CONSENSUS GUIDELINES FOR MANAGEMENT OF BONE HEALTH IN PATIENTS WITH MYELOMA

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INTRODUCTION

Multiple myeloma (MM) is a plasma cell neoplasm, characterized by clonal proliferation of plasma cells in bone marrow that jeopardizes the normal hematopoiesis and skeletal integrity. Bone involvement is a defining feature of symptomatic multiple myeloma. Tumour cells primarily disrupt the normal balance between bone formation by osteoblasts and bone resorption by osteoclasts via secretion of various factors. At the time of diagnosis, lytic bone lesions have been reported in up to 80% of the patients.(1) These lesions predispose to the development of skeletal-related events (SREs) which have a direct adverse effect on the quality of life and overall survival.(2) SREs refer to pathologic fractures, spinal cord compression as well as the need for surgery or palliative radiotherapy for bone related complications. The cost incurred in the management of SREs ultimately escalates the overall treatment expenditure.(3-5) These guidelines are mere opinions of the experts in the absence of any major studies from India on SREs among myeloma patients but available among solid tumours.(6) Most of these guidelines are based on the western guidelines and adapted to Indian setting based on expert opinion. (7-9)

CONSENSUS GUIDELINES FOR MANAGEMENT OF BONE HEALTH IN PATIENTS WITH MYELOMA

Table 1: Summary of Recommendations for Bone Protective Agents in Multiple Myeloma

Treatment modality	Parameter	Recommendation	
BISPHOSPHONATES	Target population	Newly diagnosed symptomatic multiple myeloma requiring antimyeloma treatment (with or without bone involvement)	
	Route of administration	Intravenous	
	Frequency and duration of administration	During initial therapy – every 4 weekly After 2 years – ➢ If VGPR or better achieved – discontinue therapy (restart at the time of relapse) ➢ If ≤ PR – continue therapy less frequently at three monthly interval (if tolerated)	
	Algorithm at baseline and during therapy **CARD**	**C**	**Counselling** regarding adverse events (ONJ, renal failure)
		A	**Advise** to maintain good oral hygiene
		R	**Renal** failure monitoring (at baseline, monthly thereafter) and 24 hours urine protein evaluation
		D	**Dental** check-up preferably before initiation and during therapy based on symptoms
	Choice of bisphosphonate	➢ **First choice** – Zoledronate ➢ **Second choice** – Pamidronate ➢ Ibandronate - For patients who cannot regularly attend outpatient clinic	
DENOSUMAB	Target population	➢ Newly diagnosed symptomatic multiple myeloma requiring antimyeloma treatment (with or without bone disease), **AND** ➢ Presence of renal failure (Serum creatinine > 2 mg/dL)	
	Route of administration	Subcutaneous (120 mg)	
	Frequency and duration of	During initial therapy – every 4 weekly	

	administration		
	Algorithm at baseline and during therapy **CARD**	**C**	**Counselling** regarding adverse events (ONJ, renal failure)
		A	**Advise** to maintain good oral hygiene
		R	**Renal** failure monitoring (at baseline, monthly thereafter)
		D	**Dental** check-up
BALLOON KYPHOPLASTY and VERTEBROPLASTY	Target population	➢ MM with **symptomatic** (painful) vertebral compression fractures (VCFs)	
	Choice of procedure	➢ First choice – Balloon kyphoplasty ➢ Second choice - Vertebroplasty	
RADIOTHERAPY	Target population	Transplant ineligible MM with either of the following – ➢ Uncontrolled pain from bone lesions ➢ Impending pathologic fracture ➢ Impending spinal cord compression (SCC)	
	Radiation dose and schedule	➢ First choice – 8-Gy single fraction ➢ Second choice – 30-Gy fractionated over 2 weeks	
SURGERY	Target population	MM with either of the following – ➢ Impending or actual long bone pathologic fracture ➢ Spinal cord compression (SCC) ➢ Vertebral column instability	

