Risk Stratifying Adult Patients with Suspected or Diagnosed Cancer during the COVID-19 Pandemic (exc National Screening) for Hodgkin's and Non-Hodgkin's Lymphoma (HL, NHL)

Purpose of this document:	To provide clear processes for all Provider Trusts to implement with regard to the clinical management of Adult Patients with suspected or diagnosed **Hodgkin's and Non-Hodgkin's Lymphoma** cancer through the COVID-19 pandemic, in order that patients are treated consistently and equitably across the Region. Please refer to this document in conjunction with GM Cancer COVID-19 Cancer Management SOP V1 (for instruction on processes relating to management of patients in Somerset).
Exclusions:	This paper relates to Adult Patients only. Children, Teenage and Young Adult Cancers should be managed in accordance with normal protocol. Excludes National Screening Programme
Version Control:	
V FINAL	FINAL. Authors: Eleni Tholouli with thanks to colleagues across GM for their contribution. In line with national guidance issued 17.03.20, 19.03.20)

1. Introduction

This document sets out the process to be implemented in relation to the cessation and risk stratification of Adult Patients with suspected or diagnosed cancer in the event that diagnostic and treatment resources are limited as a result of the COVID-19 pandemic, or where clinical risk exceeds normal treatment or diagnostic pathways.

Given the rapid changes, this document is expected to be updated, in line with any changes to National Guidance.

2. Key Message

ANY PATIENTS WHO MAY REQUIRE CANCER DIAGNOSTICS, EVEN IF THIS IS POST PANDEMIC, **MUST** BE RETAINED BY THE TRUST **AND** REMAIN ON A PTL, **AND** ON A DEDICATED COVID WAITING LIST.

ONLY PATIENTS WHO DO NOT NEED ANY SECONDARY CARE APPOINTMENTS OR DIAGNOSTICS ON A SUSPECTED CANCER PATHWAY CAN BE DISCHARGED.

3. PTL Management

Clinical Leads should risk stratify PTLs in accordance with the following criteria and categorise into the appropriate group:

Action	Criteria
Step Down	As per normal PTL management on receipt of all necessary diagnostic results and a non-cancer decision. No change to current practice.
Safe Discharge	Following review and no suspicions of cancer/no further diagnostics required. Telephone Assessment Criteria: Review by telephone may be appropriate if chemotherapy is not required, this should be considered especially in at risk groups

Suspend	Patients may be suspended after clinical review by a consultant if a low grade lymphoma is suspected, the patient is stable and risk of further investigation outweighs benefit. <u>Patients requiring assessment</u> • SVCO • Cord compression • B-symptoms (drenching sweats, profound fatigue, unexplained fever) • Symptomatic or bulky lymphadenopathy (>5cm) or splenomegaly (>5cm below costal margin)
Active Management	i) Outpatients/diagnostics identified as appropriate ii) Manage according to current process with clear clinical engagement Diagnosis and indications for treatment to be made according to existing regional and national guidelines. All patients should be screened for COVID19 prior to commencement of intensive chemotherapy. **General principles** Try to minimise or avoid visits to the hospital for treatment, scans or follow-up appointments. Wherever safe to do so: • Conduct consultations by telephone or videoconference to reduce hospital footfall – including patients on treatment. • Lengthen the interval between hospital appointments. • Avoid interim imaging in patients clinically responding to therapy, unless interim imaging is used to direct therapy within a standard protocol (e.g. interim PET in first line HL). • Avoid bone marrow aspirates and trephine for staging. • Consider abbreviating treatment where no overall survival advantage is expected. • Consider reducing the intensity of treatment to lower the risk of myelosuppression and immunosuppression, but balance this carefully against the risk of treatment failure. • For clinical trials that remain open, please refer to trial-by-trial guidance from the study sponsor and your institution. **Hodgkin lymphoma (HL)** As Hodgkin lymphoma is curable in most patients, delivery of dose- and time-intensive treatment remains a high priority. **Early stage HL**

