



Provided by the author(s) and University of Galway in accordance with publisher policies. Please cite the published version when available.

Title	Multiple myeloma: managing a complex blood cancer
Author(s)	Dowling, Maura; Kelly, Mary; Meenaghan, Teresa
Publication Date	2016-09-10
Publication Information	Dowling, Maura, Kelly, Mary, & Meenaghan, Teresa. (2016). Multiple myeloma: managing a complex blood cancer. <i>British Journal of Nursing</i> , 25(16), S18-S28. doi: 10.12968/bjon.2016.25.S18
Publisher	Mark Allen Healthcare
Link to publisher's version	https://doi.org/10.12968/bjon.2016.25.S18
Item record	http://hdl.handle.net/10379/14695
DOI	http://dx.doi.org/10.12968/bjon.2016.25.S18

Downloaded 2023-03-31T18:39:16Z

Some rights reserved. For more information, please see the item record link above.



Multiple Myeloma: managing a complex blood cancer

Maura Dowling

School of Nursing and Midwifery,
National University of Ireland, Galway, Ireland.
Phone: 091 493833
E-mail: maura.dowling@nuigalway.ie

Mary Kelly

Advanced Nurse Practitioner (Haematology)
Regional Oncology Haematology Day Unit
Tullamore General Hospital,
Co.Offaly,
Ireland
Phone: 057 9321501
Fax: 057 9358559

Email: marybkelly@hse.ie

Teresa Meenaghan

Advanced Nurse Practitioner (Haematology)
Galway University Hospital,
Newcastle Road,
Galway,
Ireland
Phone: 091 524222
Email: teresameenaghan@eircom.net

Abstract

This paper provides a comprehensive overview of multiple myeloma (MM), a complex blood cancer involving over production of the plasma cells. Although MM remains incurable, patients are living longer as a result of multiple treatment options. However, MM patients are also living with a higher symptom burden. The overall aim in managing MM is therefore to control disease progression, prolong survivorship and improve quality of life.

Key words: multiple myeloma, fatigue, infection, bone health, peripheral neuropathy, renal failure.

Introduction

MM is a B cell malignancy resulting in uncontrolled production of plasma cells (Palumbo *et al* 2011). These plasma cells overproduce immunoglobulins (heavy and light-chain Monoclonal proteins) known as a paraprotein which build up in the bone marrow (Kyle and Rajkumar, 2009). MM is the 17th most common cancer in the UK with approximately 5,500 new cases in 2013. This accounts for approximately 2% of cancers in the UK (Cancer Research UK, 2013). Data for England show that MM is almost twice as common in black people as in white and Asian people (Cancer Research UK, 2013). Furthermore, the median patient age at diagnosis is around 70 years, therefore co-morbidities contribute to patients' health status and treatment outcomes (Palumbo *et al* 2011).

The cause of MM is unknown, however it is known that the production of paraprotein in MM is associated with specific chromosomal abnormalities (deletions or translocations on the chromosomes- for instance t(4;14), t(14;16), and del(17p) (Tewari *et al*, 2012; Vangsted *et al*, 2012). These specific chromosomal abnormalities can determine which treatment options may be more effective against the disease and the long term prognosis.

MM is a highly treatable cancer, however it remains an incurable disease. Nonetheless, advances in treatment and symptom management have resulted in patients living longer. However, increased survival has resulted in patients living with an increasing array of treatment-related and disease-related co-morbidities (Snowden *et al*, 2011).

Reaching a diagnosis of MM

MM causes a variety of clinical signs and symptoms, most typically anaemia, bone pain as a result of lytic lesions as a result of bone destruction, renal insufficiency, hypercalcaemia, and increased risk of infection (Coleman et al, 2011). However, symptoms of MM, especially bone pain or fatigue can be misinterpreted as non-urgent which can delay the diagnosis (Drurie, no date).

A range of investigations are required to diagnose MM including, bone marrow biopsy, skeletal survey, serum protein electrophoresis (SPEP), beta 2 microglobulin, serum free light chains (SFLC), and kidney function blood tests (NICE, 2016). In addition, fluorescence in situ hybridization (FISH) studies are now recommended for all patients at diagnosis (Pratt et al, 2014; NICE, 2016). FISH uses fluorescently labelled DNA probes that can recognise and bind to damaged genes and allows the identification of genetic abnormalities (Adler, 2016). This helps in determining prognosis and what treatment is most appropriate.

Criteria used for diagnosing MM has evolved as our knowledge of this cancer has improved. Previously MM was diagnosed using criteria requiring evidence of specific end-organ damage, i.e. hypercalcemia, renal failure, anaemia, or bone lesions (CRAB features) (i.e. C=Calcium (elevated); R= Renal failure; A=Anaemia; B=Bone lesions) (Rajkumar, 2011). Patients with clonal plasma cell proliferation without CRAB feature were then classified as having: monoclonal gammopathy of undetermined significance (MGUS) or smouldering multiple myeloma (SMM). Patients with MGUS have no anaemia, hypercalcaemia, bone lesions or renal insufficiency related to M-protein production. These patients also have an M-protein of less than 3 g/dL and fewer than 10% plasma cells in the bone marrow (Kyle, no date). SMM resembles MGUS in that there is no end-stage organ damage present, however there is at least 3 g/dL of M-protein and more than 10% plasma cells in the bone marrow (Kyle et al, 2007).