CONSENSUS GUIDELINES FOR MANAGEMENT OF BONE HEALTH IN PATIENTS WITH MYELOMA

BISPHOSPHONATES IN INDIAN SETTINGS

RECOMMENDATIONS

- We strongly recommend that the newly diagnosed MM (NDMM) patients with or without demonstrable osteolytic lesions on the routine skeletal survey should be initiated on bisphosphonate (BP) therapy. MM patients without detectable lytic lesions on the routine skeletal survey should be evaluated by whole body low dose CT, MRI or PET scan depending upon the availability for additional detection of osteolytic lesions and SREs.
- We strongly recommend that the NDMM patients with osteoporosis or osteopenia should be initiated on BP therapy.
- We recommend that high risk asymptomatic MM patients and monoclonal gammopathy of undetermined significance (MGUS) patients with osteoporosis should be treated with BP therapy based on the recommendations given by osteoporosis society
- We strongly recommend that intravenous (IV) administration of BPs should be preferred. If the patient cannot attend the out-patient clinic (owing to logistics/ performance status) for the administration of the monthly dose, IV infusion at home may be an effective alternative with oral BP (Ibandronate) being an inferior choice.
- We strongly recommend that IV Zoledronate (4 mg) should be preferred over other BPs because of its survival benefit and easy availability. Although Pamidronate has similar efficacy to Zoledronate, it's restricted availability in Indian market may limit the compliance to therapy. IV Pamidronate shall be considered in patients with MM and mild to moderate renal insufficiency at diagnosis/ initiating therapy (serum creatinine 1.5 - 2 mg/dL, or CrCl 30 - 60 ml/min) who cannot afford Denosumab.
- We strongly recommend that IV BPs should be administered at 4 weeks interval for a minimum duration of two years to all the NDMM patients. For the patients maintaining complete remission (CR)/ very good partial remission (VGPR), the BP therapy shall be discontinued after two years. Earlier reduction in frequency can be considered among those achieving a CR. We recommend re-initiation of BP therapy at relapse. For the patients achieving response $\leq$ partial remission (PR), BP therapy may be considered beyond two years at a reduced frequency (every 3-4 months) till disease progression depending upon the tolerability.
- We recommend comprehensive dental evaluation and patient education regarding possible dental complications and oral hygiene before starting BP therapy. However, the BP therapy

should not be deferred in lieu of a dental evaluation. MM patients who have no obvious dental abnormality (inflamed gums, loose teeth, ill-fitting denture or any obvious dental infection) shall be started on therapy without any delay. We recommend that dental hygiene should be assessed and reinforced on each hospital visit in our settings where a substantial population consumes 'pan/ gutkha' and baseline emphasis on dental hygiene is poor. Elective dental procedures should not be advised during BP therapy (dental extraction, placement of implant, any invasive elective procedure and others as detailed below).

- We strongly recommend estimation of serum creatinine before each monthly dose of IV bisphosphonate. BP therapy should be withheld from all the patients who develop serum creatinine > 2 mg/dL (or CrCl < 30 mL/min) during treatment. The rise in serum creatinine should be attributed to BP therapy only after exclusion of all other possible causes (amyloidosis, diabetic nephropathy, urosepsis, etc.). The BP therapy shall be restarted only after the normalisation of serum creatinine.
- We strongly recommend vitamin D and calcium supplementation to MM patients receiving BP therapy. Ideally, vitamin D levels should be assessed in all the newly diagnosed MM patients. Caution should be exercised in supplementing calcium to patients with renal insufficiency (creatinine > 2mg/dL or CrCl <30ml/min).

EVIDENCE

Bisphosphonates are the first class of drugs that have been successfully used in the treatment of myeloma bone disease. They are the only class of drugs among the bone protective agents which provide survival benefit. By inhibiting farnesyl pyrophosphate synthase, bisphosphonates restrict the osteolytic activity of osteoclasts. As stated earlier the evidence is from western population with data from Indian subcontinent scarce on the field.(6-9) The summary of role of various bisphosphonates in the management of SRE is tabulated in table 2.

