoma
  - Primary effusion lymphoma
  - Intravascular B-cell lymphoma
  - Primary mediastinal B-cell lymphoma
  - Burkitt's or Burkitt-like lymphoma
  - Mantle cell lymphoma (blastoid)
  - Aggressive marginal zone lymphoma (monocytoid)
- Previously untreated disease
- CD20-positive disease
- International Prognostic Index (IPI) score 0
- No bulky disease
  - Largest single or conglomerate tumor < 7.5 cm in diameter
- No mucosa-associated lymphoid tissue (MALT) lymphoma
- No CNS involvement of lymphoma (intracerebral, meningeal, or intraspinal)

PATIENT CHARACTERISTICS:
- ECOG performance status 0-1
- Platelet count ≥ 100,000/mm³
- WBC ≥ 2,500/mm³
- Lactate dehydrogenase normal
- Not pregnant or lactating
- Fertile patients must use effective contraception during and for 1 year after study participation
- Negative pregnancy test
- No known hypersensitivity to the study medications
- No known HIV-positivity
- No active hepatitis infection
- No impaired left ventricular function
- No severe cardiac arrhythmias
- No other impaired organ function
- No other serious disorder
- No other malignancy within the past 5 years except carcinoma in situ or basal cell skin cancer

PRIOR CONCURRENT THERAPY:
- No prior chemotherapy or radiotherapy
- No prior immunosuppressive treatment with cytostatics
- No planned radiotherapy to extranodal involvement
- No concurrent participation in other treatment studies
Please refer to this study by its ClinicalTrials.gov identifier: NCT00278421

Show 78 Study Locations

Sponsors and Collaborators
German High-Grade Non-Hodgkin's Lymphoma Study Group

Investigators
Study Chair: Michael G.M. Pfreundschuh, MD, Universitaetsklinikum des Saarlandes

More Information

Additional Information:
Clinical trial summary from the National Cancer Institute's PDQ® database

No publications provided

ClinicalTrials.gov Identifier: NCT00278421
Study First Received: January 16, 2006
Last Updated: April 16, 2010
Health Authority: Unspecified

Keywords provided by National Cancer Institute (NCI):
- contiguous stage II grade 3 follicular lymphoma
- noncontiguous stage II grade 3 follicular lymphoma
- stage I grade 3 follicular lymphoma
- contiguous stage II adult diffuse large cell lymphoma
- contiguous stage II adult diffuse mixed cell lymphoma
- noncontiguous stage II adult diffuse large cell lymphoma
- noncontiguous stage II adult diffuse mixed cell lymphoma
- stage I adult diffuse large cell lymphoma
- stage I adult diffuse mixed cell lymphoma
- nodal marginal zone B-cell lymphoma
- anaplastic large cell lymphoma
- contiguous stage II adult immunoblastic large cell lymphoma
- noncontiguous stage II adult immunoblastic large cell lymphoma
- stage I adult immunoblastic large cell lymphoma
- contiguous stage II adult Burkitt lymphoma

Additional relevant MeSH terms:
- Lymphoma
- Lymphoma, Non-Hodgkin
- Lymphoma, B-Cell
- Lymphoma, Large-Cell, Immunoblastic
- Neoplasms by Histologic Type
- Neoplasms
- Lymphoproliferative Disorders
- Lymphatic Diseases
- Immunoproliferative Disorders
- Immune System Diseases
- Cyclophosphamide
- Rituximab
- Doxorubicin
- Prednisone
- Vincristine
- Immunosuppressive Agents
- Immunologic Factors
- Physiological Effects of Drugs
- Pharmacologic Actions
- Antirheumatic Agents
- Therapeutic Uses
- Antineoplastic Agents, Alkylating
- Alkylating Agents
- Molecular Mechanisms of Pharmacological Action
- Antineoplastic Agents
- Myeloablative Agonists
- Antibiotics, Antineoplastic
- Glucocorticoids
- Hormones
- Hormones, Hormone Substitutes, and Hormone Antagonists

ClinicalTrials.gov processed this record on April 15, 2012