Both conditions carry a risk of progression to malignancy, but the risk is higher with SMM (Kyle et al, 2007).

However, in 2014, the International Myeloma Working Group (IMWG) revised the disease definition of MM to enable early diagnosis before end-organ damage occurred (Rajkumar et al, 2014). This change came about for a number of reasons, including the identification of specific biomarkers that can accurately distinguish patients with SMM with a high probability of progression to MM within 2 years. This development has resulted in patients with the higher risk of SMM being treated early and the patients with low risk of progression to MM to be observed closely (Rajkumar et al, 2012).

MM is staged using the Revised International Staging System (RISS), which creates three distinct stages (Palumbo et al, 2015) (Table 1), useful in predicting survival.

Table 1

Revised International Staging System for Myeloma (Palumbo et al, 2015, Rajkumar, 2016)

Stage I	Stage II	Stage III
5 yr. survival = 82%	5 yr. survival = 62%	5 yr. survival = 40%
All of the following: -Serum albumin \geq 3.5 gm/dL -Serum beta-2-microglobulin $<$ 3.5 mg/L -No high-risk cytogenetics -Normal serum lactate dehydrogenase level	Not fitting Stage I or III	Both of the following: -Serum beta-2-microglobulin $>$ 5.5 mg/L -High-risk cytogenetics [t(4;14), t(14;16), or del(17p)] or Elevated Serum lactate dehydrogenase level

--	--	--

Developments in the management of MM are constantly evolving. For instance, an important development has been progress in the classification of MM at a molecular level which means that treatments specific to subtypes of MM can now be given (Rajkumar, 2016). Rajkumar (2016) outlines these developments highlighting examples such as the heavy chain gene translocations t(4;14) MM which appears to have less risk of bone disease at diagnosis and responds well to bortezomib-based induction and maintenance and t(14;16) which presents a higher risk of renal failure at diagnosis. It is therefore recommended that these genetic abnormalities should be actively looked for when diagnosing MM in all patients in order to identify 'high-risk' myeloma (Pratt et al, 2014). Most MM patients follow these developments with great interest and organisations such as Myeloma UK are a source of updates for patients.

Treatment options

Treatment options for MM are constantly evolving. The standard front-line treatment is high-dose chemotherapy followed by autologous stem cell transplant (ASCT) (Antanackovic and Schilling, 2013). A variety of salvage treatments are then used when patients relapse.

MM remains incurable, therefore the overall aim of treatment is to control disease progression, prolong survivorship and improve quality of life. Multidisciplinary team involvement and the use of available assessment tools e.g. International Myeloma Working Group (IMWG) frailty scoring system (Palumbo et al, 2015) are important in

the assessment and treatment planning of MM patients in order to minimise toxicity and reduce disease and treatment related complications.

A variety of treatment options are used, including proteasome inhibitors (PIs), immunomodulatory drugs, (IMiDs), chemotherapy, corticosteroids, deacetylase inhibitors (DACis), and monoclonal antibodies (mAbs) (Table 2). In addition, autologous stem cell transplant (ASCT) is a first-line treatment option for many newly diagnosed MM patients, and the decision to opt for ASCT is based on the patient's age, performance status, co-morbidities and patient preference (Muta et al, 2013).

In order to understand which treatment options are used, it is useful to consider this in the context of the three main classifications of MM. Patients who have active MM can broadly be classified into three main groups, namely, newly diagnosed eligible for stem cell transplant, newly diagnosed ineligible for stem cell transplant and relapsed and/or refractory (Bird et al 2011).

Treatment options for newly diagnosed patients

Newly diagnosed patients eligible for stem cell transplant undergo autologous stem cell transplant (ASCT) (NCCN, 2014). This treatment involves an induction regimen, such as CyBorD (cyclophosphamide, bortezomib and dexamethasone), followed by stem cell harvesting via apheresis (a process where blood is removed via a central venous catheter, the stem cells are collected and the blood is then returned to the donor), then high dose chemotherapy (melphalan) and subsequent rescue with the harvested stem cells (NCCN, 2014). An important consideration with ASCT is the timing of cell harvesting and the avoidance of particular drugs before harvesting (such as Melphalan and Lenalidomide) which adversely affect the quality of harvested stem cells or stem cell yield. Induction regimens are normally given for 3-4 cycles before harvesting (Moreau et al, 2015).

For patients who are ineligible for ASCT, treatment options include combination regimens with chemotherapy, PIs or ImiDs with corticosteroids. This treatment plan may then be followed by maintenance therapy or clinical trials (Palumbo et al, 2012). All patients should be considered for clinical trial where available. It is important to stress however, that 'one size does not fit all' and treatment choice is dependent on each patient's individual factors including side effects, convenience and continuous or fixed treatment duration which can adversely affect quality of life and symptom burden.

Treatment options for relapsed and/or refractory disease

For MM patients with relapsed and/or refractory disease, the treatment picture is quite complex and similar to patients ineligible for ASCT, decisions on the best treatment are made based on individual patient characteristics (e.g. age, other co-morbidities, organ function), and also previous treatments and outcomes from that treatment (Nooka et al, 2015). For instance, the newer proteasome inhibitor, Carfilzomib, has been shown to be clinically useful for relapsed and refractory patients who have already received at least two prior therapies including a proteasome inhibitor and an immunomodulatory agent (Steele, 2013). Moreover, a recent clinical trial demonstrated that a combination of drugs that include a proteasome inhibitor, and corticosteroid with an immunomodulatory agent and a deacetylase inhibitor (QUAD) resulted in a good response in this group of patients (Vesole et al, 2016). (See table 2).