Role in symptomatic MM patients: Oral Clodronate significantly decreased the rate of progression of osteolytic lesions, the rate of non-vertebral fractures and time to first non-vertebral fracture in NDMM patients relative to placebo. (10) Oral Clodronate has shown overall survival (OS) benefit relative to placebo in a subset of MM patients who had no vertebral fractures at baseline [HR 0.62 (0.43 – 0.87)].(11) Oral Pamidronate was ineffective in decreasing SREs in MM patients when compared to placebo. (12) Oral Ibandronate has shown no benefit in decreasing SREs and skeletal pain in MM patients relative to placebo. (13)

IV Zoledronate 4 mg and Pamidronate (90 mg) have shown similar effectiveness in reducing the incidence of SREs and bone pains in symptomatic MM patients. (14-16) IV Zoledronate showed significantly higher efficacy in comparison to oral Clodronate (MRC-IX study) reduced the risk of SREs by 26% (HR 0.74; P <0.001) in newly diagnosed MM. Zoledronate proved beneficial in decreasing SREs in MM patients with bone involvement as well as in those without it. It reduced the mortality by 16% and extended the overall survival by 5.5 months relative to clodronate (50 versus 44.5 months). However, the survival benefit of Zoledronate over Clodronate was limited to only to MM patients with bone involvement at baseline. (17) IV Pamidronate (90 mg monthly) has shown significant benefit versus placebo in reducing SREs (24% *v* 41%; P <0.001) and bone pain in newly diagnosed MM. (18) IV Pamidronate has shown marginal OS benefit versus placebo in subset of MM patients receiving second line therapy [21 versus 14 months; P = 0.083] (19)

Prospective comparison of two dosage schedules of IV Pamidronate (30 mg monthly versus 90 mg monthly) has shown similar effectiveness in delaying the occurrence of SREs with a tendency towards superior safety profile with 30 mg dose in newly diagnosed MM patients. (20) Recently, the option of less frequent Zoledronate dosing in myeloma patients was explored. In a randomized controlled trial that included 1822 patients with metastatic bone involvement (due to breast carcinoma, prostate cancer, or myeloma), Zoledronate administration every 12 weeks didn't increase the risk of skeletal related events over two years when compared to standard every 4 weekly dosing. (21) The Z-MARK study demonstrated that once in 12 weeks Zoledronate administration could safely sustain a low SRE rate among MM patients previously treated with standard (monthly) Zoledronate therapy (for 1 or 2 years). (22)

Role in asymptomatic MM patients: In 'asymptomatic' MM patients, Zoledronate and Pamidronate (60 to 90 mg) have shown benefit in decreasing bone involvement and SREs at the time of progression to symptomatic MM but they didn't alter the risk of progression per se. (23, 24)

Role in MGUS patients: Zoledronate has shown significant benefit in improving in axial and appendicular bone mineral density (BMD) in MGUS patients with osteopenia or osteoporosis. (25)

There is no evidence to support bisphosphonate therapy in solitary plasmacytoma.

Table 2: Role of various bisphosphonates in the management of SRE in Myeloma

Survival benefit and intrinsic anti-myeloma effect	IV Zoledronate only	
Efficacy in reducing SREs	IV Zoledronate ~ IV Pamedronate > Clodronate (oral) > Ibandronate	• Ibandronate has no proven benefit in reducing SREs in MM patients • Oral Pamidronate has no proven benefit in reducing SREs in MM patients • IV Pamidronate 30 mg comparable to IV Pamidronate 90 mg in terms of reduction in SREs • Zoledronate reduces SREs irrespective of patient being on Thalidomide maintenance
Efficacy in reducing bone pain	IV Zoledronate ~ IV Pamidronate (30 mg) ~ IV Pamidronate (90 mg) > Clodronate > Ibandronate	Ibandronate has no proven benefit in ameliorating bone pain in MM patients

