CancerCare Manitoba
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Practice Guideline:

Disease Management

Provincial Consensus Recommendations for the Management of Early Stage Classical Hodgkin Lymphoma

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CancerCare Manitoba Guideline

Disease Management – Hodgkin Lymphoma

Developed by: The Lymphoma DSG

1.0 Background

Preface

At CancerCare Manitoba (CCMB) the Clinical Practice Guidelines Initiative (CPGI) seeks to improve patient outcomes through the development, dissemination, implementation and evaluation of guidelines for the management of common clinical scenarios encountered by cancer patients throughout the province.

This clinical practice guideline was created through the efforts of a large interdisciplinary group from CCMB. Members of the Lymphoma Disease Site Group, as well as Members of the Medical Oncology and Hematology department have participated in its development.

The Lymphoma Disease Site Group (DSG) and Chair will review and update this document every 3-5 years, unless emerging evidence from scientific research, or practice issues requiring urgent resolution dictate a need for immediate change in content.

Aim and Purpose

Development of this clinical guide was undertaken for the purpose of knowledge translation of the current standards in practice for the management of Early Stage Classical Hodgkin Lymphoma in Manitoba. The overall aim is to improve the standard of care received by this patient population, through application of evidence-based interventions and promotion of best practices.

Development Process

A hematology trainee reviewed local practice, clinical trials and international consensus guidelines on the management of Early Stage Hodgkin Lymphoma. Based on the evidence evaluated, a preliminary approach to management was devised and presented to the Lymphoma DSG for review. After an iterative process of revisions, the following consensus guideline for the management of Early Stage Classical Hodgkin Lymphoma in Manitoba was produced.

Patient Population and Health Care Setting

The recommendations in this clinical guide are applicable to adult (age≥18) patients with Early Stage (Stages I-II) Classical Hodgkin Lymphoma in Manitoba. It is intended for use in both inpatient and outpatient settings. For this purpose, it may be used by qualified and licensed healthcare practitioners involved with the care of oncology/hematology patients, which may include (but is not limited to): physicians, surgeons, nurses, radiation therapists, pharmacists, psychosocial oncology, caregivers and dieticians at CCMB, Community Cancer Program Network (CCPN) sites, Uniting Primary Care in Oncology Network (UPCON) clinics and WRHA Community Oncology Program sites.

Disclaimer

This guideline document should be viewed as an evidence-based practice tool, and as such, it does not represent an exhaustive text on the subject of Early Stage Classical Hodgkin Lymphoma. Clinicians are advised to use it in their practice concomitantly with information from other evidence-based sources.

Use of this guideline in the clinical setting should not preclude use of the practitioner's independent clinical judgment. It is the responsibility of the practitioner to develop an individualized disease or symptom management plan for each patient under her/his care, and ideally this should take place within the context of a multidisciplinary team. The needs and preferences of the patient and the family should always be reflected in the plan of care.

2.1 Methodology

Working Group

- Lymphoma Disease Site Group (DSG)
- Author: Dr. Chantalle Menard wrote these guidelines as a required administrative project for her Hematology residency training.
- Supervisor: Dr. Pamela Skrabek
- Reviewers: Lymphoma DSG and Chair (Dr. Pamela Skrabek)
- Conflicts of Interest: None

Literature Search

A literature search identified 10 clinical trials, 2 editorials, 1 review paper and 1 individual patient-data comparison for review. 3 International guidelines and 4 provincial guidelines were reviewed. A review of local practice management strategies in the last 5 years for 78 cases of early stage Hodgkin Lymphoma was also undertaken. A summary of the existing evidence was presented at the Lymphoma DSG rounds to hematologists, radiation oncologist and nuclear medicine physicians. After several revisions, a consensus was reached among all physicians involved in the treatment of early stage Hodgkin lymphoma.

Maintenance

At CancerCare Manitoba clinical guidelines are considered 'living' documents which require ongoing evaluation, review and updating. Re-evaluation of this clinical guide is planned for 2024. The working group will revise and update the document as required, with any critical new evidence brought forward before this scheduled review.

