Chapter 80

Recent Advances in Diagnosis and Management of Multiple Myeloma: An Update

PS Ghalaut, Soumik Chaudhuri, Ragini Singh

INTRODUCTION

Multiple myeloma (from Greek myelo—bonemarrow) is one of the plasma cell dyscrasias and refers to an incurable clonal B-cell malignancy with an annual incidence of 1% of all malignancies and 10% of all hematological malignancies.1 There are approximately 19,000 new cases/year in United States of America (USA) and an Indian incidence of 6,000 new cases/year. The male/female ratio is 1.4:1 and mean 5-year survival rate of 33%.2

Plasma cell dyscrasias can be broadly subdivided into the following heads:

- Monoclonal gammopathy of unknown significance (MGUS)
- Plasmacytoma—solitary mass of neoplastic monoclonal plasma cells in either bone or soft tissue (extramedullary)
- Asymptomatic myeloma
- Symptomatic myeloma.

MONOCLONAL GAMMOPATHY OF UNKNOWN SIGNIFICANCE

It is a premalignant condition with an annual incidence of 3.2% in patients above 50 years of age. Approximately 1–2% of these patients develop multiple myeloma every year and is characterized by the following features:

- A monoclonal paraprotein band (M-protein) less than 3 g/dL
- Plasma cells less than 10% on bone marrow examination
- No evidence of hypercalcemia, renal failure, anemia or bony lesions.

A risk stratification model developed by the Mayo Clinic, USA utilizes three parameters to define the risk of progression of MGUS to multiple myeloma over a period of 5–20 years and utilizes the following parameters (Table 1):3

- Serum M-protein levels
- Heavy chain subtype [immunoglobulin G (IgG) or non-immunoglobulin G (non-IgG)]
- Free light chain (FLC) ratio.

PLASMACYTOMA

This refers to malignant plasma cell tumors present either in the skeletal system (solitary bone plasmacytoma) or in the soft tissues (extramedullary plasmacytoma) (Figure 1). The diagnostic criteria for both are as follows (Table 2):

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Patients (N)</th>
<th>Relative risk</th>
<th>Absolute risk of progression at 20 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk (serum M-protein less than 1.5 g/dL, IgG subtype, normal FLC ratio 0.26–1.65)</td>
<td>449</td>
<td>1</td>
<td>5%</td>
</tr>
<tr>
<td>Low-intermediate risk (anyone factor abnormal)</td>
<td>420</td>
<td>5.4</td>
<td>21%</td>
</tr>
<tr>
<td>High-intermediate risk (any two factors abnormal)</td>
<td>226</td>
<td>10.1</td>
<td>37%</td>
</tr>
<tr>
<td>High-risk (all three factors abnormal)</td>
<td>53</td>
<td>20.8</td>
<td>58%</td>
</tr>
</tbody>
</table>
Section 10

Recent Advances in Diagnosis and Management of Multiple Myeloma...

### TABLE 2 | Diagnostic criteria for plasmacytoma

<table>
<thead>
<tr>
<th>Solitary bone plasmacytoma</th>
<th>Soft tissue (extramedullary) plasmacytoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single area of bone destruction due to clonal plasma cells</td>
<td>Tissue biopsy showing monoclonal plasma cell histology</td>
</tr>
<tr>
<td>Bone marrow plasma cell infiltration not exceeding 5% of all nucleated cells</td>
<td>Bone marrow plasma cell infiltration not exceeding 5% of all nucleated cells</td>
</tr>
<tr>
<td>Absence of osteolytic bone lesions or other tissue involvement (no evidence of myeloma)</td>
<td>Absence of osteolytic bone lesions or other tissue involvement (no evidence of myeloma)</td>
</tr>
<tr>
<td>Absence of anemia, hypercalcemia or renal impairment attributable to myeloma</td>
<td>Absence of hypercalcemia or renal failure</td>
</tr>
<tr>
<td>Low, if present, concentrations of serum or urine monoclonal protein</td>
<td>Low serum M-protein concentration, if present</td>
</tr>
<tr>
<td>Preserved levels of uninvolved immunoglobulins</td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Enlargement of spleen, lymph nodes and gut-associated lymphoid tissue is rare in multiple myeloma.