TREATMENT DURATION

In MRC-IX trial, the survival benefit and lower incidence of SREs among MM patients receiving Zoledronate relative to clodronate were observed in those patients who received bisphosphonate therapy for at least 2 years. (26) MM patients who sustained remission for more than 2 years have been shown to exhibit improvement in bone mineral density (BMD) even without bisphosphonate therapy. Such improvement in BMD beyond 2 years has been attributed to the sustained response to antimyeloma therapy. (27)

VITAMIN D DEFICIENCY IN MM

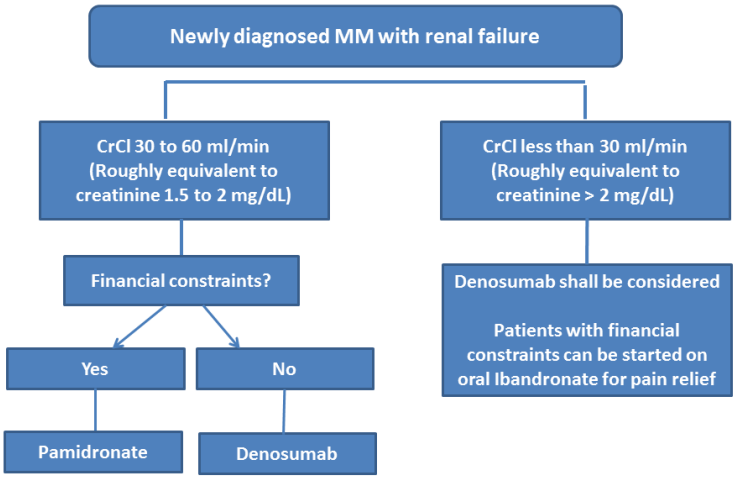
75% newly diagnosed MM patients in one study were found to have Vitamin D deficiency or insufficiency. The majority of vitamin D deficient MM patients responded to supplementation with 50000 IU vitamin D twice weekly for 6 weeks. No correlation was observed between Vitamin D status and myeloma activity. (28) The beneficial role of combination of Vitamin D and bisphosphonate therapy has been studied in other osteoporotic conditions such as postmenopausal state but similar studies are lacking in myeloma.(29) In patient with bony metastasis, the Vitamin D was found to increase the bone resorption and decrease the efficacy of the bisphosphonate therapy.(30) Considering the high incidence of baseline Vitamin D deficiency in India (31) it is a contemporary issue requiring prospective studies.

IV BISPHOSPHONATES ADMINISTRATION AND RENAL FAILURE

Higher dose and rapid infusion have been identified as the strongest risk factors for bisphosphonate therapy related renal failure. (32-34) In patients with mild to moderate renal impairment (CrCl rate

30 to 60 m/min), reduction in Zoledronate dose without changing infusion duration has been recommended. (9, 35) In patients with mild to moderate renal impairment (CrCl rate 30 to 60 m/min), reduction in Pamidronate dose and increase in infusion duration (> 4 hours) has been recommended. (9) In patients with severe renal impairment (CrCl < 30 mL/min), the use of Zoledronate and Pamidronate is not recommended. (9) The choice of bisphosphonates versus denosumab is illustrated in the flow chart in Fig. 1.

Fig 1: Selecting bone antiresorptive drugs in NDMM patients with Renal Impairment



BISPHOSPHONATES AND OSTEONECROSIS OF JAW (ONJ)

ONJ refers to an exposed bone in the mouth that doesn't heal with six to eight weeks of treatment. 4% to 11% incidence of ONJ with bisphosphonate therapy in retrospective studies. Among bisphosphonates, Zoledronate has a greater reported rate of ONJ. (36, 37) In prospective studies, ONJ incidence with Zoledronate has been reported to be approximately 1% per year. (17) Dental procedures, local infections, and corticosteroids have been described as the risk factors for ONJ. (28, 36, 37) Adoption of appropriate preventive measures has shown benefit in decreasing the risk of ONJ. (38-40)

