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Nebraska Lymphoma Study Group Scheme for the Treatment of Non-Hodgkin’s Lymphoma and Hodgkin’s Lymphoma
December 2009 Edition

LYMPHOMA STUDY GROUP

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LYMPHOMA STUDY GROUP

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The Nebraska Lymphoma Study Group (NLSG), established in 1982 by James Armitage, M.D., is a unique collaborative effort between community oncologists and pathologists, and their counterparts at the University of Nebraska Medical Center. Through this collaborative effort, patients with Hodgkin’s disease, non-Hodgkin’s lymphoma, and other neoplastic hematologic disorders are treated according to standard, state-of-the-art therapies in the community setting, while being afforded the expertise and high technology of the University setting. The majority of the patients enrolled in the study group are previously untreated, and are the most likely to benefit from their therapy. In many cases, fresh tissues are shipped to the Department of Pathology and Microbiology at the University of Nebraska Medical Center for detailed histopathologic, immunologic, and molecular characterization. Cytogenetic studies are also performed.

The table below shows the number of cases of lymphoma which have been studied and treated by the NLSG. Dr. Armitage and Julie M. Vose, M.D., direct the NLSG, while Dennis Weisenburger, M.D., leads the Hematopathology Section which reviews all tissues submitted to the NLSG. The important work of the NLSG has lead to national and international recognition of the University of Nebraska Medical Center, as well as its collaborators in the state of Nebraska.

<table>
<thead>
<tr>
<th>Standard Therapy</th>
<th># of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Patient Registrations</td>
<td>4,804</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Tissue Procurement Service</th>
<th># of Samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic Review</td>
<td>50,427</td>
</tr>
<tr>
<td>Cases with Frozen Tissue</td>
<td>7,232</td>
</tr>
</tbody>
</table>

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  (402) 559-7598
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Indolent Non-Hodgkin’s Lymphoma
Clinical Trials

Newly Diagnosed

Investigator-Initiated Studies
IRB NO: 156-95  Coordinator: Lin Bauer
(402-888-0289)
Non-Hodgkin’s Lymphoma - Blood and Bone Marrow Cellular Bank
IRB NO: 412-99  Coordinator: Marge Moragues
(402-888-5703)
Functional Genomics of Chronic Lymphocytic Leukemia and Small
Lymphocytic Lymphoma

Relapsed (Salvage)

Investigator-Initiated Studies
IRB NO: 244-07  Coordinator: Maribeth Hohenstein
(402-888-2717)
A Phase I/II Study of Dasatinib in Relapsed or Refractory Non-
Hodgkin’s Lymphoma

Industry Sponsored Studies
IRB NO: 357-08  Coordinator: Susan Blumel
(402-888-5647)
An Open-label, Phase 1 Study of MLN8237, a Novel Aurora A Kinase
Inhibitor, in Patients with Advanced Hematological Malignancies
IRB NO: 442-07  Coordinator: Maribeth Hohenstein
(402-888-2717)
A Phase I/IIa Open-label Study of Sequential Pralatrexate and
Gemcitabine with Vitamin B12 and Folic Acid Supplementation in
Patients with Relapsed or Refractory Lymphoproliferative Malignancies
IRB NO: 415-08  Coordinator: Susan Allen
(402-888-2537)
Phase I/II Dose-Escalation Study of the Pan-Histone Deacetylase
(HDAC) Inhibitor PCI-24781 in Lymphoma
Indolent Non-Hodgkin’s Lymphoma
Clinical Trials

Transplant

Investigator-Initiated Studies

IRB NO: 438-05  Coordinator:  Susan Allen
(402-888-2537)
Phase I/II Study of VELCADE® - BEAM (+/- Rituximab) and
Autologous Hematopoietic Stem Cell Transplantation for Relapsed
Indolent Non-Hodgkin’s Lymphoma, Transformed, Mantle Cell
Lymphoma or Peripheral T-Cell Lymphoma

Cooperative Group Studies

IRB NO: 441-08  Coordinator:  Cathy Basham
(402-888-0938)
A Multi-Center, Phase II Trail of Nonmyeloablative Conditioning (NST)
and Transplantation of Partially HLA-Mismatched Bone Marrow for
Patients with Hematologic Malignancies

IRB NO: 001-09  Coordinator:  Cathy Basham
(402-888-0938)
Phase II Trial of Non-Myeloablative Allogeneic Hematopoietic Cell
Transplantation for Patients with Relapsed Follicular Non-Hodgkin’s
Lymphoma Beyond First Complete Response
STANDARD THERAPY
B-CLL/Small lymphocytic lymphoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Age</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb ≥ 11 g/dl</td>
<td>Any</td>
<td>Observation</td>
</tr>
<tr>
<td>Plt ≥ 100,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dbl. time &gt; 12 mo.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\[ \text{Any of the following:} \]
\[
\begin{align*}
\text{Hb < 11 g/dl} \\
\text{Plt < 100,000} \\
\text{Symptomatic} \\
\text{Dbl. time <12 mo}
\end{align*}
\]

\[ \leq 60 \]

\[ \text{At relapse:} \]
\[
\begin{align*}
\text{Consider allogeneic or mini-allogeneic} \\
\text{transplants after first or subsequent} \\
\text{progression if the patient is a candidate} \\
\text{Campath, PCR, CHOP-R, ESHAP, RICE,} \\
\text{Bendamustine + Rituxan} \\
\text{Consider investigational study}
\end{align*}
\]

\[ > 60 \]

\[ \text{At relapse:} \]
\[
\begin{align*}
\text{Consider mini-allogeneic transplant} \\
\text{Campath, PCR, CHOP-R, ESHAP, RICE} \\
\text{Bendamustine + Rituxan} \\
\text{Consider investigational study}
\end{align*}
\]

*17p abnormalities: consider early Allogeneic transplant
# STANDARD THERAPY

**Follicular Grade I, II**

**Nodal Marginal Zone**

<table>
<thead>
<tr>
<th>Age-Adjusted IPI Score*</th>
<th>Stage</th>
<th>Age</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>I or minimal II</td>
<td>Any</td>
<td>Involved field (IF) radiotherapy only or CVP-R x 3-4 + IF (24-30 Gy) or CHOP-R x 3-4 plus IF radiotherapy (24-30 Gy)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bulky II (≥10 cm)</th>
<th>III, IV</th>
<th>≤ 60</th>
<th>Observation if asymptomatic or CVP-R or CHOP-R x 6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&gt; 60</td>
<td>Observation if asymptomatic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>or</td>
<td>If symptomatic: Rituxan weekly x 4, CVP-R, or CHOP-R</td>
</tr>
<tr>
<td></td>
<td></td>
<td>poor PS</td>
<td>(Consider maintenance 1 dose every 3 mo. x 2yrs</td>
</tr>
</tbody>
</table>

*Age Adjusted IPI Score:* Stage III, IV / LDH > upper limits of normal / Karnofsky score ≤ 70
# STANDARD THERAPY
Extranodal marginal zone, MALT type