A second (salvage) ASCT is also an option for some relapsed patients. These are usually patients who had a good response to the first ASCT for over 12 months (Pratt et al, 2014). However, MM patients with high-risk cytogenetics (Table 1) at the time of the second transplant have been shown to have a higher risk of death compared to patients with standard-risk cytogenetics (Singh et al, 2015). Moreover, relapsed MM patients with a <12 month duration of response after initial ASCT are not candidates for a second ASCT because of the high risk of ASCT-related toxicity (Atanackovic and Schilling, 2013).

Table 2: Treatment options (Adapted from Colson, 2015)

Treatment	Examples	Important nursing considerations
Proteasome inhibitors (PIs)	Bortezomib	<p>Bortezomib is effective in renal impairment and when used in combination with thalidomide acts a thromboprotective agent (Bortezomib-thalidomide-dexamethasone [VTD]), therefore reduces the risk of venous thromboembolism.</p> <p>Should be given subcutaneously to reduce incidence & severity of peripheral neuropathy (PN). Rotate injection site (less reaction from stomach area).</p> <p>Patients should not take Vitamin C, alpha lipoic acid or green tea on the days they receive bortezomib therapy to avoid interference of bortezomib's activity (Miceli et al, 2011). Advise patients re fatigue.</p>
	Carfilzomib	<p>Watch blood counts for neutropenia & thrombocytopenia. Nausea and fatigue are also common. Most common serious adverse event is pneumonia (Steel, 2013). Results in a low rate of new-onset PN and does not exacerbate previous or existing PN (Morawska et al, 2015).</p>
	Ixazomib	<p>Taken orally once weekly. Approved in US for use in combination with lenalidomide and dexamethasone for relapsed myeloma. Currently under regulatory review in the EU (Shirley, 2016). More GIT adverse effects but less neurotoxicity than bortezomib (Rajkumar, 2015).</p>
Immunomodulatory drugs, (IMiDs)	Thalidomide	<p>Anti-thrombosis prophylaxis needed. Risk of peripheral neuropathy.</p>

		Women of childbearing age must use contraception from 4 weeks before commencing thalidomide until 4 weeks after treatment has finished. Men with a partner of child bearing age should also use contraception.
	Lenalidomide	All patients on lenalidomide with dexamethasone should receive antithrombosis prophylaxis (Rajkumar 2013). Risk of rash and myelosuppression. Advice re contraception as per thalidomide.
	Pomalidomide	An analog of thalidomide and lenalidomide. Recently approved for the treatment of relapsed refractory MM (Rajkumar 2016).
Chemotherapy	Cyclophosphamide	Used in combination with a proteasome inhibitor or immunomodulatory drug in regimens for relapsed and/or refractory disease. Also used in high doses before stem cell harvest. Monitor for myelosuppression and mucositis.
	Melphalan	Used in high doses as part of the ASCT regimen. Melphalan based regimens used less often due to impact of toxicities, effect on stem cell mobilisation and risk of secondary myelodysplastic syndrome (Rajkumar, 2015). Often used in primary induction therapy for ASCT-ineligible patients. Monitor for myelosuppression and mucositis.
Corticosteroids	Dexamethasone Prednisolone	Synergistic effect when used in combination with bortezomib, carfilzomib, lenalidomide, pomalidomide, and/or thalidomide. Long-term use can result in increased

		risk of infection, osteoporosis and venous thromboembolism.
Deacetylase inhibitors (DACis)	Panobinostat	Oral administration. Approved for the treatment of relapsed or refractory MM. Enhances the activity of PIs- therefore used in combination with bortezomib and dexamethasone (Greig, 2016). The main side effect is grade 3 diarrhoea (in approx. 25% of patients) (Rajkumar, 2016). Also a risk of cardiac arrhythmias (Sharma et al, 2013).
	Vorinostat	Oral dose 400mg once daily with food (Iwamoto et al 2013). Adverse events include anaemia, thrombocytopenia, fatigue, nausea and diarrhoea.
Monoclonal antibodies (mAbs)	Elotuzumab	Recently approved in US for treatment of relapsed MM (Rajkumar, 2016). Has shown good response in relapsed or refractory MM patients when combined with lenalidomide and dexamethasone (Lonial et al 2015). Monitor for transfusion reaction.
	Daratumumab	This is a CD38-targeting monoclonal antibody (Multiple myeloma cells uniformly overexpress CD38). Monitor for infusion-related reactions, most commonly grade 1 or 2. Monitor for pneumonia and thrombocytopenia (Lokhorst et al, 2015).

Managing disease and treatment-related issues

The therapies listed in Table 2 are used in combinations in the treatment of MM. Triplet regimens containing an immunomodulatory drug and a proteasome inhibitor are known to give the best responses, for instance bortezomib-thalidomide-

dexamethasone (VTD) and bortezomib-lenalidomide-dexamethasone (VRD), and are used for initial therapy in most patients (Rajkumar, 2015). However, access to novel agents is limited in some countries and treatment regimens include the use of thalidomide (e.g. cyclophosphamide-thalidomide-dexamethasone (CTD)) for newly diagnosed patients ineligible for transplant (Hungria et al, 2016).