	Combined modality approach with reduced number of chemo regimens should be considered. Options would include: • ABVD x 2 + 20Gy ISRT for early favourable. • 'Rapid' approach: ABVD x 3 and then no further treatment if PET neg or a 4th and RT if PET positive (omitting RT would reduce footfall to the hospital considerably). • ABVDx4 and ISRT for early unfavourable. **Advanced stage HL** • A RATHL approach for most patients appears optimal. Escalated BEACOPP / BEACOPDac is more intensive and very steroid rich although for very poor risk patients it may still be optimal. Reducing the prednisolone to 7 days should be considered (this is standard in some countries). • Consider no radiotherapy to initial bulk if interim PET (iPET2) negative (standard of care in many centres now). • Interim PET (iPET2) scanning is still advisable in order to have confidence to omit the bleomycin after 2 cycles. If iPET2 is positive, escalated BEACOPP / BEACOPDac is not proven in a randomised trial to be of benefit. If iPET2 is Deauville score 4 then consider completing 6 cycles of ABVD and at the end of treatment using consolidation radiotherapy to sites of iPET2 DS 4 positivity. Patients with a Deauville 5 score at iPET2 should still be considered for a change in treatment: escBEACOPDac, BEACOPP-14 or a salvage approach. • For patients who are interim PET negative (iPET2), consider omitting end of treatment scan. **Elderly HL in ABVD / AVD unfit** • Radiotherapy alone can be considered for early stage. • A period of watch and wait maybe considered for asymptomatic patients. • If systemic treatment is needed, suggest dose modifying regimens (e.g. ChlVPP, VEPMB) and using reduced number of cycles to enter a remission. **Relapsed HL** • If early stage / low volume, could defer treatment although needs careful discussion with patient. • For early stage relapse, consider radiotherapy as consolidation without a stem cell transplant (although would need to be explained this is not standard of care). • Consider single agent brentuximab earlier in treatment algorithm to avoid salvage chemotherapy (NHSE approved)

	• Consider nivolumab earlier on and after brentuximab to replace salvage chemotherapy (NHSE approved). • Consider outpatient chemotherapy regimen for 1st line relapse such as GDP. • Bendamustine is particularly T-cell suppressive and should probably be avoided. • Allogeneic stem cell transplant is the most immunosuppressive procedure that can be performed and should if possible be avoided during the COVID-19 pandemic. **Nodular LP HL** • Watch and wait if possible, radiotherapy for symptomatic site or single agent rituximab. • If chemotherapy is needed, suggest R-CVP unless high grade transformation in which case R-CHOP is indicated. • Consider Rituximab monotherapy if available. **Low grade Non-Hodgkin's lymphoma (LG-NHL)** **Previously untreated FL, MZL and LPL** • Consider watchful waiting for patients not requiring immediate therapy. • If symptom control is required, consider local radiotherapy, corticosteroids or single agent rituximab. • For those requiring systemic therapy, consider less myelosuppressive regimens e.g. R-CVP or O-CVP (for FL). If on bendamustine or CHOP, consider dose reductions e.g. day 1 bendamustine only. Use GCSF routinely if using R-CHOP and bendamustine as per local policy. • Try to avoid escalating therapy unless patients have progressed or the risk of COVID-19 infections/infectious complications has significantly reduced. **Previously untreated MCL** • Consider watchful waiting for patients not requiring immediate therapy. • If symptom control is required, consider local radiotherapy or corticosteroids. • Consider oral ibrutininb in first line instead of IV chemotherapy (NHSE approved) • For younger patients (65 and less), high dose cytarabine regimens remains optimal. If using a Nordic approach, standard dose CHOP is acceptable. An autograft in this situation would be relatively low priority. • For older, fit patients, consider R-CHOP with GCSF cover