<table>
<thead>
<tr>
<th>Age-Adjusted IPI Score*</th>
<th>Stage</th>
<th>Age</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>Any</td>
<td>Radiotherapy or surgery</td>
</tr>
<tr>
<td></td>
<td>Non-gastric</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>II-IV</td>
<td>Any</td>
<td>Observation, Rituxan x 4, Chemotherapy + Rituxan, as per follicular</td>
</tr>
<tr>
<td></td>
<td>Non-gastric</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gastric</td>
<td>Any</td>
<td>Two trials of H. pylori irradiation therapy if H. pylori negative or no response, Observation (as per follicular), Rituxan x 4, Local radiotherapy, Chemotherapy +/- Rituxan</td>
</tr>
</tbody>
</table>

*Age Adjusted IPI Score: Stage III, IV / LDH > upper limits of normal / Karnofsky score < 70
INDOLENT NHL - Standard Therapy
Radiation Therapy Guidelines

Follicular Lymphoma Grades I-II

Principles of Radiation Therapy
Stage I – II

Radiation therapy is considered for both nodal and extramodal presentations.

Nodal Presentations:

Involved field radiation therapy is delivered usually with 3-D conformal or forward planning IMRT techniques. All lymph nodes within a region are treated, ex ipsilateral neck and supraclavicular region.

Doses 24-30Gy. An additional 6Gy may be added for bulky disease or slowly responding disease.

Extranodal Presentations:

These are usually cutaneous and are treated with involved region consisting of the target lesion with a 2.5 – 3cm radial margin around the entire lesion.

Doses 24 – 36Gy
INDOLENT NHL - Standard Therapy
Radiation Therapy Guidelines

**Nongastric Marginal Zone Lymphomas**

While marginal zone lymphomas (MZL) may occur in any location, certain clinical presentations may benefit from radiation therapy.

**Conjunctival MZL:**

These lymphomas are located on the bulbar or palpebral conjunctiva. These presentations are usually treated with an anterior enface electron field. Various techniques exist to reduce the dose to the lens of the eye. (Hanging lens eye block or commercially available tungsten contact lens eye shield.)

Radiation dose: 20-30Gy

**Orbital and Adnexal MZL:**

Tumor involving the orbit or lacrimal gland can be treated with various approaches depending on the presentation. These options can include IMRT, 3D Conformal, or Electron Beam Therapy. For retrobulbar presentations IMRT is very useful.

Radiation dose: 25-30Gy
Radiation therapy is considered in patients who have stage I or II disease and are H. pylori negative or in patients who failed initial antibiotic therapy with symptomatic or progressive disease.

Patients are treated to the entire stomach and usually the first echelon of lymph nodes. Patients should be simulated and treated in the fasting state. If oral contrast is used, the volume should be limited to 15ml during simulation.

AP/PA or slightly oblique techniques are usually adequate. Occasionally these techniques will result in an excessive dose to the left kidney. In these cases treating with a ½ beam block technique may be useful. The upper ½ of the field is treated AP/PA while the lower ½ of the field is treated an oblique pair to avoid the left kidney.

These patients benefit from being treated prophylactically with an antiemetic medication.

The radiation dose is generally between 30 and 33Gy. Fraction sizes of 1.5Gy may be selected to minimize nausea.

There may be value in repeating the treatment planning CT scan early on in treatment to confirm stability in the size of the gross target volume and coverage.
Aggressive B-cell Lymphoma
Clinical Trials

Newly Diagnosed

Investigator-Initiated Studies

IRB NO: 041-03 Coordinator: Martin Bast
(402-888-0329)
Microarray Analysis of Patients with Diffuse Large B-Cell Lymphoma Treated with CHOP/Rituximab

IRB NO: 156-95 Coordinator: Lin Bauer
(402-888-0289)
Non-Hodgkin’s Lymphoma - Blood and Bone Marrow Cellular Bank

IRB NO: 462-07 Coordinator: Mary Mailliard
(402-888-2123)
Investigator Initiated Pilot Study of Microarray Directed Therapy for Diffuse Large B-cell Lymphoma Using Genasense with CHOP-R

Relapsed (Salvage)

Investigator-Initiated Studies

IRB NO: 244-07 Coordinator: Maribeth Hohenstein
(402-888-2717)
A Phase I/II Study of Dasatinib in Relapsed or Refractory Non-Hodgkin’s Lymphoma

Industry Sponsored Studies

IRB NO: 442-07 Coordinator: Maribeth Hohenstein
(402-888-2717)
A Phase I/IIa Open-label Study of Sequential Pralatrexate and Gemcitabine with Vitamin B12 and Folic Acid Supplementation in Patients with Relapsed or Refractory Lymphoproliferative Malignancies

IRB NO: 357-08 Coordinator: Susan Blumel
(402-888-5647)
An Open-label, Phase 1 Study of MLN8237, a Novel Aurora A Kinase Inhibitor, in Patients with Advanced Hematological Malignancies
Aggressive B-cell Lymphoma
Clinical Trials

Relapsed (Salvage) — continued

**IRB NO: 416-08**  Coordinator: Maribeth Hohenstein (402-888-2717)
An Open-Label, Single-Arm, Multi-Center Phase 2 Trial With Ofatumumab in Patients with Relapsed/Progressive Diffuse Large B-Cell Lymphoma (DLBCL) Ineligible for Transplant or Relapse/Progression After Autologous Transplant

**IRB NO: 415-08**  Coordinator: Susan Allen (402-888-2537)
Phase I/II Dose-Escalation Study of the Pan-Histone Deacetylase (HDAC) Inhibitor PCI-24781 in Lymphoma

Transplant

**Investigator-Initiated Studies**

**IRB NO: 438-05**  Coordinator: Susan Allen (402-888-2537)
Phase I/II Study of VELCADE® - BEAM (+/- Rituximab) and Autologous Hematopoietic Stem Cell Transplantation for Relapsed Indolent Non-Hodgkin’s Lymphoma, Transformed, Mantle Cell Lymphoma or Peripheral T-Cell Lymphoma

**Cooperative Group Studies**

**IRB NO: 229-05**  Coordinator: Cathy Basham (402-888-0938)
Phase III Rituxan/BEAM vs. Bexxar/BEAM with Autologous Hematopoietic Stem Cell Transplantation (ASCT) for Persistent or Relapsed Chemotherapy Sensitive Diffuse Large B-cell Non-Hodgkin’s Lymphoma

**IRB NO: 441-08**  Coordinator: Cathy Basham (402-888-0938)
A Multi-Center, Phase II Trail of Nonmyeloablative Conditioning (NST) and Transplantation of Partially HLA-Mismatched Bone Marrow for Patients with Hematologic Malignancies
### STANDARD THERAPY

