Clinical Guidelines for Plasma Cell Malignancies

Reference Number	Version	Status	Executive Lead(s) Name and Job Title	Author(s) Name and Job Title	
13-2H-108	5		Dr Helen Barker MDT Lead Clinician	Professor J Snowden Dr A Chantry Dr Y Ezaydi	
Approval Body		SY Region Haematology MDT		**Date Approved**	31/05/2019
Ratified by		The Sheffield Teaching Hospitals NHS Foundation Trust (STHFT), Barnsley Hospital NHS Foundation Trust (BHNFT), Chesterfield Royal Hospital NHS Foundation Trust (CRHFT), Doncaster and Bassetlaw Hospitals NHS Foundation Trust (DBHNFT) and The Rotherham NHS Foundation Trust (TRFT)		**Date Ratified**	31/05/2019
Date Issued		May 2019		**Review Date**	May 2020
Contact for Review Name and Job Title: Sarah Platton, MDT Coordinator					

For more information on this document please contact:-

Insert names of authors of the section: **Professor J Snowden**
Dr A Chantry
Dr Y Ezaydi

Version History

Version	Date Issued	Brief Summary of amendments	Owner's Name:
1			Professor J Snowden Dr A Chantry Dr Y Ezaydi
2	24/05/16	Imaging investigations updated Solitary Plasmacytoma of Bone and Extramedullary Plasmacytoma treatment updated	Professor J Snowden Dr A Chantry Dr Y Ezaydi
3	05/05/17	New Myeloma late effects guidelines added	Professor J Snowden
4	09/05/18	Additional treatment lines added including Carfilzomib and Dexamethasone Ixazomib, Lenalidamide and Dexamethasone Daratumumab Monotherapy	Dr A Chantry
5	May 2019	Lenalidomide maintenance Lenalidomide 1st line DVd 2nd line and Lenalidomide 2nd line Pomalidomide for 4th and later lines	Dr Y Ezaydi Dr Y Ezaydi Dr Y Ezaydi Dr Y Ezaydi

(Please note that if there is insufficient space on this page to show all versions, it is only necessary to show the previous 2 versions)

Contact Details
Dr Helen Barker, Haematology MDT Lead Clinician.
Helen.barker@sth.nhs.uk

Sarah Platton, Haematology MDT Coordinator
Sarah.platton@sth.nhs.uk

Index

Important: these South Yorkshire Regional network guidelines should be read in conjunction with:

1) **BCSH Guidelines for Diagnosis and Treatment of Multiple Myeloma (BSH Website)**
2) **BCSH Guidelines for Supportive Care in Multiple Myeloma 2011 (BSH website)**
3) **IMWG Update criteria for the diagnosis of Multiple Myeloma (Lancet Oncology 2014;15:e538-48)**
4) **NICE Guideline – Myeloma: diagnosis and management (nice.org.uk, 2016)**
5) **BSH Guidelines for screening and management of late and long-term consequences of myeloma and its treatment. (BSH Website, 2017)**

Definition of Multiple Myeloma and other plasma cell malignancies

Diagnostic Criteria

The International Myeloma Working Group 2013 & Revised IMWG diagnostic criteria October 2014

Diagnosis	Diagnostic Criteria: All Three Required
Symptomatic multiple myeloma	• Monoclonal plasma cells in the bone marrow >/=10% and/or presence of a biopsy-proven plasmacytoma • Monoclonal protein present in the serum and/or urine • Myeloma-related organ dysfunction (>/=1) **[C] Calcium elevation** in the blood (Corrected serum calcium >0.25 mmol/l above the upper limit of normal or >2.75 mmol/l) **[R] Renal insufficiency** (serum Creatinine>173 µmol/l) **[A] Anaemia** (hemoglobin 20 g/l below the lower limit of normal or haemoglobin <100 g/l) **[B] Lytic bone lesions** (MRI, CT or PET scan may clarify)