### CLINICAL FEATURES

- No myeloma-related organ or tissue impairment viz. Hypercalcemia, Renal insufficiency, Anemia and Bone lesions (CRAB).
- The average duration of progression from smoldering myeloma to symptomatic disease is less than 2 years.

### Symptomatic Multiple Myeloma

As defined by the International Myeloma Working Group (IMWG) in 2003 and subsequently revised in 2009, the criteria for symptomatic multiple myeloma includes:

- Clonal plasma cells greater than 10% on bone marrow biopsy or (in any quantity) in a biopsy from other tissues (plasmacytoma)
- A monoclonal protein (paraprotein) in either serum or urine
- Evidence of end-organ damage related to the plasma cell disorder (commonly referred to as “CRAB” symptoms):
  - Hypercalcemia (> 10.5 mg/dL or > 0.5 mg above normal limits)
  - Renal insufficiency attributable to myeloma (creatinine > 2 mg/dL)
  - Anemia (hemoglobin <10 g/dL or <2 g/dL below normal limits)
  - Bone lesions (lytic lesions or osteoporosis with compression fractures).

### TYPES OF PARAPROTEINS IN MULTIPLE MYELOMA

- Serum heavy chain immunoglobulins (77%):
  - Immunoglobulin G kappa or lambda multiple myeloma
  - Immunoglobulin A kappa or lambda multiple myeloma
- Urinary light chain immunoglobulins or Bence-Jones proteins (20%):
  - Kappa light chain multiple myeloma
  - Lambda light chain multiple myeloma
- No serum or urinary M-protein (3%):
  - Nonsecretory multiple myeloma.

### STAGING OF MULTIPLE MYELOMA

There are currently two staging systems in vogue for the staging of multiple myeloma. The older system is known as Durie-Salmon staging and is more popular (Table 3). The newer International Staging System (ISS) was formulated in 2005 and is more of a prognostic index and ideally combined with the Durie-Salmon staging (Table 4). The parameters used in both these systems are as follows:

**Note:** Serum β₂-microglobulin levels are an independent prognosticator of mean survival and can substitute staging systems in clinical practice.

### INVESTIGATIONS AND MONITORING

All patients of multiple myeloma should undergo a battery of investigations which would aid in diagnosis as well as direct prognosis and monitoring. Ideal investigations would include:

- Complete and differential blood counts
- Serum albumin, serum calcium, serum creatinine
- Serum β₂-microglobulin, C-reactive protein, lactate dehydrogenase (LDH)
- Quantitative immunoglobulins
- Free light chain assay
- Serum and urine electrophoresis
- Serum protein immunofixation
- Radiological skeletal bone survey
- Cytogenetics, fluorescent in situ hybridization (FISH)
- Gene expression profiling (GEP).

Monoclonal gammopathy of unknown significance and smoldering myeloma are both premalignant condition with a definite proportion transforming into overt multiple myeloma every year. Hence, it is imperative that monitoring of such patients be undertaken at regular intervals so as to identify and arrest the disease at an early stage. An ideal calendar would include follow-ups at these durations (Table 5):

### TREATMENT OF MULTIPLE MYELOMA

Treatment of multiple myeloma should be focused on therapies to improve symptoms of the disease and decrease the clonal plasma cell population. Asymptomatic disease (e.g. smoldering myeloma) should be carefully monitored for progression and treatment ideally deferred.

The initial treatment for a myeloma patient would depend upon whether or not the patient is a candidate for stem cell transplantation. In eligible patients, high-dose chemotherapy with
Hematology

### Table 3: Durie-Salmon staging system for multiple myeloma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria</th>
<th>Estimated tumor burden ($&lt;10^{15}$/m$^3$)</th>
</tr>
</thead>
</table>
| I     | All of the following:  
- Hemoglobin $>$ 10 g/dL  
- Serum calcium $<$ 12 mg/dL  
- Normal bone X-ray or solitary lesion  
- Low M-component production  
  - IgG level $<$ 50 g/L ($<$ 5 g/dL)  
  - IgA level $<$ 30 g/L ($<$ 3 g/dL)  
  - Urine light chain $<$ 4 g/24 hours |
| Fitting neither I nor III  | $<$ 0.6 (low) |
| II    | One or more of the following:  
- Hemoglobin $<$ 8.5 g/dL  
- Serum calcium $>$ 12 mg/dL  
- Advanced lytic bone lesions  
- High M-component production  
  - IgG level $>$ 70 g/L ($>$ 7 g/dL)  
  - IgA level $>$ 50 g/L ($>$ 5 g/dL)  
  - Urine light chains $>$ 12 g/24 hours |
| III   | 0.6–1.20 (intermediate) |

