Contents

1. Introduction ............................................................................................................................................... 4
2. Referral Pathways from Primary Care........................................................................................................ 4
3. Investigation and Diagnosis ....................................................................................................................... 5
   3.1. Initial assessment and investigation ............................................................................................... 5
   3.2. Pathology ......................................................................................................................................... 5
   3.3. Staging and risk assessment ............................................................................................................ 6
4. Service Configuration across the LCA ......................................................................................................... 8
   4.1. Children, teenagers and young adults ............................................................................................. 8
5. Patient Information and Support ............................................................................................................... 9
6. Treatment Recommendations ................................................................................................................. 10
   6.1. Treatment of early stage favourable classical Hodgkin lymphoma .............................................. 10
   6.2. Treatment of early unfavourable and advanced stage classical Hodgkin lymphoma ................... 10
   6.3. Treatment of Hodgkin lymphoma in special circumstances ......................................................... 11
   6.4. The use of 18F-FDG PET in classical Hodgkin lymphoma ................................................................ 12
   6.5. Management of relapsed classical Hodgkin lymphoma ................................................................ 14
7. Management of Common Disease and Treatment-related Complications ............................................. 16
   7.1. Superior vena cava obstruction ..................................................................................................... 16
   7.2. Cord compression .......................................................................................................................... 16
   7.3. Febrile neutropenia ....................................................................................................................... 16
   7.4. Nausea and vomiting ..................................................................................................................... 17
   7.5. Tumour lysis syndrome and hyperuricaemia ................................................................................ 17
   7.6. Bleomycin lung toxicity ................................................................................................................. 17
8. Supportive Care ........................................................................................................................................ 18
   8.1. Transfusions .................................................................................................................................. 18
   8.2. Thrombosis/haemostasis .............................................................................................................. 18
   8.3. Breathlessness ............................................................................................................................... 18
   8.4. Weight loss .................................................................................................................................... 18
   8.5. Pain ................................................................................................................................................ 19
   8.6. Complex symptom management .................................................................................................. 19
<table>
<thead>
<tr>
<th>Chapter</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>9. End of Treatment Information</td>
<td>20</td>
</tr>
<tr>
<td>9.1. Treatment summary and care plan</td>
<td>20</td>
</tr>
<tr>
<td>10. Follow-up Arrangements</td>
<td>21</td>
</tr>
<tr>
<td>11. Rehabilitation and Survivorship</td>
<td>22</td>
</tr>
<tr>
<td>12. Research and Clinical Trials</td>
<td>22</td>
</tr>
<tr>
<td>13. End-of-life Care</td>
<td>23</td>
</tr>
<tr>
<td>14. Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL)</td>
<td>24</td>
</tr>
<tr>
<td>14.1. Diagnostic criteria</td>
<td>24</td>
</tr>
<tr>
<td>14.2. Essential investigations</td>
<td>24</td>
</tr>
<tr>
<td>14.3. Primary treatment</td>
<td>25</td>
</tr>
<tr>
<td>14.4. Treatment of relapsed NLPHL</td>
<td>25</td>
</tr>
<tr>
<td>References</td>
<td>26</td>
</tr>
<tr>
<td>Annex 1: Multidisciplinary Teams (MDTs) and Constituent Hospital Trusts</td>
<td>28</td>
</tr>
<tr>
<td>Annex 2: SIHMDS or Current Diagnostic Services and Contacts</td>
<td>29</td>
</tr>
<tr>
<td>Annex 3: Guideline for the Management of Tumour Lysis Syndrome (TLS)</td>
<td>30</td>
</tr>
<tr>
<td>Annex 4: Guidelines for Use of Rasburicase in Adult Haematology and Oncology Patients</td>
<td>32</td>
</tr>
<tr>
<td>Appendices</td>
<td>34</td>
</tr>
</tbody>
</table>
1. Introduction

Hodgkin lymphoma (HL) accounts for approximately 15% of all lymphomas in the UK; around 1,700 people are diagnosed with HL each year and it is slightly more common in men than in women.\(^1\) The majority of these cases fall under the category of ‘classical Hodgkin lymphoma’ while the remaining are nodular lymphocyte predominant Hodgkin lymphoma (NLPHL). The latter is a separate disease entity from classical HL and more information on NLPHL can be found in section 14. Classical HL is the most common form of haematological cancer in teenagers and young adults, with peak incidence between 15 and 35 years. After young adults, the most frequently affected age group are the over-55s, although any age group can be affected. It is extremely rare in young children.

Overall, patients with classical HL have a good outcome and the majority are cured with first-line treatment. With current treatment, around 8 out of 10 patients survive this lymphoma. In particular, young adults, if diagnosed early, have an excellent prognosis and almost all survive. Most patients do very well and suffer minimal side effects in the long and short term. However, it is important that selected patients, for example those receiving radiotherapy to the mediastinum, continue to be followed up because of long-term risks associated with the treatment used for Hodgkin lymphoma.

2. Referral Pathways from Primary Care

Rapid referral for investigation of significant lymphadenopathy, especially in the presence of B-symptoms, should be made on the same day on a 2 week wait pathway (see Appendix 1: 2 Week Wait Referral Forms). Triggers for referral may come from an enlarged lymph node from GPs or from specialist medical or surgical teams. Most patients will present with painless lymphadenopathy and diagnosis is made from lymph node biopsy.
3. Investigation and Diagnosis

An accurate diagnosis of HL requires an adequately sized surgical specimen or excisional lymph node biopsy and should be made according to the World Health Organization (WHO) classification.

In classical HL, scattered binucleate or multinucleate Hodgkin and Reed–Sternberg (HRS) cells and mononuclear Hodgkin cells are seen, associated with a reactive cellular infiltrate of lymphoid cells, eosinophils and other inflammatory cells. Immunohistochemistry is an important aid to diagnosis in HL. In classical HL, HRS cells are positive for CD30 in nearly all cases and CD15 in approximately 80%. They are usually CD4S negative and are J chain negative. CD20 is variably expressed as is the EBV encoded latent membrane protein (LMP1).

Classical HL includes nodular sclerosing (NS), mixed cellularity (MC), lymphocyte-rich (LR) and lymphocyte-depleted (LD) sub-types.

3.1. Initial assessment and investigation

These should include:

- full blood count (FBC) + differential, erythrocyte sedimentation rate (ESR)
- serum biochemistry: renal profile, liver profile, bone profile, uric acid, albumin, lactate dehydrogenase (LDH) and C-reactive protein (CRP)
- serum immunoglobulins and electrophoresis
- HIV, hepatitis B and C testing
- bone marrow aspirate and trephine is not mandatory if PET-CT is performed\(^2\)
- contrast enhanced CT scan of the neck, chest, abdomen and pelvis
- FDG-PET
- MUGA/ECHO for left ventricular ejection fraction measurement prior to either induction chemotherapy or ablative therapy (optional)
- pulmonary function tests (optional) – request TLCO and KCO
- sperm cryopreservation or referral for egg/embryo harvesting if appropriate plus referral for reproductive counselling. Consideration of fertility preservation should be made for those of reproductive age (men below the age of 55 and women below the age of 40). Please see the LCA Guidance and recommendations for referral to fertility services for more information on referral criteria and contact details for services.