Monoclonal gammopathy of undetermined significance (MGUS)	• Serum monoclonal protein low[e]
	• Monoclonal bone marrow plasma cells <10%
	• No evidence of end-organ damage attributable to the clonal plasma cell disorder:
	  ○ Normal serum calcium, haemoglobin level and serum creatinine
	  ○ No bone lesions on full skeletal X-ray survey and/or other imaging if performed

	○ No clinical or laboratory features of amyloidosis or light chain deposition disease
Smouldering or indolent myeloma[f]	• Monoclonal protein present in the serum 3 g per 100 ml or higher or • Monoclonal plasma cells 10% or greater present in the bone marrow and/or a tissue biopsy • No evidence of end-organ damage attributable to the clonal plasma cell disorder: ○ Normal serum calcium, haemoglobin level and serum creatinine ○ No bone lesions on full skeletal X-ray survey and/or other imaging if performed ○ No clinical or laboratory features of amyloidosis or light chain deposition disease
Solitary plasmacytoma of bone	• Biopsy-proven plasmacytoma of bone in a single site only. X-rays and magnetic resonance imaging and/or • FDG PET imaging (if performed) must be negative outside the primary site. • The primary lesion may be associated with a low serum and/or urine M-component • The bone marrow contains no monoclonal plasma cells • No other myeloma-related organ dysfunction

Revised International Myeloma Working Group diagnostic criteria for multiple Myeloma and smouldering multiple myeloma October 2014:

NB: Recommends that the name 'asymptomatic myeloma' be replaced by 'smouldering myeloma'

Definition of multiple myeloma:

Clonal bone marrow plasma cells ≥10% or biopsy-proven bony or extramedullary Plasmacytoma* and any one or more of the following myeloma defining events:
· Myeloma defining events:

· **Evidence of end organ damage** that can be attributed to the underlying plasma cell proliferative disorder, specifically:
  · **[C]** Hypercalcaemia: serum calcium >0.25 mmol/L (>1 mg/dL) higher than the upper limit of normal or >2.75 mmol/L (>11 mg/dL)
  · **[R]** Renal insufficiency: creatinine clearance <40 mL per min † or serum creatinine >177 μ mol/L (>2 mg/dL)
  · **[A]** Anaemia: haemoglobin value of >20 g/L below the lower limit of normal, or a haemoglobin value <100 g/L
  · **[B]** Bone lesions: one or more osteolytic lesions on skeletal radiography, CT, or PET-CT ‡

· **Any one or more of the following biomarkers of malignancy**:
  · Clonal bone marrow plasma cell percentage* ≥60%
  · Involved:uninvolved serum free light chain ratio§ ≥100
  · >1 focal lesions on MRI

Definition of smouldering multiple myeloma
Both criteria must be met:
· Serum monoclonal protein (IgG or IgA) ≥30 g/L or urinary monoclonal protein ≥500 mg per 24 h and/or clonal bone marrow plasma cells 10–60%
· Absence of myeloma defining events or amyloidosis

Non-secretory Myeloma

· No M-protein in serum and/or urine with immunofixation
· Bone marrow clonal plasmacytosis ≥10% or plasmacytoma
· Related organ or tissue impairment (end organ damage, including bone lesions)

Solitary Plasmacytoma of Bone

1. Plasma cell features as for myeloma with aberrant phenotype by immunohistochemistry +/- clonal Ig.
2. The criteria for risk assessment used in MGUS will also apply.

Extramedullary Plasmacytoma

1. Extra-medullary mass of clonal plasma cells with aberrant phenotype, determined using imaging and biopsy confirmation.
2. Normal results on skeletal survey including radiology of long bones
3. Histologically normal marrow aspirate and trephine.

Monoclonal Deposition Disease (including amyloidosis)

This includes **primary amyloidosis** and **light chain deposition disease**. Almost all cases will have neoplastic plasma cells in the bone marrow.

