



**PRINCESS MARGARET CANCER CENTRE  
CLINICAL PRACTICE GUIDELINES**

**LYMPHOMA**

**AGGRESSIVE LYMPHOMA**

## Site Group: Lymphoma – Aggressive Lymphoma

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<b>1. INTRODUCTION</b>	<b>3</b>
<b>2. PREVENTION</b>	<b>3</b>
<b>3. SCREENING AND EARLY DETECTION</b>	<b>3</b>
<b>4. DIAGNOSIS</b>	<b>3</b>
<b>5. PATHOLOGY</b>	<b>3</b>
<b>6. MANAGEMENT</b>	<b>5</b>
6.1 MANAGEMENT ALGORITHMS	5
6.2 SURGERY	13
6.3 CHEMOTHERAPY	13
6.4 RADIATION THERAPY	13
6.5 OTHER THERAPY	13
6.6 ONCOLOGY NURSING PRACTICE	13
<b>7. SUPPORTIVE CARE</b>	<b>13</b>
7.1 PATIENT EDUCATION	13
7.2 PSYCHOSOCIAL CARE	14
7.3 SYMPTOM MANAGEMENT	14
7.4 CLINICAL NUTRITION	14
7.5 PALLIATIVE CARE	14
<b>8. FOLLOW-UP CARE</b>	<b>14</b>
<b>9. REFERENCES</b>	<b>16</b>

## **1. Introduction**

Aggressive lymphomas include a variety of clinical and pathological conditions that may affect adults at any age. This guideline relates to the management of these disorders currently at the Princess Margaret Cancer Centre.

## **2. Prevention**

Prevention strategies are not currently available for aggressive lymphomas. While it is recognized that persons with Human Immunodeficiency Virus infection, chronic HTLV-1 infection, and iatrogenic immunosuppression because of organ transplantation or chronic inflammatory diseases are at higher risk for developing lymphoma, there are no current prevention strategies that can be endorsed in these patient populations.

## **3. Screening and Early Detection**

Screening and early detection do not play a role in the diagnosis and management of aggressive lymphomas.

## **4. Diagnosis**

The diagnosis of aggressive lymphoma is dependent on histologic assessment of a surgically acquired incisional or excisional biopsy of an involved lymph node or other extra-nodal tissue, to ensure adequate evaluation based on morphology, immunohistochemistry and flow cytometry for accurate sub-typing. The diagnosis of T-cell lymphoma is very difficult to make using the limited tissue obtained by needle core biopsy. However, increasingly, core biopsies obtained under image guidance (CT scan or ultrasound) are used to obtain diagnostic material; such biopsies may be supplemented by fine needle aspiration for flow cytometry and / or cytogenetic testing (by fluorescence in situ hybridization or FISH). Bone marrow aspiration and biopsy are currently standard for completion of staging at diagnosis, and on rare occasions represent the primary biopsy site for final diagnosis.

## **5. Pathology**

Patients are treated based on a diagnosis conforming to those described according to World Health Organization criteria, most often after primary evaluation or pathology review by an expert hematopathologist at the University Health Network.

The diagnosis of diffuse large B-cell is made by histology and immunophenotypic analysis using a panel of antibodies: CD5, CD10, CD20, CD23, CD30, BCL6, BCL2, MYC, MUM1, KI67, CCND1 and EBER.

This panel is used to ascertain proper diagnosis of the diverse types of large B cell lymphoma, such as diffuse large B-cell lymphoma, NOS, EBV positive large B-cell lymphoma, primary mediastinal large B-cell lymphoma or high grade B-cell lymphoma. In addition, the panel includes markers that distinguish between prognostic subgroups of diffuse large B-cell lymphoma, NOS. Prognostic subgroups comprise those with the immunophenotype of activated B-cells (ABC) and of germinal centre B-cells (GCB), the former having a worse prognosis than the latter. In addition, the expression CD5 or the co-expression of BCL2 and MYC protein, with respective cut offs of 50% and 40%, are also considered adverse prognostic markers. Additionally, all lymphoma with the histology of diffuse large B-cell lymphoma or high grade B-cell lymphoma are tested for MYC gene translocation by fluorescence in situ hybridization (FISH). Those cases showing MYC gene translocation are further tested for BCL2 and BCL6 gene translocation, in order to properly diagnose high grade B-cell lymphoma with MYC translocation and BCL2 or BCL6 translocation (so-called double-hit lymphoma). This lymphoma type has an adverse prognosis.

