Lancashire and South Cumbria Haematology NSSG Guidelines for mature T-cell Lymphoma

1.0 Scope

This guideline covers the management of mature (or peripheral) T-cell lymphomas and excludes lymphoblastic T-cell, prolymphocytic T-cell, T/NK large granular lymphocytic, adult T-cell leukaemia/lymphoma (ATLL) and cutaneous T-cell lymphomas. Patients with cutaneous T-cell lymphoma must be referred to the regional Skin Lymphoma MDT at The Christie Hospital, Manchester

2.0 Pre-treatment evaluation

The following tests should be performed:

- FBC, ESR, U&Es, creat, LFTs, calcium, LDH, urate, (immunoglobulins, DCT if angioimmunoblastic T-cell lymphoma is suspected)
- Hepatitis B, C and HIV serology (HTLV serology in selected cases)
- PET-CT scan if feasible and where treatment is with curative intent
- MRI scan for assessment of disease in the oropharynx and Waldeyer's ring, sinuses and nasal cavity, and paraspinal areas where there is a suspicion of spinal cord compromise
- Bone marrow aspiration and trephine biopsy if PET-CT scan has no definite evidence of marrow infiltration and where this might alter treatment e.g upstaging may result in a change of treatment, indication for CNS prophylaxis. It must be noted that the sensitivity of PET scanning for bone marrow disease may be lower than for aggressive B-cell lymphomas.
- CT scan brain and CSF exam at high risk of CNS lymphoma or CNS disease suspected on clinical grounds.
- Assessment of cardiac function in patients with a history of or risk factors for cardiac disease or when mediastinal irradiation may be indicated
- The IPI/age-adjusted IPI must be calculated.

2.1 Post-treatment evaluation

- On completion of treatment the patient must be reassessed clinically and where treatment is given with curative intent all abnormal tests at baseline repeated followed by MDT discussion with review of an end of treatment PET-CT scan performed at least 6 weeks after the last dose of chemotherapy, or three months after the last dose of radiotherapy.
- There should be rebiopsy or at least close follow up of residual FDG-avid lesions with repeat PET-CT scan before additional treatment.
- Where possible re-biopsy should be performed at relapse.

3.1 Peripheral T-cell lymphoma-unspecified (PTCL-NOS)

- Stage I-II disease should be treated with CHOP for 6 cycles, followed by and 30Gy involved-site radiotherapy where this is not associated with unacceptable short or long term toxicity.
- Stage III-IV should be treated with CHOP x 6 cycles.

- Where CHOP is not feasible management options are gemcitabine, palliative oral chemotherapy, radiotherapy and steroids.
- Consolidation of a first complete remission with high dose therapy and autologous stem cell transplant should be considered but it must be noted that the benefits of this approach remain unclear. In young fit patients referral for consideration of allogeneic stem cell transplant should be offered.
- In fit patients with relapsed/refractory disease salvage chemotherapy e.g GDP for 3 cycles, should be offered followed in responsive patients by high dose therapy and autologous stem cell transplant if not done in first response. In younger patients referral for consideration of allogeneic stem cell transplant should be considered.
- In relapsed/refractory patients unfit for intensive therapy options are gemcitabine or gemcitabine combinations e.g gem-ox, bendamustine, palliative oral chemotherapy, radiotherapy, steroids. Note newer agents e.g romidepsin, may be available on compassionate use grounds.

3.2 Angioimmunoblastic T-cell (AILT) lymphoma

- Careful clinico-pathologic correlation at the MDT is particularly important for this form of lymphoma.
- It should be noted that occasional spontaneous and durable remissions may occur.
- Newly-diagnosed patients often respond well to high dose steroids, these may be used to improve performance status but responses are rarely durable.
- Stage I-II disease should be treated with CHOP for 6 cycles, followed by 30Gy involved-site radiotherapy where this is not associated with unacceptable short or long term toxicity.
- Stage III-IV should be treated with CHOP x 6 cycles.
- Consolidation of a first complete remission with high dose therapy and autologous stem cell transplant should be considered but it must be noted that the benefits of this approach remain unclear. In young fit patients referral for consideration of allogeneic stem cell transplant should be offered.
- In fit patients with relapsed/refractory disease salvage chemotherapy e.g GDP for 3 cycles, should be offered followed in responsive patients by high dose therapy and autologous stem cell transplant if not done in first response. In younger patients referral for consideration of allogeneic stem cell transplant should be considered.
- In relapsed/refractory patients unfit for intensive therapy options are gemcitabine or gemcitabine combinations e.g gem-ox, bendamustine, palliative oral chemotherapy, radiotherapy, steroids. Note that there is limited evidence of benefit for thalidomide, fludarabine-cyclophosphamide, lenalidomide, cyclosporin A, azacitidine. Note newer agents e.g romidepsin, may be available on compassionate use grounds.