	and add maintenance rituximab when possible. Bendamustine should probably be avoided. • Consider dose reduced R-CHOP, R-CVP or R-chlorambucil for older/frailer patients. **Any patients on induction treatment** • Consider switching to a less myelosuppressive regimen especially if patients are experiencing infective complications, myelosuppression or hypogammaglobulinaemia. • Consider shortening the course of treatment e.g. 4 cycles instead of 6 for patients responding to treatment. • Try to avoid escalating therapy unless patients have PD or have transformed. **Patients on maintenance treatment** • Consider temporarily stopping (or not starting) maintenance therapy for all patients. Maintenance therapy may be started/re-started after the pandemic, especially for patients with mantle cell lymphoma. • For any patient planned for ASCT, consider deferring this if possible (liaise with transplant team if appropriate). **High grade Non-Hodgkin's Lymphoma (HG-NHL)** For most patients with aggressive lymphoma subtypes, treatment is delivered with curative intent so this remains the clinical priority. **First-line Burkitt's lymphoma** • First-line therapy with standard protocols (R-CODox-M/R-IVAC or DA-EPOCH-R) remain the recommended approaches for BL. Use of ambulatory care to reduce exposure time to hospital should be accommodated wherever possible. For CODox-M, consider giving the methotrexate 3g/m2 over 3h as probably less toxicity. **First line DLBCL (includes DHL and histological transformation of indolent NHL)** • Consider R-CHOP with GCSF support cover for the vast majority of patients with all (non-Burkitt) aggressive B cell lymphomas. There are no randomised data to support a survival advantage of using more intensive regimens, which are likely to confer additional risk during the COVID-19 pandemic. • Consider the omission of consolidation radiotherapy to bulk

	unless there is convincing evidence of residual disease on the end-of-treatment PET-CT. • Where radiotherapy is employed, consider a hypofractionated approach. • Consider restricting CNS prophylaxis to those in the highest risk groups (e.g. testicular, adrenal or renal involvement). **First-line primary mediastinal B cell lymphoma (PMBL)** • Consider using RCHOP14 as a dose-intensive outpatient regimen. • Randomised evidence to support the omission of consolidation radiotherapy after RCHOP is not yet available although retrospective data supports this. Consider omission for those who are PET negative at EOT. • Consider hypofractionated radiotherapy consolidation in line with current guidance. • If DA-EPOCH-R can be delivered in an ambulatory setting and the strategy is to omit consolidation radiotherapy for those in CR, this may be a reasonable option for selected patients. **First line primary CNS lymphoma** • Please refer to existing BSH guidance for primary CNS lymphoma. • Consider reducing the number of dose cytarabine doses per cycle within the MATRix regimen to avoid early toxicity, prolongation of inpatient stay and reduced risk of admission to intensive care. Also consider reducing / omitting thiotepa in patients > 60 or 65 years, taking into account PS and co-morbidities. • However, such decisions need to be balanced carefully against the risk of early disease progression and the consequences thereof. • For ASCT consolidation, consider reducing the thiotepa dose to a total of 10mg/kg (rather than 20mg/kg) given that there are no data to support superiority of 20mg/kg over 10mg/kg and that the higher dose is associated with higher toxicity, risking a longer inpatient stay and risk of ICU admission. **Secondary CNS lymphoma** • Treatment pathways and protocols are expected to largely follow existing practice with additional consideration for dose reductions of myelosuppressive chemotherapy agents, carefully balancing risk and benefit for individual patients.

	Peripheral T-cell lymphomas • CHOP with GCSF support remains the standard of care for first-line therapy of peripheral T cell lymphomas. • On an individual patient basis, consider the omission of ASCT consolidation, for which a survival benefit has not yet been clearly established. **Relapsed/refractory aggressive lymphoma** • Treatment pathways for relapsed aggressive lymphoma are largely expected to follow existing pathways with the caveat that restricted bed and/or ICU capacity at some institutions may restrict therapies such as stem cell transplantation and/or CAR-T cell therapy. • Wherever possible, deliver salvage regimens in the ambulatory setting. • Consider restricting multi-agent salvage therapy to those patients on a curative pathway. • Consider polatuzumab + rituximab +/- bendamustin as bridging therapy for approved CAR-T, for before and after apheresis **Relapsed FL** • Switch IV rituximab to SC when combined with lenalidomide in FL • Use GCSF liberal after chemotherapy to minimise neutropenic periods. All patients should receive quinolone, cotrimoxazole and acyclovir prophylaxis. • High grade NHL and HL will be treated following regional guidelines and standard protocols. • Low grade lymphoma with life threatening complications will require treatment, otherwise a watch & wait approach is recommended, deferring treatment for 8-12 weeks. Consider using RCVP or RCHOP rather than Bendamustine or Fludarabine based regimes as these may be less immunosuppressive. Consider administering chemo at 4 instead of 3-weekly intervals pending patient and disease factors. For patients on maintenance antibody therapy should be deferred for 4 months as risk is likely to outweigh any benefit. Maintenance can be reinstated when COVID19 is controlled. • Autologous and allogeneic SCTs with curative intent continue to be performed as per clinical indication.