The diagnosis of primary mediastinal B-cell lymphoma is made by histology using the immunophenotypic panel mentioned above, in a patient with chest x-ray or CT scan demonstrating an anterior mediastinal mass.

The diagnosis of mantle cell lymphoma is made by histology using a panel of antibodies for small B cell lymphoma. The following panel is used for immunohistochemistry: CD20, CD79a, PAX5, CD3, CD5, CD10, CD21, CD23, BCL6, BCL2, IgK, IgL, CCND1, KI67. In cases where CCND1 is negative and mantle cell lymphoma is still suspected, SOX11 is added to the panel. SOX11 is also added in case of suspected non-nodal leukemic mantle cell lymphoma to prove absence of SOX11 expression in the presence of CCND1 expression. Cytogenetic analysis for CCND1 gene translocation is not required for diagnosis but is frequently helpful when IHC testing is not definitive or is ambiguous. The proliferation rate, one of the important prognostic indicators in mantle cell lymphoma, must be reported.

Diagnosis of T cell lymphoma and NK/T-cell lymphoma requires histologic and immunophenotypic analysis using the following panel: CD20, CD3, CD2, CD5, CD7, CD4, CD8, TCRb, CD279, CD10, BCL6, FOXP3, CD21, CD25, CD30, TIA1, Granzyme B, ALK1, KI67, EBER(ISH). It is advised to complement the diagnosis with T-cell receptor gene rearrangement analysis to prove clonal rearrangements in T cell lymphoma and frequent absence thereof in NK/T-cell lymphoma. These studies are performed on paraffin-embedded tissues.

Diagnosis of anaplastic large cell lymphoma requires histologic and immunophenotypic analysis using the T-cell lymphoma panel given above. Genetic analysis of ALK gene translocation is not required for diagnosis as currently only NPM-ALK analysis is being

tested whereas multiple other ALK partners are possible. Therefore, immunohistochemistry for ALK protein suffices. By contrast, DUSP22 gene translocation has been described in anaplastic large cell lymphoma and should be tested for in cases that do not express ALK, in view of the similar prognosis as ALK positive anaplastic large cell lymphoma.

## **6. Management**

### **6.1 Management Algorithms**

#### **Aggressive histology lymphomas**

##### **Histologies:**

B cell: Diffuse large B-cell lymphoma (include transformed follicular and transformed MALT) and variants (T cell rich B cell lymphoma, etc)  
High grade B cell lymphoma with MYC and BCL2 or BCL6 gene translocation  
High grade B cell lymphoma, NOS  
Primary mediastinal lymphoma  
Follicular Grade 3B lymphoma

T cell: Anaplastic large cell lymphoma, ALK positive  
Peripheral T cell lymphoma and variants (angioimmunoblastic T cell, ALCL ALK negative, etc)

Others (see below):

Mantle cell lymphoma  
Extranodal NK cell lymphoma  
Burkitt lymphoma

#### **Pretreatment evaluation and staging:**

##### **a) Staging Investigations:**

Staging of aggressive lymphomas is described according to the Ann Arbor staging classification system. Pre-treatment evaluation should include:

- Full history and physical examination including performance status
- CBC, albumin, LDH, LFTs (bilirubin, ALT, AST, ALP), creatinine
- CT Head and Neck, thorax, abdomen, pelvis, FDG-PET/CT
- MUGA scan or 2D echocardiogram (patients for whom doxorubicin is considered appropriate, who are age  $\geq 60$ , or those with risk factors for cardiac disease)