Diagnostic Criteria

1. Diagnosis of amyloid by Congo red stain.
2. Low level of marrow infiltration by neoplastic plasma cells. The diagnostic criteria used for MGUS and myeloma will apply.

Plasma cell leukaemia (PCL)

PCL is a rare, yet aggressive form of multiple myeloma characterized by high levels of plasma cells circulating in the peripheral blood. PCL can either originate de novo (primary or PPCL) or as a secondary leukemic transformation of multiple myeloma (secondary PCL). The diagnosis requires that:

- WBC >10×109/L, at least 2×109/L are circulating plasma cells, or
- WBC <10×109/L, at least 20% must be plasma cells.

In an analysis of the Surveillance, Epidemiology, and End Results (SEER) database, there were 49,106 patients with multiple myeloma; 291 had plasma cell leukemia (0.5%).

Laboratory and Clinical Features

Bone Marrow Features:

1. At least 10% plasma cells by morphology or flow cytometry.
2. Interstitial, diffuse or nodular patterns of marrow infiltration.

Myeloma Related Organ or Tissue Impairment (end organ damage) Due to the Plasma Cell Proliferative Process

- Calcium levels increased: serum calcium 0.25 mmol/L (>10 mg/L) above normal or >110 mg/L (2.75 mmol/L)
- Renal Insufficiency:eGFR <40ml/min or serum creatinine >177 µmol/L (>2 mg/dL)
  .
- Anaemia: haemoglobin 2 g/dL below normal or haemoglobin <10 g/dL
- Bone lesions: Lytic lesions or osteoporosis with compression fractures (MRI or CT may clarify)
- Other: symptomatic hyperviscosity, amyloidosis.

(****CRAB)

Lab Investigation

Essential Investigations for all patients with suspected plasma cell disorders

- Full Blood Count
- Serum immunoglobulins, serum electrophoresis/immunofixation & serum free light chains
- Urinary Bence-Jones protein
- Urea, creatinine and calcium
- Bone Marrow aspirate and trephine and cytogenetics – essential if MRD is to be used to determine risk though may not be appropriate for all suspected MGUS patients.
- ß2 microglobulin and albumin – used to calculate the International Staging System (ISS), see section

Prognostic Factors

Laboratory investigations to provide prognostic information

Use the same sample for all diagnostic and prognostic tests on bone marrow, so people only have to have one bone marrow aspirate and trephine biopsy.

When performing a bone marrow aspirate and trephine biopsy to provide prognostic information:

- Perform fluorescence in-situ hybridisation (FISH) on CD138-selected bone marrow plasma cells to identify the adverse risk abnormalities t(4;14), t(14;16), 1q gain, del(1p) and del(17p)(TP53 deletion). Use these abnormalities alongside International Staging System (ISS) scores to identify people with high-risk myeloma.
- Consider performing FISH on CD138-selected bone marrow plasma cells to identify the adverse risk abnormality t(14;20), and the standard risk abnormalities t(11;14) and hyperdiploidy.
- Consider performing immunophenotyping of bone marrow to identify plasma cell phenotype, and to inform subsequent monitoring.

- Consider performing immunohistochemistry (including Ki-67 staining and p53 expression) on the trephine biopsy to identify plasma cell phenotype and give an indication of cell proliferation, to provide further prognostic information.
- Perform serum-free light-chain assay and use serum-free light-chain ratio to assess prognosis.

Imaging investigations

Imaging for people with suspected myeloma

- Offer imaging to all people with a plasma cell disorder suspected to be myeloma.
- Consider whole-body MRI as first-line imaging.
- Consider whole-body low-dose CT as first-line imaging if whole-body MRI is unsuitable or the person declines it, or depending on local availability
- Only consider skeletal survey as first-line imaging if whole-body MRI and whole-body low-dose CT are unsuitable or the person declines them or depending on local availability
- Do not use isotope bone scans to identify myeloma-related bone disease in people with a plasma cell disorder suspected to be myeloma.

