Appendices

Appendix 1: International Myeloma Working Group diagnostic criteria

Symptomatic myeloma

All three criteria needed for diagnosis:

- Monoclonal plasma cells in marrow ≥10%
- Monoclonal protein in serum or urine (unless non-secretory; if so, need ≥30% monoclonal plasma cells in bone marrow)
- Evidence of myeloma related organ or tissue impairment:
  - Hypercalcaemia (>10.5 mg/dL (2.6 mmol/L) or upper limit of normal)
  - Renal insufficiency (serum creatinine >2 mg/dL (176.8 µmol/L)
  - Anaemia: haemoglobin <100 g/L or 20 g below normal range
  - Lytic bone lesions, osteoporosis, or pathological fractures

Asymptomatic myeloma

Both criteria needed for diagnosis:

- Monoclonal protein ≥30 g/L or monoclonal plasma cells in marrow ≥10%
- Absence of myeloma related organ or tissue impairment

MGUS

All three criteria needed for diagnosis:

- Monoclonal protein <30 g/L
- Monoclonal plasma cells in bone marrow <10%
- Absence of myeloma related organ or tissue impairment

Appendix 2: Main side effects of drugs used to treat myeloma[4]

Corticosteroids
Gastrointestinal side effects, hyperglycaemia, immunosuppression, insomnia and altered mood

Alkylating agents (cyclophosphamide, melphalan)
Nausea, myelosuppression

High dose melphalan
Mucositis, gastrointestinal toxicity, alopecia

Thalidomide*
Constipation, somnolence, sensorimotor peripheral neuropathy, autonomic neuropathy (less common), bradycardia, altered thyroid function, increased thrombotic risk

Bortezomib
Sensory neuropathy—can be painful, autonomic neuropathy—postural hypotension, altered bowel habit, thrombocytopenia, reactivation of varicella zoster virus

Lenalidomide*
Constipation, fatigue, myelosuppression, Increased risk of thrombosis.

*Because this drug has teratogenic effects, conditions of a pregnancy prevention programme must be fulfilled for all male and female patients before the drug is prescribed.

Appendix 3: Staging of non-Hodgkin lymphoma based on Ann Arbor classification

Early stage

- I—Single nodal area
- II—More than one nodal area, but does not cross the diaphragm

Advanced stage

- III—Both sides of diaphragm involved
- IV—Extranodal or bone marrow involvement

Suffix

- A—No B symptoms
- B—B symptoms (fever, night sweats, and weight loss)
- E—Extranodal disease (localised extranodal disease, Stage 1E)

Reference: Lister TA, Crowther D, Sutcliffe SB Report of a committee convened to discuss the evaluation and staging of patients with Hodgkin's disease: Cotswolds meeting J Clin Oncol 1989 7(11) 1630-6

Appendix 4: Sources of information and support

For patients with lymphoma

- Lymphoma Action (https://lymphoma-action.org.uk/) provides information literature and support to patients with lymphoma and runs a "buddy" scheme that matches newly diagnosed patients with a patient who has already been through a similar diagnosis
- Macmillan Cancer Support (www.macmillan.org.uk) offers medical, psychological, and financial support to patients diagnosed with cancer
- Several helpful patient groups exist, such as "Living with follicular lymphoma" on Facebook (www.facebook.com/follicularlymphoma1/)
- Cancer Research UK (www.cancerresearchuk.org/about-cancer/non-hodgkin-lymphoma) provides information about symptoms, risk factors, incidence statistics, treatment, and trials for non-Hodgkin lymphoma

For patients with myeloma

- Macmillan Cancer Support gives information for patients with MGUS (www.macmillan.org.uk/information-and-support/diagnosing/causes-and-risk-factors/pre-cancerous-conditions/mgus.html) and myeloma (www.macmillan.org.uk/information-and-support/myeloma).
- Myeloma UK (www.myeloma.org.uk) provides information for patients with myeloma
- Cancer Research UK (www.cancerresearchuk.org/about-cancer/myeloma), provides information about symptoms, risk factors, incidence statistics, treatment, and trials for myeloma

For patients with CLL

- Cancer Research UK provides specific help for patients living with CLL www.cancerresearchuk.org/about-cancer/chronic-lymphocytic-leukaemia-cll
- CLL Support Association is a patient led UK charity, whose mission is to support and empower Chronic Lymphocytic Leukaemia (CLL) patients, their families and their carers through education and access to reliable, relevant and current information. www.cllsupport.org.uk
- The Chronic Lymphocytic Leukaemia Support Association (CLLSA) is also a patient led charity founded in the UK in 2005 which aims to provide support to patients with CLL and their families/carers. They provide information about developments in CLL treatment and research and provide opportunities for awareness raising and mutual support, including the opportunity to meet at UK conferences several times each year www.healthunlocked.com/cllsupport

Appendix 5: Binet and Rai Staging Systems

Staging systems for chronic lymphocytic leukaemia (CLL)

Stage	Definition	Median survival
Binet system		
Binet A	Hb ≥ 10.0 g/dl, thrombocytes ≥100 × 10^9 /l, <3 lymph node regions	>10 years
Binet B	Hb ≥ 10.0 g/dl, thrombocytes ≥100 × 10^9 /l, ≥3 lymph node regions	>8 years
Binet C	Hb < 10.0 g/dl, thrombocytes <100 × 10^9 /l	6.5 years

Each of the following would constitute "1 lymph node region" -

- Head and neck (this counts as one area, even if more than one group of nodes is enlarged).
- Axillae (involvement of both axillae counts as one area).
- Groins, including superficial femorals (involvement of both groins counts as one area).
- Palpable spleen and/or liver

Rai system		
Low risk		
Rai 0	Lymphocytosis >15 × 10^9 /l	>10 years
Intermediate risk		
Rai I	Lymphocytosis and lymphadenopathy	>8 years
Rai II	Lymphocytosis and hepatomegaly and/or splenomegaly with/without lymphadenopathy	
High risk		
Rai III	Lymphocytosis and Hb < 11.0 g/dl with/without lymphadenopathy/organomegaly	6.5 years
Rai IV	Lymphocytosis and thrombocytes <100 × 10^9 /l with/without lymphadenopathy/organomegaly	

Appendix 5: Diagnostic work up for CLL

Table 1.
Diagnostic and staging work-up

	Pretreatment evaluation	Response evaluation
History, physical examination and performance status	+	+
Complete blood count and differential	+	+
Serum chemistry including serum immunoglobulin and direct antiglobulin test	+	+
Cytogenetics (FISH) for del (17p)/molecular genetics for *TP53* mutation	+	–
Marrow aspirate and biopsy	+[a]	+[b]
Hepatitis B and C, CMV and HIV serology	+	–

[a] Only if clinically indicated.
[b] Only for confirmation of CR within clinical studies.
FISH, fluorescence *in situ* hybridisation; CMV, cytomegalovirus; HIV, human immunodeficiency virus; CR, complete remission.