- Additional blood tests and imaging tests, e.g. MRI, bone scan, ultrasound, as determined by symptoms or clinical circumstances
- BM aspirate and biopsy for morphology, immunohistochemistry, flow cytometry; cytogenetics/FISH depending on histology
- Lumbar puncture for protein, glucose, cell count and cytology/flow cytometry – for those considered at risk for CNS involvement
- HBsAg, HBsAb, HBcoreAb; HCV antibody
- HIV test if risk factors present
- Review of Pathology at University Health Network

**b) Re-Staging Investigations:**

(Applicable for patients receiving combined modality therapy, to document response after receiving chemotherapy, prior to radiation therapy)

- History and physical examination; including adverse events and performance status
- Repeat of imaging tests previously demonstrating involvement by lymphoma (generally PET/CT scan and/or contrast-enhanced CT scan of neck, chest, abdomen, pelvis; MRI in selected cases). End of treatment PET/CT with contrast enhancement is the recommended approach. Interim PET/CT is not currently recommended and response assessment should be determined using contrast-enhanced CTs.
- CBC, LDH; bone marrow biopsy if involved and documentation of complete response to treatment is required/desirable
- A complete or partial response is required to proceed to planned radiation therapy (by CT scan +/- functional imaging). A less than partial response may require repeat biopsy and alternate treatment strategy.
- Complete metabolic response (CMR) corresponds to a Deauville score of 1-3 on a five point scale.

**Diffuse Large B cell lymphoma: Stage I/II**

Risk-adapted therapy, treatment recommendation based on the presence or absence of the following prognostic factors and response assessed by CT-PET scan:

**Prognostic factors:**

IPI factors:    age > 60  
                   abnormal LDH  
                   stage II

Tumour size: bulk > 7 cm

Extranodal: testis, stomach, breast, bone (epidural), etc.

**Treatment:**

No risk factors: **R-CHOP x 4 cycles, then PET/CT**  
**IF CMR: observation**  
**IF PET positive (Deauville 4.5): RT 35-40 Gy in 20 fractions**

≥ 1 factor(s): **R-CHOP x 6 cycles, then PET/CT**  
**IF CMR and no initial bulk (<7cm): observation**  
**IF PET positive or initial bulk >7cm: Involved site RT 30 Gy for initial bulk, 40 Gy if PET positive (Deauville 4) at the end of chemotherapy**

**Additional considerations:**

Chemotherapy sanctuary sites (e.g. testes), or clinically critical sites (e.g. orbit, airway or spinal cord compression at presentation) should still be considered for post-chemotherapy IF RT to achieve optimal local control (i.e. combined modality therapy).

Stage I-II testis and epidural presentations should receive CNS prophylaxis: 2 cycles of high-dose methotrexate without IT chemotherapy if tolerable on basis of age, renal function GFR.

Patients with localized gastric DLBCL should receive involved field radiation following CR or PR following R-CHOP, even for presentations that do not meet conventional criteria for bulky disease, based on phase II and cohort data suggesting optimal treatment outcomes with combined modality therapy. Patients with localized DLBCL of the breast should be considered for combined modality therapy.

**Diffuse Large B cell lymphoma: Stage III/IV**

**Treatment:**

**R-CHOP x 6 cycles**

CT scan after cycle 3 or 4 to ensure response and after cycle 6; FDG-PET/CT with contrast enhancement at end of chemotherapy for response assessment.

If residual mass post completion of systemic chemotherapy is FDG-avid, consider biopsy and salvage chemotherapy and stem cell transplant if biopsy is positive (no limiting comorbidities). For those not eligible for autologous stem cell transplant, and for those for whom combined modality treatment was a consideration due to bulk of

disease at diagnosis, if the residual mass is localized, radiation should be considered (30 – 40 Gy in 20 fractions).

Radiation is not considered standard for patients with advanced DLBCL and is currently being investigated in prospective clinical trials. However, in certain clinical circumstances, involved field radiation may be appropriate, to reduce the risk of local recurrence or decrease future morbidity. Such circumstances include but are not limited to patients presenting with bulky masses (> 10 cm), extradural tumour with spinal cord/nerve root compression, impending or actual organ compromise (orbit, airway, long bone or weight-bearing bone fracture, etc).