The combination of drugs used in the management of MM has resulted in increased survivorship but it also presents a challenge for nurses in view of the myriad of possible side effects (Table 2). MM patients have reported that the side effects of treatments are the single most important predictors of unmet needs (Molassiotis et al, 2011).

Bone health

Bone lesions are usually present at diagnosis, with the most frequent sites being the vertebrae (65%), ribs (45%), skull (40%), shoulders (40%), pelvis (30%) and long bones (25%) (Zamagni and Cavo, 2012). This impacts greatly on patients' morbidity and quality of life. Bone pain is a common symptom with MM and managed with the use of analgesics.

Other complications associated with myeloma affecting the bone can be as a result of hypercalcaemia. Symptoms of hypercalcaemia occur when the damage caused by myeloma to the bone structure releases calcium into the blood. These symptoms include: loss of appetite, nausea, fatigue, confusion, thirst, muscle weakness and restlessness. These symptoms are often initially detected by nursing staff on routine patient assessments and are managed with the use of intravenous fluids and bisphosphonates treatment.

Several studies have confirmed the clinical benefit of bisphosphonates (clodronate, pamidronate and zoledronate) in the prevention and treatment of bone disease associated with MM (Alegre et al 2014). Bisphosphonates are effective inhibitors of bone resorption, while also exerting an anti-myeloma effect when combined with

other therapies (Morgan et al, 2012). Trial evidence indicates that denosumab is superior to zoledronic acid in delaying the development of skeletal-related events (Lipton et al, 2012). It is recommended that MM patients on bisphosphonate therapy should be monitored to determine if calcium and vitamin D3 supplements are required (Terpos et al, 2015).

Dental assessment and completion of dental work prior to commencing bisphosphonates is important to reduce the risk of osteonecrosis of the jaw (ONJ), a rare complication of bisphosphonate therapy, as demonstrated in a recent MRC study. The study reported 36 (3.7%) confirmed cases of ONJ in the group of MM patients who received zoledronic group compared with 5 (0.5%) confirmed cases in the clodronate group (Jackson et al, 2014). Nevertheless, Nurses who administer bisphosphonates need to be aware of ONJ, clinical signs of ONJ and its prevention and management (Morris and Cruickshank, 2010).

Fatigue

Chemotherapy and other treatments for MM can result in myelosuppression. (Table 2). A reduction in red cells will often lead to symptoms such as fatigue or shortness of breath and it is important that nurses encourage patients to talk about any symptoms of fatigue and alert them to the symptoms. Management includes blood transfusion and strategies to combat fatigue, including exercise. Erythropoietic-stimulating agents can also be used, although they are associated with thromboembolic complications (Terpos et al, 2015). However, while there is limited evidence in their use in MM patients, both the American Society of Hematology (ASH) and American Society of Clinical Oncology (ASCO) recommend their use (at the lowest possible dose) to help avoid the need for transfusions to manage anaemia (Terpos et al, 2015).

There is much evidence on the role of exercise in managing cancer-related fatigue (CRF), however, less is known in its role in MM. Groeneveldt et al, (2013) found that MM patients (n=37) who underwent stretching, aerobic and resistance exercises showed improved fatigue scores over time. Moreover, high exercise rates were reported for all MM patients, including patients aged over 70 in a recent retrospective study with 41 patients and the researchers recommend that even in the presence of bone lesions and skeletal fragility, most MM patients can safely exercise when following individualised recommendations (Shallwani et al, 2015). A chartered physiotherapist specialised in the care of cancer patients is the most suitable professional to develop a suitable exercise plan for MM patients.

Peripheral neuropathy

Peripheral neuropathy is a major issue for MM patients and can develop both from the disease and treatments used (Morowska et al, 2015). More attention is now being paid to determine if PN is present in newly diagnosed patients. In one study of newly diagnosed MM patients, mild PN was found in 19% (12 of 64) patients (Richardson et al, 2009). Treatments related to PN in MM patients include thalidomide and the proteasome inhibitor bortezomib. However, carfilzomib results in a lower rate of new-onset PN (Morowska et al, 2015) (Table 2).

Nurses can play a central role in assessing for the presence of PN among all myeloma patients. A useful tool for assessment is 11-item neurotoxicity assessment tool originally developed by Calhoun *et al* (2003) because of its ease of completion.

Pain

MM patients can experience pain early in their disease most commonly from pathological fractures to the spine (Zamagni and Cavo 2012).

Pain later in the disease most often arises from treatment –related peripheral neuropathy. A MDT and multifaceted approach (including the expertise of the palliative care team or chronic pain team) to pain management is often required. Treating the myeloma with anti-myeloma drugs (Table 2) helps alleviate the pain. Radiotherapy can also bring rapid pain relief but if undertaken prior to peripheral blood stem cells (PBSC) mobilisation (and depending on the bone sites treated) can result in some destruction of marrow stem cells which subsequently impairs stem cell collection (i.e. stem cell yield at apheresis may be reduced) (Olivieri et al, 2012). Percutaneous vertebroplasty is currently being investigated as an approach to relieve painful vertebral compression fractures and evidence suggests that it does not interfere with PBSC mobilisation, collection and transplant (Tosi et al, 2014).