**CD20+ Follicular large cell (grade III) Diffuse large B-cell**

<table>
<thead>
<tr>
<th>Age Adj IPI Score*</th>
<th>Tumor Bulk</th>
<th>Stage</th>
<th>Age</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>I-II</td>
<td>Any</td>
<td>CHOP-R x (3-4) + 40 Gy</td>
</tr>
<tr>
<td>0-1</td>
<td>Non-bulky</td>
<td>III- IV</td>
<td>Any</td>
<td>CHOP-R x 6-8 (2 past CR)</td>
</tr>
<tr>
<td></td>
<td>Bulky ≥ 10 cm</td>
<td>Any</td>
<td>Any</td>
<td>CHOP-R x 6-8 (2 past CR) + 40 Gy</td>
</tr>
<tr>
<td>≥ 2</td>
<td>Non-bulky</td>
<td>CHOP-R x 6</td>
<td>Any</td>
<td>If &lt; CR transplant or CR→consider ABMT (if transplant candidate)</td>
</tr>
<tr>
<td></td>
<td>Bulky ≥ 10 cm</td>
<td>Any</td>
<td>Any</td>
<td>CHOP-R x 6 + 40 Gy If &lt; CR transplant or CR → consider ABMT (if transplant candidate)</td>
</tr>
</tbody>
</table>

*For Patients with a low ejection fraction consider CNOP-R.*

*Age Adjusted IPI Score: Stage III, IV / LDH > upper limits of normal / Karnofsky score < 70*
# STANDARD THERAPY

## Mantle Cell

<table>
<thead>
<tr>
<th>Age Adj IPI Score*</th>
<th>Tumor Bulk</th>
<th>Stage</th>
<th>Age</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>&lt; 60</td>
<td>R-Hyper CVAD/R-M/A x 4-6 (2-3 A+B)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(if young and good PS) ABMT in PR1 or CR1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt; 60 or Poor PS</td>
<td>CHOP-R x 6-8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 past CR→ ABMT (if transplant candidate) in PR1 or CR1</td>
</tr>
</tbody>
</table>

## Lymphoblastic

<table>
<thead>
<tr>
<th>Age adjusted IPI Score</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>Hyper CVAD- 6-8 (3-4 A+B) + maintenance or auto PSC in CR1 (+ Rituximab if CD20+)</td>
</tr>
</tbody>
</table>

## Burkitt

<table>
<thead>
<tr>
<th>Age Adj IPI Score</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 60</td>
<td>R-Magrath regimen x 2 full cycles</td>
</tr>
<tr>
<td></td>
<td>R-CODOX-M x 3 –low risk</td>
</tr>
<tr>
<td></td>
<td>R-CODOX-M/IVAC x 2-3 (1 cycle = 1A+1B)</td>
</tr>
<tr>
<td></td>
<td>-high risk or R-Hyper CVAD x 3-4</td>
</tr>
<tr>
<td>&gt; 60 or Poor PS</td>
<td>R-EPOCH x 6</td>
</tr>
</tbody>
</table>

* Age Adjusted IPI Score: Stage III, IV / LDH > upper limits of normal / Karnofsky score ≤ 70
AGGRESSIVE B-CELL NHL - Standard Therapy
Radiation Therapy Guidelines

Diffuse Large B-Cell Lymphoma

Radiation therapy may be used in conjunction with chemotherapy and very rarely as an alternative to chemotherapy in selected patients. Bulky versus Non bulky disease is based on contiguous nodal masses of $\geq$ 10cm versus smaller volumes. Generally 3-D conformal techniques are used although occasionally IMRT techniques are used to limit dose to nearby sensitive structures. Treatment nodal regions are based on the staging PET/CT, although treatment volumes are based on post chemotherapy imaging.

Stage I, II Non bulky (<10cm) are usually treated to the post chemotherapy treatment volume to a dose of 30-40Gy (36Gy)

If six or eight cycles are given there may not be indications for radiation therapy with Non bulky disease.

Stage I, II Bulky ($\geq$ 10cm) are usually treated to the post chemotherapy treatment volume to a dose of 30 – 40Gy (36Gy)
T-cell Lymphoma Clinical Trials

**Newly Diagnosed**

**Multi-Center Institutional Studies**

IRB NO: 415-06   Coordinator: Martin Bast  
(402-888-0329)

T-Cell Project: Prospective Collection of Data in Patients with Peripheral T-Cell Lymphoma

**Relapsed (Salvage)**

**Investigator-Initiated Studies**

IRB NO: 244-07   Coordinator: Maribeth Hohenstein  
(402-888-2717)

A Phase I/II Study of Dasatinib in Relapsed or Refractory Non-Hodgkin’s Lymphoma

**Industry Sponsored Studies**

IRB NO: 305-07   Coordinator: Susan Allen  
(402-888-2537)

A Phase II Study of Oral LBH589 in Adult Patients With Cutaneous T-Cell Lymphoma Resistant to Prior HDAC Inhibitor Therapy

IRB NO: 442-07   Coordinator: Maribeth Hohenstein  
(402-888-2717)

A Phase I/IIa Open-label Study of Sequential Pralatrexate and Gemcitabine with Vitamin B12 and Folic Acid Supplementation in Patients with Relapsed or Refractory Lymphoproliferative Malignancies

IRB NO: 415-08   Coordinator: Susan Allen  
(402-888-2537)

Phase I/II Dose-Escalation Study of the Pan-Histone Deacetylase (HDAC) Inhibitor PCI-24781 in Lymphoma

IRB NO: 533-08   Coordinator: Susan Allen  
(402-888-2537)

Phase II, Multi-center, Simon Two-Stage Study of R788 in Patients with Relapsed or Refractory T-Cell Lymphoma
T-cell Lymphoma
Clinical Trials

Transplant

Investigator-Initiated Studies

IRB NO: 438-05 Coordinator: Susan Allen
(402-888-2537)
Phase I/II Study of VELCADE® - BEAM (+/- Rituximab) and Autologous Hematopoietic Stem Cell Transplantation for Relapsed Indolent Non-Hodgkin’s Lymphoma, Transformed, Mantle Cell Lymphoma or Peripheral T-Cell Lymphoma
### STANDARD THERAPY

**Anaplastic Large cell-T/Null ALK pos**

<table>
<thead>
<tr>
<th>Tumor Bulk</th>
<th>Stage</th>
<th>Age</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-II</td>
<td>Any</td>
<td></td>
<td>CHOP x 3-4 + 40 Gy</td>
</tr>
<tr>
<td>Non-bulky</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III-IV</td>
<td>Any</td>
<td></td>
<td>CHOP x 6-8 (2 past CR)</td>
</tr>
<tr>
<td>Bulky ≥ 10cm</td>
<td>I-IV</td>
<td>Any</td>
<td>CHOP x 6-8 (2 past CR) + 40 Gy</td>
</tr>
</tbody>
</table>

For patients with low ejection fraction – CNOP may be substituted
## STANDARD THERAPY