### **Additional considerations:**

**CNS prophylaxis:** While CNS relapse rates following rituximab-based chemotherapy are generally low, some patients with DLBCL are at higher risk of CNS recurrence. The CNS-IPI score appears to be a useful, validated score predicting risk of CNS relapse. Evaluation of CSF with cytology supplemented by flow cytometry at diagnosis is recommended to detect CSF involvement.

Patients subsets that warrant consideration of this therapy include patients with:

- CNS-IPI scores 5-6;
- CNS-IPI score of 4 in younger pts with other individual high risk factors
- On a case by case basis for high risk sites: testicular involvement, adrenal, renal, epidural
- High grade B cell lymphoma with C-MYC and BCL2 and or BCL6 translocation (double or triple hit), who appear to have a higher risk of CNS involvement and recurrence.

Intrathecal chemotherapy with methotrexate and cytarabine has not been shown to be effective, and patients at high risk should receive prophylaxis with high-dose methotrexate 3.5 g/m<sup>2</sup> and leucovorin rescue, 2 cycles starting at the earliest with cycle 3 of RCHOP, or beyond. If given along with RCHOP, it should be administered on D9- 10 of the cycle. CNS prophylaxis is recommended for patients up to the age of 70 with normal renal function; safety and optimum dosing strategy for older patients or those with mild degrees of renal impairment are not known. If HD MTX is given after the completion of systemic therapy, it should be administered every 2 wks.

**Dose-intensity and the use of granulocyte colony-stimulating factor (G-CSF):** Current recommendations (ASCO) are for patients with a risk of febrile neutropenia of >20% to receive primary prophylaxis with G-CSF. Secondary prophylaxis is recommended for those with low treatment day neutrophil counts (rather than treatment delay) or for patients experiencing febrile neutropenia who have otherwise tolerated full dose R-CHOP (rather than dose reduction for subsequent treatments). Patients presenting with bone marrow compromise from lymphoma, elderly patients with significant comorbidities, patients with poor performance status (ECOG >3) and immunocompromised patients



(HIV+, organ transplant recipients) should be considered for primary prophylaxis with G-CSF.

Patients who are HIV positive and are fit to receive combination chemotherapy should be treated in the same approach as HIV negative patients, generally receive 6 cycles of R-CHOP with antiretroviral therapy and anti-infectious prophylaxis as appropriate for their CD4 counts during treatment. Those with stage I and II DLBCL should receive IFRT following completion of chemotherapy.

**High grade B cell lymphoma with C-MYC and BCL2 and or BCL6 translocation (double or triple hit):**

**DA-R-EPOCH X 6**

Double hit lymphoma:

In 5-10% of cases of denovo DLBCL, translocations involving CMYC and BCL2 and or BCL6 can be detected by FISH. Retrospective analyses of these patients report poor outcomes with RCHOP, and intensification with alternative regimens may result in better response rates and PFS; the impact of such regimens on OS is less clear. It is recommended that fit patients with DHL receive 6 cycles of dose-adjusted R-EPOCH and CNS prophylaxis (preferably with HD MTX, see section on CNS prophylaxis); addition of autologous stem cell transplantation does not appear to improve outcomes for these patients. Evaluation of CSF with cytology supplemented by flow cytometry at diagnosis is recommended to detect CSF involvement. If the CSF is involved, recommend twice weekly IT chemotherapy until clearance. If the CSF is negative, the addition of 2 cycles of HDMTX q2wks is recommended at the completion of systemic therapy (see CNS prophylaxis section).

Double Expressor lymphoma:

Approximately 30% of DLBCL will overexpress C-MYC and BCL2 protein by immunohistochemistry; these patients have been reported to have worse progression-free and overall survival than those with overexpression of either one or neither of these proteins. However, there is no consensus on whether this population of patients benefits from intensification of therapy, and the current recommendation remains to manage such patients with limited stage DLBCL based on IPI risk factors at diagnosis, and 6 cycles of RCHOP for patients with advanced stage disease.