Infection

Infection in MM patients is a major concern. Bilmark et al's (2015) large population study found that the risk of both bacterial and viral infection was seven times higher among MM patients when compared to matched controls. Rates of specific infections such as pneumonia and septicaemia, and viral infections such as herpes zoster and influenza were particularly high (Bilmark et al, 2015).

Another recent study which examined the clinical and microbiology records of MM patients (n = 199) identified 771 episodes of infection. Of these 771 episodes of infection, 44.6% were clinically defined, 35.5% were microbiologically defined and 19.9% were fever of unknown cause and a higher risk of infection overall was linked to treatment with chemotherapy regimens (high-dose melphalan, IV cyclophosphamide, corticosteroids), while use of ImiDs and PIs were not (Teh et al, 2016). However, Terpos et al (2015) report on studies that have shown a 14% risk of infection on regimens with lenalidomide and 30% with pomalidomide, and the European Myeloma Network recommend prophylactic antibiotics for the first three months of therapy involving these IMiDs (Terpos et al, 2015).

Viral respiratory tract infection also pose a major risk for MM patients with advanced disease being managed on multiple lines of therapy and these patients require appropriate influenza vaccination and early identification of infection (Teh et al, 2015). There is some evidence that double vaccination against influenza in MM patients appears to offer protection, however more evidence is required (Hahn et al, 2015).

There is a higher risk of herpes zoster reactivation among MM patients being treated with bortezomib-based regimens, regardless of regimen and total dose of bortezomib, and may occur in any phase of the treatment (Minarik et al, 2012). Lower doses of acyclovir or valacyclovir can be used to provide adequate prophylaxis, and should be maintained for the duration of bortezomib therapy (Minarik et al, 2012). For patients with a low IgG level and a history of severe recurrent infections immunoglobulin therapy may be beneficial (Terpos et al, 2015). Neutropenic sepsis is a risk for MM patients because of lower immunoglobulin levels and side effects from combination chemotherapy. Nurses are at the forefront in ensuring that MM patients are aware of the symptoms of impending sepsis and to seek medical help immediately if these symptoms occur.

Renal complications

All myeloma patients either have renal complications or are at risk of developing renal complications (Faiman et al, 2011). Treating myeloma with novel agents can reduce tumour burden and therefore reduce the risk of renal complications. In addition, renal disease can be reversed with use of bortezomib-based regimens (Rousseau et al, 2010). More recently, it has been shown that SC bortezomib resulted in a 30% rate of renal impairment reversal in relapsed MM patients (Moreau et al, 2015). Bortezomib-based regimens are now considered fundamental in the management of myeloma-related renal impairment (Dimopolous et al, 2016). In addition, renal assessment is recommended for these patients before receiving contrast for CT scanning. Patients

found to have renal impairment may be given a non-contrast scan or MRI because contrast CT impairs renal function.

Nurses play a unique role in early identification of renal complications and ensuring regular monitoring of serum calcium and creatine levels. Nurses are at the forefront in assessing patients' fluid intake and output and daily weights; these indicators may be the first warning of declining kidney function. Furthermore, patients should be advised on the importance of taking adequate fluids and avoiding medications that can cause renal impairment, such as non-steroidal anti-inflammatory agents (Faiman et al, 2011).

Conclusion

MM patients are experts on their illness. They have to 'work' to manage the many physical and emotional issues they face daily (Stephens et al, 2014). Therefore, they should be encouraged to be actively involved in their management. Tariman et al (2014) report on their study where all but one of the 20 older newly diagnosed symptomatic MM patients wanted to be actively involved in treatment decisions. In this study, 55% of participants preferred a shared decision-making role with their doctor and 40% preferred to reach their treatment decision in light of their doctor's opinion. Oncology/Haematology nurses, in their capacity as patients' point of contact can play a central role in promoting patient participation in shared decision-making with the medical team. This can be achieved by ensuring patients are provided with clear and comprehensive details of the treatment options being considered and encouraging patients to 'speak out' and share their preferences for decision-making with their consultant (Tariman et al, 2014). This role also includes advice on managing symptoms and educating patients on what symptoms require urgent medical assessment. Interestingly, a recent Irish study found that haematology doctors welcomed shared decision making with relapsed MM patients. The doctors interviewed expressed the view that informed patients were more aware of the

consequences and outcomes of treatment options, and shared decision making relieved them of some of the pressure when making difficult decisions regarding treatment options (Cormican and Dowling, 2016).

Patients with MM are often willing to take their chances with new treatments they are offered (Maher and De Vries, 2011). However, over time, their disease does relapse and disease progression is evident. Despite this, patients still opt for salvage therapies at the end stages of their illness which gives them false hope (Howell et al, 2010). This is the time that conversations about palliative care for symptom management should be introduced, but this is difficult, mainly because MM patients are known as 'fighters', and may not want to give up on active treatment. Nevertheless, McGrath (2013) reports that most patients with haematological malignancies are open to information on palliative care because it allows them time to plan ahead. In response to this need, Myeloma UK have recently launched a 'Planning ahead' info pack for MM patients. The pack provides patients with practical information on a number of topics related to end of life, including advice on planning ahead (Myeloma UK 2016).

