Hull University Teaching Hospitals NHS Trust

Hull University Teaching Hospitals and North Lincolnshire NHS Trusts Haematology Multidisciplinary Team Guideline and Pathway

Follicular Lymphoma

1 BACKGROUND

The Hull and North Lincolnshire Haematology Multidisciplinary team manages patients with haematological malignancies on three sites, Diana Princess of Wales Hospital Grimsby, the Queens Centre for Haematology and Oncology at Castle Hill Hospital Hull University Teaching Hospitals NHS Trust and Scunthorpe Hospital.

Levels of service provided in these organisations is as defined in the NICE guidance "Haematological Cancers: improving outcomes NG47" 25th May 2016.

Low-to-intermediate intensity chemotherapy is delivered in Grimsby, the Queens Centre Castle Hill Hospital and Scunthorpe Hospital.

High-intensity chemotherapy and autologous stem cell transplantation is delivered at the Queens Centre, Castle Hill Hospital.

The following chemotherapy regimens for follicular lymphoma can be delivered in centres providing low-to intermediate intensity chemotherapy:

Rituximab single agent (maintenance)
Rituximab in combination with: Bendamustine, Chlorambucil or FC
Obinutuzumab single agent (maintenance)
Obinutuzumab in combination with: Bendamustine,

The following chemotherapy regimens for follicular lymphoma can only be delivered in centres providing high intensity chemotherapy:

Rituximab in combination with: CVP, CHOP
Obinutuzumab in combination with: CVP, CHOP
RDHAP
RIVE
RICE

BEAM with autologous peripheral blood stem cell support (autoPBSC)

LEAM autoPBSC

2 POLICY / PROCEDURE / GUIDELINE DETAILS

Diagnosis of follicular lymphoma

Follicular lymphoma will be diagnosed in line with Non-Hodgkin's Lymphoma: diagnosis and management NICE guideline NG52.

Diagnostic material (lymph node or soft tissue biopsies, bone marrow) is to be sent directly to HMDS, Leeds. Lymph node excision biopsy is preferred, but if the risk of a surgical procedure outweighs the potential benefits of an excision biopsy - needle core biopsy is an alternative.

Full body PET/CT scan or CT neck/thorax/abdomen/pelvis with contrast are the recommended staging modalities. FDG PET is preferred in accordance with Consensus of the International Conference on Malignant Lymphomas Imaging Working Group, Lugano 2014 based on evidence of more accurate staging. (Compared to standard radiological means in follicular lymphoma - PET/CT was able to upstage as much as 62% of the patients in early stage (I and II) by CT, with the highest sensitivity for extranodal disease - first among them, bone marrow).

A strong suspicion of disease transformation on PET/CT should be confirmed histologically with the additional biopsy of the most FDG avid site. If histological confirmation is not possible (i.e. anatomical site unsafe for biopsy) the MDT will consider upfront treatment with anthracycline containing regimen (RCHOP).

The Follicular Lymphoma International Prognostic Index (FLIPI) indices (both FLIPI and FLIPI2) should be recorded for all patients at diagnosis.

Staging bone marrow biopsy should be considered and performed if ambiguous bone marrow involvement by PET/CT or if staging modality was CT rather than PET/CT.

MRI is the imaging method of choice in the rare cases of CNS follicular lymphoma including brain, leptomeninges and/or spinal cord.

Patients with neurological symptoms and/or imaging studies suggestive of central nervous system involvement should undergo diagnostic lumbar puncture with cerebrospinal fluid sample to be sent to HMDS, Leeds

All newly diagnosed cases of follicular lymphoma are to be discussed at the network MDT.

Management of follicular lymphoma

Follicular lymphoma will be managed within the Hull and North Lincolnshire MDT in line with Non-Hodgkin's Lymphoma: diagnosis and management NICE guideline NG52.

The local management of follicular lymphoma will also take account of the following BSH guidelines and NICE pathways and guidance:

Investigation and management of follicular lymphoma BSH guideline – published 23 December 2011.

Rituximab for the first-line treatment of stage III-IV follicular lymphoma –
NICE guidance TA243, published 25/01/2012.

Rituximab for the first-line maintenance treatment of follicular non-Hodgkin's lymphoma –
NICE guidance TA226, published 22 June 2011.

Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma – NICE guidance TA137, published 27 February 2008.

Obinutuzumab for untreated advanced follicular lymphoma – NICE recommendation TA513, published 21 March 2018.