## **Primary Mediastinal Large B-cell Lymphoma**

RCHOP x 6 cycles ± involved site radiation 30-36 Gy. If non-bulky (<7cm) and CMR on end of treatment PET/CT (Deauville 1-3), can omit radiotherapy on a case-by-case basis. DA-EPOCH-R x 6 cycles (for those with high risk of radiation toxicity (acute or late effects) or advanced stage disease)

## **Mantle cell lymphoma:**

**Initial period of observation:** asymptomatic, no bone marrow compromise, no impending organ compromise (see watch and wait criteria for indolent lymphomas)

### **Limited stage (I)**

Patients with limited stage MCL based on routine laboratory testing and CT scans should have complete staging with CT/PET and bone marrow aspiration and biopsy to rule out more extensive disease, endoscopy.

Treatment: **BR or RCHOP x 4 - 6 cycles + involved site RT + maintenance as below**

**Advanced stage (II, III, IV)** - No hard cutoff for age, generally < 70 years, no comorbidities precluding intensive therapy, consider fitness and ability to tolerate induction chemotherapy if older: plan for autologous stem cell transplantation (ASCT). PET/CT with contrast enhancement should be completed for all patients.

**All patients of transplant-eligible age should undergo tp53 and 17p deletion if available.**

Treatment: **R-CHOP alternating with R-DHAP (dexamethasone, cytarabine, cisplatin) for 6 cycles**

**CR, PR (after cycle 4) □ stem cell mobilization □ PET/CT - autologous stem cell transplantation**

Intensive therapy:

Total Body Radiation (TBI)\*: 1000 cGy/6 fractions/bid days -7, -6, -5

Cytarabine 1.5 g/m<sup>2</sup> q12h 4 doses days -4, -3

Melphalan 140 mg/m<sup>2</sup>, i.v., day -2

Stem cell infusion day 0

\*TBI will be included in the conditioning regimen, for patients age < 60 and for those over 60 without comorbidities and with normal lung function, no TBI for patients over the age of 65.

**Maintenance Rituximab 375 mg/m<sup>2</sup> q3mo x 8 cycles, commencing 3 months**

**following completion of chemoimmunotherapy.**

**Age > 70, or not considered eligible for ASCT**

Treatment: **bendamustine + rituximab x q4wks 6 cycles**

Alternative chemotherapy regimens:

CHOP + rituximab q3weeks x 6 cycles

CVP + rituximab q3weeks x 6-8 cycles

RBAC; RCHP-bortezomib

Elderly patients with significant co-morbidities or who wish to avoid the toxicity of combination chemotherapy may be treated with chlorambucil 0.1 mg/kg/d for 4-6 months as tolerated.

**Maintenance/ consolidation therapy:** Is recommended for patients with CR or PR after primary therapy (or second-line treatment, if rituximab naïve): **Rituximab 375 mg/m<sup>2</sup> q3mo x 8 cycles, commencing 3 months following completion of chemoimmunotherapy.**

Additional considerations: Recommendation for the use of bendamustine as front line therapy is based on a subset of MCL patients in the larger indolent lymphoma cohort of the trial by Rummel et al; this subset analysis did show a large improvement in PFS compared to RCHOP, with significantly less toxicity. However the PFS from RCHOP in that trial appears much less that reported in other trials (e.g., Kluin-Nelemans et al), and to date there are no data suggesting overall survival with bendamustine as initial therapy. Use of bendamustine-rituximab as induction therapy as induction therapy prior to ASCT is not recommended outside of a clinical trial.

**Retrospective data from patients undergoing ASCT as primary therapy suggest that the benefit from ASCT is considerably less for those who have MCL harboring TP53 mutations, and alternative strategies for this population may be considered, such as consolidation with allogeneic transplantation rather than ASCT, in young, fit patients.**

**Peripheral T cell lymphoma and variants (including Anaplastic Large Cell lymphoma):**

The prognosis for PTCL and its variants (including CD30+ ALK negative ALCL) is generally inferior to that for DLBCL. Chemotherapy and radiation treatment recommendations are derived by extrapolation from results in aggressive B cell lymphomas or from retrospective analyses of large case series of PTCL. Small controlled trials of alternative regimens (VIP-ABVD, GEM-P) have not provided support for a different approach.