3.2. Pathology

Careful attention must be paid to the labelling of forms and samples before sending to the SIHMDS (see Annex 2). Samples are unlikely to be processed unless clearly and correctly labelled.
3.3. Staging and risk assessment

Using the Modified Ann Arbor staging system, HL is divided into early stage I–II or advanced stage III–IV disease.

Table 1. Ann Arbor staging system

<table>
<thead>
<tr>
<th>Stage</th>
<th>Prognostic groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>Involvement of a single lymph node region (I) or of a single extralymphatic organ or site (IE)</td>
</tr>
<tr>
<td>Stage II</td>
<td>Involvement of two or more lymph node regions (number to be stated) on the same side of the diaphragm (II) or localised involvement of extralymphatic organ or site and of one or more lymph node regions on the same side of the diaphragm (IIIE)</td>
</tr>
<tr>
<td>Stage III</td>
<td>Involvement of lymph node regions on both sides of the diaphragm (III) which may also be accompanied by localised involvement of extralymphatic organ or site (IIIIE) or by involvement of the spleen (IIIS) or both (IIISE)</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Diffuse or disseminated involvement of one or more extralymphatic organs or tissues with or without associated lymph node enlargement. Organ should be identified by symbols</td>
</tr>
</tbody>
</table>

A – No symptoms
B – Fever, drenching night sweats, loss of more than 10% of body weight over 6 months
X: Bulky disease: >1/3 mediastinum at the widest point; >10cm maximum diameter of nodal mass
E: Involvement of single, contiguous or proximal, extra nodal site

Classification of early stage HL into favourable and unfavourable categories can guide treatment decisions. The German Hodgkin Study Group (GHSG) and the European Organisation for the Research and Treatment of Cancer (EORTC) criteria for favourable and unfavourable disease are listed below.

Table 2. Criteria for favourable and unfavourable disease

<table>
<thead>
<tr>
<th>EORTC</th>
<th>GHSG</th>
</tr>
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<tbody>
<tr>
<td>Favourable risk factors</td>
<td></td>
</tr>
<tr>
<td>No large mediastinal adenopathy</td>
<td>No large mediastinal adenopathy</td>
</tr>
<tr>
<td>ESR &lt;50 with no B-symptoms</td>
<td>ESR &lt;50 with no B-symptoms</td>
</tr>
<tr>
<td>ESR &lt;30 with B-symptoms</td>
<td>ESR &lt;30 with B-symptoms</td>
</tr>
<tr>
<td>Age &lt;50</td>
<td>No extranodal disease</td>
</tr>
<tr>
<td>1–3 lymph node sites</td>
<td>1–2 lymph node sites</td>
</tr>
<tr>
<td>Unfavourable risk factors</td>
<td></td>
</tr>
<tr>
<td>Large mediastinal adenopathy</td>
<td>Large mediastinal adenopathy</td>
</tr>
<tr>
<td>ESR &gt;50 with no B-symptoms</td>
<td>ESR &gt;50 with no B-symptoms</td>
</tr>
<tr>
<td>ESR &gt;30 with B-symptoms</td>
<td>ESR &gt;30 with B-symptoms</td>
</tr>
<tr>
<td>Age &gt;50</td>
<td>Extranodal disease</td>
</tr>
<tr>
<td>&gt;4 lymph node sites</td>
<td>&gt;3 lymph node sites</td>
</tr>
</tbody>
</table>
In advanced stage HL, the International Hodgkin’s Lymphoma Prognostic Score (IHDPS)\(^3\) should be calculated. One point is assigned to each of the following seven prognostic factors:

- age >45 years
- male sex
- serum albumin concentration <40g/L
- haemoglobin concentration <105g/L
- Stage IV disease
- leucocytosis >15 x 10\(^9\)/L
- lymphopenia <0.6 x 10\(^9\)/L or <8% of total white cell count.

The rates of freedom from progression and overall survival according to the IHDPS or ‘Hasenclever score’ are listed in the table below.

**Table 3. Freedom from progression and overall survival**

<table>
<thead>
<tr>
<th>Prognostic score</th>
<th>Freedom from progression</th>
<th>Overall survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>84%</td>
<td>89%</td>
</tr>
<tr>
<td>1</td>
<td>77%</td>
<td>90%</td>
</tr>
<tr>
<td>2</td>
<td>67%</td>
<td>81%</td>
</tr>
<tr>
<td>3</td>
<td>60%</td>
<td>78%</td>
</tr>
<tr>
<td>4</td>
<td>51%</td>
<td>61%</td>
</tr>
<tr>
<td>≥5</td>
<td>42%</td>
<td>56%</td>
</tr>
</tbody>
</table>
4. Service Configuration across the LCA

All patients with a diagnosis of Hodgkin lymphoma should be seen in a British Committee for Standards in Haematology (BCSH) Level 2 centre or above within 2 weeks of referral.

All patients must be discussed at diagnosis and relapse at the local network multidisciplinary team (MDT) meeting (see Annex 1). This should ensure consistency and quality of treatment from specialist expertise and access to the latest clinical trials. Each MDT meeting should be composed of the recognised quorate membership as dictated by the Improving Outcomes for haematological malignancies.

All new diagnoses should be centrally reviewed by a specialist haematopathologist. Histopathology laboratories reporting lymphoma should have the facility to carry out immunohistochemistry using a basic panel of antibodies locally, with access within the network to a wider range of antibodies and to molecular techniques should they be required to formulate complex cases. All laboratory methods including immunohistochemistry and molecular technique are subject to standard quality assurance systems. (See Annex 2 for details of SIHMDs.)

The MDT referral form requires full patient details including NHS number, DOB, clinical history, presence of associated co-morbid illness and performance status. The outcome reported requires the stage of the disease (Ann Arbor), classification of the histological diagnosis, ICD code and prognostic index score if appropriate. Details of the key worker should be recorded.

The MDT should recommend a management plan including treatment modality and response assessment details. The final decision should be signed off by the MDT lead or designated cover and communicated to the patient’s GP within 24 hours.

4.1. Children, teenagers and young adults

Children below the age of 16 years with a diagnosis of Hodgkin lymphoma or suspected Hodgkin lymphoma must be referred to the paediatric oncology team at the principal treatment centre (PTC) and must not be managed exclusively by adult site-specific teams.

- The joint PTC for children aged below 16 years for South Thames is The Royal Marsden (Sutton)/St George’s Hospital.
- The PTC for North Thames (including North West London) is Great Ormond Street Hospital/University College London Hospitals.

All patients <1 year from both North and South Thames should be referred to Great Ormond Street Hospital. Please see Appendix 2 for contact information for the children’s PTCs.

Teenagers aged 16–18 should be managed at a PTC for teenage and young adult (TYA) cancers. Young adults aged 19–24 should be given the choice of being managed at a PTC or TYC designated hospital.

- The PTC for TYA for South Thames is The Royal Marsden (Sutton).
- The PTC for North Thames (including North West London) is University College London Hospitals.

