Lancashire and South Cumbria Haematology NSSG Guidelines for Management of Primary CNS Diffuse Large B-cell Lymphoma (PCNSL)

1.1 Pre-treatment evaluation

Note pre-diagnostic biopsy steroids should be avoided where possible since this may lead to non-diagnostic rates of 30-60%

The following tests should be performed:

- FBC, ESR, U&Es, creat, LFTs, calcium, LDH, urate, immunoglobulins and electrophoresis
- Hepatitis B, C and HIV serology
- Chest X-ray
- Contrast-enhanced MRI scan of brain
- PET-CT scan if treatable with curative intent
- Ophthalmoscopy and ocular slit-lamp examination followed where necessary by vitreous biopsy +/- chorioretinal biopsy where necessary to exclude intra-ocular involvement which is present in up to 20% of patients at presentation,
- Bone marrow aspiration and trephine biopsy if PET-CT scan or abnormal blood count suggest marrow disease, or there is paraproteinaemia to suggest a concordant indolent lymphoma
- CSF cytopsin and protein estimation where feasible
- Testicular ultrasound scan
- ECG and assessment of cardiac function
- Establish fitness for intensive therapy and high dose methotrexate based on age and physiological factors
- Recording of mini-mental status examination (MMSE)

1.2 Post-treatment evaluation

- On completion of treatment the patient must be reassessed clinically and with a repeat MRI scan of brain, +/- ophthalmic examination +/- CSF cytospin examination followed by MDT review
- Patients on high-dose methotrexate regimens should have a MRI scan after every 2 cycles and consider after cycle 1 if PBSC mobilisation is planned after cycle 1. A scan should also be performed 2 months after completing any consolidation therapy.

2.0 Treatment of newly diagnosed patients

2.1 Patients eligible for intensive combination chemo-immunotherapy incorporating high-dose methotrexate

- MATRIX regimen x 4 cycles (with 3.5g/m^2 methotrexate over 4hours) if responsive after cycle 2
- Consider a 25% dose reduction with cycle 1 for patients with poor performance status: ECOG score ≥2, age >65 years, significant comorbidity
- Primary GCSF and anti-infective prophylaxis
- For PBSC mobilisation with 1st or 2nd cycle

2.2 Consolidation therapy following high-dose methotrexate–based induction

- Patients who are sufficiently fit and if they have achieved at least stable disease should be considered for consolidation of a first response with a BCNU-thiotepa autograft
- Whole-brain RT should considered for patients who are ineligible for autograft if they have residual disease following induction therapy.
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2.3 Patients eligible for high-dose methotrexate based immune-chemotherapy but not intensive combination chemotherapy

- High-dose methotrexate ($3.5g/m^2$) for up to 6 cycles at 1-3 week intervals together with rituximab. Consider addition of an alkylating agent e.g procarbazine followed by procarbazine maintenance (PRIMAIN regimen)

2.4 Therapy for patients ineligible for high-dose methotrexate-based chemotherapy

- There is a lack of good data to guide management and decisions should be based on performance status, comorbidity, risks of neurotoxicity, quality of life, life expectancy and the patient's wishes.
- Options are: whole-brain RT, temazolamide, steroids alone

2.5 Intraocular lymphoma

- Intra-ocular lymphoma with or without CNS involvement should be treated with high dose methotrexate-based regimens. For eligible patients the MATRIX regimen should be considered.
- For patients who have responded to intensive methotrexate chemotherapy and remain fit enough consolidation BCNU-thiotepa autograft should be offered, or consider bilateral ocular RT for primary intraocular lymphoma
- If the patient is unfit for intensive chemotherapy regimens and has isolated intraocular lymphoma consider intravitreal methotrexate.

3.0 Treatment of relapsed and refractory patients

- Consider repeat biopsy for atypical brain lesions or relapses later than 2 years after completing initial therapy especially if intensive salvage therapy is being considered.
- Relapsed patients should undergo full restaging if further treatment is being planned.
- Since the prognosis is poor consider referral for clinical trials.
- Consider previous treatment, response duration, age, performance status, physiological fitness and neurocognitive function.
- If a previous response to high dose methotrexate treatment was > two years repeating this is an option. This may be consolidated with a BCNU-thiotepa autograft if not previously performed. Alternatively consolidation with whole brain RT should be offered.
- For early relapses consider rituximab-ifosfamide-etoposide (R-IE) chemotherapy and consolidation with autograft or whole brain RT.
- If the patient is unfit for intensive therapy options are whole brain RT, steroids, temozolamide.

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Date	27th November 2018
Ratified by LSCCN Haematology NSSG	11th Dec 2018
Review date:	Dec 2019