In contrast, the outcome of ALCL that expresses anaplastic lymphoma kinase (ALK) detected preferentially by immunohistochemistry, and alternatively with t (2;5) by FISH (ALK + ALCL) (detecting only a subset, hence not preferred) may have a better prognosis when treated with standard CHOP +/- etoposide. The same holds true for ALCL with DUSP22 gene translocation, which may be detected by FISH. Prospective evaluation of treatment interval (CHOP-14 vs CHOP-21) has not been performed, but retrospective data do not support a 14 day cycle. A retrospective analysis by the German High Grade Lymphoma Study Group did find an advantage for the addition of etoposide to CHOP, predominantly in the ALK positive ALCL subgroup.

A recent trial in of the addition of the CD30 chemoimmunoconjugate brentuximab vedotin (BV) to CHP compared to CHOP in CD30+ in ALCL and T cell lymphomas expressing CD30 (IHC cutoff >10%) demonstrated improved response rate, progression-free and overall survival from the inclusion of BV. The majority of patients in this trial (70%) had ALCL, and the study was not powered to detect a difference in outcome in other CD30+ PTCL subtypes.

### **Stage I/II**

Treatment: **CHOP q21 days x 6 cycles + ISRT 30-35 Gy in 20 fractions (in PET/CT demonstrated CMR post-CHOP, can omit radiation in a non-bulky, non-invasive presentation)**

Stage I cutaneous ALCL, ALK positive: RT alone (35 Gy) is appropriate

### **Stage III/IV**

Treatment: **CHP + BV x 6 cycles (ALCL, CD30 +ve PTCLs)  
CHOEP q21 days x 6 cycles for fit pts ≤ 65 who are CD30 negative  
CHOP q21 days x 6 cycles**

Additional considerations: Cohort studies have reported encouraging outcomes from the addition of autologous stem cell transplantation in first remission, but this therapy has not been compared prospectively to standard dose chemotherapy and is not presently recommended in this setting.

Hepatosplenic gamma delta T cell lymphoma is a very rare clinical and pathological subtype with poor response to and low likelihood of cure from standard chemotherapy. A platinum-containing regimen (eg GDP) is the preferred approach for first line therapy in these patients. There is some information from small case series that allogeneic stem cell transplantation in first remission may be potentially curative therapy for those responding to primary chemotherapy.

### **Extranodal NK lymphoma, nasal type:**

#### **Stage IE/IIIE**

Treatment: **1) Concurrent weekly cisplatin 30 mg/m<sup>2</sup> with ISRT 45 – 50 Gy in 25 fractions over 5 weeks**), followed by  
2) VIPD (etoposide, ifosfamide, cisplatin, dexamethasone) chemotherapy every 3 weeks x 3 cycles (If chemotherapy contraindicated and the disease is limited to nasal cavity with no invasion into surrounding structures, RT alone to 50 Gy in 25 fractions can be considered)

### **Stage III/IV**

Treatment: **DDGPx6 cycles, if access to PEG-asparaginase**

**Alternative: SMILE chemotherapy (dexamethasone, methotrexate, ifosfamide, L-asparaginase, and etoposide) 3-6 cycles**

A recent small randomized phase II trial reported higher complete and overall response rates with a gemcitabine-containing regimen including PEG-asparaginase (DDGP), compared to SMILE, with improved progression-free and overall survival and significantly less toxicity.

### **6.2 Surgery**

Surgery does not play a role in the primary management of most patients with aggressive lymphoma, outside of the need for an adequate excisional biopsy for accurate diagnosis.

### **6.3 Chemotherapy**

The role of chemotherapy for primary therapy of aggressive lymphoma is described above in the treatment algorithms.