Imaging for people with newly diagnosed myeloma

- For people with newly diagnosed myeloma or smouldering myeloma who have not had whole-body imaging with 1 of the following, consider whole-body imaging to assess for myeloma-related bone disease and extra-medullary plasmacytomas with one of:
    - MRI
    - CT
    - fluorodeoxyglucose positron emission tomography CT (FDG PET-CT).
- Consider baseline whole-body imaging with MRI or FDG PET-CT for people who have non-secretory myeloma or suspected or confirmed soft tissue plasmacytomas and have not already had either of these tests.

(For guidance on imaging for people with suspected spinal cord compression, see the NICE guideline on metastatic spinal cord compression.)

Prognostic Factors in MGUS

The presence of normal plasma cells by multi-parameter flow cytometry and a normal serum free light chain ratio are associated with a low risk of progression. Abnormal serum free light chain (FLC) ratio is an important risk factor for progression and is independent of the size and type of the serum monoclonal protein.

Treatment

Assessment of response

Rajkumar et al., Blood, 2011

The overall response assessment to therapy i.e. PR, VGPR, CR, stringent CR, is a combination of bone marrow assessment, serological assessment (paraprotein, serum free light chains) and imaging where appropriate.

Response subcategory	**Response criteria**
Stringent Complete Response (sCR)	Negative immunofixation on the serum and urine and Disappearance of any soft tissue plasmacytomas and ≤5% plasma cells in bone marrow[a] and Normal free light chain (FLC) ratio and Absence of clonal cells in the bone marrow[a] by immunohistochemistry or immunofluorescence[b]
Complete response (CR)	Negative immunofixation on the serum and urine and Disappearance of any soft tissue plasmacytomas and ≤5% plasma cells in bone marrow[a]
Very Good Partial Response (VGPR)	Serum and urine M-protein detectable by immunofixation but not on electrophoresis or 90% or greater reduction in serum M-protein plus urine M-protein level <100mg per 24 hour.
Partial Response (PR)	≥50% reduction in the serum M-protein and reduction in 24-h urinary M-protein by ≥90% or to <200mg per 24h. If the serum and urine M-protein are unmeasurable, a ≥50% decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria. If the serum and urine M-protein are unmeasurable and serum free light assay is also unmeasurable, ≥50% reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma cells percentage was ≥30% In addition to the above listed criteria, if present at baseline, a ≥50% reduction in the size of soft tissue plasmacytomas is also required.
Stable disease (SD)	Not meeting the criteria for CR, VGPR, PR or progressive disease.
Progressive disease (PD)	Any one or more of the following: Increase of 25% from baseline in • Serum M-component and/or (the absolute increase must be ≥0.5g/dL) • Urine M-component and/or (the absolute increase must be ≥200mg/24h *Only in patients without measurable serum and urine M-proteins levels*: • the difference between involved and uninvolved FLC levels. The absolute increase must be >10mg/dL • Bone marrow plasma cell percentage; the absolute % must be ≥10% • Definite development of new bone lesions or soft tissue plasmacytomas or definite increase in the size of existing bone lesions or soft tissue plasmacytomas • Development of hypercalcaemia (corrected serum calcium >11.5mg/dL or 2.65mmol/L) that can be attributed solely to the plasma cell proliferative disorder

[a] Confirmation with repeat bone marrow biopsy is not needed

[b] Presence/absence of clonal cells is based upon the K/λ ratio. An abnormal K/λ ratio by immunohistochemistry and/or immunofluorescence requires a minimum of 100 plasma cells for analysis. An abnormal ratio reflecting presence of an abnormal clone is K/λ of >4:1 or <1:2.

