Protocol for Planning and Treatment

The process to be followed when a course of chemotherapy is required to treat:

HIGH GRADE B CELL NHL

Patient information given at each stage following agreed information pathway

1. DIAGNOSIS
Treatments for specifically diffuse large B cell NHL.

2. STAGING
Diagnosis, staging and treatment to be discussed at MDT (BCSH recommendation). Patients to be defined as follows:

A. Early Stage Disease (I or II, non-bulky).
B. Advance Stage Disease (bulky I or II, stages III or IV).
C. Relapsed/Refractory Disease-Patient Fit For High Dose Therapy
D. Relapsed/Refractory Disease In Patients Unfit For High Dose Therapy
E. Allogeneic Transplant
F. Grade 3b Follicular Lymphoma

References

3. INVESTIGATIONS
Patients require a lymph node biopsy to make the diagnosis. Staging investigations required include CT scan of neck, chest, abdomen and pelvis and bone marrow aspirate and trephine. PET scanning is not currently recommended unless within the auspices of a clinical trial. CT is repeated to assess response at the mid-point and following the end of planned chemotherapy.

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### 4. RADIOTHERAPY
Referral for involved field radiotherapy in early stage disease following 3 courses of chemotherapy with R-CHOP21. Consider in patients with advanced stage if a single area of residual lymphadenopathy is apparent on CT at the end of treatment.

### 5. CHEMOTHERAPY

#### A. Early Stage Disease

1. No trial currently available.
2. Stage I nodal, non-bulky (less than 10cm; mediastinal mass less than third of thoracic diameter): R-CHOP 3 cycles plus involved field radiotherapy.
3. Stage I/II bulky, RCHOP 6-8 cycles. CT after 3-4 cycles to assess response if appropriate. Consider boosting radiotherapy for bulky disease. Radiotherapy for mediastinal large B cell lymphoma is recommended.
4. Patients unfit for R-CHOP: radiotherapy or palliation should be considered following discussion with patient.

#### B. Advance Stage Disease (bulky I/II or stages III/IV)

1. RCHOPx6/8 q21days. 6 cycles would normally be given based on data from MINT study. The use of 6 cycles rather than 8 is in disagreement with practice in some areas of the UK which is based on the GELA study, but is deemed to be acceptable given the response rates seen in the MINT study. Option to extending to 8 if evidence of ongoing response is observed on CT, or if clinical concern about risk of relapse is deemed very high. Radiotherapy to bulk disease may be appropriate subsequently.
2. If performance status significantly impaired, consider ‘staggering’ agents or pre-treatment with steroids/vincristine.
3. Patients unfit for R-CHOP: consider reducing anthracycline dose of RCHOP. If patient tolerates this and/or has good left ventricular function the dose could be increased in subsequent cycles. If decision is taken to omit doxorubicin altogether, CVP without Rituximab should be given, as this signals a change from treatment with curative intent to palliation. If unfit for chemotherapy consider palliation following discussion with patient e.g. dexamethasone 4mg bd.

#### C. Relapsed/Refractory Disease-Patient Fit For High Dose Therapy
Consider eligibility for high dose treatment: biologically fit; responds to salvage therapy. R-IVe recommended, but if a concern about cumulative anthracycline toxicity following R-CHOP or patient has low serum albumen, R-ESHAP is an alternative. If patient has primary resistant disease, Rituximab should be omitted from the salvage regimen. BEAM as conditioning agent-only in those who respond to salvage treatment.

#### D. Relapsed/Refractory Disease In Patients Unfit For High Dose Therapy
Consider oral PECC or palliative treatment e.g. Dexamethasone.

#### E. Allogeneic Transplant
Occasional patient may be eligible. Discuss at MDT prior to referral.
F. Grade 3 Follicular Lymphoma
(i) Grade 3b is considered to be the same disease as DLBCL in guidelines with plateauing of survival curves and should be treated as above.
(ii) Grade 3a should be treated as follicular NHL.

G. CNS prophylaxis
No consensus at present. Consider in patients with involvement of following sites: testes, breast, sinuses, epidural space or if LDH raised + >1 extranodal site. Possible regimens include IT MTX 4-6; high dose IV MTX; combination of these.

6. TREATMENT DEFINITIONS

RCHOP given q21days
Rituximab 375mg/m² IV Infusion Day 1
FOLLOWED BY
Doxorubicin 50mg/m² IV Bolus Day 1
Vincristine 1.4mg/m² IV Bolus Day 1 (Max 2mg)
Cyclophosphamide 750mg/m² IV Bolus Day 1
Prednisolone 40mg PO Days 1 to 5
Repeated every 3 weeks. For diffuse large B-cell NHL

R-IVE

R-ESHAP

BEAM
Carmustine 300mg/m² IV Infusion Day 1
Cytarabine 200mg/m² BD IV Infusion Days 2 to 5
Etoposide 200mg/m² IV Infusion Days 2 to 5
Melphalan 140mg/m² IV Infusion Day 6
Conditioning regimen prior to autologous stem cell transplantation

PECC
Prednisolone 40mg PO Daily Days 1-7
Etoposide 200mg/m² PO Daily Days 1-3
Lomustine (CCNU) 100mg/m² PO Daily Day 1
Chlorambucil 20mg/m² PO Daily Days 1-4
Repeated every 42 days