Hull and East Yorkshire and North Lincolnshire NHS Trusts Haematology Multidisciplinary Team Guideline and Pathway

Diffuse Large B-cell 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 and East Yorkshire 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 protocols for Diffuse Large-B-cell Lymphoma (DLBCL) can be delivered in centres providing low-to intermediate intensity chemotherapy:

Palliative treatment with steroids and/or Etoposide

The following chemotherapy protocols for Diffuse Large-B-cell Lymphoma (DLBL) should only be delivered in centres providing high intensity chemotherapy:

RCHOP
RGCVP
RGDP
RDHAP
RIVE
RCODOXM/RIVAC
Cyclophosphamide or Plerixafor priming
BEAM autologous stem cell transplant
LEAM autologous stem cell transplant
High dose Methotrexate
Intrathecal chemotherapy

2 POLICY / PROCEDURE / GUIDELINE DETAILS

Diagnosis of DLBCL

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

Diagnostic material (lymph node, soft tissue biopsies or 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 a viable alternative.

All cases of DLBCL should be tested for *MYC* rearrangement by FISH and if detected, further testing should be performed for *BCL2* and *BCL6* rearrangements.

Full body PET/CT scan is the recommended staging modality. CT neck/thorax/abdomen/pelvis with contrast is an alternative in exceptional/urgent clinical situations.

Revised International Prognostic Index (R-IPI) is to be calculated for all patients.

Bone marrow involvement is to be assessed by PET/CT scan.

Bone marrow biopsy should be considered for patients who underwent CT scan for staging or if there is a clinical suspicion of underlying low grade lymphoma.

Patients with neurological symptoms and/or imaging studies suggestive of central nervous system involvement should undergo additional MRI imaging and diagnostic lumbar puncture with cerebrospinal fluid sample to be sent to HMDS, Leeds. It is recommended to consider administration of intrathecal Methotrexate at the same time as diagnostic lumbar puncture.

Fertility-preserving treatments, such as sperm cryopreservation should be offered to eligible patients.

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

Management of DLBCL

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

Intrathecal chemotherapy is to be administered in line with:

1) Updated national guidance on the safe administration of intrathecal chemotherapy
   HSC 2008/001.
2) Safe administration of Cytotoxic Intrathecal Injections
   Hull and East Yorkshire Hospitals, Policy CP153.

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

1) BSH Guidelines for the management of diffuse large B-cell lymphoma – published 16th May 2016.
2) BSH Guideline for the prevention of secondary central nervous system lymphoma – published 27th August 2013.
3) Radiotherapy in first line treatment of diffuse large b-cell lymphoma at sites of bulky disease NICE recommendation NG52/3.
4) Metastatic spinal cord compression in adults: risk assessment, diagnosis and management. NICE guideline CG 75.

First line-treatment of DLBCL

Treatment decisions are to be based on assessment of fitness/frailty and co-morbidities rather than age alone. Patients with clinical symptoms of heart failure causing limitation of ordinary physical activity (NYHA II and above) should be referred for echocardiogram and/or cardiology assessment prior to anthracycline containing chemotherapy regimen.

Patients fit for chemotherapy with stage IA non bulky (<7.5 cm) DLBCL are to be offered treatment with 3 cycles of RCHOP chemotherapy followed by radiotherapy to the initial site of the disease.

If the anatomical site of lymphoma is associated with high risk radiotherapy complications - 6 cycles of RCHOP is an alternative.

Patients fit for chemotherapy with DLBCL stage IIA and above are to be offered treatment with 6 cycles of RCHOP.

Patients with cardiac impairment or other comorbidities may be considered for treatment with RGCVP.

Radiotherapy to the initial site of bulky disease (>7.5 cm) is to be considered upon the completion of chemotherapy. MDT decision is based on clinical situation and follow-up imaging studies results.

Patients with: 1) very high risk by R-IPI, 2) presence of adverse molecular features or 3) CNS involvement at presentation, are to be considered for escalation of first line chemotherapy with RCODOXM/RIVAC.

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

Patient identified as high risk of CNS relapse (in accordance with BSH guidelines criteria) should receive Methotrexate-based CNS directed therapy. The recommendation of CNS

directed therapy must be recorded in the MDT treatment plan. The treatment options are: 3-6 doses of intrathecal Methotrexate during primary therapy or 3 cycles of high dose i.v. Methotrexate at 2 – 3 weekly intervals directly after primary chemotherapy. CNS directed treatment is to be delivered in Queens Centre for Haematology and Oncology at Castle Hill Hospital Hull.

First line treatment response assessment and monitoring.

Patients with DLBCL stage IIA and above are to be referred for PET/CT scan after the 4th cycle of RCHOP chemotherapy.

Treatment is to be continued to planned 6 cycles of RCHOP chemotherapy unless there is clear evidence of disease progression on interval scan. Transplant eligible patients with primary refractory disease will be offered salvage chemotherapy followed by high dose chemotherapy with autologous peripheral blood stem cell transplant (autoPBSCT).

Patients with a negative (Deauville 2) PET/CT scan post 4 cycles of RCHOP do not require an end of treatment scan.

Patients with partial response on interim scan will require repeated PET/CT upon the completion of chemotherapy.