[c] Measurable disease is defined by at least one of the following 3 measurements: serum M-protein ≥1g/dL (≥10g/L); urine M-protein ≥200mg/24h; serum FLC assay: involved FLC level ≥10mg/dL (≥100mg/L) provided serum FLC ratio is abnormal

Primary Treatment

All patients should receive bisphosphonate therapy in the form of iv Zoledronic acid or Oral sodium clodronate unless otherwise contra-indicated.
All suitable patients should be considered for NCRI-supported clinical intervention studies. Patients should be divided into 2 groups according to suitability for transplant.

Suitable for transplant

For patients where HDT with autologous stem cell re-infusion (ASCT) is planned, or is a possible future option, the aim of initial treatment is to:

- Induce high remission rates (>VGPR optimally) quickly and easily with minimal toxicity
- Mobilise adequate numbers of stem cells
- Complete ASCT safely with quick engraftment
- Obtain high remission rates (>VGPR, ideally CR/sCR) post-ASCT with long PFS and OS

Patients should be offered entry into a NCRI portfolio clinical trial, if available .
Phase III RCT data supports the use of IMIDs, in combination with proteasome inhibitors and steroids, in previously untreated patients. Therefore, VTD, thalidomide in combination with a steroid (e.g. Dexamethasone) and Bortezomib are recommended as first line therapy for patients proceeding to high dose therapy.
For patients intolerant of or refractory to a Bortezomib -based combination, CTD induction therapy is recommended.
In patients with renal impairment or in those with PCL, a Bortezomib-based induction therapy is recommended as first-line.
Lenalidomide maintenance should be considered although not funded in NHS yet, but has good evidence from Myeloma XI trial.

A thorough Thrombo-embolic risk assessment should be conducted (see table) in patients receiving thalidomide-based therapy and patients should be closely monitored for clinical evidence of VTE. In patients with high-risk scores (>1 additional major risk factor for VTE) LMWH is recommended. In patients with no other VTE risk factors, aspirin 75-150 mg o.d. may be considered as VTE prophylaxis unless contraindicated.

For selected patients, an Allogeneic stem cell transplant may be appropriate (http://bsbmt.org/indications-table/) and should be discussed with the Transplant Team.

Venous thrombo-embolic disease risk factors and management in MM

Individual/Myeloma risk factors 1. New diagnosis MM 2. Hyperviscosity 3. Personal/family history of VTE 4. Obesity (Body Mass Index >30) 5. Co-morbidities: cardiac, diabetes, AKI/CKD, chronic inflammatory disease 6. Immobility (acute or chronic) 7. Thrombophilias, myeloproliferative disorders haemoglobinopathies 8. Recent surgery (within 6 weeks): neuro-, trauma, orthopaedic, general, other 9. Medications: erythropoiesis stimulating agents, hormone replacement therapy, tamoxifen/stilboestrol	If no risk factors (RF) or only 1 RF consider aspirin If 2 or more RF present consider either: LMWH (high risk prophylactic dose e.g. enoxaparin 40 mg od) or Warfarin (target INR 2.5)
Myeloma therapy 1. Doxorubicin 2. High-dose steroid (≥480 mg/month dexamethasone or equivalent) 3. Combination chemotherapy	LMWH (high risk prophylactic dose e.g. enoxaparin 40 mg od) or Warfarin (target INR 2.5)
Bleeding risk factors: 1. Active bleeding 2. Haemophilia or other known bleeding disorder 3. Platelet count <$100x10^9$/l 4. Acute stroke in previous month (haemorrhagic or ischaemic) 5. Blood pressure >200 mmHg systolic or >120 mmHg diastolic 6. Severe liver disease (abnormal PT or known varices) 7. Severe renal disease (Creatinine clearance <30 ml/min) 8. Undergoing procedure or intervention with high bleeding risk	The presence of a bleeding risk factor should prompt clinicians to consider whether bleeding risk is sufficient to preclude pharmacological thrombo-prophylaxis.