### Other aggressive PTCL, Peripheral T-cell, NOS

#### Angioimmunoblastic T-cell

**ALCL, ALK neg**

<table>
<thead>
<tr>
<th>Age Adj IPI Score*</th>
<th>Tumor Bulk</th>
<th>Stage</th>
<th>Age</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHOP x 6-8</td>
<td>good PR or CR → consider ABMT</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**<10 cm**

<table>
<thead>
<tr>
<th>I-I</th>
<th>&lt; 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHOP x 6-8</td>
<td></td>
</tr>
</tbody>
</table>

**>10 cm**

<table>
<thead>
<tr>
<th>III-IV</th>
<th>≥ 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHOP 6-8, x 40 Gy</td>
<td>good PR or CR → consider ABMT (if transplant candidate)</td>
</tr>
</tbody>
</table>

**Consider CNOP if ejection fraction is low**

### T-cell Lymphoblastic

<table>
<thead>
<tr>
<th>Age Adj IPI Score*</th>
<th>Tumor Bulk</th>
<th>Stage</th>
<th>Age</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyper CVAD x 3-4 + maintenance or auto PSC in CR1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Age Adjusted IPI Score: Stage III, IV / LDH > upper limits of normal / Karnofsky score ≤ 70*
Electron beam irradiation is the treatment of choice for unilesional disease. Recommended dose is 24-36Gy.

Electron beam irradiation may be used to treat lesions that are refractory to systemic therapy, when disease control is otherwise favorable. Recommended dose is 30-36Gy.

Involved field electron beam irradiation may be combined with Phototherapy for treatment of thicker lesions. Recommended dose is 24-36Gy.

Total Skin Electron Beam therapy is no longer considered first choice of therapy due to the addition of newer systemic therapies. It is still used for widespread skin disease that is refractory to other therapies. Doses of 30-36Gy are recommended.
I. ELIGIBILITY
Any biopsy proven non-Hodgkin’s lymphoma with the following WHO classification subtypes: FL3, Diffuse large B-cell, or Mantle cell. CD20+ on immunophenotype of pathology.

II. STANDARD STAGING EVALUATION
Modify as needed to document all initial disease sites adequately for follow-up evaluation.

A. History and physical examination.
B. Chest x-ray.
C. Laboratory: CBC, differential, platelet count, Serum LDH, AST (SGOT), alkaline phosphatase, bilirubin, creatinine, uric acid, calcium, beta-2-microglobulin (if available).
D. Bone marrow aspiration and biopsy.
E. CT of chest/abdomen/pelvis with lymph nodes sizes.
F. Whenever possible, PET or PET/CT scan should be done as part of the initial evaluation.
G. Additional scans and biopsy as needed to unequivocally document the extent of disease especially sites of extra-nodal involvement.
H. MUGA scan or ECHO to document ejection fraction, if appropriate.
I. CSF examination for lymphomatous involvement will be done if the lymphoma involves the sinuses, orbit, testes, or paraspinous areas. A dose of 12 mg of IT Methotrexate will be administered at this time.
J. Colonoscopy and EGD if MCL with blind biopsies
K. Pregnancy test if applicable
L. Hepatitis B antigen if Rituximab given
## A. SCHEDULE AND DOSES

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE</th>
<th>ROUTE</th>
<th>DAYS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituxan *+</td>
<td>375 mg/M²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>750 mg/M²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>50 mg/M²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Vincristine</td>
<td>1.4 mg/M²/day (max. 2.0 mg)</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Prednisone</td>
<td>100 mg (total dose)</td>
<td>PO</td>
<td>1 – 5</td>
</tr>
</tbody>
</table>

* On cycle 1 Rituxan may be given on day 1 and CHOP on day 2 due to prolonged duration of infusion.
* Delete Rituxan for T-cell lymphomas

Repeat sequence at 21 days unless counts are not acceptable, then repeat at 28 day intervals.

## CENTRAL NERVOUS SYSTEM THERAPY FOR PATIENTS WITH POSITIVE CSF CYTOLOGY

Patients with positive CSF cytology at diagnosis will receive intrathecal Methotrexate at a dose of 12 mg plus Ara-C at a dose of 50 mg two times a week until the CSF is clear and then once a week for 2 doses, and continue with one dose at the start of each remaining CHOP cycle.

## PROPHYLACTIC THERAPY FOR PATIENTS WITH LYMPHOMA INVOLVING THE SINUSES, ORBIT, TESTES, OR PARASPINOUS AREAS

Patients with aggressive NHL with sites of involvement mentioned above will receive prophylactic CSF treatment starting with cycle 1 of CHOP. They should receive intrathecal Methotrexate at a dose of 12 mg with each cycle of CHOP.
NLSG Treatment for NHL

CHOP + Rituxan

Systemic Therapy for Non-Hodgkin’s Lymphoma Using Cyclophosphamide, Mitoxantrone, Vincristine, Prednisone and Rituxan

CNOP +/- Rituxan
(Effective: January 1, 2001)

I. ELIGIBILITY
Any biopsy proven non-Hodgkin’s lymphoma with the following WHO classification subtypes: FL3, Diffuse large B-cell, or Mantle cell. CD20+ on immunophenotype of pathology, for patients > age 60 with poor ejection fraction or performance status.

STANDARD STAGING EVALUATION
Same as CHOP-R

A. SCHEDULE AND DOSES

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE</th>
<th>ROUTE</th>
<th>DAYS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituxan *+</td>
<td>375 mg/M²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>750 mg/M²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Mitoxantrone</td>
<td>12 mg/M²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Vincristine</td>
<td>1.4 mg/M²/day (max. 2.0 mg)</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Prednisone</td>
<td>100 mg (total dose)</td>
<td>PO</td>
<td>1 – 5</td>
</tr>
</tbody>
</table>

*On cycle 1 Rituxan may be given on day 1 and CNOP on day 2 due to prolonged duration of infusion.
+Delete Rituxan for T-cell lymphomas

Repeat sequence at 21 days unless counts are not acceptable, then repeat at 28 day intervals.
NLSG Treatment for NHL

Systemic Therapy for Non-Hodgkin’s Lymphoma Using Cyclophosphamide, Mesna, Doxorubicin, Vincristine and Rituximab

R-HyperCVAD
for Mantle Cell, LBL, Burkitt NHL
(Effective January 1, 2000)

I. ELIGIBILITY
Any biopsy proven non-Hodgkin’s lymphoma with the following WHO classification subtype: Mantle Cell, LBL, Burkitt NHL

II. STANDARD STAGING EVALUATION
Modify as needed to document all initial disease sites adequately for follow-up evaluation.
A. History and physical examination.
B. Chest x-ray.
C. Laboratory: CBC, differential, platelet count, Serum LDH, AST (SGOT), alkaline phosphatase, bilirubin, creatinine, uric acid, calcium, beta-2-microglobulin (if available).
D. Bone marrow aspiration and biopsy.
E. CT of chest/abdomen and pelvis.
F. Whenever possible, PET or PET/CT scan should be done as part of the initial evaluation.
G. Additional scans and biopsy as needed to unequivocally document the extent of the disease, especially sites of extra-nodal involvement.
H. CSF examination for lymphomatous involvement will be done if the lymphoma involves the sinuses, orbit, testes or paraspinous areas. A dose of 12 mg of IT Methotrexate will be administered at this time.
J. EGD & colonoscopy for MCL
A. **SCHEDULE AND DOSES**