In conclusion, because of treatment advances, MM patients can now be managed long-term, but this advance has resulted in high symptom burden (Johnsen et al., 2009; Molassiotis et al, 2011). It is therefore essential that they are actively supported to improve their quality of life (Molassiotis et al, 2011). Nurses play a key role in supporting MM patients. This role is evident in for instance, the standardised nurse-led risk assessment tool developed by Tolan et al (2015). This risk assessment tool (the BRAIN assessment tool) assesses patients under the following: bone, renal, anaemia, infection and neuropathy, and is used on all myeloma patients at each visit in the centre's ambulatory day service (Tolan et al, 2015). Nurses should make patients aware of available support networks and specific support avenues including the International Myeloma Foundation (IMF), Myeloma UK, Multiple Myeloma Ireland and the Myeloma Research Foundation (USA).

MM affects individual patients and families in different ways and information should therefore be tailored to meet patients' unique needs. Nurses play a key role in the delivery and co-ordination of support and information so that each MM patient can achieve the best quality of life for them.

References

- Adler EM (2016) *Living with lymphoma. A patient's guide* (2nd edition). John Hopkins University Press: Baltimore.
- Alegre A, Gironella M, Bailén A, Giraldo P (2014) Zoledronic acid in the management of bone disease as a consequence of multiple myeloma: A review. *European Journal of Haematology* **92**:181-8.
- Atanackovic D, Schilling G (2013) Second autologous transplant as salvage therapy in multiple myeloma. *British Journal of Haematology* **163**:565-72.
- Blimark C, Holmberg E, Mellqvist UH, Landgren O, Bjorkholm M, Hultkrantz ML, Kjellander C, Turesson I, Kristinsson SY (2015) Multiple myeloma and infections: a population-based study on 9253 multiple myeloma patients. *Haematologica* **100**: 107–113.
- Bird JM, Owen RG, D'Sa S, Snowden JA, Pratt G, et al (2011) Haemato-oncology Task Force of British Committee for Standards in Haematology (BCSH) and UKMyeloma Forum Guidelines for the diagnosis and management of multiple myeloma (2011). *Br J Haematol* **154**:32–75
- Cancer Research UK (2013) <http://www.cancerresearchuk.org/health-professional/cancer-statistics> accessed March 11th 2016
- Colson K (2015) Treatment-related symptom management in patients with multiple myeloma: a review. *Supportive Care in Cancer* **23**:1431-45.
- Cormican O, Dowling M (2016) Managing relapsed myeloma: the views of patients, nurses and doctors. *European Journal of Oncology Nursing* **23**: 51-58
- Dimopolous MA, Sonneveld P, Leung N, Merlini G, Ludwig H et al (2016) International Myeloma Working Group Recommendations for the Diagnosis and Management of Myeloma-Related Renal Impairment. *Journal of Clinical Oncology* **34** (in press)
- Drurie B (no date) What makes it so difficult to diagnose Multiple Myeloma. International Myeloma Foundation. <http://myeloma.org/ArticlePage.action?articleId=640> (Last accessed June 15th 2016)

Faiman BM, Mangan P, Spong J, Tariman JD (2011) Renal complications in multiple myeloma and related disorders: Survivorship care plan of the international myeloma foundation nurse leadership board. *Clinical Journal of Oncology Nursing* **15** (SUPPL.), 66-76.

Greig SL (2016) Panobinostat: A Review in Relapsed or Refractory Multiple Myeloma. *Targeted Oncology* **11**:107-14.

Hahn M, Schnitzler P, Schweiger B, Kunz C, Ho AD, Goldschmidt H, et al. (2015) Efficacy of single versus boost vaccination against influenza virus in patients with multiple myeloma *Haematologica* **100**:e285-e8.

Hungria VTM, Crusoé EQ, Maiolino A, Bittencourt R, Fantl D, Maciel JFR, et al. (2016) Phase 3 trial of three thalidomide-containing regimens in patients with newly diagnosed multiple myeloma not transplant-eligible. *Annals of Hematology* **95**(2):271-8.

Iwamoto M, Friedman EJ, Sandhu P, Agrawal NGB, Rubin EH, Wagner JA (2013) Clinical pharmacology profile of vorinostat, a histone deacetylase inhibitor. *Cancer Chemotherapy and Pharmacology* **72**:493-508.

Jackson GH, Morgan GJ, Davies FE, Wu P, Gregory WM, Bell SE, et al. (2014) Osteonecrosis of the jaw and renal safety in patients with newly diagnosed multiple myeloma: Medical Research Council Myeloma IX Study results. *British Journal of Haematology* **166**:109-17.

Johnsen AT, Tholstrup D, Petersen M., Pedersen L, Groenvold M (2009) Health related quality of life in a nationally representative sample of haematological patients. *European Journal of Haematology* **83**: 139-148.

Kyle RA (no date) What is MGUS? What is the difference between MGUS and multiple myeloma? International Myeloma Foundation.
<http://myeloma.org/ArticlePage.action?articleId=638>. Accessed June 15th 2016

Kyle RA, Rajkumar SV (2009) Treatment of multiple myeloma: a comprehensive review. *Clin Lymphoma Myeloma* **9**:278–288

Kyle RA, Remstein ED, Therneau TM, et al. (2007) Clinical course and prognosis of smoldering (asymptomatic) multiple myeloma. *N Engl J Med* **356**:2582–2590.

Lokhorst HM, Plesner T, Laubach JP, Nahi H, Gimsing P, Hansson M, et al. (2015) Targeting CD38 with daratumumab monotherapy in multiple myeloma. *New England Journal of Medicine* **373**:1207-19.