Unsuitable for transplant:

Older and/or less fit patients should be offered entry into a NCRI portfolio clinical trial or other Myeloma UK clinical trials, if available. For such patients, RCT evidence indicates that initial therapy should consist of a thalidomide-containing regimen in combination with an alkylating agent and steroid e.g. CTDa, MPT. In instances where thalidomide is not tolerated or contra-indicated, then a Bortezomib-based combination may be used e.g. VMP.
The other option where thalidomide is not tolerated or contra-indicated is Lenalidomide with Dexamethasone to be continued till disease progression as per recent NICE guidelines.

Primary plasma cell leukaemia

Consider Bortezomib-based and/or Lenalidomide-based combination induction chemotherapy for people with primary plasma cell leukaemia.
Consider high-dose melphalan-based autologous stem cell transplantation for people with primary plasma cell leukaemia if they are suitable. Younger patients should also be considered for allogeneic transplantation, given the poorer prognosis of plasma cell leukaemia.

Managing acute renal disease caused by myeloma

Consider immediately starting a Bortezomib- and dexamethasone-based combination regimen for people with untreated, newly diagnosed, myeloma-induced acute renal disease.
If a Bortezomib-based combination regimen is unsuitable for people with untreated, newly diagnosed, myeloma-induced acute renal disease, consider immediately starting a thalidomide- and dexamethasone-based combination regimen[1].
Do not perform plasma exchange for myeloma-induced acute renal disease.

Second Line and subsequent Treatment

Patients should again be divided into 2 groups according to suitability for transplant:

Suitable for transplant in second line

- Patients should be offered entry into a NCRI or MUK CTN portfolio clinical trial, if available.
- If not entering into a clinical trial, all suitable patients at first relapse should receive a Bortezomib-based re-induction regimen (Vd or DVd: Daratumumab, Velcade, Dex). Patients failing to achieve >PR at 4 cycles are eligible for refund of the drug costs as per the VRS.
- A second ASCT is an appropriate consolidation modality in second line in patients who have either not received an ASCT in first-line or who have attained >12 months freedom-from-disease progression from a prior ASCT (http://bsbmt.org/indications-table/)
- If Bortezomib is contra-indicated or has been utlilised in first line, then a thalidomide-based combination may be used. In some circumstances (e.g. prior neuropathy) where a Bortezomib-based combination has been used in first-line, then Lenalidomide and dexamethasone may be used. However, though within the license of Lenalidomide, this is currently not approved by NICE and warrants funding requests. Thrombo-prophylaxis while on thalidomide/Lenalidomide should be individually risk-assessed and managed with the determined risk category.
- Allogeneic transplants may be suitable for selected patients and should be discussed with the STH Myeloma/Transplant Team.
- If poor response to a Bortezomib-based or thalidomide-based combination (i.e. no response after 4 courses) then consider instituting a Lenalidomide-based combination or a more intensified chemotherapy regimen e.g. DT-PACE, VD-PACE, intermediate-dose melphalan (70-100mg/m2).

Unsuitable for transplant in second line

- Patients should be offered entry into a clinical trial if available .
- Under the NICE FAD, all suitable patients at first relapse should receive Bortezomib based combination Vd or DVd: Daratumumab, Velcade, Dex
- If Bortezomib is contra-indicated, the other option is Lenalidomide Dex as per recent NICE guidelines.
- Melphalan Prednisolone/ melphalan & prednisolone & Thalidomide / C-weekly/ dexamethasone alone
- Consider tertiary referral for novel therapies
- EPO should be considered for continuing anaemia following chemotherapy
- Palliative RT for symptoms, nerve compression-related symptoms and bone disease as indicated.

Carfilzomib and Dexamethasone

- Carfilzomib in combination with dexamethasone is recommended as an option for treating multiple myeloma in adults, only if they have had only 1 previous therapy, which did not include Bortezomib (Carfilzomib for previously treated multiple myeloma NICE Technology Appraisal TA457)

Subsequent Therapy

Patients should be offered entry into a NCRI portfolio clinical trial (including Myeloma UK CTN trials) or a NCRI Industry portfolio trial, if available.