All patients within this age range, regardless of place of care, should be referred to the TYA MDT at the relevant PTC. Please see Appendix 3 for information about how to make a referral and contact information for the PTC and TYA designated centres in the LCA.
5. Patient Information and Support

If a diagnosis of Hodgkin lymphoma is confirmed, patients should be informed that HL is a cancer of the blood, bone marrow and immune system. Their prognosis, based on the parameters listed in Table 3 (section 3.3) and other co-morbidities, should be discussed along with possible treatment options and clinical trials or research studies currently available.

All patients must have access to a key worker. This is usually (but not always) the clinical nurse specialist. The LCA has produced a key worker policy (see Appendix 4: LCA Key Worker Policy) which sets out the definition of a key worker and provides an overview of their role and responsibilities.

The key worker/clinical nurse specialist should ensure that all patients are offered a holistic needs assessment (HNA) (see Appendix 5: LCA Holistic Needs Assessment Tool) at key pathway points, including within 31 days of diagnosis; at the end of each treatment regime; and whenever a person requests one. Following each HNA, every patient should be offered a written care plan. This plan should be developed with the patient and communicated to all appropriate healthcare and allied healthcare professionals.

Written and verbal information are essential and the key worker/clinical nurse specialist plays a key role in ensuring that patients have access to appropriate and relevant written information about their condition.

The Lymphoma Association, Leukaemia & Lymphoma Research or Macmillan Cancer Support information booklets and the NHS Information Prescription are good sources of patient information at diagnosis. Patient leaflets are available for all treatment options and are also available for download on the following websites:

www.macmillan.org.uk/information-and-support/lymphoma/lymphoma-hodgkin/understanding-cancer
www.lymphomas.org.uk/about-lymphoma/types/hodgkin-lymphoma
www.nhs.uk/ipg/pages/ipstart.aspx

Particularly important aspects of communication and patient information may include:

- treatment intent – whether the condition is curable/incurable
- the range and types of therapy (including novel treatments and stem cell transplantation (SCT))
- clinical trials
- the fact that follow-up will be time-limited for potentially curable disease
- fertility, if appropriate
- treatment toxicity and late effects.
6. Treatment Recommendations

All patients should, if appropriate should be offered the opportunity to participate in clinical trials and consideration should be given to referring a patient to a centre where a suitable trial may be open. Please refer to the LCA website for an up-to-date directory of clinical trials.

6.1. Treatment of early stage favourable classical Hodgkin lymphoma

Patients with early stage disease and favourable prognostic factors (GHSG or EORTC; see section 3.3) generally have excellent outcomes. In the GHSG multicentre HD10 trial, 1,190 patients with early stage HL were prospectively randomised to receive treatment in a 4-way randomisation of 2 versus 4 cycles of ABVD followed by consolidation with either 20Gy or 30Gy of involved field radiotherapy (IFRT). The 8-year freedom from progression and overall survival (OS) rates were 87.1% and 94.5% respectively, with no significant difference between the four arms.\(^4\) On the basis of this study, the standard of care for patients with early stage, favourable HL should be 2 cycles of ABVD followed by 20Gy IFRT.

However, the decision on whether or not to proceed with radiotherapy should be made in conjunction with a radiation oncologist, in order to minimise long-term sequelae. Particularly in females below 35 years of age with mediastinal or axillary sites of HL, consideration should be given to additional courses of ABVD without radiotherapy.

The NCIC and ECOG study, comparing 4–6 cycles of ABVD against therapy involving subtotal nodal irradiation in 405 patients with stage I–IIA classical HL, showed that omitting radiotherapy increased the risk of early relapse. However, it also demonstrated an excellent OS of 94% at 12 years for those patients treated with ABVD alone. A cross-trial comparison between ABVD x 2 followed by IFRT (GSHG HD10/11) with ABVD x 4 (NCIC HD6), in patients with stage I or IIA HL, showed that patients had excellent outcomes with either treatment provided they achieved a complete remission (CR) on CT scanning after 2 cycles of ABVD.\(^5\)

There is no evidence to recommend omission of radiotherapy in bulky disease.

The question of whether \(^{18}\)F-FDG PET scan can be utilised for response-adapted therapy in these patients is being addressed in clinical trials. This is discussed further in section 6.4.

**Recommendations:** Patients with early stage favourable classical HL should be treated with 2 cycles of ABVD and 20Gy IFRT.

However, decisions on radiotherapy should be made together with a radiation oncologist, taking the potential long-term sequelae into consideration. Additional cycles of ABVD and omission of radiotherapy may be appropriate, particularly if a CR is achieved after 2 cycles of ABVD.

6.2. Treatment of early unfavourable and advanced stage classical Hodgkin lymphoma

In the UK, traditionally, early stage HL patients with bulky disease or B-symptoms have been treated with advanced stage HL protocols.\(^6\)

For early unfavourable HL, evidence in recent years suggests that a combined modality protocol with ABVD x 4 followed by IFRT (30Gy) is a very effective alternative approach for these patients. The evidence for this
comes from the GHSG HD11 study\(^7\) in which 1,395 patients with early unfavourable HL were assigned to one of two chemotherapy arms – ABVD x 4 or BEACOPP x 4. This was followed by consolidation with either 20Gy or 30Gy IFRT resulting in four possible randomisations. There was no significant difference in OS (94.5% at 5 years) but ABVD x 4 and 20Gy IFRT was inferior to the other three arms in terms of freedom from treatment failure and progression free survival (PFS). Greater toxicity was observed in the BEACOPP arms, making ABVD x 4 followed by 30Gy IFRT the most attractive among the four arms. It should, however, be borne in mind that greater toxicity was also seen in patients who received 30Gy compared with 20Gy IFRT (12% v 5.7%).

In advanced stage HL, a number of trials using ABVD have shown a failure free survival of 73–78% with an OS in the range of 82–90%.\(^8,9\)

In a recent meta-analysis, 6 cycles of escalated BEACOPP was shown be superior to 6–8 cycles of ABVD in advance stage HL (OS advantage of 10% at 5 years)\(^10,11\) but ABVD is thought to have a more favourable toxicity profile in terms of side effects, including infections, transfusion requirements as well as fertility.\(^12,13\)

As far as possible, ABVD should be delivered on schedule with infusions given every 14 days irrespective of neutropenia, particularly when this is isolated. Granulocyte colony-stimulating factor (G-CSF) is required only for patients with infectious complications.\(^14–16\)

Radiotherapy should be considered to original sites of bulk disease for patients receiving ABVD.

**Recommendations:** For patients with early unfavourable HL, ABVD x 4 followed by 30Gy IFRT is an effective treatment option. However, decisions on radiotherapy should be made together with a radiation oncologist, taking the potential long-term sequelae into consideration. In selected cases, 6 cycles of ABVD and omission of radiotherapy may be appropriate.

For patients with advanced stage HL not treated on a clinical trial, 6–8 cycles of ABVD is the current standard of care. Radiotherapy should be considered to sites of bulk disease at the end of treatment.

In younger, fitter patients, escalated BEACOPP should be considered, particularly in the presence of adverse prognostic factors, as there is evidence of a significant overall survival advantage with this regimen over ABVD. However, this should be balanced against the increased risk of side effects and infertility associated with this regimen.

