Multiple Myeloma

2019-2020

Definition

TTP

Duration from start of treatment to disease progression, with deaths from causes other than progression censored.

PFS

Duration from start of the treatment to disease progression or death (regardless of cause of death), whichever comes first.

EFS

The definition for EFS depends on how “event” is defined. In many studies, the definition of EFS used is the same as PFS. EFS may include additional “events” that are considered to be of importance besides death and progression, including serious drug toxicity.

DFS

Duration from the start of MRD negativity to the time of reappearance of MRD. DFS applies only to patients in MRD negative state.

DOR

Duration from first observation of PR to the time of disease progression, with deaths from causes other than progression censored.* Duration of MRD, CR and PR should each be reported as appropriate.

Diagnosis and investigation:

- Complete blood count+film &ESR
- C-reactive protein.
- Urea, creatinine, uric acid, electrolytes, blood sugar, serum calcium &LFT.
- B2 microglobuline, LDH.
- Serum and urin protein electrophoresis.
- Serum and 24hour urine protein immuno-fixation.
- Serum immunoglobulin assay
- Serum free light chain ratio
- Urine free light chain ratio
- Bone marrow aspirates and trephine biopsy.
- Skeletal survey(X-ray, total body CT- scanning).
- Coagulation screen.
- Immunophenotyping for clonality assessment(flowcytometry or immuno-histochemistry).
- Cytogenetic study to assess the risk stratification (if available)
  - FISH study for: Del 13, Del 17, t(4;14), t(11;14), t(14;16), t(14;20), 1q21 amplification1p abnormalities.
- MRD assessment**(optional)**: Bone marrow flowcytometry

Plasma cell related disorder diagnostic criteria:

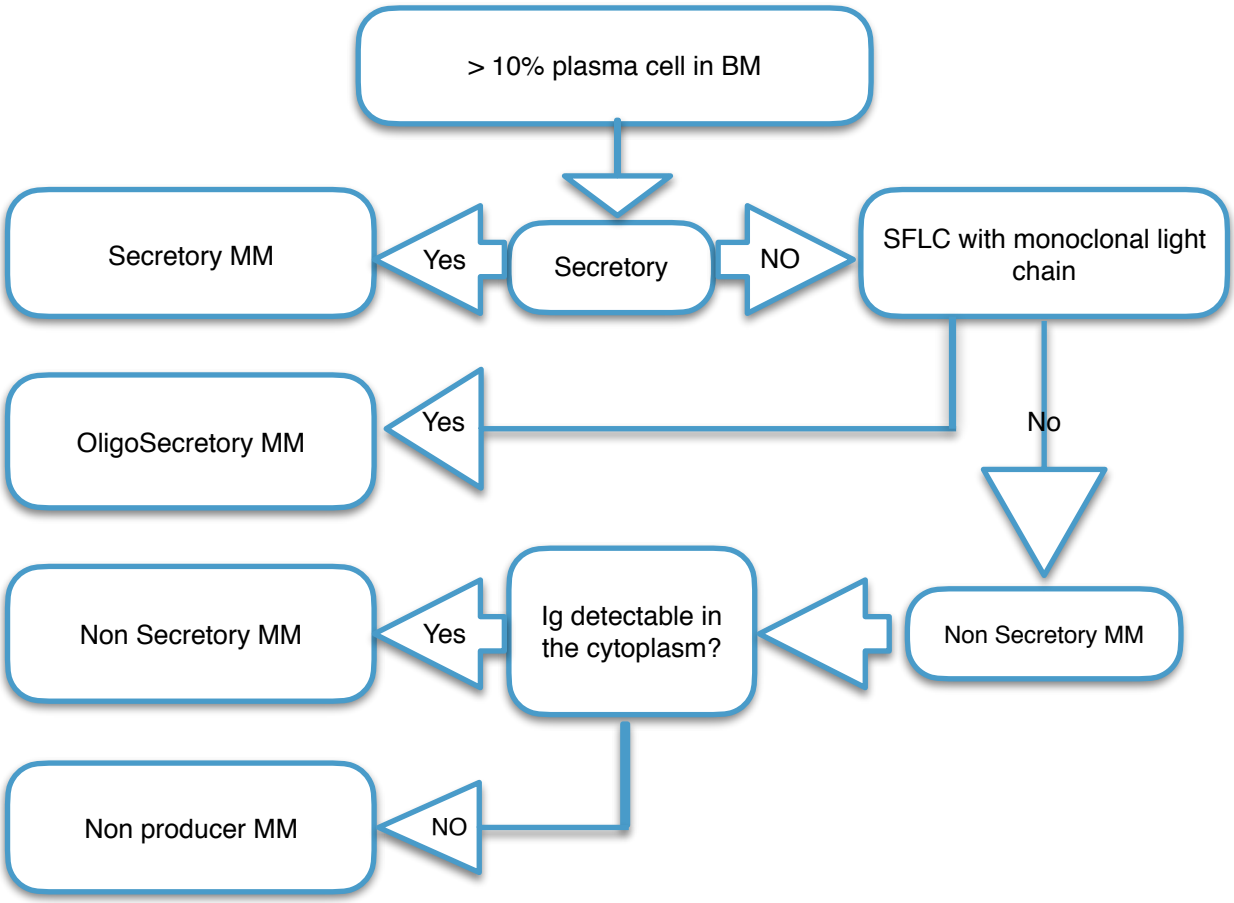
We need:

