Protocol for Planning and Treatment

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

Low grade B cell/ follicular NHL

Patient information given at each stage following agreed information pathway

1. DIAGNOSIS

Biopsy of enlarged lymph node is mandatory if diagnosis is suspected.

2. STAGING

Patients require clinical examination, CT of neck, chest, abdomen and pelvis and bone marrow aspirate and trephine.

3. INVESTIGATIONS

CT, bone marrow, full blood count, biochemical screen including LDH. Consider investigation of ventricular function if using anthracyclines.

4. CHEMOTHERAPY

First Presentation
Discussion at MDT is mandatory (BCSH recommendation).

a. Stage I-small volume disease. Recommendation is to use involved field radiotherapy (IF RT), unless concerned about toxicity, especially if fully excised.

b. Stage II, III, IV
- Asymptomatic, low bulk, no marrow failure: watch and wait.
- If treatment required: RCVP (SMC) recommendation, but chlorambucil+/- dexamethasone is still considered reasonable depending on age/patient preference. The PRIMA study has suggested a benefit of maintenance Rituximab once response has been achieved (PR or CR), but this indication has not yet been assessed by SMC/NICE.
- RCHOP is a reasonable first line approach if a rapid response is desired.

Relapse
Discussion at MDT is mandatory (BCSH recommendation).

a. Localised: consider IFRT.

b. Widespread relapse
   - >1 years since primary treatment. Consider re-biopsy if clinical concern re possibility of high grade transformation. Consider repeating first line treatment (unless first line treatment was RT, in which case treat as above).
   - Relapse <1 years since primary treatment. The following options are available: 1) R-Fludarabine combination or single agent regimen, 2) R-CVP if not previously given (a progressively smaller number of patients), 3) R-CHOP, 4)R- IVE if considering stem cell collection (see later).
   - Primary resistant disease (relapse on 1st line therapy or within 6 months of completion). There is no evidence to support further rituximab use in this setting. Median survival in primary resistant disease is very poor- consider switching to an alternative drug regimen e.g. fludarabine based (FMD) or salvage therapy such as IVE/ESHAP if considered suitable for high dose therapy.

c. Second and subsequent relapse. Consider further chemotherapy, depending on previous treatment and acquisition of drug resistance e.g. fludarabine containing regimen, CVP, CHOP. Use of Rituximab is recommended in patients who have reached last line (NICE) and not yet received in previous treatment. Palliative care +/- steroids can be considered.

d. Maintenance therapy. SMC advice has acknowledged it can be appropriate to administer this in first or second remission, but no evidence currently exists to support maintenance therapy on both occasions. It is recommended that maintenance treatment with Rituximab 375mg/m^2 every two months for two years or until relapse be considered in all patients in first remission. Patients who did not receive first line maintenance can be considered for maintenance in 2nd remission, with rituximab 375mg/m^2 every three months for 2 years or until relapse. Patients with a late relapse following first line maintenance who respond well to reinduction could be considered for repeat second line maintenance on a case by case basis, but must be discussed at the Haematology MDT.

The Role of High Dose Therapy
The role of autografting in follicular lymphoma is currently unproven, and discussion at MDT prior to priming regimen is mandatory (BCSH recommendation). Given that transplanted related mortality is higher in heavily pre-treated patients it is recommended patients be treated early in the disease course (level 4 evidence). Consideration should be given to patients deemed fit enough for treatment who have a short/incomplete first remission or who undergo high grade transformation. Autografting in later disease is associated with more morbidity/mortality and the balance of risks should be discussed at the MDT and with the patient.

Allogeneic Transplantation
There is no clear evidence of allografting in follicular lymphoma is currently, and discussion at MDT prior to priming regimen is mandatory (BCSH recommendation). Consideration should be given to patients deemed fit enough for treatment who have a short/incomplete first remission. Transplantation in later disease is associated with more morbidity/mortality and the balance of risks should be discussed with the transplant centre and patient.

5. TREATMENT DEFINITIONS

R-CVP
Rituximab 375mg/m² IV Infusion Day 1
FOLLOWED BY
Cyclophosphamide 750mg/m² IV Bolus Day 1
Vincristine 1.4mg/m² IV Bolus Day 1 (max 2mg)
Prednisolone 50mg PO Daily Days 1 to 5
Repeated every 3 weeks

Fludarabine
Fludarabine 25mg/m² IV Infusion on Days 1 to 5
Repeat every 28 days
Or in combination with Cyclophosphamide

Oral Option for Fludarabine
Fludarabine 40mg/m2 PO Days 1to 5 (repeated every 28 days)

R-IVE
Rituximab 375mg/m² IV Day 1
Epirubicin 50mg/m² IV Bolus Day 1
Etoposide 200mg/m² IV Infusion Days 1 to 3
Ifosfamide 3g/m² IV Infusion Days 1 to 3
Repeated as required (minimum of 28 days)

Rituximab maintenance
Rituximab 375mg/m² IV Day 1 Repeated every 3 months for 4 cycles
One-Off cycle
For follicular NHL

RCHOP
FMD

Author: …… Signature: …….. Date: ……

Chair: …… Signature: …….. Date: ……
(on behalf of OHMMG)

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