### 6.3. Treatment of Hodgkin lymphoma in special circumstances

#### 6.3.1. Elderly patients

- Old age is recognised as an independent adverse prognostic factor for HL. Five-year survival for patients over the age of 60 is 58%.\(^17\)

- Increased toxicity and treatment-related mortality have been observed in patients aged over 60 years treated with ABVD, compared with patients aged less than 60 years. This includes increased incidence of neutropenia, infections and bleomycin-induced lung toxicity (BLT).\(^18\) BLT occurred in 43% of patients over 60 years receiving ABVD in the latter study, with associated mortality of 18%.

- The SHIELD study in the UK evaluated VEPEM-B in the treatment of 103 patients over the age of 60. In 31 patients with early stage disease (VEPEM-B x 3 and radiotherapy) the 3-year PFS and OS were 74%
and 81% respectively. In patients with advanced stage HL (N=72, VEPEM-B x 6), 3-year PFS and OS were 58% and 66% respectively.19 Of note, frail patients were excluded from this study.

- The non-anthracycline containing regimen ChlVPP is another option in elderly patients or in those unable to have anthracyclines. However, response rates in patients over 50 years of age are not very encouraging.20
- There is a need for clinical trials specifically addressing the treatment of HL in older patients. Where clinical trial entry is not available, treatment recommendation is according to performance status, cardiac and respiratory assessment, and patient preference.

6.3.2. Pregnancy

- There is very limited evidence for management of HL in pregnancy. Some case reports, case series and reviews have been published on this subject.21
- HL in pregnancy should always be managed in conjunction with an obstetrician experienced in high-risk pregnancy.
- In some cases it may be possible to delay treatment until after delivery but this should be done with caution.
- MRI and ultrasound can be used for staging and response assessment to avoid X-ray exposure.
- ABVD is the treatment of choice in this situation. As far as possible, chemotherapy exposure should be avoided in the first trimester as the risk to the developing foetus is theoretically at its highest.
- Radiotherapy should be delayed until after delivery wherever possible.

6.3.3. HIV

- HIV-positive patients have more extensive disease and adverse prognostic features compared with HIV-negative patients.
- Standard management with ABVD combined with antiretroviral therapy can achieve responses approaching those seen in the HIV-negative population.22
- Stage and risk-adapted treatment is both feasible and effective in this group of patients in the era of highly active antiretroviral therapy.23

6.4. The use of 18F-FDG PET in classical Hodgkin lymphoma

- HL is a highly FDG-avid lymphoma and nearly 100% of cases demonstrate high FDG uptake.
- The use of FDG-PET is recommended in the staging of HL because of greater accuracy compared with CT alone. In prospective studies, FDG-PET has been shown to upstage 13–24% of patients when compared with CT.
- Interim FDG-PET scans are not currently considered standard of care but early interim FDG-PET, after 2 cycles of treatment, has been widely accepted as a prognostic tool for ABVD-treated early unfavourable or advanced-stage HL.
- A number of randomised trials in both early stage and advanced HL have included interim FDG-PET in a response-adapted strategy to improve outcome. A five-point scale, also known as Deauville criteria,
Treatment recommendations

has been used for response reporting in these trials because of high inter-observer agreement using this score.

Table 4. The Deauville scale

<table>
<thead>
<tr>
<th>Deauville score</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No uptake</td>
</tr>
<tr>
<td>2</td>
<td>Uptake less than or equal to the mediastinum</td>
</tr>
<tr>
<td>3</td>
<td>Uptake greater than the mediastinum but less than the liver</td>
</tr>
<tr>
<td>4</td>
<td>Uptake moderately higher than the liver</td>
</tr>
<tr>
<td>5</td>
<td>Uptake markedly higher than the liver</td>
</tr>
</tbody>
</table>

- In the UK ‘RAPID’ study of stage I and IIA non-bulky HL, patients with a PET negative remission (Deauville score of 1 or 2) after 3 cycles of ABVD had superior PFS compared with those who were PET positive. Patients who were PET negative were randomised to receive or omit radiotherapy. Those who received radiotherapy had a slight early benefit in PFS but there was no significant difference in OS between the radiotherapy and no radiotherapy groups.

- In the RATHL study evaluating response adapted treatment based on interim FDG-PET after 2 cycles of ABVD, a Deauville score of 1–3 was considered negative while a score of 4–5 was considered positive. PET negative patients were randomised to further ABVD or de-escalation to AVD while PET positive patients were randomised to either BEACOPP-14 or escalated BEACOPP. Interim analysis suggests escalation of chemotherapy in PET positive patients can lead to ‘substantial response rate’ and de-escalation in PET negative case could reduce toxicity. However, longer follow up is needed and the final analysis is awaited.

- The GSHG HD15 study of patients with advanced stage HL, comparing three schedules of BEACOPP (escalated BEACOPP x 6, escalated BEACOPP x 8 and BEACOPP-14 x 8), demonstrated a high negative predictive value of FDG-PET 94.5% at 12 months, suggesting that additional radiotherapy in this setting can be guided by end of treatment PET-CT.

**Recommendations:** FDG-PET is more accurate than CT alone in HL and is therefore recommended for staging and for evaluation of end of treatment responses.

Interim PET scan is not currently considered standard of care but is recommended if feasible. This should be performed after 2 cycles of ABVD (as close to 2 weeks after cycle 2B as possible) and the results should be discussed at an MDT.

In patients with early stage HL with mediastinal or axillary sites of disease where radiotherapy is associated with potential long-term risks, a negative PET-CT after 2 cycles (Deauville 1 or 2) can support the decision to omit radiotherapy. Additional cycles of ABVD may be considered as an alternative in these cases depending on risk factors.

Although treatment stratification on the basis of interim 18F-FDG-PET is not yet considered standard of care, a Deauville score of 4 or 5 on an interim PET-CT should be considered an inadequate response. There is insufficient evidence to recommend a particular treatment regimen but in advanced stage HL BEACOPP (standard or escalated) or a salvage regimen such as Gem-P or ESHAP may be appropriate.
Patients with a Deauville score of 3 on interim PET-CT should continue on the same regimen as there is insufficient evidence to recommend a change in treatment.

For patients treated with advanced stage HL and residual masses, especially in those treated with escalated BEACOPP, radiotherapy can be omitted if a complete metabolic remission is seen on FDG-PET at the end of treatment.

Note that interim PET scan should be done as close to 2 weeks after day 1 ABVD 2B and not sooner than 10 days to minimise false-positive readings introduced by the inflammatory response to therapy.

6.5. Management of relapsed classical Hodgkin lymphoma


The key recommendation is:

- Repeat biopsy is generally recommended in patients thought to have relapsed, and should be considered in those who have residual FDG-avid lesions post-therapy.

6.5.1. Treatment

- The choice of a first-line salvage regimen in patients eligible for autologous stem cell transplantation (ASCT) should be based on patient factors and the familiarity of the treatment centre with the regimen; usually a platinum-based regimen, e.g. GEM-P, ICE, ESHAP.

- Regimens containing stem cell toxic agents (such as carmustine and melphalan) should be avoided if possible until stem cells have been successfully collected and cryopreserved if ASCT is planned.