3.1 Definitions

WHO Classification of Histological Subtypes of Classical Hodgkin Lymphoma[1]

- Nodular Sclerosis
- Mixed Cellularity
- Lymphocyte Rich
- Lymphocyte Depleted

The Lugano Classification: Staging[2]

Stage I: involvement of a single node region (**I**) or localized involvement of a single extralymphatic organ or site without nodal involvement ($\mathbf{I_E}$)

Stage II: involvement of two or more lymph node regions on the same side of the diaphragm **(II)**, or localized involvement of a single contiguous extralymphatic organ or site and its regional lymph node(s), with or without involvement of other lymph node regions on the same side of the diaphragm ($\mathbf{II_E}$)

Stage III: involvement of lymph node regions on both sides of the diaphragm, or nodes above the diaphragm with spleen involvement. There may also be localized involvement of an associated extralymphatic organ or site ($\mathbf{III_E}$).

Stage IV: Disseminated multifocal involvement of one or more extralymphatic organs, with or without associated lymph node involvement, or isolated extralymphatic organ involvement with distant (non-regional) nodal involvement.

A No systemic symptoms present
B Unexplained fevers >38°C; drenching night sweats; or weight loss >10% of body weight in the preceding 6 months

Unfavourable (U) Disease Characteristics[3]

German Hodgkin Study Group (GHSG)

- Mediastinal adenopathy >1/3 maximum transverse diameter
- >2 lymph node groups
- B-Symptoms + ESR ≥30
- ESR ≥50
- Extranodal disease

5- Point Scale Deauville Criteria for Response Assessment[4]

Score	18-FDG Uptake
1	No uptake
2	≤Mediastinal blood pool
3	>Mediastinum but ≤liver
4	Moderately >liver at any site
5	Markedly >liver (>2x SUVmax) at any site
X	New areas of uptake unlikely to be related to lymphoma

The Lugano Classification: Response Assessment/FDG-PET Interpretation[2]

Score 1 or 2: Considered to represent complete metabolic response (CMR) at both interim and end of treatment

Score 3: Dependent on the timing of the assessment, the clinical context and the treatment. At the end of standard treatment, this is a CMR. If using a response-adapted treatment approach to guide de-escalation strategies, score 3 on interim scan may be deemed an inadequate treatment response so as to avoid under-treatment.

Score 4 or 5 at interim: If there is a reduction from baseline, it suggests chemo-sensitive disease and a partial metabolic response (**PMR**). If there is no change from baseline, this suggests no metabolic response (**NMR**). If

there is an increase from baseline or a new lesion is identified, this is progressive metabolic disease (**PMD**). Both NMR and PMD are considered treatment failure at interim.

Score 4 or 5 at end of treatment: Represents residual metabolic disease, even if the uptake has reduced from baseline.

4.1 Recommendations

Staging Investigations

1) **It is recommended that all patients undergo PET scans of the neck, chest, abdomen and pelvis prior to initiating therapy to adequately determine disease stage[5]. If PET scan is performed, a bone marrow biopsy is not necessary[2].**

2) **All patients should undergo an assessment of cardiac function, pulmonary function testing, and staging CTs prior to chemotherapy.**

3) **All patients should be tested for HIV, Hepatitis B, and Hepatitis C prior to starting treatment.**

4) **Patients should be categorized as favourable or unfavourable according to the GHSG characteristics.**

5) **Bulk will be defined as any nodal mass >10cm, or mediastinal adenopathy >1/3 the maximum intrathoracic diameter of the chest.**

Response Assessment

1) **A PET2 score of 1 or 2 will be considered negative for the purpose of de-escalating treatment (omission of radiation therapy). A PET2 score of 3 or higher will be deemed insufficient to de-escalate therapy.**

