Treatment of diffuse large B cell lymphoma – a historical overview

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Lymphoma Tumor Board
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Relative Incidence of NHL Subtypes

>71,000 new cases in US in 2015

- DLBCL: 32%
- FL: 22%
- Composite: 13%
- Burkitt’s-like: 2%
- LL: 2%
- LPL: 1%
- ALCL: 2%
- PMLBCL: 2%
- MZL: 6%
- PTCL: 6%
- MCL: 6%
- SLL: 6%

NHL = non-Hodgkin lymphoma.

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Outline

• Fisher et al. – non-inferiority of CHOP to more complex regimens

• Coiffier et al. – superiority of R-CHOP to CHOP
  – Short term results
  – Long term results

• Récher et al. – superiority of R-ACVBP to R-CHOP in low-risk DLBCL

• Wilson et al. – DA-R-EPOCH for DLBCL

• Dunleavey et al. – DA-R-EPOCH for PMLBCL
Time to Treatment Failure in the Treatment Groups

Overall Survival in the Treatment Groups

Event-free Survival among 399 Patients Assigned to Chemotherapy with Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (CHOP) or with CHOP plus Rituximab
Overall Survival among 399 Patients Assigned to Chemotherapy with Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (CHOP) or with CHOP plus Rituximab

Progression-free survival in patients treated with CHOP and R-CHOP

Overall survival in patients treated with CHOP and R-CHOP

Figure 1. Protocol outline

R-ACVBP=rituximab, doxorubicin, cyclophosphamide, vindesine, bleomycin, and prednisone.
R-CHOP=rituximab, doxorubicin, cyclophosphamide, vincristine, and prednisone.

Christian Récher, Bertrand Coiffier, Corinne Haioun, Thierry Jo Molina, Christophe Fermé, Olivier Casasnovas, Catherine Thiéblemont, André Bosly, Guy Laurent, Franck Morschhauser, Hervé Ghesquières, Fabrice Jardin, Serge Bologna, Christophe Fruchart, Bernadette Corront, Jean Gabarre, Christophe Bonnet, Maud Janvier, Danielle Canioni, Jean-Philippe Jais, Gilles Salles, Hervé Tilly

Intensified chemotherapy with ACVBP plus rituximab versus standard CHOP plus rituximab for the treatment of diffuse large B-cell lymphoma (LNH03-2B): an open-label randomised phase 3 trial


http://dx.doi.org/10.1016/S0140-6736(11)61040-4
Figure 3. Kaplan-Meier estimates of outcomes by treatment group. Event-free survival for the 379 patients in the intention-to-treat population (A). Progression-free survival for the 379 patients in the intention-to-treat population (B). Disease-free survival for...

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Kaplan-Meier plots of survival outcomes of all patients

Kaplan-Meier plots of survival outcomes patients with biomarkers

Kaplan–Meier Estimates of Event-free and Overall Survival of Patients with Primary Mediastinal B-Cell Lymphoma Receiving DA-EPOCH-R, According to Study Group

A. Event-free Survival (NCI Patients)

B. Overall Survival (NCI Patients)

C. Event-free Survival (Stanford Patients)

D. Overall Survival (Stanford Patients)
Rituximab and Combination Chemotherapy in Treating Patients With Diffuse Large B-Cell Lymphoma

This study is ongoing, but not recruiting participants.

Sponsor:
Alliance for Clinical Trials in Oncology

Collaborator:
National Cancer Institute (NCI)

Information provided by (Responsible Party):
Alliance for Clinical Trials in Oncology

ClinicalTrials.gov Identifier:
NCT00118209

First received: July 8, 2005
Last updated: September 18, 2015
Last verified: September 2015
History of Changes

Purpose

RATIONALE: Monoclonal antibodies, such as rituximab, can block cancer growth in different ways. Some block the ability of cancer cells to grow and spread. Others find cancer cells and help kill them or carry cancer-killing substances to them. Drugs used in chemotherapy 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 combination chemotherapy regimen is more effective when given with rituximab in treating diffuse large B-cell lymphoma.

PURPOSE: This randomized phase III trial is studying rituximab when given together with two different combination chemotherapy regimens to compare how well they work in treating patients with diffuse large B-cell lymphoma.
### Arms

**Active Comparator: Arm A - R-CHOP**

Patients receive the following treatment:

- Rituximab 375 mg/m² IV infusion on Day 1 prior to CHOP chemotherapy
- Cyclophosphamide 750 mg/m² IV on Day 1
- Doxorubicin 50 mg/m² IV on Day 1
- Vincristine 1.4 mg/m² IV (2 mg cap) on Day 1
- Prednisone 40 mg/m²/day PO on Days 1-5
- Filgrastim or pegfilgrastim as defined in the protocol

Required ancillary medications is administered during all cycles as defined in the protocol.

Cycles will be repeated every 21 days for 6 treatment cycles. Restaging will occur after Cycles 4 and 6.

### Assigned Interventions

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<th>Biological: rituximab</th>
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<th>Drug: cyclophosphamide</th>
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<th>Drug: vincristine</th>
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<th>Drug: prednisone oral</th>
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<td>Drug: filgrastim IV</td>
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<th>Drug: pegfilgrastim IV</th>
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### Experimental: Arm B - DA-EPOCH-R

Patients receive the following treatment:

**Cycle 1 Doses:**

- Rituximab 375 mg/m² IV infusion on Day 1 prior to EPOCH chemotherapy
- Doxorubicin 10 mg/m²/day CIVI on Days 1-4
- Etoposide 50 mg/m²/day CIVI on Days 1-4
- Vincristine 0.4 mg/m²/day (no cap) CIVI on Days 1-4 (total 1.6 mg/m² over 96 hours)
- Cyclophosphamide 750 mg/m² IV on Day 5 (following completion of 96 hour infusions)
- Prednisone 60 mg/m² PO BID on Days 1-5

- Administer filgrastim 480 mcg subcutaneous daily from Day 6 until ANC > 5000 after the nadir (nadir usually between Days 10-12) or for 10 days (Days 6-15) if the ANC is not being monitored, during every cycle.

Doses for subsequent cycles will be determined by the absolute neutrophil (ANC) or platelet nadir from the previous cycle.

Required ancillary medications are administered during all cycles as defined in the protocol.

Cycles will be repeated every 21 days for a maximum of 6 cycles. Restaging will occur after Cycles 4 and 6.