- In patients not eligible for ASCT, combined modality therapy should be considered, especially in early stage relapse and in patients who have not received prior radiotherapy or who have relapsed outside of the initial radiotherapy field.

- In patients who fail to respond to conventional combination regimens, brentuximab vedotin is available via the Cancer Drugs Fund for relapsed CD30+ HL following at least two prior therapies. Suitable responding patients can then proceed to SCT.

- In the rare event of late relapse >5 years after primary therapy occurring at a localised site without B-symptoms, treatment with standard-dose chemotherapy and IFRT alone may be appropriate.

- In patients unlikely to tolerate the toxicities associated with more intensive regimens, palliation with either a single agent or with a multiagent oral regimen with or without intravenous vinblastine should be considered.

- The use of radiotherapy should be given serious consideration in cases of local relapse or relapse at sites where local disease is dominating the clinical picture.

- Salvage radiotherapy alone may be considered a reasonable treatment option in selected patients not eligible for ASCT, especially for older patients with relapsed HL who lack B-symptoms and have limited stage disease at relapse.
• Consideration of entry to clinical trials with novel agents should be given. For more details on clinical trials see section 12.

• Early consideration of involvement of palliative care services is recommended, particularly in those not eligible for high-dose therapy. For more detail on end-of-life care, see section 13.

6.5.2. Response assessment and consolidation

• Although it is acknowledged that an adequate response to salvage therapy is currently defined as a partial response by conventional CT criteria, the authors refer to reported poor outcomes after ASCT in patients with residual FDG-PET-positive tumour uptake post-salvage chemotherapy, and propose a PET-based response-adjusted treatment algorithm.

• PET-CT is the preferred restaging modality after salvage therapy.

• The aim of salvage treatment should be to achieve an FDG-PET-negative remission.

• Consider switching to an alternative non-cross-resistant salvage regimen if there are residual FDG-avid lesions after first-line salvage treatment and the intent is to proceed to ASCT.

• ASCT is the standard treatment for patients with relapsed or primary resistant disease who achieve an adequate response to salvage therapy.

• Choice of conditioning regimen should be based on familiarity of the treatment centre with the regimen.

• ASCT is not recommended in those failing to achieve an adequate response.

• Allogeneic transplantation using a reduced intensity conditioning regimen is the treatment of choice for younger patients with a suitable donor and chemo-sensitive disease following failure of ASCT.

• An appropriately human leukocyte antigen- (HLA-) matched unrelated donor should be considered when there is no HLA-matched sibling.

• Investigation of the use of allogeneic transplantation earlier in the treatment pathway should be performed in the context of prospective clinical trials, but may be justified in selected patients who have required multiple lines of therapy to achieve a response.

• Peri-transplant (ASCT) radiotherapy should be considered in patients who have a dominant site of local relapse at an initially involved site.
7. Management of Common Disease and Treatment-related Complications

7.1. Superior vena cava obstruction

Superior vena cava obstruction (SVCO) is nearly always associated with malignancy, usually lung cancer (80% of cases) but sometimes lymphoma, breast cancer or germ cell tumours. It occurs most commonly in patients with known cancer, but can be the presenting feature of a new diagnosis.

7.1.1. Signs

Although the signs of SVCO are characteristic, they are often absent and so an index of suspicion is needed based on tumour type and symptoms. These include:

- thoracic vein distension (65%)
- neck vein distension (55%)
- tachypnoea
- facial/conjunctival oedema (55%)
- central/peripheral cyanosis (15%)
- arm oedema (10%)
- plethora (15%)
- vocal cord paresis (3%).

For more information, see the LCA Acute Oncology Clinical Guidelines.

7.2. Cord compression

Spinal cord compression due to malignant infiltration or vertebral collapse requires immediate management and referral. The LCA Acute Oncology Clinical Guidelines contain detailed information about management and referral for spinal cord compression and can be found here.

7.3. Febrile neutropenia

Suspected or proven infection in a neutropenic patient is a medical emergency and is an indication for immediate assessment and prompt treatment with intravenous antibiotics within 1 hour of presentation to anywhere within the hospital. Patients who are neutropenic following anti-cancer treatment may initially appear well. However, infections may progress within hours to shock or death, especially when due to gram-negative bacilli. The LCA Acute Oncology Clinical Guidelines provide guidance to admitting clinicians when faced with a case of suspected infection and neutropenia in both solid tumour oncology and haematology oncology. If there is clinical suspicion of neutropenic sepsis in existing inpatients, they should be treated within 1 hour of clinical onset, as defined by baseline observations, early warning score (EWS) or clinical suspicion. Local policy should be followed for antibiotic cover.

Patients with neutropenic pyrexia or sepsis should be treated according to local protocols for neutropenic sepsis (and following NICE guidance).

In addition, for haematology oncology patients the following are mandatory:

- urinalysis
- midstream specimen of urine
- chest X-ray
• swabs: throat (bacterial and viral), central venous access device (CVAD) site if present and any other focal lesions as appropriate
• sputum and stool culture
• cytomegalovirus (CMV), EBV, adeno PCR if indicated.

Such patients should ideally be cared for by specially trained nurses on a BCSH Level 2b–3 unit. The use of G-CSF is highly dependent upon the context of the disease and the chemotherapy protocol in which it is being used. G-CSF is used to hasten recovery of the neutrophil count, decrease risk of infection and reduce hospital stay. However, evidence supporting improved survival with G-CSF is lacking.

7.4. Nausea and vomiting

Follow pan-London nausea and vomiting protocol and local policy or the *LCA Acute Oncology Clinical Guidelines.*

7.5. Tumour lysis syndrome and hyperuricaemia

See *Annex 3* for information on tumour lysis syndrome (TLS) and *Annex 4* for guidance on the use of rasburicase.

Patients with aggressive disease may already be in tumour lysis prior to the initiation of chemotherapy. Tumour lysis is indicated by a high LDH, uric acid, hyperkalaemia, hyperphosphataemia, hypocalcaemia and renal failure. The mainstay of treatment is avoidance by aggressive IV hydration from diagnosis and especially at the start of cytoreductive therapy, rasburicase as per protocol (if G6PD is normal) followed by allopurinol. If TLS does occur, patients undergoing intensive therapy must be supported with appropriate fluid and electrolyte management and, if necessary, ICU transfer with haemofiltration until TLS resolves and renal function improves.

7.6. Bleomycin lung toxicity

Bleomycin lung toxicity (BLT) is a disabling side effect of therapy of HL and is associated with a significant mortality risk. In a retrospective analysis of 141 patients receiving bleomycin-based chemotherapy for HL, 18% developed BLT. In this study, an association was found with increasing age and the use of G-CSF. Mortality in those who developed lung toxicity was 24%.

The following measures should be taken to minimise the risk of this serious complication:
• regular clinical assessment for breathing problems in patients on bleomycin-based therapy
• a low threshold for omitting bleomycin in cases where respiratory symptoms develop with no obvious cause, particularly in patients who achieved a good response on interim PET-CT
• omission of regular G-CSF in treatment protocols containing bleomycin wherever possible.