https://www.myeloma.org/resource-library/international-myeloma-working-group-consensus-criteria-response-minimal-residual

Plasma Cell Disorder	Definition
Symptomatic multiple myeloma	• Monoclonal plasma in the BM≥10%&/or presence of biopsy proven plasmacytoma • Monoclonal protein present in serum&/or urine • Myeloma related organ dysfunction: ➢ C-Calcium. elevation>10.5(11.5)mg/L or upper limit of normal ➢ R-Renal insufficiency(s.cr>2(1.73)mg%) ➢ A-Anemia()Hb<10g% or<2g of normal ➢ L-Lytic bone lesion or osteopenia.
Smoldering multiple myeloma	Both criteria must be met: • Serum monoclonal protein (IgG or IgA ≥ 30g/L or urinary monoclonal protein ≥ 500mg per 24h and/or clonal bone marrow plasma cells 10-60% • Absence of myeloma-defining events or amyloidosis
Non-IgM monoclonal gammopathy of undetermined significance (MGUS)	• Serum monoclonal protein ≤ 30g/L • Clonal bone marrow plasma cells ≤ 10% • Absence of end-organ damage such as hypercalcemia, renal insufficiency, anemia, and bone lesions (CRAB) or amyloidosis that can be attributed to the plasma cell proliferative disorder
IgM MGUS	• Serum IgM monoclonal protein ≤ 30g/L • No evidence of anemia, constitutional symptoms, hyperviscosity, lymphadenopathy, hepatosplenomegaly, or other end-organ damage that can be attributed to the plasma cell proliferative disorder
Light chain MGUS	• Abnormal FLC ratio (≤0.26 or ≧1.65) • Increased level of the appropriate free light chain (increased s. FLC in patients with ratio≧1.65 and increased s. FLC in patients with ratio≤ 0.26) • No immunoglobulin heavy chain expression on immunofixation • Absence of end-organ damage such as hypercalcemia, renal insufficiency, anemia, and bone lesions (CRAB) or amyloidosis that can be attributed to the plasma cell proliferative disorder • Clonal bone marrow plasma cells≤10% • Urinary monoclonal protein≤ 500mg/24h

Solitary plasmacytoma	• Biopsy-proven solitary lesion of bone or soft tissue with evidence of clonal plasma cells • Normal bone marrow with no evidence of clonal plasma cells • Normal skeletal survey and MRI (or CT) of spine and pelvis (except for the primary solitary lesion) • Absence of end-organ damage such as hypercalcemia, renal insufficiency, anemia, and bone lesions (CRAB) or amyloidosis that can be attributed to the plasma cell proliferative disorder
Solitary plasmacytoma with minimal marrow involvement	• Biopsy-proven solitary lesion of bone or soft tissue with evidence of clonal plasma cells • Clonal bone marrow plasma cells ≤ 10% • Normal skeletal survey and MRI (or CT) of spine and pelvis (except for the primary solitary lesion) • Absence of end-organ damage such as hypercalcemia, renal insufficiency, anemia, and bone lesions (CRAB) or amyloidosis that can be attributed to the plasma cell proliferative disorder
POEMS syndrome	• Polyneuropathy • Monoclonal plasma cell proliferative disorder • Any one of the 3 other major criteria: sclerotic bone lesions, Castleman's disease, elevated levels of VEGFA • Any one of the following 6 minor criteria: • Organomegaly (splenomegaly, hepatomegaly, or lymphadenopathy) • Extravascular volume overload (edema, pleurl effusion, or ascites) • Endocrinopathy (adrenal, thyroid,pituitary, gonadal, parathyroid, pancreatic) • Skin changes (hyperpigmentation, hypertrichosis, glomeruloid hemangiomata, plethora, acrocyanosis, flushing, white nails) • Papilloedema • Thrombocytosis/polycythemia
Systemic AL amyloidosis	• Presence of an amyloid-related systemic syndrome (e.g., renal, liver, heart, gastrointestinal tract, or peripheral nerve involvement) • Positive amyloid staining by Congo red in any tissue (e.g., fat aspirate, bone marrow, or organ biopsy) • Evidence that amyloid is light-chain-related established by direct exmination of the amyloid using mass spectrometry-based proteomic analysis or immunoeletronmicroscopy • Evidence of a monoclonal plasma cell proliferative disorder (serum monoclonal protein, abnormal free light chain ratio, or clonal plasma cells in the bone marrow)