Obinutuzumab with Bendamustine for treating follicular lymphoma refractory to Rituximab –
NICE guidance TA472, published 30 August 2017.

Metastatic spinal cord compression in adults: risk assessment, diagnosis and management.
NICE guideline CG 75.

First line-treatment of follicular lymphoma

Treatment decisions are to be based on assessment of fitness/frailty and co-morbidities rather than age alone. The therapeutic risk-to-benefit ratio and individualized aim of therapy (i.e., palliation, best response, durable remission) should be considered for each patient.

Follicular lymphoma stage I and stage II, where the involved nodes are contiguous and can be safely encompassed within a radiation field, are to be considered for local radiotherapy. These patients should have a bone marrow examination performed if radical radiotherapy is under consideration. Observation of patients with early stage disease is acceptable if radiotherapy is thought to be undesirable or due to patient choice.

Management of stage III and IV follicular lymphoma is dependent upon whether disease is symptomatic or not. "Symptomatic disease" is defined by the British National Lymphoma Investigation (BNLI) and Groupe d'Etude des Lymphomes Folliculaires (GELF) criteria.

Patients with asymptomatic advanced-stage disease are to be offered active monitoring. The option of 4 doses of weekly Rituximab "induction" therapy should be discussed with patient.

Patients fit for chemotherapy with symptomatic stage III/IV follicular lymphoma are to be offered 6-8 cycles of Rituximab or Obinutuzumab in combination with CVP or CHOP. Elderly and frail patients are to be considered for chemotherapy treatment with Rituximab-Chlorambucil, Chlorambucil monotherapy or purely palliative management.

Symptomatic areas of disease bulk (>7 cm) or non-bulky disease causing compression of vital organs is to be considered for local radiotherapy.

Suspected, or proven, spinal cord compression associated with follicular lymphoma is to be managed in-line with the NICE guidelines: Diagnosis and management of adults at risk of and with metastatic spinal cord compression – guidance CG75.

Rituximab or Obinutuzumab maintenance is to be offered for patients that have responded to first-line anti CD 20 based induction chemotherapy.

First line treatment response assessment and monitoring.

Patients on first line chemotherapy undergo regular clinical assessment and response to treatment is to be monitored clinically (reduction of palpable masses, resolving B symptoms etc.). Repeat PET or CT scan is performed after 4 cycles of therapy and upon the completion of first line chemotherapy unless interim imaging indicates CR.

Treatment of relapsed follicular lymphoma

Relapsed disease is to be reassessed with PET/CT scan. Repeated biopsy is strongly recommended and patients should be evaluated for possibility of transformed disease (constitutional symptoms, target biopsy of the most FDG avid site of disease, LDH)

All relapsed cases of follicular lymphoma are to be discussed at the network MDT. Treatment decisions must be highly individualized in the context of the patient's goals (palliative vs durable remission), performance status, previous treatments and response.

Relapsed, asymptomatic follicular lymphoma is not necessary an indication for further treatment – active monitoring should be considered. If symptoms are associated only with localized site of disease - radiotherapy to the symptomatic area is an option in the context of more palliative approach.

Patients fit for systemic chemotherapy, but transplant ineligible and previously treated with Rituximab-based chemotherapy are to be considered for Bendamustine-Obinutuzumab chemotherapy.

If relapse occurred > 2 years since initial treatment with good response the patient is to be considered for the same / similar chemotherapy as during first line treatment.

Rituximab or Obinutuzumab maintenance therapy is to be offered following response to second line therapy.

Transplant eligible patients with short duration of remission (< 2 years since initial treatment) or suspected/confirmed disease transformation are to be considered for salvage chemotherapy with RDHAP, RIVE, or RICE protocols followed by high dose chemotherapy with autologous stem cell transplant. Response to salvage chemotherapy should be assessed with PET/CT scan prior to proceeding with autologous stem cell transplant.

Patients with an unsatisfactory response to initial salvage chemotherapy are to be considered for alternative salvage regimen, clinical trial or palliative treatment.

If autologous stem cell transplantation has not resulted in long lasting remission or if a patient failed stem cell harvesting but being still fit enough for transplantation and suitable donor can be found - allogenic stem cell transplantation should be discussed with patient and the transplant team in Leeds or Sheffield.

Transplant ineligible patients in second relapse and fit for systemic treatment are to be considered for FCR chemotherapy, clinical trial or palliative treatment. The optimum course for any patient is dependent on the nature of their disease and the wishes and expectations of the patient.