### **6.4 Radiation Therapy**

The role of radiation for primary therapy of aggressive lymphoma is described above in the treatment algorithms.

### **6.5 Other Therapy**

Autologous or allogeneic stem cell transplantation do not have a role in the primary therapy of aggressive lymphomas; the exception to this is ASCT as consolidation for younger patients with mantle cell lymphoma in first remission, discussed above. ‘

Oncology Nursing

Refer to [general oncology nursing practices](#)

## **7. Supportive Care**

### **7.1 Patient Education**

Refer to [general patient education practices](#)

## 7.2 Psychosocial Care

Special concerns for young adults

- Fertility preservation should be offered to all patients if age appropriate, in advance of starting treatment
- Referral to the Adolescent & Young Adult (AYA) Program for psychosocial, financial and other support as indicated

Refer to [general psychosocial oncology care guidelines](#)

## 7.3 Symptom Management

Venous thromboembolism (VTE) prophylaxis

- For patients with new VTE and active lymphoma
  - Treatment with either LMWH or DOACs are acceptable (preferred DOAC edoxaban 60mg PO OD)
  - Continue until complete remission and resolution of thrombosis, or indefinitely if not in remission

Refer to [general symptom management care guidelines](#)

## 7.4 Clinical Nutrition

Refer to [general clinical nutrition care guidelines](#)

## 7.5 Palliative Care

Refer to [general oncology palliative care guidelines](#)

## 8. Follow-up Care

**Follow up guidelines (NHL):**

### Monitoring

Response assessment at 1 month post treatment:

- Document with physical exam, contrast-enhanced CTs of head and neck/chest/abdo/pelvis and FDG-PET/CT scan following completion of chemotherapy for aggressive histology lymphomas. Repeat biopsy is indicated if there is a strong suspicion of residual disease or progression, and documentation of persistent disease will change management (e.g., salvage therapy and ASCT). Repeat CT imaging 2-3 months after IFRT for bulky disease is appropriate to document response. A repeat BM should be performed at completion of systemic therapy if previously positive with aggressive histology lymphoma.

At each subsequent visit:

- Document history and physical examination, residual toxicity, measure CBC if blood counts have not returned to normal at prior visit, (add TSH every 6 months if radiation to thyroid gland). Consider repeat imaging study only if symptoms suggesting possible disease recurrence. Patients with previously demonstrated stable post-treatment masses need not be followed with CT scan if asymptomatic.
- Counseling re: physical and psychological health issues, including impact of treatment on quality of life, reproduction, cardiovascular fitness, risk of recurrence, and risk of second malignancy. Smoking cessation for smokers. Attention to age-specific screening for breast, colorectal, and lung cancers (patient may be study-eligible).
- Ensure appropriate advice and care from family doctor or cardiologist re: cardiac risk factors and strategies to minimize risk (smoking cessation, BP, cholesterol, lipids, exercise, weight control), particularly for patients who received mediastinal radiation. Consider cardiac stress test for 10-year survivors who received mediastinal RT, particularly if other cardiac risk factors present.
- For women who received involved field radiation therapy which included breast tissue (axilla, infraclavicular, mediastinal): screening mammography and MRI starting 8-10 years post treatment, or age 30, whichever comes later. MRI + mammogram is recommended for survivors under age 40. Survivors over age 50 can be screened with mammography alone.

#### Oncology Clinic Follow-up Frequency:

First year	-	Visits every 3 months
2 - 3 years	-	Visits every 4 months
4 - 5 years	-	Visits every 6 months
> 5 years	-	annual follow up

In general, alternate follow up visits between attending medical oncologist/hematologist and radiation oncologist. Family physicians are encouraged to participate in the follow up as outlined, particularly for visits beyond 5 years from treatment. The majority of patients may be discharged to the care of their primary care practitioner by 10 years post-treatment.

#### **Second malignancy screening**

- Routine primary care follow-up
- For women who receive chest irradiation for PMBCL or other aggressive lymphomas at age <40, breast cancer screening with mammography and breast MRI is recommended to commence 8 years after completion of radiation

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