Off trial, available treatment regimens include

- Lenalidomide and dexamethasone (Rd) - Lenalidomide 25mg/Day PO D1-21 with Dexamethasone 40mg Day 1, 8, 15, 22

- Ixazomib, Lenalidomide and Dexamethasone Triplet Regimen now available for suitable

patients via CDF after NICE Technology Appraisal TA505 07/02/2018 (Supporting refs include Moreau et al, NEJM Vol 374; 17 April 2016, Chrissy et al, JCO Vol 35:12 April 2017)

Nb - a thorough Thrombo-embolic risk assessment should be conducted in patients receiving Lenalidomide-based therapy and patients should be closely monitored for clinical evidence of VTE. In patients with high-risk scores (>1 additional major risk factor for VTE) LMWH is recommended. In patients with no other VTE risk factors, aspirin 75-150 mg o.d. may be considered as VTE prophylaxis unless contraindicated.

- Daratumumab monotherapy is now NICE approved as a fourth line treatment (Usmani S et al, Blood, 2016); NICE Technology Appraisal TA10076

- Panobinostat, Bortezomib and Dexamethasone may also be considered as a subsequent line of therapy in patients who have received an IMID and Bortezomib previously.
- Pomalidomide and Dexamethasone via CDF after NICE guidelines.

Subsequent therapy should be considered on an individual patient basis taking into account prior treatment responses and treatment tolerability, alongside available independent patient funding. Patients should be offered entry into a suitable NCRI portfolio clinical trial (including Myeloma UK CTN trials) or a NCRI Industry portfolio trial.

Examples of potentially suitable regimens include:

- Bortezomib, thalidomide and dexamethasone (VTD)

- Bendamustine, Thalidomide and Dexamethasone (BTD)

- Thalidomide, Dexamethasone, Etoposide, Doxorubicin, Cyclophosphamide & cis-Platin (DT-PACE)

- Thalidomide, Idarubicin, Dexamethasone and Etoposide (TIDE).

Solitary Plasmacytoma of Bone and Extramedullary Plasmacytoma

Single, isolated lesions are potentially curable with radical radiotherapy, if patient sufficiently fit. Recommend referral to Clinical Oncology. Patients require indefinite follow-up on a 3 monthly basis in view of the risk of evolution to myeloma.

Amyloidosis

Primary and Relapse Treatment

- Consider referral to the National Amyloid Centre, Royal Free Hospital
- Treatment options include:
    1. VCD or CTD chemotherapy
    2. Stem cell transplantation (discuss with STH Myeloma/Transplant Team).
    3. Intermediate-dose melphalan
    4. Melphalan and prednisolone
    5. Bortezomib containing therapy
    6. Radiotherapy

All suitable patients should be considered for NCRI-supported clinical intervention studies.

For detailed guidance refer to BCSH Amyloid guideline from the following link:
http://www.bcshguidelines.com/pdf/ALamyloidosis_210604.

Late effects and long term consequences of myeloma and its treatments

The publication of national British Society for Haematology (BSH) Guidelines on Late Effects and Long Term Consequences of Myeloma (Snowden, Greenfield et al 2017 accessible via the guidelines section of the BSH website) includes routine (mainly annual or at change of treatment) physical and psychosocial screening assessments for patients with myeloma, whether they have been treated with transplant or not.
There are also recommendations for vaccinations and other measures for infection prophylaxis, where appropriate.
We recommend that clinicians implement these guidelines locally in their units with input and coordination for clinical nurse specialist and other colleagues.
Professor Diana Greenfield is also able to take referrals in her Late Effects Clinic in Sheffield, with input from Professor Snowden and linked endocrinology, cardiovascular, bone, respiratory, infection/vaccination and psychological services as required.
Referrals should be directed to Professor Greenfield with Professor Snowden copied in, although patients will be seen according to current waiting list prioritisation and this should be balanced against local implementation of the BSH Guidelines and assessment of patients by their routine myeloma team.