EVALUATION PRIOR TO STARTING AND DURING THERAPY

- **Dental evaluation prior to starting therapy –** Ideally, all patients must be advised a complete dental examination by a dental specialist before starting treatment* (Try not to give the impression that until the patient consults a dental specialist he can't be treated with bisphosphonates or Denosumab. Risks and benefits of anti-bone resorptive agents should be openly discussed with the patient. Substantial risk of SREs and life-threatening complications without antiresorptive therapy must be clearly explained.) Inaccessibility of a specialist dental consultation should not preclude or delay treatment. Atleast, history of any recent dental trauma or dental procedure must be elicited and

examination of the oral cavity for inflamed gums, loose teeth, ill-fitting denture or any obvious dental infection must be performed. Patients requiring a major procedure (like extraction) must be referred to a dental specialist. The antiresorptive therapy must be started at least 8 weeks after the invasive procedure (provided complete local healing has taken place). Least invasive procedures (involving endodontic techniques) shall be preferable. Dental scaling, cavity repair, crown placement and root canal treatment can be performed but wherever possible elective dental procedures must be avoided. Strongly advise **"NOT to undergo ANY dental procedure without prior consultation with the treating physician (Hematologist/ Oncologist)"**. All patients must be counselled regarding the risk of osteonecrosis of jaw. All patients must be advised to maintain good oral hygiene.

- **Monitoring during Bisphosphonate therapy:**
  - **Dental aspects in patients on bisphosphonates:** Ideally, a complete dental examination by a dental specialist must be performed at baseline and annually thereafter. Emphasis on dental hygiene at beginning and at each follow up visit. High risk patients must be identified before putting them on bisphosphonates. Ideally, any invasive dental procedure (dental extraction, placement of implant, any invasive elective procedure) must be avoided while being on bisphosphonates.
  - **Unexplained albuminuria:** Ideally, 24 hours urine albumin must be monitored every 3 to 6 monthly intervals. In case of unexplained (not attributable to amyloidosis or diabetic nephropathy) albuminuria (> 500 mg/ 24 hours), withhold IV bisphosphonate therapy until the normalisation of 24-hour urine albumin. For the sake of convenience, urine routine examination by dipstick may be performed at 3 to 6 monthly intervals and in case of positive urine dipstick for albumin, 24-hour urine examination shall be performed.
  - **Serum creatinine: A**ssessment of Serum creatinine is required before each monthly dose of IV bisphosphonate. For unexplained increase (not likely to be explained by myeloma disease activity) in serum creatinine (increase by 0.5 mg if baseline creatinine normal; increase by 1 mg if baseline creatinine abnormal), subsequent IV dose must be withheld until the normalisation of serum creatinine. Close monitoring essential particularly in elderly patients.

Table 3: Bisphosphonates available in Indian Market with price list. (The list is not all inclusive and is based on market survey)

S. No.	Brand Name	Pharma Company	MRP (in INR)	Approx cost to the patient (in INR)
INJ. ZOLEDRONATE (4 mg) preparations available in India				
1	**ZOMETA**	**NOVARTIS**	**15213**	**3600**
2	ZYCLASTIN	ZYDUS	3097	INR 300 - 900 per vial. ##These products are available in AMRIT Pharmacy (Govt of India initiative) in the price range of INR 300 - 400. However, their availability is inconsistent.
3	ZOLTERO	HETERO	2650	
4	BIDOLENIC	BDR	2700	
5	ZOLDONAT	NATCO	2990	
6	**ZOBONE**##	SUN PHARMA	3017	
7	ZORRENT	TORRENT	2500	
8	ZOLDREA	CIPLA	2800	
9	ZOLEDAC	AUREATE	2850	
10	**ZOLASTA**##	INTAS	3334	
11	ZOLDRO	UNITED BIOTECH	2745	
12	ZOLDRONE	GETWEL	2650	
13	ZOLGET	GETWEL	2650	
14	ZOLCARE	HUMO	3375	
15	ZOLTRUST	PANACEA	1595	
16	BLAZTERE	DR REDDY'S	3212	
17	**ZOLON**##	CELON	3100	
18	ZOLDRIC	ZUVIUS	3200	
19	ZYFOSS	FRESENIUS KABI	2933	
20	ZOLEBENZ	CADMA	1450	
21	ZOLTER	BARTER & MARCIN PHARMA	3100	
INJ. PAMIDRONATE (90 mg) preparations available in India				
1	MEDRONATE	HEALTH BIOTECH	3490	1500
2	AREDIA*	NOVARTIS	***Manufacturing & marketing of these products has been stopped by the respective pharma companies for the last 5 – 6 years**	
3	PAMIRED*	DR REDDY'S		
4	PAMIPHOS*	DABUR/FRESENIUS KABI		
5	BIODRONATE*	UNITED BIOTECH		
INJ. IBANDRONATE (90 mg) preparations available in India				
1	BONIMET	INTAS	2703	1500
2	BANDRONE	NATCO	2762	1500
3	IDROFOS	SUN PHARMA		