**Cycle A**

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE</th>
<th>ROUTE</th>
<th>DAYS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab</td>
<td>375 mg/m²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Cytoxan</td>
<td>300 mg/m² (q 12 hrs x 6 doses)</td>
<td>IV</td>
<td>1 – 3</td>
</tr>
<tr>
<td>Mesna</td>
<td>600 mg/m² each (24 hrs by CI)</td>
<td>IV</td>
<td>1 – 4</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>25 mg/m²/day (total dose 50 mg/m² over 48 hrs)</td>
<td>IV (By CI over 24 hrs x 2)</td>
<td>4 &amp; 5</td>
</tr>
<tr>
<td>Vincristine</td>
<td>1.4 mg/m² (Max 2.0 mg)</td>
<td>IV</td>
<td>4 &amp; 11</td>
</tr>
<tr>
<td>Methotrexate*</td>
<td>12 mg</td>
<td>IT</td>
<td>2</td>
</tr>
<tr>
<td>Cytarabamine*</td>
<td>50 mg</td>
<td>IT</td>
<td>8</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>40 mg</td>
<td>PO or IV</td>
<td>1–4 &amp; 11–14</td>
</tr>
<tr>
<td>G-CSF or Neulasta 24 hours after chemo</td>
<td>5 μg/kg-G-CSF or 6 mg-Neulasta</td>
<td>SC</td>
<td>7 - … (until ANC &gt;1500)</td>
</tr>
</tbody>
</table>

* IT Methotrexate and Cytarabine for LBL and Burkitt’s only

**Prescriptions:**
Cipro, Valacyclovir, Fluconazole - optional
Add Bactrim DS 1 tablet PO BID twice per week for PCP prophylaxis.
Urine pH > 7.0 to start Methotrexate
### Cycle B – on or before day 21 (when ANC >1500 off G-CSF)

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE</th>
<th>ROUTE</th>
<th>DAYS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab</td>
<td>375 mg/m²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>200 mg/m² (over 2 hrs) then 800 mg/m² (over 22 hrs)</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Leucovorin</td>
<td>50 mg IV (12 hrs after MTX infusion) then 15 mg IV or po (q 6 hrs x 8 doses)</td>
<td>PO</td>
<td>3 - … (until MTX level &lt;0.05)</td>
</tr>
<tr>
<td>ARA-C</td>
<td>3 gms/m² over 2 hrs q 12 hrs x 4 doses (1 gm/m² if age &gt;65 or creatinine is &gt;1.5)</td>
<td>IV</td>
<td>2 &amp; 3</td>
</tr>
<tr>
<td>Methotrexate*</td>
<td>12 mg</td>
<td>IT</td>
<td>2</td>
</tr>
<tr>
<td>Cytarabamine*</td>
<td>50 mg</td>
<td>IT</td>
<td>8</td>
</tr>
<tr>
<td>G-CSF or Neulasta 24 hours after chemo</td>
<td>5 μg/kg-G-CSF or 6 mg-Neulasta</td>
<td>IV or SC</td>
<td>4 - …(until ANC &gt;1500)</td>
</tr>
</tbody>
</table>

* IT Methotrexate and Cytarabine for LBL and Burkitt’s only

If Methotrexate levels were > 1 umol/L at 24 hours after the methotrexate infusion ended or 0.1 umol/L at 48 hours after the end of the methotrexate infusion, the leucovorin dose should be increased to 100 mg IV every 3 hours.

**Prescriptions:**
- Leucovorin 15 mg po q 6 hrs x 8 (total doses)
- Pred-Forte Poth Drops – 2 gtts QID x 7 days after ARA-C
- Cipro, Fluconazole, Valacyclovir – optional
- Bactrim DS one orally BID twice per week

Start cycle A again at day 21 or when ANC >1500 off G-CSF
Dose Reductions:
1. MTX levels – leucovorin adjusted by nanogram.
2. For severe mucositis reduce Methotrexate by 25% and for pleural, pericardial effusion or ascites reduce the Methotrexate by 50%.

Restage after 2 of each cycles (A+B). Maximum for non-transplant patients would be 4 cycles of each cycle A and B.

CENTRAL NERVOUS SYSTEM THERAPY FOR PATIENTS WITH POSITIVE CSF CYTOLOGY (LBL & Burkitt’s only)
Patients with positive CSF cytology at diagnosis will receive intrathecal Methotrexate at a dose of 12 mg plus Ara-C at a dose of 50 mg two times a week until the CSF is clear and then once a week for 2 doses, and continue with one dose on the days indicated in the tables above for each remaining cycle.

DOSE ATTENUATION SCHEDULE FOR AGE
Age ≥ 60 years: Reduce Ara-C to 1 gm/M²
Systemic Therapy for Non-Hodgkin’s Lymphoma Using Cytarabine, Vincristine, Doxorubicin, Methotrexate, Leucovorin, and Cyclophosphamide Alternating with Cytarabine, Methotrexate, Ifosfamide, and Etoposide

Magrath Hybrid Protocol

for Burkitt’s NHL

(Effective: January 1, 2000)

I. ELIGIBILITY
Any biopsy proven non-Hodgkin’s lymphoma with the following WHO classification subtype: Burkitt’s

II. STANDARD STAGING EVALUATION
A. History and physical examination.
B. Chest x-ray.
C. Laboratory: CBC, differential, platelet count, Serum LDH, AST (SGOT), alkaline phosphatase, bilirubin, creatinine, uric acid, calcium, beta-2-microglobulin (if available).
D. Bone marrow aspiration and biopsy.
E. CT of chest/abdomen/pelvis.
F. When possible, PET or PET/CT scan should be done as part of initial evaluation.
G. Additional scans and biopsy as needed to unequivocally document the extent of the disease, especially sites of extra-nodal involvement.
H. CSF Fluid examination for lymphomatous involvement will be done regardless of disease sites.