### Table 4: International staging system for multiple myeloma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria</th>
<th>Median survival</th>
</tr>
</thead>
</table>
| I     | Serum $\beta_2$-microglobulin ($\beta_2$M) $<$ 3.5 mg/L  
  Serum albumin $\geq$ 3.5 g/dL |
|       | 62 months |
| II    | Serum $\beta_2$-microglobulin $<$ 3.5 mg/L and albumin $<$ 3.5–5.5 mg/dL, or $\beta_2$M $<$ 3.5–5.5 mg/L, irrespective of the serum albumin |
|       | 44 months |
| III   | Serum $\beta_2$-microglobulin $>$ 5.5 mg/L |
|       | 29 months |

### Table 5: Follow-up calendar for plasma cell dyscrasias

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Monitoring</th>
<th>Supportive therapy</th>
<th>Disease-specific therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monoclonal gammopathy of unknown significance</td>
<td>Annual</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Smoldering myeloma</td>
<td>Every 2–3 months</td>
<td>Usually none</td>
<td>None</td>
</tr>
<tr>
<td>Indolent myeloma</td>
<td>Every 1–2 months</td>
<td>+/-</td>
<td>None</td>
</tr>
<tr>
<td>Stage I myeloma</td>
<td>Every 1–2 months</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Stage II, III myeloma</td>
<td>Every month</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

autologous hematopoietic stem-cell transplantation (ASCT) has become the preferred treatment for patients under the age of 65. An initial induction chemotherapy is administered before stem cell transplantation. This includes both conventional and novel induction agents like:

- Conventional therapy:
  - Glucocorticoids + anthracycline/alkylator
  - Melphalan
  - Melphalan + prednisone
  - VAD (vincristine + doxorubicin + dexamethasone).

This produces a remission in about 40% of cases.¹¹

### Novel therapy:
- Immnomodulators: Thalidomide, lenalidomide
- Proteasome inhibitors: Bortezomib.

This produces remission in more than 70% of patients. Novel agents may also overcome poor prognostic factors [del(13q), t(4;14)] and prolong event-free and overall survival.¹²

### NOVEL AGENTS IN MULTIPLE MYELOMA

#### Bortezomib

- Class of drug: Proteasome inhibitor
- Mechanism of action: As a reversible inhibitor of the 26S proteasome complex, bortezomib prevents proteolysis, thus affecting a number of cellular signaling cascades and ultimately leading to cellular death or apoptosis. Its half-life ranges from 15–19 hours
- Recommended dosage: The recommended dose of bortezomib is 1.3 mg/m² as 3–5 second bolus intravenous (IV) injection twice weekly for 2 weeks (days 1, 4, 8 and 11) followed by a 10-day rest period (days 12–21) for 8 cycles
- Adverse events: Thrombocytopenia, neutropenia, asthenia, peripheral neuropathy, anemia
- Precautions and dose alterations: Renal failure—dose alteration
- Thalidomide is an immunomodulator and has a number of mechanisms of action including antiangiogenic activity, inhibition of tumor necrosis factor-α (TNF-α), secretion of interferon-α (IFN-α) and interleukin-2 (IL-2), induction of apoptosis and regulation of adhesion molecule expression.¹⁴

- The usual adult dose is 200 mg orally once a day with water, preferably at bedtime and at least 1 hour after the evening meal. Thalidomide is administered in combination with dexamethasone in 28-day treatment cycles. The dexamethasone dose is 40 mg orally daily, administered on days 1 through 4, 9 through 12 and 17 through 20, every 28 days. Adverse effects include venous thromboembolism (VTE), sensory neuropathy, constipation and rashes. It is absolutely contraindicated in pregnancy or young females.