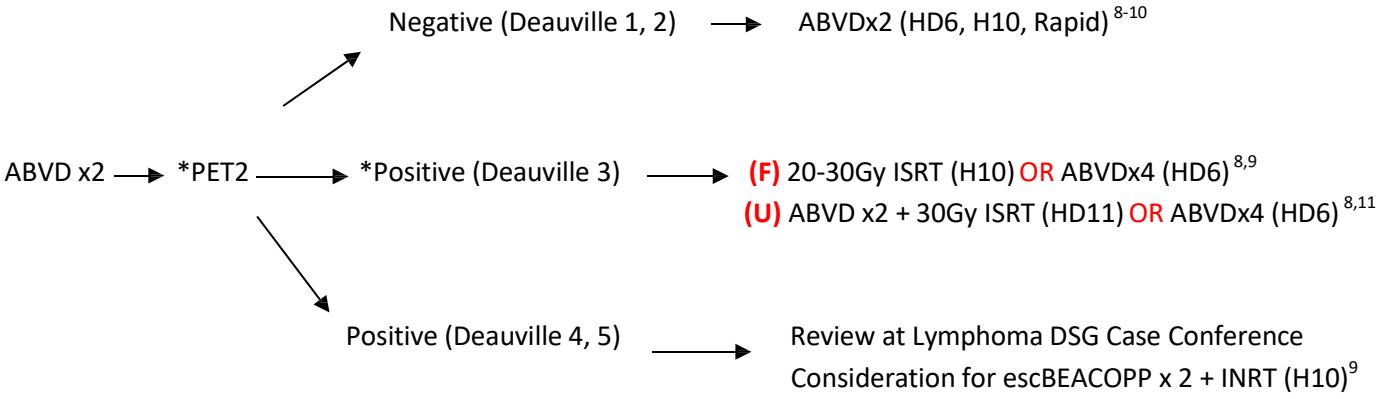
2) **End of treatment PET scanning is recommended to be ideally no sooner than 6-8 weeks (but at least 3 weeks) after the completion of chemotherapy, and ≥3 months after radiation therapy[2].**

3) **The Lugano Classification FDG/PET interpretation using the Deauville Criteria 5-point scale is recommended for response assessment at the end of treatment.**

Stage I-II Favourable (F) & Unfavourable (U) Disease without Bulk or B Symptoms

On the balance of managing progression free survival (PFS), overall survival (OS) and long-term toxicities, the decision for combined modality treatment (CMT: Chemotherapy + Involved Site Radiation Therapy (ISRT)) vs. chemotherapy alone must be individualized. In young patients in whom exists the concern for long term toxicities related to radiation (secondary cancers, coronary artery disease), a chemotherapy alone approach is reasonable. For older patients, in whom the toxicities and risks associated with disease relapse and a need for secondary treatments (including autologous stem cell transplant) are likely to be of concern, a CMT approach may be preferred. In either situation, the patient must be made aware of the probable mild reduction of roughly 5-8% in PFS that is associated with a chemotherapy alone approach, as well as the potential long-term toxicities related to radiation therapy[6,7,8].

4) **A PET-adapted strategy is suggested:**



*PET2 should be completed between Days 22-25 of cycle 2 ABVD[9].

5) **If CMT is preferred at the outset of therapy for early favourable disease without bulk or B symptoms, the recommended treatment course is ABVD x2 + 20 Gy ISRT (HD10) [12]. An interim PET is not required.**

6) **If CMT is preferred at the outset of therapy for early unfavourable disease without bulk or B symptoms, the recommended treatment course is ABVD x4 + 30 Gy ISRT (HD11, H9-U) [11,13]. An interim PET is not required.**

Stage I-II Disease with Bulk or B Symptoms

7) **It is recommended that all patients with bulk or B symptoms be treated according to advanced stage treatment algorithms.**

Follow-Up[5, 14]

8) **History & Physical every 3 months for the first 2 years, every 6 months for the next 3 years, and then annually.**

9) **Laboratory investigations: CBC with differential, ESR (if elevated at diagnosis), chemistry profile as clinically indicated, TSH (if received radiation therapy to the neck).**

10) **Imaging investigations (CT/PET/Chest X-Ray) are not required unless clinically indicated.**

11) **If radiation therapy was administered, annual assessment and appropriate counselling for late toxicities (cardiovascular, lung, secondary malignancies) are appropriate. Age-appropriate cancer screening should be conducted regularly. For patients with chest or axillary irradiation, mammography should be conducted annually, beginning 8-10 years after radiation therapy. For women who were ≤30 years of age at the time of radiation therapy, breast MRI should be performed in addition to mammography.**

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