Criteria for non secretory myeloma
Biopsy proven clonal cells
< 0.5 mg/dl SPE
< 200mg/24hrs of light chain proteinuria by UPEP
Unquantiable free light chain measurement
Evidence of CRAB criteria which must be attributable to clonal plasma cell infiltration



Definition of eligibility for auto - BMT

- Age ≤ 65 year old
- > 65-70 years old according ECOG status and presence the cormorbidities, revised myeloma comorbidity index (R-MCI) score.
- http://www.myelomacomorbidityindex.org/en_calc.html.

Myeloma-defining events include the following :

- Serum calcium level >0.25 mmol/L (>1 mg/dL) higher than the upper limit of normal or >2.75 mmol/L (>11 mg/dL)
- Renal insufficiency (creatinine >2 mg/dL [>177 μmol/L] or creatinine clearance < 40 mL/min)
- Anemia (hemoglobin < 10 g/dL or hemoglobin >2 g/dL below the lower limit of normal)
- One or more osteolytic bone lesions on skeletal radiography, CT, or PET-CT
- Clonal bone marrow plasma cells ≥60%
- Abnormal serum free light chain (FLC) ratio ≥100 (involved kappa) or < 0.01 (involved lambda)
- One or more focal >5 mm lesions on MRI scans

****The International Myeloma Working Group added the following criteria to the CRAB criteria for smoldering multiple myeloma(indications of treatment) **((SLiM criteria))**:

- Bone marrow plasma cells (BMPCs) ≥60%
- Involved/uninvolved serum free light chain ratio ≥100
- Abnormal MRI with more than one focal lesion, with each lesion >5 mm.

****The researchers were able to categorize patients as having low, intermediate, or high risk of progression of smoldering myeloma based on three features: presence of >20% bone marrow plasma cells, a serum M protein spike of >2 g/dL, and a free light chain ratio of >20.

Each factor is an independent predictor of a shorter time to progression.

- The low-risk group, with none of the features, had a 5% risk of disease progression at 2 years.
- Intermediate-risk patients had at least one of these features and a 17% risk of progression,
- High-risk patients had at least two features and a 46% risk of progression.

"For patients who have a risk of progression of 50% at 2 years, as a community, we think we are comfortable about discussing the potential for early interventions with those patients.

Staging system:

International staging system:-

Stage	Characteristics	Median survival/ months
I	S.β-2 microglobulin<3.5mg/L S.Albumin≥35g/L	62
II	S.β-2 microglobulin<3.5mg/L S.Albumin<35g/L or S.β-2 microglobulin3.5-5.5mg/L	44
III	S.β-2 microglobulin ≥5.5mg/L	29

REVISED INTERNATIONAL STAGING SYSTEM (R-ISS) FOR MULTIPLE MYELOMA

Stage	Criteria
I	Serum β2 microglobulin < 3.5 mg/l Serum albumin ≥ 3.5 g/dl Standard-risk chromosomal abnormalities (CA) Normal LDH
II	Not R-ISS stage I or III
III	Serum β2 microglobulin ≥ 5.5 mg/L and either High-risk CA by FISH OR High LDH

Revised international staging system:-

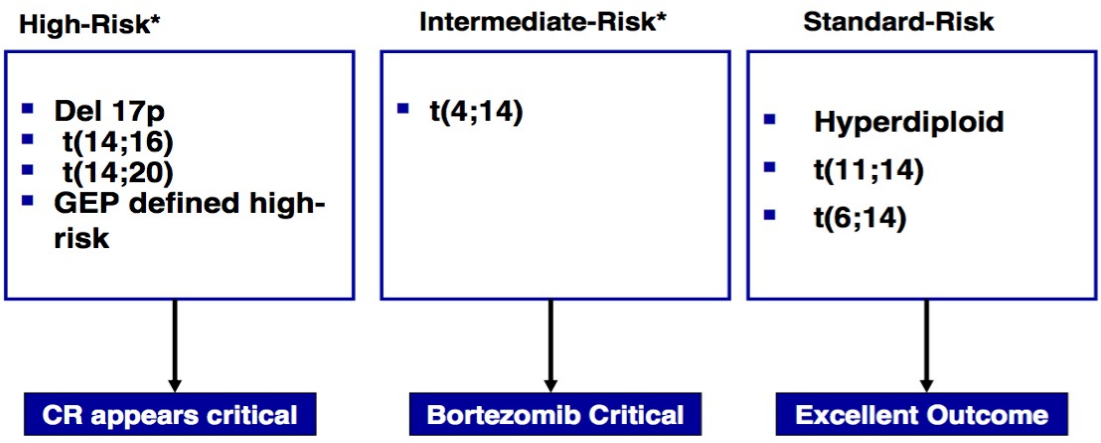
https://www.mdcalc.com/revised-multiple-myeloma-international-staging-system-r-iss