III. TREATMENT AND DOSE ALTERATIONS
It is very important that treatment be given on time finishing in the planned number of cycles. All drugs should be given in FULL doses on time unless SPECIFIC toxicity requires dose reduction.
A. **SCHEDULE AND DOSES**

*ALTERNATE CYCLES OF CYCLES A and B (following page) for a total of four cycles.*

**Cycle A: CODOX-M**

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE</th>
<th>ROUTE</th>
<th>DAYS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab</td>
<td>375 mg/m²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Cytarabine</td>
<td>70 mg</td>
<td>IT</td>
<td>1 &amp; 3</td>
</tr>
<tr>
<td>Vincristine</td>
<td>1.5 mg/m²</td>
<td>IV</td>
<td>1, 8, 15*</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>40 mg/m²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>12 mg</td>
<td>IT</td>
<td>15</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>800 mg/m² (Day 1) then 200 mg/m² (Days 2-5)</td>
<td>IV</td>
<td>1 – 5</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>1200 mg/m² over 1 hr then 240 mg/m²/hr (for 23 hrs)</td>
<td>IV</td>
<td>10</td>
</tr>
<tr>
<td>Leucovorin</td>
<td>200 mg/m² (at hour 36) then 12 mg/m² (q 6 hrs until MTX level 0.05)</td>
<td>IV</td>
<td>11 - 14</td>
</tr>
<tr>
<td>G-CSF or Neulasta</td>
<td>5 μg/kg-G-CSF or 6 mg-Neulasta</td>
<td>IV or SC</td>
<td>13-… (until ANC &gt;1000)</td>
</tr>
</tbody>
</table>

* The Day 15 dose of VCR is not given on cycle 1 and only if no neuropathy in cycle 2A
**Cycle B: IVAC**

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE</th>
<th>ROUTE</th>
<th>DAYS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab</td>
<td>375 mg/m²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Cytarabine</td>
<td>2 GM/m²(q 12 hrs x 4 doses)</td>
<td>IV</td>
<td>1 &amp; 2*</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>12 mg</td>
<td>IT</td>
<td>5</td>
</tr>
<tr>
<td>Mesna</td>
<td>1500 mg/m²/day (1 hr prior to Ifosfamide &amp; continue for 12 hrs post Ifosfamide)</td>
<td>IV (CI)</td>
<td>1 - 5</td>
</tr>
<tr>
<td>Ifosfamide</td>
<td>1500 mg/m²/day</td>
<td>IV</td>
<td>1 - 5</td>
</tr>
<tr>
<td>Etoposide</td>
<td>60 mg/m²/day</td>
<td>IV</td>
<td>1 – 5</td>
</tr>
<tr>
<td>G-CSF or Neulasta</td>
<td>5 µg/kg-G-CSF or 6 mg-Neulasta</td>
<td>IV or SC</td>
<td>7 - ... (until ANC &gt;1000)</td>
</tr>
</tbody>
</table>

*Pred-Forte ophthalmic drops x 7 days post Cytarabine

Repeat sequence at 21 days if ANC ≥ 1000 and platelet count ≥ 50,000/µL, if not repeat at 28 day intervals. Complete a total of 2 cycles of A + B.

**CENTRAL NERVOUS SYSTEM THERAPY FOR PATIENTS WITH POSITIVE CSF CYTOLOGY**

Patients with positive CSF cytology at diagnosis will receive intrathecal Methotrexate at a dose of 12 mg plus Ara-C at a dose of 50 mg two times a week until the CSF is clear and then once a week for 2 doses, and continue with prophylactic treatment as indicated in tables above for each remaining cycle.
Systemic Therapy for Non-Hodgkin’s Lymphoma Using Etoposide, Doxorubicin, Vincristine, Cyclophosphamide, Prednisone and Rituxan

**R-EPOCH**
*For HIV+ NHL and Burkitt’s (patients > age 50)*

**I. ELIGIBILITY**
Any biopsy proven non-Hodgkin’s lymphoma with the following WHO classification subtypes: HIV+ NHL and Burkitt NHL (patients > age 50)

**II. STANDARD STAGING EVALUATION**
Modify as needed to document all initial disease sites adequately for follow-up evaluation.

- **A.** History and physical examination (including performance status).
- **B.** Chest x-ray.
- **C.** Laboratory: CBC, differential, platelet count, Serum LDH, AST (SGOT), alkaline phosphatase, bilirubin, creatinine, uric acid, calcium, beta-2-microglobulin (if available).
- **D.** Bone marrow aspiration and biopsy.
- **E.** CT of chest/abdomen/pelvis with lymph nodes sizes.
- **F.** Whenever possible, PET or PET/CT scan should be done as part of the initial evaluation.
- **G.** Additional scans and biopsy as needed to unequivocally document the extent of disease especially sites of extra-nodal involvement.
- **H.** MUGA scan or ECHO to document ejection fraction, if appropriate.
- **I.** CSF examination for lymphomatous involvement will be done if the lymphoma involves the sinuses, orbit, testes, or paraspinous areas. A dose of 12 mg of IT Methotrexate will be administered at this time.
- **J.** Lumbar Puncture
- **K.** HIV testing
- **L.** Pregnancy test if applicable
- **M.** Hepatitis B antigen if Rituximab given
A. SCHEDULE AND DOSES

**R-EPOCH STARTING DOSE LEVEL**

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE</th>
<th>ROUTE</th>
<th>DAYS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituxan</td>
<td>375 mg/M²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Etoposide</td>
<td>50 mg/M²/day</td>
<td>CIV</td>
<td>1,2,3,4 (96 hours)</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>10 mg/M²/day</td>
<td>CIV</td>
<td>1,2,3,4 (96 hours)</td>
</tr>
<tr>
<td>Vincristine</td>
<td>0.4 mg/M²/day</td>
<td>CIV</td>
<td>1,2,3,4 (96 hours)</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>750 mg/M²</td>
<td>IV</td>
<td>5</td>
</tr>
<tr>
<td>Prednisone</td>
<td>60 mg/M²/bid</td>
<td>PO</td>
<td>1-5</td>
</tr>
<tr>
<td>G-CSF</td>
<td>5 μg/kg/day</td>
<td>SC</td>
<td>6-…(to ANC &gt; 5x10⁹/L past nadir)</td>
</tr>
</tbody>
</table>

Repeat sequence at 21 days unless ANC < 1 x 10⁹/L and the platelet count < 100 x 10⁹/L.
## DOSE ADJUSTMENTS

<table>
<thead>
<tr>
<th>Nadir measurements*</th>
<th>Dose-adjustment+</th>
</tr>
</thead>
<tbody>
<tr>
<td>If Nadir ANC at least 0.5 x 10⁹/L</td>
<td>20% increase in etoposide, doxorubicin, &amp; cyclophosphamide above last cycle</td>
</tr>
<tr>
<td>If Nadir ANC less than 0.5 x 10⁹/L on 1 or 2 measurements</td>
<td>Same dose(s) as last cycle</td>
</tr>
<tr>
<td>If Nadir ANC less than 0.5 x 10⁹/L on at least 3 measurements</td>
<td>20% decrease in etoposide, doxorubicin, &amp; cyclophosphamide below last cycle</td>
</tr>
</tbody>
</table>

OR

| If Nadir platelet count less than 25 x 10⁹/L on 1 measurement | 20% decrease in etoposide, doxorubicin, & cyclophosphamide below last cycle |

* Measurements of ANC and platelet nadir are based on **twice weekly CBC only.**
+ Dose adjustments **above starting dose level** apply to etoposide, doxorubicin and cyclophosphamide. Dose adjustments **below starting dose level** apply to cyclophosphamide only.
CENTRAL NERVOUS SYSTEM THERAPY FOR PATIENTS WITH POSITIVE CSF CYTOLOGY

Patients with positive CSF cytology at diagnosis will receive the following standard chemotherapy:

- **Induction** - intrathecal methotrexate (6 mg by Ommaya or 12 mg by lumbar route) or cytarabine (70 mg by Ommaya or lumbar route). Alternatively, if combined with methotrexate, administer cytarabine 30 mg (by Ommaya or lumbar route) and hydrocortisone (15 mg by Ommaya or lumbar route). Administer induction treatment twice a week for 2 weeks past negative cytology with a minimum of 4 weeks treatment.