CONSENSUS GUIDELINES FOR MANAGEMENT OF BONE HEALTH IN PATIENTS WITH MYELOMA

DENOSUMAB IN INDIAN SETTINGS

RECOMMENDATIONS

- We recommend monthly treatment with subcutaneous Denosumab in NDMM patients with bone involvement who have serum creatinine > 2 mg/dL at baseline (or CrCl < 30 ml/min).
- We recommend comprehensive dental evaluation and patient education regarding possible dental complications (ONJ) and oral hygiene before starting Denosumab. However, therapy should not be deferred in lieu of a dental evaluation. MM patients who have no obvious dental abnormality shall be started on therapy without any delay. Dental hygiene should be assessed and reinforced on each hospital visit. Elective dental procedures should not be advised during BP therapy.

EVIDENCE

Denosumab is a fully human monoclonal antibody that inhibits osteoclast function by binding to RANKL. Contrary to bisphosphonates, it is given via subcutaneous route and it does not depend on renal clearance for its elimination owing to its removal by the reticuloendothelial system. Denosumab is FDA approved for treatment of postmenopausal women with osteoporosis at high risk for fracture and prevention of SREs in patients with bone metastases from solid tumours. FDA approved the use of Denosumab in MM on 05 Jan 2018 based on data of 482 patients demonstrating non inferiority to zoledronic acid at delaying the time to first SRE (HR, 0.98; 95% CI, 0.85-1.14; *P* = .01) presented at International Myeloma Workshop 2017 at Delhi.(41) The "244 study" concluded that there was no significant difference in survival when all patients were analysed together. Although inferior survival was observed in MM patients who received Denosumab, the trial faced criticism for multiple shortcomings which confused the outcomes pertaining to MM patients (10% of the study population).(42) Recently, a large phase III trial between Denosumab and Zoledronate comprising of 1718 newly diagnosed MM patients with bone involvement showed that the effectiveness of Denosumab in preventing SREs was similar to Zoledronate. The patients receiving Denosumab also displayed a favourable safety profile particularly about renal toxicity. Interestingly, Denosumab was observed to have longer progression free survival (PFS) than Zoledronate although there was no difference in overall survival (Table 3).(43)

Table 4: Comparison of bisphosphonates and Denosumab in the management of SRE in Myeloma

Study	Year	Drug	No. of patients (in each arm)	Median time to first SRE (months)	Hazard ratio	ONJ	Renal failure
Raje *et al.*(43)	2017	Denosumab	859	22.83	0.98 (0.85–1.14) (P = 0.01)	4.1%	10%
		Zoledronate	859	23.98	-	2.8%	17.1%

Table 5: Densoumab available in Indian Market with price list. (The list is not all inclusive and is based on market survey)

S. No.	Brand Name	Pharma company	MRP (in INR)	Approximate cost to the patient (in INR)
1	XGEVA	AMGEN/Dr Reddy's	28787	23000

BALLOON KYPHOPLASTY AND VERTEBROPLASTY

RECOMMENDATIONS

- We recommend that balloon kyphoplasty or vertebroplasty can be performed in MM patients with symptomatic (painful) vertebral compression fractures (VCFs) **without** epidural disease and retropulsed bony fragments into the spinal cord.
- If possible, Balloon kyphoplasty shall be preferred over vertebroplasty in view of its greater efficacy in prospective studies. The choice between kyphoplasty and vertebroplasty shall depend on the expertise of the practitioner who is performing these procedures in the institute.