Lipton A, Fizazi K, Stopeck AT, Henry DH, Brown JE, Yardley DA, et al. (2012) Superiority of denosumab to zoledronic acid for prevention of skeletal-related events: A combined analysis of 3 pivotal, randomised, phase 3 trials. *European Journal of Cancer* **48**:3082-92.

Lonial S, Dimopoulos M, Palumbo A, White D, Grosicki S, Spicka I, et al. (2015) Elotuzumab therapy for relapsed or refractory multiple myeloma. *New England Journal of Medicine* **373**:621-31.

Maher K, De Vries K (2011) An exploration of the lived experiences of individuals with relapsed Multiple Myeloma. *European Journal of Cancer Care* **20**: 267-275.

Mateos M-V, Hernández M-T, Giraldo P, et al. (2013) Lenalidomide plus dexamethasone for high-risk smoldering multiple myeloma. *N Engl J Med* **369**:438-447.

McGrath P (2013) End-of-Life Care in Hematology: Update From Australia. *Journal of Social Work in End-of-Life and Palliative Care* **9**: 96-110.

Minarik J, Pika T, Bacovsky J, Langova K, Scudla V (2012) Low-dose acyclovir prophylaxis for bortezomib-induced herpes zoster in multiple myeloma patients. *British Journal of Haematology* **159**:111-3.

Molassiotis A, Wilson B, Blair S, Howe T, Cavet J (2011). Unmet supportive care needs, psychological well-being and quality of life in patients living with multiple myeloma and their partners. *Psycho-Oncology* **20**: 88-97.

Morgan GJ, Davies FE, Gregory WM, et al. (2012) Effects of induction and maintenance plus long-term bisphosphonates on bone disease in patients with multiple myeloma: The Medical Research Council Myeloma IX Trial. *Blood* **119**: 5374-83.

Morawska M, Grzasko N, Kostyra M, Wojciechowicz J, Hus M (2015) Therapy-related peripheral neuropathy in multiple myeloma patients. *Hematological Oncology* **33**:113-9.

Moreau P, Attal M, Facon T (2015). Frontline therapy of multiple myeloma. *Blood* **125**(20), 3076-3084.

Moreau P, Pylypenko H, Grosicki S, Karamanesht I, Leleu X, Rekhtman G, et al. (2015) Subcutaneous versus intravenous bortezomib in patients with relapsed multiple myeloma: Subanalysis of patients with renal impairment in the phase iii MMY-3021 study. *Haematologica* **100**(5):e207-e10.

Muta T, Miyamoto T, Fujisaki T, et al. (2013) Evaluation of the feasibility and efficacy of autologous stem cell transplantation in elderly patients with multiple myeloma. *Internal Medicine* **52**: 63-70.

Myeloma UK (2016) *Planning ahead- an info pack for myeloma patients*. Available at <http://www.myeloma.org.uk/information/myeloma-uk-publications-list/essentials/planning-ahead-an-infopack-for-myeloma-patients/> accessed March 24th 2016

National Comprehensive Cancer Network (2014) *NCCN clinical practice guidelines in oncology, Multiple Myeloma V2.2014*

National Institute for Health and Care Excellence (NICE) (2016) Myeloma: Diagnosis and Management. NICE guidelines NU35 <https://www.nice.org.uk/guidance/ng35/chapter/Recommendations#laboratory-investigations>. Accessed June 15th 2016

Nooka A K, Kastritis E, Dimopoulos M A, Lonial S (2015). Treatment options for relapsed and refractory multiple myeloma. *Blood* **125**: 3085-3099.

Olivieri A, Marchetti M, Lemoli R, Tarella C, Iacone A, Lanza F, Rambaldi A, Bosi A (2012) Proposed definition of 'poor mobilizer' in lymphoma and multiple myeloma: an analytic hierarchy process by ad hoc working group Gruppo Italiano Trapianto di Midollo Osseo. *Bone Marrow Transplantation* **47**: 342-351.

Palumbo A, Bringhen S, Ludwig H, et al. (2011) Personalized therapy in multiple myeloma according to patient age and vulnerability: A report of the European Myeloma Network (EMN). *Blood* **118**: 4519-29.

Palumbo A, Hajek R, Delforge M, Kropff M, Petrucci MT, Catalano J, Gisslinger H, Wiktor-Jędrzejczak W, Zodelava M, Weisel K *et al* (2012) Continuous lenalidomide treatment for newly diagnosed multiple myeloma. *New England Journal of Medicine* **366**:1759-1769.

Palumbo A, Avet-Loiseau H, Oliva S, et al. (2015) Revised international staging system for multiple myeloma: A report from international myeloma working group. *J Clin Oncol* **33**:2863–2869.

Palumbo A, Bringhen S, Mateos M, Larocca A et al (2015) Geriatric assessment predicts survival and toxicities in elderly myeloma patients: an International Myeloma Working group report. *Blood* **125**: 2068-2074

Pratt G, Jenner M, Owen R, Snowden JA, Ashcroft J, Yong K, et al. (2014) Updates to the guidelines for the diagnosis and management of multiple myeloma. *British Journal of Haematology* **167**:131-3.

Rajkumar SV, Dimopoulos MA, Palumbo A, et al. (2014) International myeloma working group updated criteria for the diagnosis of multiple myeloma. *Lancet Oncol* **15**:e538–e548.