4. Management of Long Term Follow Up/CNS lists/Recently treated patients (patients NOT on a live PTL)

Clinical Leads to review FU clinic waiting lists/recent treatment lists and categorise into groups to safely discharge/suspend with review date/actively manage.

Action	Criteria
Safe Discharge	Following review and no further input from secondary care required. No specific guidance. Continue normal follow up
Suspend	Consider telephone consults or deferring stable patients for 3-6 months.
Active Management	Manage according to current process with clear clinical engagement Remote consultations (eg by telephone) should be offered to patients. Blood test monitoring may be required although the risk of attendance should be minimised where possible (eg symptomatic patients should not attend, appointments should be made to avoid congestion in waiting rooms, blood tests in GP surgeries or other less busy phlebotomy services at a different hospital). Arrangements for this will vary according to local policies. Consider deferring any monitoring scans for 3-6 months

5. Management of New GP/Dental Referrals (excludes National Screening Programmes)

Each tumour group should ensure processes are in place for the daily triage of referrals and follow the following tumour specific guidance:

PLEASE NOTE:
Referrals cannot be rejected without discussion with primary care. Patients may be discharged after telephone appointments **if cancer is no longer suspected and there is no longer need for any cancer diagnostics**. Telephone appointments can now be counted as 'first seen appointment' as per national guidance.

1. Cancer Services / Booking Centre: distribute referrals as per tumour group decision.
2. Cancer Services / Booking Centre: Register patients on PAS as per normal process

3. Clinical leads: review emails daily in accordance with criteria of safely discharge after review if cancer no longer suspected and no further cancer investigations needed/suspend with review date/actively manage and respond to generic email.

Action	Criteria
Safe Discharge (following review and no further input from secondary care required)	No haematological malignancy is found. May be referred to other speciality.
Suspend	As per PTL
Active Management	Manage according to current process with clear clinical engagement – see point 3 as per PTL

MDT/sMDT Guidance:

- Maintain weekly MDT: remotely if needed
- Aim to minimise number of staff present at MDT e.g. 1 surgeon, 1 oncologist, 1 pathologist, 1 radiologist and one Breast Care Nurse

6. Annotation - delays/treatment plan changes on Cancer Tracking system

If general delays (identified through referral management and tracking) are observed, the recording of formal clinical prioritisation (following PTL clinical review and prioritising), and the recording of treatment types offered that would not normally be considered outside of the COVID-19 pandemic (From MDT / treatment planning) must be formally documented for each patient (see SOP).

7. Clinical Prioritisation

Surgery	If theatre space is limited consider interventional radiology for lymph node / mass biopsy Note that lymphomas can be difficult to diagnose on core biopsy, then those with indications for treatment or suspected high grade lymphoma should be prioritised
Radiotherapy	Prioritise for life or organ threatening lymphadenopathy, SVCO and cord compression. All other indications should be discussed at MDT, balancing risks and benefits carefully.
SACT	High grade NHL and HL, both have cure rates above 50% and should be considered as per NICE guidance as priority 1.

	Consideration should be given in old and frail patients as to the risk/benefit of treatment.

8. Alternative treatment given / recommended

Clinical Leads should use the following criteria when making decisions that result in changes to a patient's treatment from that which would have been offered prior to the COVID-19 pandemic.

9. Research

NA

10. References

1. https://lymphoma-action.org.uk/healthcare-professionals/lymphoma-treatment-and-covid-19-healthcare-professionals

2. https://www.nice.org.uk/guidance/ng161

3. http://www.bsbmtct.org/wp-content/uploads/2020/03/BSBMTCT-recommendations-for-COVID-Adult-BMT-27th-March-2020.pdf

4. https://www.ebmt.org/ebmt/news/coronavirus-disease-covid-19-ebmt-recommendations-update-march-23-2020