It is difficult to recommend omitting bleomycin from chemotherapy regimens in elderly HL as response rates with ChlVPP in this age group are poor. However, omission of bleomycin should be considered either at the start or if a good response is seen on interim staging scans.
8. Supportive Care

Supportive care is very important for all patients with haematological malignancies. There are many aspects to consider and they are carefully documented in current clinical trial protocols. These protocols are available for download and should be consulted for precise details of appropriate supportive care, even if patients are not entering the clinical trial.

Patients should ideally be nursed in isolation rooms with appropriate protocols to prevent infections. Clean, neutropenic diets should be instituted and appropriate infection control measures should be undertaken. Prophylaxis and treatment of infection from presentation should be instituted based on local protocols with antibiotic choice largely dependent on local microbiological flora. For patients who will undergo intensive treatment schedules, a CVAD should be inserted as soon as is safely possible.

8.1. Transfusions

All patients with Hodgkin lymphoma should receive irradiated blood products indefinitely from diagnosis onwards.

Transfusion triggers should be chosen in advance for patients, depending on co-morbidities. For patients with no co-morbidities or bleeding risk, and in those who do not lead active lifestyles, it would be reasonable to aim for a target Hb >80g/dL.

Administer leucodepleted blood products.

Platelets should be transfused when the platelet count is <10 x 10^9 /L, or <20 x 10^9 /L in the setting of sepsis.

All platelet products should be single donor collections in order to limit the risk of allo-sensitisation.

HLA-typing should be done prior to starting treatment in order to address donor status if transplantation is appropriate for the patient, and in case HLA-matched platelets become necessary during treatment (as often occurs in women who have had children).

8.2. Thrombosis/haemostasis

Avoid aspirin/non-steroidal anti-inflammatory drugs (NSAIDs) and intramuscular injections (unless platelets >50 x 10^9 /L). Avoid arterial blood gases unless absolutely necessary – ensure platelets >50 x 10^9 /L.

A proton-pump inhibitor (PPI) should be administered if a steroid-containing treatment is used.

8.3. Breathlessness

Any inpatient showing signs of respiratory distress should be assessed by a physician with knowledge of treatment for patients with classical HL and, if appropriate, referred for respiratory physiotherapy assessment in accordance with local on-call guidelines, unless of overt metabolic cause.

Ongoing breathlessness management strategies can be provided by occupational therapy or physiotherapy.

8.4. Weight loss

A screening tool for the assessment of dietary issues should be completed weekly for inpatients and, if issues are identified, a referral should be made to a specialist dietitian.
Referral for specialist dietetic input should be made in the following instances.

- Any patient with neutropenia should be provided with information and education on the neutropenic diet and be referred to a specialist dietitian.
- If artificial feeding is being considered, a referral to the specialist dietitian should be made.
- Any patient with mucositis should be referred for dietetic assessment, as well as for specialist speech and language assessment.
- Weight loss/malnutrition should be identified through weekly screening of inpatients.

8.5. Pain

People reporting pain should be considered for non-pharmacological intervention including, but not limited to, TENS (transcutaneous electrical nerve stimulation), complementary therapies and psychological interventions such as mindfulness.

8.6. Complex symptom management

Discuss with the specialist palliative care team for advice on symptom management (e.g. pain, mucositis) when there is no/poor response to standard interventions. If appropriate, referral can be made to the specialist palliative care team using the LCA referral form to specialist palliative care (see Appendix 7).
9. End of Treatment Information

An end of treatment consultation should be offered to every patient. This should include an end of treatment HNA and associated written care plan and should also include the discussion and provision of a comprehensive treatment summary. On successful completion of treatment, both the patient and their GP should be made aware of follow-up plans and potential future disease or treatment-related issues.

9.1. Treatment summary and care plan

There are two related but distinct documents which patients should be given at the end of their treatment.

- A **treatment summary** provides a summary of the cancer treatments received by the end of the first treatment, planned follow-ups (including mechanisms for these), and signs and symptoms of which to be aware. Their aim is to provide information not only to the patient but also to the GP about possible consequences of cancer and its treatment, signs of recurrence and other important information. The treatment summary should be completed by the named clinical nurse specialist/key worker using the LCA template with the patient and a copy sent to the GP and the patient (see Appendix 6: NCSI Treatment Summary).

- A **care plan** is generated as a result of an HNA and is the agreed plan between the patient and healthcare professional about how the identified areas of concern will be addressed. This may cover provision of information (e.g. through an information prescription), onward referral for specialist assessment and intervention (e.g. breathlessness management), or things which the patient themselves can do (e.g. contact their HR department about graduated return to work options).

**Recommendation:** An end of treatment consultation should be offered to every patient. This should include an end of treatment HNA and associated written care plan, and should also include the discussion and provision of a comprehensive treatment summary.

Lymphoma team, key worker and patient support group contact details should be reiterated and details of future follow-up arrangements provided.

Patients should be educated regarding the potential symptoms and signs that might indicate disease progression or recurrence and counselled on the need to re-present to the unit should these occur.

People should be offered access to a health and wellbeing event at the end of treatment. This should provide information to enable a person to self-manage any expected consequences of their cancer and its treatment, as well as general health promotion information, including diet and physical activity.

The MDT outcome form and clinic letters will serve to communicate diagnosis, treatment initiation and new lines of treatment with the GP.
10. Follow-up Arrangements

All patients need clinical assessment, imaging as dictated by the clinical condition plus additional tests as below. If the patient is in study, check if any additional tests are necessary and check follow-up interval. Remember that hormonal failure can occur in various systems after both radiotherapy and chemotherapy.

CT scan is routinely performed at 3 months after completion of chemotherapy except for low-grade lymphoma. Discuss with consultant if symptoms of relapse or refer to study protocol. Surveillance imaging is not recommended.

The nature and frequency of follow-up review and investigations for patients will be somewhat tailored by their disease, treatment type, treatment toxicities, disease-related effects, co-morbidities and psycho-social factors.

<table>
<thead>
<tr>
<th>Standard lymphoma following chemotherapy (adjusted to patient risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
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<tr>
<td>6 months</td>
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<tr>
<td>9 months</td>
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<tr>
<td>12 months</td>
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<tr>
<td>18 months</td>
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<tr>
<td>24 months</td>
</tr>
<tr>
<td>Annually until 5 years</td>
</tr>
<tr>
<td>When discharged can be considered and discussed with consultant (see below)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Long-term follow-up – patients with lymphoma in remission for five years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can be considered for discharge after 5 years with the exception of:</td>
</tr>
<tr>
<td>• females treated with mantle radiotherapy, radiotherapy to the neck where the thyroid gland was within the field or radiotherapy to breast tissue who can be discharged at five years but must be referred to the appropriate breast team (as above) for screening and their GP must monitor TFTs yearly (or if symptomatic) commencing 5 years post radiotherapy</td>
</tr>
<tr>
<td>• males treated with mantle radiotherapy or radiotherapy to the neck where the thyroid gland was within the field may be discharged after 5 years but will require their GP to monitor TFTs yearly (or if symptomatic) commencing at 5 years post radiotherapy</td>
</tr>
<tr>
<td>• those who had high-dose chemotherapy who remain on surveillance indefinitely unless felt suitable for discharge by the consultant</td>
</tr>
<tr>
<td>• indolent lymphomas with significant risk of recurrence.</td>
</tr>
</tbody>
</table>

Those with nodular lymphocyte predominant Hodgkin lymphoma should remain on follow-up indefinitely as for indolent NHLs unless deemed suitable for discharge by the consultant.
End of treatment $^{18}$F-FDG-PET scan is advised as above. Routine imaging following a negative PET scan is not advised during follow-up, with clinical follow-up at decreasing frequency until discontinuation after 5 years.