- **Consolidation** - Following induction, change therapy frequency to weekly x 6.

- **Maintenance** - Following consolidation, change therapy frequency to monthly x 4. Due to unforeseeable events, the above therapy may be modified as clinically indicated. In some cases, it may be necessary to administer radiation to the head and/or spine or to administer intrathecal therapy using methotrexate 12 mg I.T. b.i.w. for 4 treatments beyond clearing, then once every other week for 4 treatments, and then once monthly for 6 treatments. Patients who fail to clear or relapse in the CSF will be considered for other intraventricular therapy and/or radiation.
Hodgkin’s Lymphoma
Clinical Trials

**Newly Diagnosed**

**Investigator-Initiated Studies**

IRB NO: 156-95    Coordinator: Lin Bauer
                 (402-888-0289)
Non-Hodgkin’s Lymphoma - Blood and Bone Marrow Cellular Bank

**Relapsed (Salvage)**

**Industry Sponsored Studies**

IRB NO: 069-07    Coordinator: Maribeth Hohenstein
                   (402-888-2717)
A Phase II Study of MGCD0103 (MG-0103) in Patients with Relapsed or Refractory Hodgkin’s Lymphoma

IRB NO: 442-07    Coordinator: Maribeth Hohenstein
                   (402-888-2717)
A Phase I/IIa Open-label Study of Sequential Pralatrexate and Gemcitabine with Vitamin B12 and Folic Acid Supplementation in Patients with Relapsed or Refractory Lymphoproliferative Malignancies

IRB NO: 415-08    Coordinator: Susan Allen
                   (402-888-2537)
Phase I/II Dose-Escalation Study of the Pan-Histone Deacetylase (HDAC) Inhibitor PCI-24781 in Lymphoma

**Transplant**

**Cooperative Group Studies**

IRB NO: 441-08    Coordinator: Cathy Basham
                    (402-888-0938)
A Multi-Center, Phase II Trail of Nonmyeloablative Conditioning (NST) and Transplantation of Partially HLA-Mismatched Bone Marrow for Patients with Hematologic Malignancies
STANDARD THERAPY
Classical Hodgkin’s Lymphoma

<table>
<thead>
<tr>
<th>Age</th>
<th>Stage</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60</td>
<td>I-IIA</td>
<td>Stanford V x 8 weeks and Radiotherapy (30Gy to involved field if &lt;5cm; 35 Gy to involved field if ≥5 cm) Or ABVD (x 16 wks/4 cycles) followed by involved field Radiotherapy (if maintenance of fertility is an over riding factor)</td>
</tr>
<tr>
<td>≥60</td>
<td>I-IIA</td>
<td>ABVD x 4 and Radiotherapy Or Ch1VPP/ABV x 6 (30 Gy to involved field if&lt;5 cm ; 35 Gy to involved field if ≥5 cm)</td>
</tr>
<tr>
<td></td>
<td>IIB, III, IV or 10 cm mass</td>
<td>ABVD Or Ch1VPP/ABV x 6 Or Ch1VPP x 6 Radiation for mass &gt; 10cm</td>
</tr>
</tbody>
</table>

LPHD

<table>
<thead>
<tr>
<th>Age</th>
<th>Stage</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I-IIA</td>
<td>Radiation or observation Or same as above for localized</td>
</tr>
<tr>
<td></td>
<td>IIB, III, IV</td>
<td>Treat like advanced stage classical HD (if CD20+ - add Rituximab)</td>
</tr>
</tbody>
</table>
Radiation therapy is generally combined with chemotherapy. The timing of radiation therapy is usually within three weeks of completing chemotherapy. A staging PET/CT is very valuable to identify the sites of disease and the size of the disease prior to chemotherapy. The treatment volume is based on post chemotherapy imaging, while the region to be treated is based on the initial PET/CT findings. Patients with disease above the diaphragm are usually treated in an “arms overhead position” instead of “akimbo.” This is useful to reduce the dose to breast tissue in women and lung dose when axillary nodes are to be treated.

Radiation therapy is usually delivered with 3D conformal technique. Forward planning IMRT techniques are frequently used to achieve dose uniformity. True IMRT is occasionally used to treat disease adjacent to a critical or dose limiting structure.

Most treatment fields are Involved-field: limiting treatment to the involved lymphoid region(s). Involved-field usually treats a larger volume than Involved Nodal-field.

**Combined Modality Therapy Stage I – II:**

**Stanford V treated patients:**
Non-bulky  30Gy  
Bulky (>5cm or large mediastinal mass ie > than 1/3 diameter) 36Gy

**ABVD treated patients:**
Non bulky stage I-II 30Gy  
Bulky (any mass > 10cm or larger or mediastinal mass ie > 1/3 diameter) 36Gy

**Radiation Therapy Alone:**
Patients with early stage lymphocyte predominant Hodgkin’s lymphoma may be considered for treatment with radiation therapy alone with either Involved-field or Regional-field techniques”

Involved regions:  30- 36Gy  
Uninvolved regions:  25 – 30Gy
I. **ELIGIBILITY**
A. **Required:**
   1. Biopsy proven Hodgkin’s Lymphoma (any subtype)
   2. Age <60 years old.

II. **STANDARD STAGING EVALUATION**
Modify as needed to document all initial disease sites adequately for
follow-up evaluation:
A. History and physical examination.
B. Chest x-ray.
C. Laboratory: CBC, differential, platelet count, Sed Rate, AST
   (SGOT), alkaline phosphatase, bilirubin, creatinine, uric acid,
   albumin, calcium.
D. Bone marrow aspiration and biopsy.
E. CT of chest/abdomen/pelvis.
F. Whenever possible, PET or PET/CT should be done as part of the
   initial evaluation.
G. Additional scans and biopsy as needed to unequivocally document
   the extent of the disease especially sites of extra-nodal involvement.
**III. TREATMENT AND DOSE ALTERATIONS**

It is very important that treatment be given on time finishing in the planned number of cycles. All drugs should be given in FULL doses on time unless SPECIFIC toxicity requires dose reduction.