EVIDENCE

Vertebroplasty is a technique that involves the percutaneous injection of bone cement under fluoroscopic guidance into a collapsed vertebral body. Kyphoplasty involves the introduction of inflatable bone tamps into the collapsed vertebral body. Bone tamps restore the height of the vertebral body while creating a cavity that can be filled with bone cement. Kyphoplasty is significantly expensive as compared to vertebroplasty. Kyphoplasty and vertebroplasty have never been compared in a prospective trial in MM. In comparison to conservative management, Balloon kyphoplasty in MM patients with painful vertebral compression fractures (VCFs) has shown significant and durable improvement in pain and quality of life. It has also shown improvement in vertebral height loss and spine deformity in such patients. (44, 45) Retrospective studies have

demonstrated significant improvement in pain, mobility and quality of life with vertebroplasty in MM patients with painful vertebral compression fractures (VCFs).(46) In prospective studies, vertebroplasty has not shown any advantage over conservative management in patients with osteoporotic fractures. (47, 48) A meta-analysis suggested the superiority of balloon kyphoplasty over vertebroplasty in decreasing pain associated with malignancy related VCFs. (45)

RADIOTHERAPY

RECOMMENDATIONS FOR RADIOTHERAPY

- We recommend that low dose radiotherapy (single fraction 8-Gy or 30-Gy fractionated over 2 weeks) can be administered to **transplant ineligible** MM patients with uncontrolled pain arising from impending or pathological fracture or impending spinal cord compression.
- A higher dose of radiotherapy (40 to 50-Gy fractionated over 4 weeks) shall be considered for the management of solitary plasmacytoma and MM patients with actual spinal cord compression.

EVIDENCE FOR RADIOTHERAPY

Impending pathologic fracture of a long bone is defined as "greater than 2 or 3 cm of cortical involvement, lytic destruction of 50% of the width of the bone, or avulsion of the lesser trochanter on plain radiograph." Comparison of single 8-Gy fraction and a fractionated 30-Gy (over two weeks) in MM patients with bony pains have shown similar efficacy in pain relief. (49) Higher radiation dose (40 to 50-Gy) has been recommended for the management of spinal cord compression or solitary plasmacytoma. (9) Radiotherapy alone has demonstrated meaningful improvement in motor functions of 75% MM patients with spinal cord compression (SCC). (50)

SURGERY

RECOMMENDATIONS FOR SURGERY

- We recommend that surgeon's consultation should be sought in all MM patients with – impending or pathologic fracture, actual spinal cord compression associated epidural disease or retropulsed bone fragments into the spinal cord and vertebral instability.
- We recommend that surgeon's consultation should be sought in MM patients with painful skeletal complications (plasmacytoma or fracture) that don't respond to anti-myeloma therapy and radiotherapy.