#### Lenalidomide

Lenalidomide is an orally administered thalidomide analogue with a different side-effect profile. It has more potent in vitro activity, including the inhibition of angiogenesis, cytokine modulation and T-cell costimulation than thalidomide. It is better tolerated than thalidomide and does not cause significant somnolence, neuropathy or constipation. The most frequently seen toxicities occurring grade greater than 3 are myelosuppression (which can usually be managed with dose reduction and growth factor support if necessary) and thrombosis.¹⁵

- It is also prudent at this juncture to review the terms used in describing the response to treatment and assessment of remission status. The IMWG uniform response criteria defines the following terms as (Table 6):
  - There has been a paradigm shift in the traditional way that this disease has been approached and managed in recent years. The previous emphasis was on treating the clinical phenotype but was limited by the observation that the overall survival in some subgroups had not improved, despite the availability of new treatment options. This led to the realization that molecular cytogenetic type is an important criterion which influences choice of, as well as response...
to, treatment. The correlation between cytogenetic subtypes and prognostic risk could be summed up in the following (Table 7):17

High-risk cytogenetic factors: del(17p), del(13q), t(14;16) and hypodiploid.

Some of the primary induction regimens that have been utilized to produce remission in multiple myeloma have included the following combination schedules as shown in Table 8.18

A proposed treatment algorithm (as developed by the Mayo Clinic, USA) for transplant eligible and transplant ineligible patients has prolonged overall survival and complete remission (Flow charts 1 and 2):34

### TABLE 6 | International Myeloma Working Group uniform response criteria for multiple myeloma16

<table>
<thead>
<tr>
<th>Response subcategory</th>
<th>Response criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Stringent complete response (sCR)</td>
<td>Complete response (CR) as defined below +plus&lt;br&gt;• Normal serum free light chain (SFLC) ratio&lt;br&gt;• Absence of phenotypically aberrant plasma cells by multiparameter flow cytometry</td>
</tr>
<tr>
<td>2. Complete response</td>
<td>• Negative immunofixation on the serum and urine&lt;br&gt;• Disappearance of any soft tissue plasmacytomas&lt;br&gt;• Less than 5% bone marrow plasma cells</td>
</tr>
<tr>
<td>3. Very good partial response (VGPR)</td>
<td>• Serum and urine M-protein detectable by immunofixation but not on electrophoresis&lt;br&gt;Or&lt;br&gt;• Greater than 90% reduction in serum M-protein plus reduction in 24 hours urinary M-protein by greater than 90% or to greater than 100 mg/24 hours</td>
</tr>
<tr>
<td>4. Partial response (PR)</td>
<td>• Greater than 50% reduction of serum M-protein and reduction in 24 hours urinary M-protein by greater than 90% or to less than 200 mg/24 hours</td>
</tr>
<tr>
<td>5. Stable disease (SD)</td>
<td>• Not meeting criteria for CR, VGPR, PR or progressive disease</td>
</tr>
</tbody>
</table>

### TABLE 7 | Risk stratification for multiple myeloma

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk factors</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk multiple myeloma</td>
<td>Absence of intermediate and high-risk factors.</td>
<td>~75%</td>
</tr>
<tr>
<td>Intermediate-risk multiple myeloma</td>
<td>t(4;14) plus absence of 17p deletion or high-risk gene expression profiling signature.</td>
<td>~10%</td>
</tr>
<tr>
<td>High-risk multiple myeloma</td>
<td>Presence of 17p deletion or high-risk gene-expression profiling signature.</td>
<td>~15%</td>
</tr>
</tbody>
</table>