### A. SCHEDULE AND DOSES

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE</th>
<th>ROUTE</th>
<th>DAYS*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxorubicin</td>
<td>25 mg/m²</td>
<td>IV</td>
<td>1 &amp; 15</td>
</tr>
<tr>
<td>Vinblastine†</td>
<td>6 mg/m²</td>
<td>IV</td>
<td>1 &amp; 15</td>
</tr>
<tr>
<td>Mechlorethamine</td>
<td>6 mg/m²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Vincristine†</td>
<td>1.4 mg/m²</td>
<td>IV §</td>
<td>8 &amp; 22</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>5 U/m²</td>
<td>IV</td>
<td>8 &amp; 22</td>
</tr>
<tr>
<td>Etoposide</td>
<td>60 mg/m²</td>
<td>IV</td>
<td>15 &amp; 16</td>
</tr>
<tr>
<td>Prednisone ‡</td>
<td>40 mg/m²</td>
<td>PO</td>
<td>QOD</td>
</tr>
</tbody>
</table>

**Abbreviations:**  IV, intravenous; PO, oral; QOD, every other day.

*  Treatment cycle repeated every 28 days, for total of 3 cycles.
†  Vinblastine dose decreased to 4 mg/m² and vincristine dose to 1 mg/m² during cycle 3 for patients ≥ 50 years of age.
‡  Tapered by 10 mg QOD starting at week 10.
§  Maximum dose, 2.0 mg.

**Follow with radiotherapy to bulk disease.**

**Prophylactic antimicrobial, antifungal and antibiotic dose and schedule:**

- Acyclovir (#252) 200 mg, 1 tab, PO TID
- Fluconazole (#84) 200 mg, 1 tab, PO qd until gone
- Bactrim, DS (#48) 1 tab, PO BID (Saturday and Sunday)
I. ELIGIBILITY
A. Biopsy proven Hodgkin’s Lymphoma (any subtype)
   1. Age $\geq 60$ years old.
   2. Stage II B, III A, III B, IV A, or IV B.

II. STANDARD STAGING EVALUATION
Modify as needed to document all initial disease sites adequately for follow-up evaluation.
A. History and physical examination.
B. Chest x-ray.
C. Laboratory: CBC, differential, platelet count, Sed Rate, AST (SGOT), alkaline phosphatase, bilirubin, creatinine, uric acid, albumin, calcium.
D. Bone marrow aspiration and biopsy.
E. CT of chest/abdomen/pelvis.
F. Whenever possible, PET should be done as part of the initial evaluation.
G. Additional scans and biopsy as needed to unequivocally document the extent of the disease especially sites of extra-nodal involvement.
III. TREATMENT AND DOSE ALTERATIONS
It is very important that treatment be given on time finishing in the planned number of cycles. All drugs should be given in FULL doses on time unless SPECIFIC toxicity requires dose reduction.

A. SCHEDULE AND DOSES

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</thead>
<tbody>
<tr>
<td>Chlorambucil</td>
<td>6 mg/m²/day</td>
<td>PO</td>
<td>1 – 7</td>
</tr>
<tr>
<td>Vinblastine</td>
<td>6 mg/m²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Procarbazine</td>
<td>100 mg/m²/day</td>
<td>PO</td>
<td>1 – 7</td>
</tr>
<tr>
<td>Prednisone</td>
<td>40 mg/day</td>
<td>PO</td>
<td>1 – 14</td>
</tr>
<tr>
<td>Adriamycin</td>
<td>25 mg/m²</td>
<td>IV</td>
<td>8</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>10 U/m²</td>
<td>IV</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>(max. 15 U)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vincristine</td>
<td>1.4 mg/m²</td>
<td>IV</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>(max. 2 mg)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Repeat cycle every 28 days for 6 cycles.

Follow with radiotherapy to bulk disease.
Systemic Therapy for Hodgkin’s Lymphoma Using Doxorubicin, Bleomycin, Vinblastine, and Dacarbazine

**ABVD**
(Effective: January 1, 2000)

**I. ELIGIBILITY**
A. Biopsy proven Hodgkin’s Lymphoma (any subtype)

**II. STANDARD STAGING EVALUATION**
Modify as needed to document all initial disease sites adequately for follow-up evaluation.
A. History and physical examination.
B. Chest x-ray.
C. Laboratory: CBC, differential, platelet count, sed rate, AST (SGOT), alkaline phosphatase, bilirubin, creatinine, uric acid, albumin, calcium.
D. Bone marrow aspiration and biopsy.
E. CT of chest/abdomen/pelvis
G. Whenever possible, PET or PET/CT should be done as part of the initial evaluation.
H. Additional scans and biopsy as needed to unequivocally document the extent of the disease, especially sites of extra-nodal involvement.
III. TREATMENT AND DOSE ALTERATIONS
It is very important that treatment be given on time finishing in the planned number of cycles. All drugs should be given in FULL doses on time unless SPECIFIC toxicity requires dose reduction.

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<tr>
<td>Bleomycin*</td>
<td>10 U/m²</td>
<td>IV</td>
<td>1 &amp; 15</td>
</tr>
<tr>
<td>Vinblastine</td>
<td>6 mg/m²</td>
<td>IV</td>
<td>1 &amp; 15</td>
</tr>
<tr>
<td>Dacarbazine</td>
<td>375 mg/m²</td>
<td>IV</td>
<td>1 &amp; 15</td>
</tr>
</tbody>
</table>

* Bleomycin (give 1 unit test before first dose)
Premeds for Bleomycin (after test dose):
  Acetaminophen (650 mg)
  Diphenhydramine
  Repeat cycle every 28 days.
Systemic Therapy for Hodgkin’s Disease Using Chlorambucil, Vinblastine, Procarbazine, Prednisone for Patients with Good Prognostic Factors at Diagnosis

**ChlVPP**
(Effective: May 2, 1991)

I. **ELIGIBILITY**
A. Biopsy proven Hodgkin’s Lymphoma (any subtype)
B. Age > 60 years old

II. **STANDARD STAGING EVALUATION**
Modify as needed to document all initial disease sites adequately for follow-up evaluation.
A. History and physical examination.
B. Chest x-ray.
C. Laboratory: CBC, differential, platelet count, erythrocyte sedimentation rate, AST (SGOT), alkaline phosphatase, bilirubin, creatinine, uric acid, albumin, calcium.
D. Bone marrow aspiration and biopsy.
E. CT of chest/abdomen/pelvis
F. PET or PET/CT should be done as part of the initial evaluation.
H. Additional scans and biopsy as needed to unequivocally document the extent of the disease

A. **SCHEDULE AND DOSES**

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<td>6 mg/m²</td>
<td>IV</td>
<td>1 &amp; 8</td>
</tr>
<tr>
<td>Procarbazine</td>
<td>100 mg/m²/day</td>
<td>PO</td>
<td>1 – 14</td>
</tr>
<tr>
<td>Prednisone</td>
<td>40 mg/day</td>
<td>PO</td>
<td>1 - 14</td>
</tr>
</tbody>
</table>

Repeat cycle every 28 days for 6 cycles.
**Follow with radiotherapy to bulk disease (i.e. ≤ 5 cm).**