All patients should be made aware of the risks of secondary cancers and participate in national cancer screening programmes, and of the increased risk of cardiovascular disease with the need for periodic monitoring of risk factors in general practice.

11. Rehabilitation and Survivorship

Issues in relation to rehabilitation and the long-term consequences of treatment should be monitored throughout the patient pathway and highlighted to the appropriate allied health professionals if required. Survivorship issues can relate to the effects of the disease process and/or management of long-term adverse effects of treatment. Please refer to the LCA Survivorship Guidelines for more information.

Any patient experiencing or reporting reduced mobility and/or ability to perform activities of daily living should be referred for occupational therapy and physiotherapy assessment.

People reporting ongoing consequences such as fatigue, anxiety and pain should be considered for non-pharmacological intervention including, but not limited to, TENS (transcutaneous electrical nerve stimulation), complementary therapies and psychological interventions such as mindfulness.

Onward referrals may include:

- physiotherapist/occupational therapist (fatigue management, rehabilitation)
- dietitian if symptoms are affecting intake/nutritional status, especially in cases of gastrointestinal disturbances and mucositis, and weight loss
- speech and language therapist (weight loss, dysphagia or concerns about aspiration).

12. Research and Clinical Trials

All patients should be entered into clinical trials and tissue stored where possible. Ideally, all patient diagnostic material should be bio-banked in an ethically approved research framework.

For an up-to-date list of all clinical trials which are currently recruiting patients with Hodgkin lymphoma, please see the LCA website.
13. End-of-life Care

Full integration with palliative care services should be seamless and end-of-life treatment decisions discussed with patients and their families where appropriate, fully respecting the dignity of patients and the sensitivities of traumatic difficult situations.

For older patients and in those with poor performance status and/or high risk disease, discussions regarding prognosis and treatment options should also include discussions on end-of-life care. These are to facilitate transitions between active disease-modifying therapy to clinical trials, or supportive care only at the time of disease progression/non-response.

To support consideration of referral to specialist palliative care, please refer to the LCA Referral Criteria for Specialist Palliative Care (see Appendix 8). The LCA form for referral to specialist palliative care can be found in Appendix 7: LCA Specialist Palliative Care Referral Form.

The named clinical nurse specialist/key worker, patient, family members and palliative care teams as well as members of the inpatient ward team may be involved. Clear documentation of the discussion with guidance to the treating teams is helpful in communicating these discussions and outputs to the wider team that may care for the individual.
14. Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL)

NLPHL is recognised as a separate disease entity and comprises 5% of all cases of HL. It is clinically, pathologically and prognostically distinct from classical HL. The majority of patients are aged 30 to 50 years. Most patients (70–80%) present with localised disease and have a 10-year overall survival of >80%. Late relapses are well recognised. Those with advanced disease experience multiple relapses over years. There is a significant risk of transformation (30% at 20 years)\(^2\) to diffuse large B-cell lymphoma (DLBCL). For more information please see the LCA Haemato-Oncology Clinical Guidelines on DLBCL.

14.1. Diagnostic criteria

- Abnormal expanded B-cell follicles with mixture of mantle and germinal centre B-cells and reactive T-cells including a CD4+, CD57+ population.
- Polylobulated and large mononuclear B-cells, usually associated with T-cell rosettes.

14.2. Essential investigations

Work up is as for classical Hodgkin lymphoma. See section 3: Investigation and Diagnosis.

14.3. Primary treatment

- **Stage IA**
  IFRT (30Gy).

- **Stages other than IA**
  The rarity of NLPHL means that there is a lack of data from large randomised trials. However, the idea that alkylator-based therapy may have an advantage over non-alkylator-based therapy is supported by a retrospective analysis from CALGB, and a retrospective series from MDACC.\(^2\), \(^3\) Of note, previous GHSG regimens included higher doses of alkylating agents than ABVD (e.g. COPP/ABVD). The potentially higher toxicity of ABVD is an additional factor in recommending alternative alkylator-based regimens.

  The addition of rituximab to chemotherapy is recommended and rituximab maintenance can be considered although not commissioned.

- **Stages IB and IIA**
  IFRT alone may be an option for selected cases of Stage IIA NLPHL.

  Patients not entering a trial should receive 3 cycles of R-CVP with MDT decision as regards a PET scan and either further chemotherapy, IFRT or no further therapy.

- **All other stages**
  Note the risk of occult transformation to aggressive NHL.

  Treat with 6 cycles of R-CVP or R-CHOP or R-ABVD (noting the increased toxicity of this regimen in a non-curative setting).
14.4. Treatment of relapsed NLPHL

- Re-biopsy is essential, as transformation to aggressive NHL must be excluded.
- For localised relapse: IFRT.
- For advanced stage asymptomatic patients with low tumour burden, consider watch and wait.
- For advanced relapse with symptoms/bulk, consider second-line + high-dose therapy.
References

1. www.hmrn.org/statistics


Annex 1: Multidisciplinary Teams (MDTs) and Constituent Hospital Trusts

<table>
<thead>
<tr>
<th>South East London MDT 1</th>
<th>Guy’s &amp; St Thomas’ NHS Foundation Trust/Lewisham and Greenwich NHS Trust (Lewisham Hospital and Queen Elizabeth Hospital)</th>
</tr>
</thead>
<tbody>
<tr>
<td>South East London MDT 2</td>
<td>King’s College Hospital NHS Foundation Trust (including Princess Royal University Hospital)</td>
</tr>
<tr>
<td>South West London MDT 1</td>
<td>Kingston Hospital NHS Foundation Trust/St George’s University Hospitals NHS Foundation Trust</td>
</tr>
<tr>
<td>South West London MDT 2</td>
<td>Epsom and St Helier University Hospitals NHS Trust/Croydon Health Services NHS Trust</td>
</tr>
<tr>
<td>South West London MDT 3</td>
<td>The Royal Marsden NHS Foundation Trust</td>
</tr>
<tr>
<td>North West London MDT 1</td>
<td>Imperial College Healthcare NHS Trust/The Hillingdon Hospitals NHS Foundation Trust/Chelsea and Westminster Hospital NHS Foundation Trust/West Middlesex University Hospital NHS Trust/Ealing Hospital</td>
</tr>
<tr>
<td>North West London MDT 2</td>
<td>London North West Healthcare NHS Trust (Northwick Park Hospital and Central Middlesex Hospital)</td>
</tr>
</tbody>
</table>
Annex 2: SIHMDS or Current Diagnostic Services and Contacts

Guy’s & St Thomas’ NHS Foundation Trust
Cytogenetics/Flow Lab
ViaPath Pathology
4th Floor, Southwark Wing
Guy’s Hospital
Great Maze Street
London, SE1 9RT