Rajkumar SV (2011) Treatment of multiple myeloma. *Nature Rev Clin Oncol* **8**:479–491.

Rajkumar SV, Merlini G, San Miguel JF (2012) Redefining myeloma. *Nature Rev Clin Oncol* **9**:494–496.

Rajkumar SV (2016) Myeloma today: Disease definitions and treatment advances. *American Journal of Hematology* **91**:90-100.

Richardson PG, Xie W, Mitsiades C et al. (2009) Single-agent bortezomib in previously untreated multiple myeloma: efficacy, characterization of peripheral neuropathy, and molecular correlations with response and neuropathy. *J Clin Oncol* **27**: 3518–3525.

Roussou M, Kastiris E, Christoulas D, Migkou M, Gavriatopoulou M, Grapsa I, Psimenou E, Gika D, Terpos E, Dimopoulos MA (2010) Reversibility of renal failure in newly diagnosed patients with multiple myeloma and the role of novel agents. *Leuk Res* **34**:1395-7.

Shallwani S, Dalzell MA, Sateren W, O'Brien S (2015) Exercise compliance among patients with multiple myeloma undergoing chemotherapy: a retrospective study. *Supportive Care in Cancer* **23**:3081-8.

Sharma S, Beck J, Mita M, Paul S, Woo MM, Squier M, et al (2013) A phase I dose-escalation study of intravenous panobinostat in patients with lymphoma and solid tumors. *Investigational New Drugs* **31**:974-85.

Shirley M (2016) Ixazomib: First global approval. *Drugs* **76**:405-11.

Singh Abbi KK, Zheng J, Devlin SM, Giralt S, Landau H (2015) Second Autologous Stem Cell Transplant: An Effective Therapy for Relapsed Multiple Myeloma. *Biology of Blood and Marrow Transplantation* **21**:468-72.

Snowden JA, Ahmedzai SH, Ashcroft J, D'Sa S, Littlewood T, Low E, et al (2011) Haemato-oncology Task Force of British Committee for Standards in Haematology and UK Myeloma Forum (2011) Guidelines for supportive care in multiple myeloma 2011. *Br J Haematol* **154**:76–103

Steele JM (2013) Carfilzomib: A new proteasome inhibitor for relapsed or refractory multiple myeloma. *Journal of Oncology Pharmacy Practice* **19**:348-54.

Stephens M, McKenzie H, Jordens CFC (2014) The work of living with a rare cancer: Multiple myeloma. *Journal of Advanced Nursing* **70**: 2800-2809.

Tariman JD, Doorenbos A, Schepp KG, Singhal S, Berry DL (2014) Older adults newly diagnosed with symptomatic myeloma and treatment decision making. *Oncology Nursing Forum* **41**:411-9.

Teh BW, Worth LJ, Harrison SJ, Thursky KA, Slavin MA (2015) Risks and burden of viral respiratory tract infections in patients with multiple myeloma in the era of immunomodulatory drugs and bortezomib: experience at an Australian Cancer Hospital. *Supportive Care in Cancer* **23**:1901-6.

Teh BW, Harrison SJ, Worth LJ, Spelman T, Thursky KA, Slavin MA (2016) Risks, severity and timing of infections in patients with multiple myeloma: A longitudinal cohort study in the era of immunomodulatory drug therapy. *British Journal of Haematology* **171**:100-8.

Terpos E, Kleber M, Engelhardt M, Zweegman S, Gay F, Kastiris E, et al. (2015) European myeloma network guidelines for the management of multiple myeloma-related complications. *Haematologica* **100**:1254-66.

Tewari P, Ryan AW, Hayden PJ, Catherwood M, Drain S, Staines A, et al (2012) Genetic variation at the 8q24 locus confers risk to multiple myeloma. *British Journal of Haematology* **156**:133-6.

Tolan C, Marry L, Lovett S, Summersby E, McCloy M, Sargent J (2015) *Using your BRAIN: a nursing risk assessment tool for myeloma patients*. Haematology Association of Ireland Annual Meeting 2015, Galway, Ireland.

Tosi P, Sintini M, Molinari AL, Imola M, Ciotta G, Tomassetti S, et al (2014) Early application of percutaneous vertebroplasty reduces pain without affecting peripheral blood stem cell (PBSC) collection and transplant in newly diagnosed multiple myeloma (MM) patients. *European Journal of Cancer Care* **23**:773-8.

Vangsted A, Klausen TW, Vogel U (2012) Genetic variations in multiple myeloma I: Effect on risk of multiple myeloma. *European Journal of Haematology* **88**:8-30.

Vesole DH, Bilotti E, Richter JR, McNeill A, McBride L, Raucci L, et al. (2016) Phase I study of carfilzomib, lenalidomide, vorinostat, and dexamethasone in patients with relapsed and/or refractory multiple myeloma. *British Journal of Haematology* **171**:52-9.

Waxman AJ, Mink PJ, Devesa SS, Anderson WF, Weiss BM, Kristinsson SY, McGlynn KA, Landgren O (2010) Racial disparities in incidence and outcome in multiple myeloma: a population-based study. *Blood* **116**: 5501–5506

Zamagni E, Cavo M (2012) The role of imaging techniques in the management of multiple myeloma. *British Journal of Haematology* **159**:499-513.