Clinical Trials

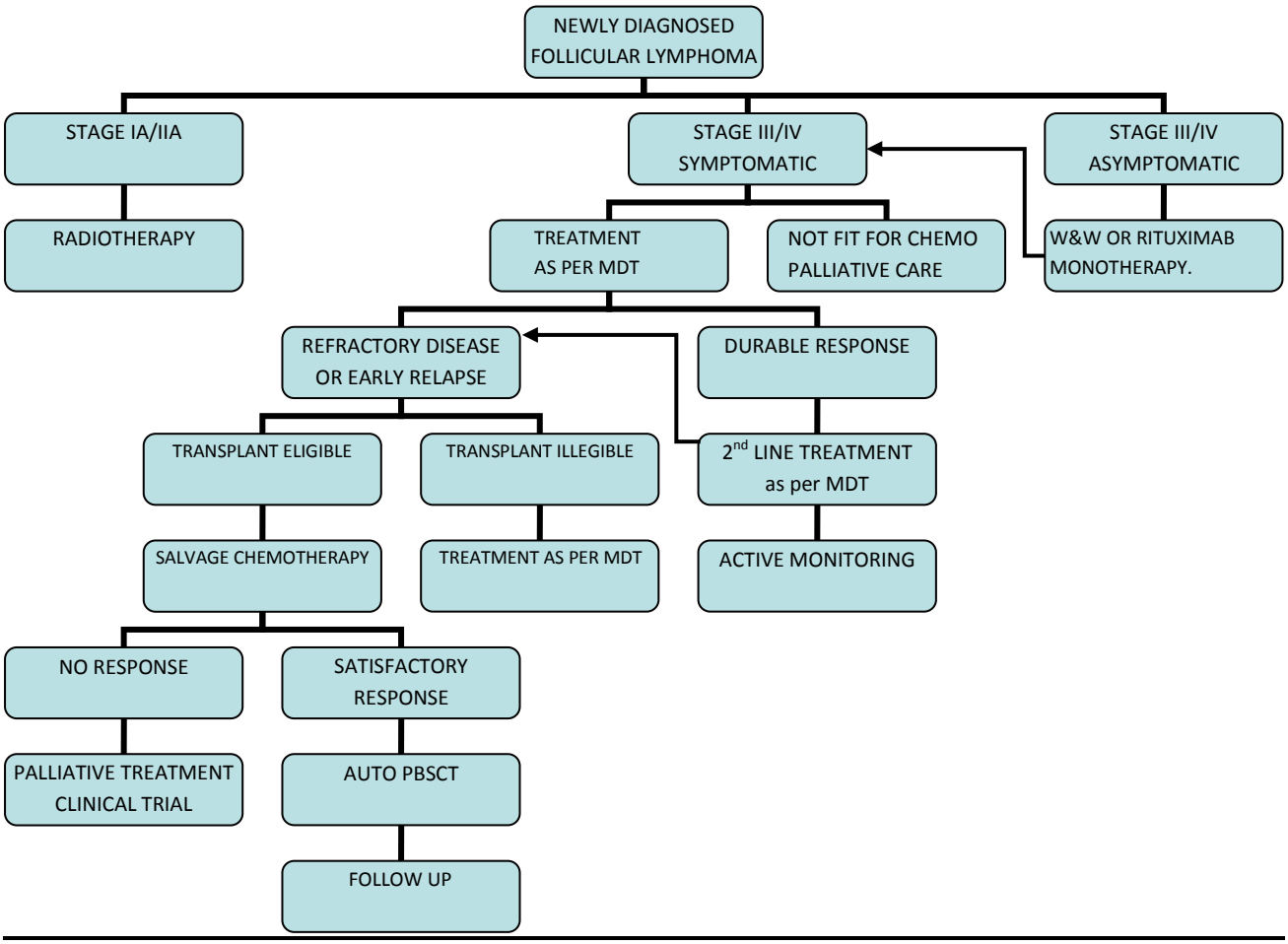
All patients should be considered for, and offered entry into clinical trials where available.

Palliative care services

All follicular lymphoma patients will have a named key-worker who will undertake a holistic needs assessment and provide support and advice based upon this.

Referral to hospital or community palliative care services should be considered for patients unfit for chemotherapy and those with poor prognosis relapsed/refractory disease.

Patient Pathway, newly diagnosed follicular lymphoma



3 PROCESS FOR MONITORING COMPLIANCE

Compliance will be audited within the MDT audit programme.

4 REFERENCES

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