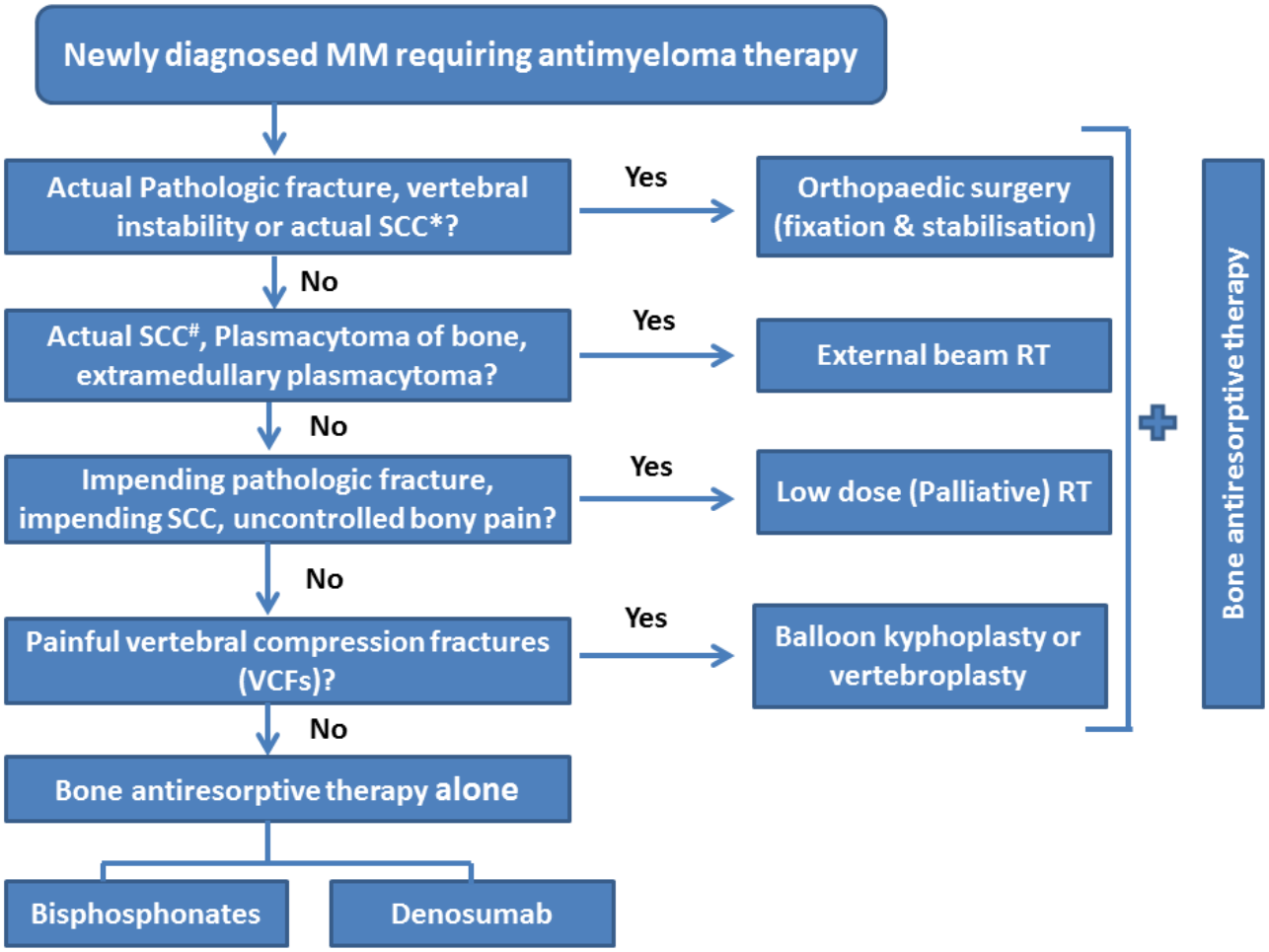
PROCEDURES

- Decompressive laminectomy with or without vertebroplasty
- Plate fixation or intramedullary devices (e.g., nails, rods, etc.)

EVIDENCE

Role of surgery in MM is generally palliative. Surgery is mainly performed in patients with impending or existing pathological fracture with pain refractory to anti-myeloma therapy and radiotherapy, spinal cord compression, or vertebral instability. Elective fixation prevents the loss of function and intense pain consequent to a pathologic fracture. However, surgical risks must be weighed against life expectancy and quality of life to justify surgical intervention. Apart from the clinical status of the patient, the decision for a surgical procedure must take into the consideration the survival estimates based on prognostic factors. A retrospective analysis showed that surgical management was well tolerated by seventy-five MM patients with debilitating skeletal involvement (impending or pathologic fracture or spinal cord compression). Five year survival was 37% (median survival 4.5 years).(51)

Fig 2: Choice of different therapeutic modalities for NDMM with SRE



*Spinal Cord Compression (SCC) with epidural disease component or retropulsion of bone fragments into spinal cord

Spinal Cord Compression (SCC) without epidural disease component and retropulsed bone fragments

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