3.3 Anaplastic CD30-positive T-cell lymphoma

- The role of abbreviated chemotherapy followed by consolidation radiotherapy in limited stage disease is unclear. Where possible all stages should be treated with a full course of chemotherapy.
- First line treatment should be CHP-brentuximab x 6 cycles
- If consolidation of a first response with involved-site consolidation radiotherapy with 30Gy should be considered for patients with stage I-II disease

- In alk negative cases and alk +positive cases with a high or high intermediate IPI, consolidation of a first complete remission with high dose therapy and autologous stem cell transplant should be considered. However, it must be noted that the benefits remain unclear, especially in patients treated with brentuximab.
- Where treatment with CHOP is not feasible management options are gemcitabine, CVP, palliative oral chemotherapy, radiotherapy and steroids.
- In relapsed patients not previously treated with brentuximab consider treatment with brentuximab
- Consider retreatment with brentuximab in relapsed patients who previously responded.
- In fit patients with relapsed/refractory disease salvage chemotherapy e.g GDP for 3 cycles, should be offered followed in responsive patients by high dose therapy and autologous stem cell transplant if not done in first response. In younger patients referral for consideration of allogeneic stem cell transplant should be considered.
- In patients unfit for intensive therapy options are gemcitabine or gemcitabine combinations e.g gem-ox, bendamustine, palliative oral chemotherapy, radiotherapy, steroids. Note newer agents e.g romidepsin, may be available on compassionate use grounds.

3.4 Aggressive intestinal T-cell lymphoma

- This entity covers enteropathy-associated T-cell lymphoma (formerly EATL type 1) and monomorphic intestinal T-cell lymphoma (MEITL, formerly EATL type 2).
- Treatment must involve gastroenterology and nutritional support.
- The high risk of gastrointestinal perforation must be noted and initial surgical resection considered.
- For younger patients a more intensive approach should be considered: CHOP x 1 cycle initially, then alternating IVE-intermediate dose methotrexate (SNLG protocol) followed by autologous stem cell transplant in responders with adequate performance status.
- For other patients CHOP x 6 cycles.
- Where CHOP is not feasible management options are gemcitabine, palliative oral chemotherapy, radiotherapy and steroids.
- The prognosis of relapsed disease is very poor. Management is palliation.

3.5 Extranodal NK/T-cell (nasal type) lymphoma

- Note this form is associated with a high rate of CNS disease therefore CT/MRI scan and CSF examination must be performed.
- EBV should be quantitated in the peripheral blood in patients with extranodal NK/T-cell (nasal type) lymphoma (and monitored to evaluate response).
- Early radiotherapy in doses of at least 50Gy is central to the management.
- In stage I-II disease combined chemotherapy-radiotherapy regimens should be considered e.g a non-anthracycline, platinum-based regimen with either concurrent or sequential radiotherapy e.g 6 cycles L-asparaginase, etoposide, cisplatin, dexamethasone (LVDP) with ‘sandwiched’ 56Gy radiotherapy after cycle 2, gemcitabine, oxaliplatin, L-asparaginase (GELOX) followed by radiotherapy, carboplatin, etoposide, ifosfamide, dexamethasone (DeVIC) with concurrent radiotherapy.

- In advanced stage disease offer multiagent, non-anthracycline, L-asparaginase-based regimens e.g SMILE (dexamethasone, methotrexate, ifosfamide, L-asparaginase, etoposide), DDGP (dexamethasone, cisplatin, gemcitabine, pegylated asparaginase).
- Consider consolidation of a first response with autologous or allogeneic stem cell transplantation.
- In aggressive NK-cell leukaemia consider an intensive L-asparaginase-based regimen as for advanced stage NK/T-cell lymphoma, consolidated with allogeneic stem cell transplantation.

3.6 Hepato-splenic T-cell lymphoma

- This is an aggressive systemic lymphoma, typically in young people, with liver and splenic involvement and multiple sites of extranodal disease and requires urgent treatment.
- Disease control may be achieved with non-anthracycline based regimens incorporating ifosfamide with high-dose cytarabine or carboplatin.
- Allogeneic stem cell transplantation is potentially curative and patients must be referred early in the disease course

3.7 CNS prophylaxis

- CNS relapse in T-cell lymphomas occurs at a similar rate to that seen in diffuse large B-cell lymphoma and has similarly poor outcomes, driven rather by associated systemic relapse than CNS disease itself.
- CNS prophylaxis should be offered to patients with risk factors similar to those used for diffuse large B-cell lymphoma. In particular involvement of >1 extranodal site has been identified as a risk factor, particularly in alk +ve anaplastic T-cell lymphoma.

Author	Dr MP Macheta
Date	19th Dec 2022
Ratified by LSCCN Haematology NSSG	
Review date:	Dec 2024