### TABLE 8 | Primary induction regimens (combination) in multiple myeloma

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Usual dosing schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melphalan-prednisone (7-day schedule)19</td>
<td>Melphalan: 8–10 mg oral days 1–7&lt;br&gt;Prednisone: 60 mg/day oral days 1–7&lt;br&gt;Repeated every 6 weeks</td>
</tr>
<tr>
<td>Thalidomide-dexamethasone20,21</td>
<td>Thalidomide: 200 mg oral days 1–28&lt;br&gt;Dexamethasone: 40 mg oral days 1, 8, 15 and 22&lt;br&gt;Repeated every 4 weeks</td>
</tr>
<tr>
<td>Lenalidomide-dexamethasone22</td>
<td>Lenalidomide: 25 mg oral days 1–21 every 28 days&lt;br&gt;Dexamethasone: 40 mg oral days 1, 8, 15 and 22 every 28 days&lt;br&gt;Repeated every 4 weeks</td>
</tr>
<tr>
<td>Bortezomib-dexamethasone23</td>
<td>Bortezomib: 1.3 mg/m² subcutaneous or IV days 1, 8, 15 and 22&lt;br&gt;Dexamethasone: 20 mg oral on day of and day after bortezomib (or 40 mg days 1, 8, 15 and 22)&lt;br&gt;Repeated every 4 weeks</td>
</tr>
<tr>
<td>Melphalan-prednisone-thalidomide24,25</td>
<td>Melphalan: 0.25 mg/kg oral days 1–4 (use 0.20 mg/kg/day oral; days 1–4 in patients more than 75 years)&lt;br&gt;Prednisone: 2 mg/kg oral days 1–4&lt;br&gt;Thalidomide: 100–200 mg oral days 1–28 (use 100 mg dose in patients more than 75 years)&lt;br&gt;Repeated every 6 weeks</td>
</tr>
<tr>
<td>Bortezomib-melphalan-prednisone26-28</td>
<td>Bortezomib: 1.3 mg/m² subcutaneous or IV days 1, 8, 15, and 22&lt;br&gt;Melphalan: 9 mg/m² oral days 1–4&lt;br&gt;Prednisone: 60 mg/m² oral days 1–4&lt;br&gt;Repeated every 35 days</td>
</tr>
<tr>
<td>Bortezomib-thalidomide-dexamethasone29</td>
<td>Bortezomib: 1.3 mg/m² subcutaneous or IV days 1, 8, 15 and 22&lt;br&gt;Thalidomide: 100–200 mg oral days 1–21&lt;br&gt;Dexamethasone: 20 mg oral on day of and day after bortezomib (or 40 mg days 1, 8, 15 and 22)&lt;br&gt;Repeated every 4 weeks × 4 cycles as pretransplant induction therapy</td>
</tr>
<tr>
<td>Bortezomib-cyclophosphamide-dexamethasone (VCD)30,31</td>
<td>Cyclophosphamide: 300 mg/m² orally on days 1, 8, 15 and 22&lt;br&gt;Bortezomib: 1.3 mg/m² subcutaneous or intravenously on days 1, 8, 15 and 22&lt;br&gt;Dexamethasone: 40 mg orally on days 1, 8, 15 and 22&lt;br&gt;Repeated every 4 weeks</td>
</tr>
<tr>
<td>Bortezomib-lenalidomide-dexamethasone32,33</td>
<td>Bortezomib: 1.3 mg/m² subcutaneous or IV days 1, 8 and 15&lt;br&gt;Lenalidomide: 25 mg oral days 1–14&lt;br&gt;Dexamethasone: 20 mg oral on day of and day after bortezomib (or 40 mg days 1, 8, 15 and 22)&lt;br&gt;Repeated every 3 weeks</td>
</tr>
</tbody>
</table>
**NEWER THERAPIES**

A number of newer agents have been tried in multiple myeloma with variable results (Table 9).

**EXPERIENCE WITH MULTIPLE MYELOMA AT POST-GRADUATE INSTITUTE OF MEDICAL SCIENCES, ROHTAK, HARYANA**

A total of 100 new patients of multiple myeloma have been evaluated at our hematologic clinic over the past two decades (1992–2012), with 88 being male and 12 being female patients. It constituted 2.5% of total hematological malignancies. 67% of our patients were over 50 years of age and only 11% were younger than 30 years at presentation. Most males presented at a later mean age (56 ± 5.6 years) as compared to females (51 ± 6.2 years).

The most common presenting features were bony pain (58%), generalized weakness/anemia (54%), renal failure (35%), fever (26%), pathological fractures (20%) and paraplegia (6%). This correlated well with the data published by Kyle at al. from Mayo Clinic, who found bony lesions (79%), anemia (73%) and renal failure (32%) as the most common presenting signs and symptoms. The treatment options in multiple myeloma have undergone a paradigm shift in the past two decades and this is reflected in our data as well. Melphalan-prednisolone (MP) was used in 48 patients, whereas 18 patients were treated with the Vincristine-Doxorubicin-Dexamethasone (VAD) regimen. Fourteen received MP + thalidomide and 10 were treated with thalidomide-dexamethasone. Five patients received bortezomib alone. Seventy-eight percent of patients have expired over a 20-year review period whereas 12% are still under monitoring. Ten patients were lost in follow-up. The overall prognosis was poor due to poor socioeconomic conditions precluding use of novel therapeutic options.