Imperial College Healthcare NHS Trust
Imperial Molecular Pathology Laboratory
G Block, North Corridor
Hammersmith Hospital
Du Cane Road
London, W12 0HS

London North West Healthcare NHS Trust
Processed centrally in TDL laboratories on-site for SIHMDS (in progress), cytogenetics/molecular to:
North West Thames Regional Genetics Service, Haematology Section
Northwick Park Hospital
Watford Road
Harrow, HA1 3UJ

The Royal Marsden Hospital NHS Foundation Trust
The Centre for Molecular Pathology
Downs Road
Sutton, SM2 5PT
Tel: 020 8915 6570
Immunophenotyping Tel: 020 8915 6517 or 020 8915 6518
Cytogenetics Tel: 020 8722 4232
Molecular Genetics Tel: 020 8915 6565

For APML diagnostic and MRD
Dr Yvonne Morgan
Molecular Oncology Diagnostics Unit
GSTT Pathology, 4th Floor, Southwark Wing
Guy’s Hospital
Great Maze Street
London, SE1 9RT

King’s College Hospital NHS Foundation Trust
KingsPath: Clinical Diagnostic Pathology Service
Haematological Medicine
King’s College Hospital
Denmark Hill
London, SE5 9RS
Annex 3: Guideline for the Management of Tumour Lysis Syndrome (TLS)

To be read in conjunction with Annex 4: Guidelines for Use of Rasburicase in Adult Haematology and Oncology Patients.

TLS is life-threatening. Rapid lysis of tumour cells leads to the release of cellular contents into circulation resulting in hyperkalaemia, hyperphosphataemia, hyperuricaemia and hypocalcaemia which may lead to acute oliguric renal failure and cardiac arrhythmias. TLS can occur spontaneously in tumours with a very high proliferative rate, and/or during induction treatment. It can be classified as laboratory TLS (no clinical manifestations) or clinical TLS (life-threatening clinical abnormalities). Symptoms during TLS/rasburicase include fever, haemolysis, headaches, vomiting, diarrhoea, rash and hypersensitivity reactions.

Prevention of TLS

1. Standard care is hydration and allopurinol and these help prevent TLS
2. Check urate, renal function and LDH prior to starting chemotherapy and hydrate with 3L/m² over 24 hours
3. For high risk patients rasburicase should be considered

Management (see separate rasburicase protocol): Rasburicase is to be used immediately prior to and during treatment-induction for the indications below and when authorised by a consultant haematologist.

TLS Screen is to be ordered 1–4 times per day according to patient’s clinical condition until resolves: urea, creatinine, uric acid, phosphate, potassium, corrected calcium and LDH (FBC if AML/ALL/CML/MPN).

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Diagnosis</th>
<th>Preventative Strategies</th>
</tr>
</thead>
</table>
| High       | Burkitt lymphoma | 1. IVF (~3L/m²/day, to maintain UOP >100ml/m²/hr) or aggressive hydration as per chemotherapy protocols.  
2. Rasburicase* as per rasburicase protocol |
|            | Burkitt-type ALL | |
|            | AML or ALL with WBC >100 x 10⁹/L | |
| Moderate   | AML with WBC > 50 x 10⁹/L | 1. IVF (~3L/m²/day, to maintain UOP >100ml/m²/hr) or aggressive hydration as per chemotherapy protocols.  
2. Rasburicase* as per rasburicase protocol |
|            | Other ALL | |
|            | High grade NHL with bulky disease | |
|            | CML accelerated/blast phase, or where rapid response to therapy expected | |
| Minor      | Other AML | Use allopurinol.  
Use rasburicase* where clinically indicated (high risk):  
High LDH (>ULN)  
Renal failure  
High proliferation index  
High uric acid (>420 umol/L or 7mg/ml) |
|            | Myeloma | |
|            | Other lymphoma/CLL | |
|            | Other CML and MPN | |

* No dose adjustment in renal/hepatic impairment. Ensure normal G6PD level prior to rasburicase (if low, use aggressive hydration & allopurinol).
References:


Annex 4: Guidelines for Use of Rasburicase in Adult Haematology and Oncology Patients

Criteria for use

Rasburicase may be used only for the following indications, when authorised by a consultant haematologist or oncologist:

Urate oxidase (rasburicase) is an enzyme which catalyses the oxidation of uric acid to allantoin, which is more easily excreted in the urine.

**Used in the treatment of:**

- hyperuricaemia associated with high grade haematological malignancies
- prevention of complications of tumour lysis syndrome

**Indications (see also separate guideline):**

- Induction or salvage therapy of AML, ALL, high grade lymphoma, high grade multiple myeloma with
  - High LDH (>ULN)
  - Renal failure
  - High proliferation index (Ki67>80%; consider if Ki67>50%)
  - High uric acid (>420 umol/L or 7mg/ml)

Further to the above, consider using rasburicase in those patients unable to tolerate aggressive hydration.

**Protocol for use:**

1. Ensure patient (male or female) is G6PD negative prior to use (if positive, use aggressive hydration with allopurinol – consider higher doses based on risk of TLS and creat level).
2. Ensure aggressive hydration as per chemotherapy protocols.
3. At initiation of treatment, for uric acid levels of:
   - a) < 420 umol/L (7mg/L), give a single 3mg dose of rasburicase.
   - b) >420 umol/L (7mg/L), give a single 6mg dose of rasburicase.
4. Local policies should be followed with regard to collecting blood samples and laboratory monitoring.
5. Start allopurinol as per protocols the morning after rasburicase given.
6. Measure uric acid levels as per tumour lysis (TLS) protocols and at least daily until TLS resolved.
7. During TLS monitoring, if uric acid levels >20 umol/L (>0.3 mg/L), or renal failure worsens, give another 1.5–6 mg rasburicase, as indicated by level and clinical parameters of TLS.

**References:**


**Special warnings and precautions for use**

Allergic reactions may occur with this product, patients should be closely monitored and full resuscitation facilities should be at hand. Should any serious allergic or anaphylactic reaction occur treatment should be immediately discontinued and appropriate resuscitation given.

Caution should be exercised in patients with a history of atopic allergies.

Administration of rasburicase decreases serum uric acid to below normal levels, **but has no direct effect in reversing hyperphosphataemia, hyperkalaemia and hypocalcaemia. If severe these abnormalities should be corrected following standard treatment guidelines.**

There are limited data available to recommend the sequential use of rasburicase and allopurinol.

To ensure accurate measurement of uric acid plasma level during treatment with rasburicase, a strict sample handling procedure must be followed to minimise ex vivo degradation of the analyte. Local policies should be followed with regard to collecting blood samples and laboratory monitoring.
Appendices

Appendix 1: 2 Week Wait Referral Forms
- North West London
- South East London
- South West London

Appendix 2: Treatment of Children

Appendix 3: Treatment of Teenagers and Young Adults
- Teenagers and Young Adults PTC Referrals
- Teenagers and Young Adults MDT Proforma

Appendix 4: LCA Key Worker Policy

Appendix 5: LCA Holistic Needs Assessment Tool

Appendix 6: NCSI Treatment Summary

Appendix 7: LCA Specialist Palliative Care Referral Form

Appendix 8: LCA Referral Criteria to Specialist Palliative Care