Partial or equivocal response at end of treatment PET/CT is to be discussed at the MDT with consideration of radiotherapy, interval scan monitoring or salvage chemotherapy depending on clinical situation and individual circumstances.

Patients who achieved complete remission following treatment are to be followed up on a 3–4 monthly basis for up to 2 years. Beyond 2 years, if no additional risk factors, patients will be discharged from regular follow-up and offered nurse led survivorship clinic.

Treatment of relapsed DLBCL

Relapsed disease is to be reassessed with PET/CT scan. Repeated biopsy is strongly recommended. All relapsed cases of DLBCL are to be discussed at the network MDT.

Transplant eligible patients are to be offered salvage chemotherapy (RGDP, RDHAP or RIVE). After two cycles of salvage chemotherapy response to treatment is to be assessed with PET/CT scan. Responding patients are to be offered high dose chemotherapy with autoPBST.

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

Patients transplant illegible with relapsed disease or salvage refractory disease have very poor prognosis, with minimal chance of prolonged control of disease. This group of patients is to be mainly offered palliative treatment with steroids and radiotherapy to symptomatic masses or entry into clinical trials if available, either locally or regionally. The optimum course for any

patient is dependent on the nature of their disease and the wishes and expectations of the patient.

Clinical Trials

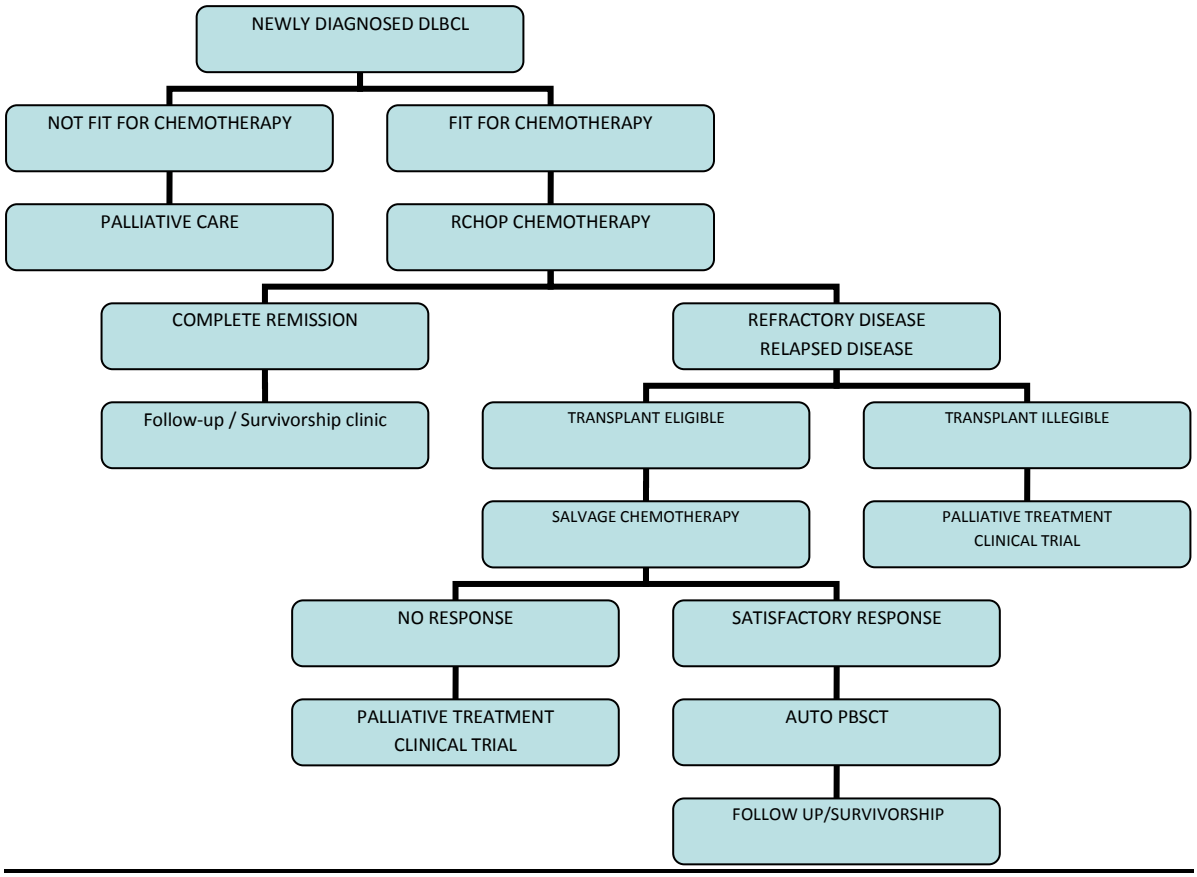
All patients should be considered for, and offered entry into clinical trials where available.

Palliative care services

All DLBCL 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 DLBCL



3 PROCESS FOR MONITORING COMPLIANCE

Compliance will be audited within the MDT audit programme.

4 REFERENCES

- Hull and North Lincolnshire Haematology MDT operational policy. September 2017.
- Hull and East Yorkshire Hospitals. Safe administration of Cytotoxic Intrathecal Injections Policy CP153, November 2017
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