**TREATMENT OF RELAPSED DISEASE**

The treatment of relapsed disease remains an area of concern as the response in such patients is generally poor. Since no therapy is curative, all options need to be tried sequentially and there is no good data on optimum sequence or regimen. All patients should be encouraged to participate in ongoing clinical trials and cumulative toxicities from prior therapies may influence decision. The salvage therapies available include:

- Thalidomide-dexamethasone: Induces PR in 30% of patients (47% if combined with dexamethasone) but increased risk of neuropathies and VTE
- Lenalidomide-dexamethasone: More potent immunomodulator than thalidomide but causes greater myelosuppression
- Bortezomib-dexamethasone: Then, apex trial (2011) found a significant increase in mean survival (6.22 vs 3.49 months; p < 0.001) and 1 year survival rates (80 vs 60%; p = 0.003) with bortezomib as opposed to high-dose dexamethasone alone.
- Pegylated liposomal doxorubicin (PLD) based regimens: Significant increase in thrombotic thrombocytopenic purpura (TTP) at the cost of higher adverse effects.

**SUPPORIVE THERAPY IN MULTIPLE MYELOMA**

- **Treatment of bone disease**: Bisphosphonates, surgical procedures like vertebroplasty and balloon kyphoplasty and radiotherapy [American Society of Clinical Oncology (ASCO) guidelines]
- **Treatment of anemia**: Improve iron and vitamin B12/folate levels, erythropoietin therapy, packed cell blood transfusions (ASCO guidelines)
- **Treatment of renal failure**: Avoid dehydration and toxic drugs, consider dialysis
- **Treatment of infections**: Prophylactic antibiotics, aseptic precautions
- **Venous thromboembolism prevention**: Low-molecular weight heparin and full dose warfarin are recommended. Consider aspirin in low-risk patients.

**TABLE 9**

<table>
<thead>
<tr>
<th>New therapeutic agents for multiple myeloma</th>
<th>Therapeutic target or class of agent</th>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunomodulatory agents</td>
<td>Pomalidomide</td>
<td></td>
</tr>
<tr>
<td>Proteasome inhibitors</td>
<td>Carfilzomib, MLN9708</td>
<td></td>
</tr>
<tr>
<td>Histone deacetylase inhibitors</td>
<td>Vorinostat, panobinostat</td>
<td></td>
</tr>
<tr>
<td>Phosphatidylinositol-3 kinase pathway</td>
<td>Perifosine</td>
<td></td>
</tr>
<tr>
<td>inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-CS1</td>
<td>Elotuzumab</td>
<td></td>
</tr>
<tr>
<td>Heat shock protein 90 inhibitors</td>
<td>Tanespimycin</td>
<td></td>
</tr>
</tbody>
</table>

**Flow chart 2**

```
High-risk

MP + Bortezomib

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Standard risk

MP + Thalidomide or Ro

Observation

Observation

*Clinical trials strongly recommended as the first option.

Rd maintenance is an option for patients responding well to induction therapy with low toxicities; dexamethasone is typically discontinued after the first year.

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**TABLE 9**

<table>
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<td>Perifosine</td>
<td></td>
</tr>
<tr>
<td>inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-CS1</td>
<td>Elotuzumab</td>
<td></td>
</tr>
<tr>
<td>Heat shock protein 90 inhibitors</td>
<td>Tanespimycin</td>
<td></td>
</tr>
</tbody>
</table>
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Chapter 80 Recent Advances in Diagnosis and Management of Multiple Myeloma...

SUMMARY AND CONCLUSION

Multiple myeloma is not uncommon in our country and constituted 2.5% of all hematological malignancies. The disease presentation is similar to that seen in the west. The introduction of novel agents like thalidomide, lenalidomide and bortezomib have altered the present day management of myeloma and made it possible to convert it into a chronic disease with which one can live for a decade or more. The outcome in our patients was poor probably because of late presentation, treatment failure and nonavailability of latest modes of treatment due to socioeconomic factor.

REFERENCES