Standard Risk Factors for MM and the R-ISS

Prognostic Factor	Criteria
ISS stage	
I	Serum β2-microglobulin < 3.5 mg/L, serum albumin ≥ 3.5 g/dL
II	Not ISS stage I or III
III	Serum β2-microglobulin ≥ 5.5 mg/L
CA by iFISH	
High risk	Presence of del(17p) and/or translocation t(4;14) and/or translocation t(14;16)
Standard risk	No high-risk CA
LDH	
Normal	Serum LDH < the upper limit of normal
High	Serum LDH > the upper limit of normal
A new model for risk stratification for MM	
R-ISS stage	
I	ISS stage I and standard-risk CA by iFISH and normal LDH
II	Not R-ISS stage I or III
III	ISS stage III and either high-risk CA by iFISH or high LDH

Abbreviations: CA, chromosomal abnormalities; iFISH, interphase fluorescent in situ hybridization; ISS, International Staging System; LDH, lactate dehydrogenase; MM, multiple myeloma; R-ISS, revised International Staging System.

Myeloma Risk-Stratification



*Presence of trisomies ameliorates high risk

Response criteria subcategory(IMWG):

Response subcategory	Response criteria
Sustained MRD-negative*	• MRD negativity in the marrow by next-generation sequencing (NGS) or next-generation flow (NGF), or both, and MRD negativity by imaging, as defined below, confirmed minimum of 1 year apart
Flow MRD-negative**	• Absence of phenotypically aberrant plasma cells by NGF on bone marrow aspirates with a minimum sensitivity of 1 in 105 nucleated cells
Sequencing MRD-negative***	• Absence of clonal plasma cells by NGS on bone marrow aspirate with a minimum sensitivity of 1 in 105 nucleated cells
Imaging-positive MRD-negative	• MRD negativity as defined by NGF or NGS, and • Disappearance of every area of increased tracer uptake found at baseline or a preceding PET/CT or decrease to less mediastinal blood pool standardised uptake values or decrease to less than that of surrounding normal tissue
Standaed IMWG response criteria	
Stringent complete response (sCR)	• CR as defined below, and • Normal FLC ratio, and • Absence of clonal plasma cells by immunohistochemistry
Complete response (CR)	• Negative IFE of serum and urine, and • Disappearance of any soft tissue plasmacytomas, and • <5% plasma cells in bone marrow aspirates • In patients in whom the only measurable disease is by sFLC levels, CR is defined as a normal FLC ratio (0.26-1.65) in addition to the CR criteria listed above
Very good partial response (VGPR)	• Serum and urine M-protein detectable by IFE but not on electrophoresis, or • ≥90% reduction in serum M-protein plus urine M-protein <100 mg per 24 hours • In patients in whom the only measurable disease is by sFLC levels, VGPR is defined as a >90% decrease in the difference between involved and uninvolved sFLC levels

Partial response (PR)	• ≥50% reduction of serum M-protein and reduction in 24-hour urinary M-protein by ≥90% or to <200 mg per 24 hours • In patients in whom the only measurable disease is by sFLC levels, PR is defined as a ≥50% decrease in the difference between involved and uninvolved sFLC levels • If serum and urine M-protein are unmeasurable, and sFLCs are also unmeasurable, ≥50% reduction in bone marrow plasma cells is required in place of M-protein, provided baseline percentage was ≥30% • In addition to the above criteria, if present at baseline, ≥50% reduction in the size of soft tissue plasmacytomas is also required
Minimal Response	• ≥25% but ≤49% reduction of serum M-protein, and • Reduction in 24-h urine M-protein by 50-89%, and • If present at baseline, a ≥50% reduction in the size of soft tissue plasmacytomas
Stable disease (SD)	Not meeting criteria for CR, VGPR, PR or progressive disease
Relapse from CR	Require one or more of the following: Reappearance of serum or urinary paraprotien on immunofixation or routine electrophoresis. Development of ≥ 5% of plasma cell in bone marrow. Appearance of any other sign of progression.
Clinical relapse	Require one or more of: Development of new soft tissue plsmacytoma or bone lesions Increasing size of plsmacytoma or bone lesions(a 50% and at least 1cm. increasing). Hypercalcimia(11.5mg%) Full of Hb.of≥ 2g/dl Rise s.creatinine by 2mg/dl or more.
Refractory myeloma	is defined as disease that is non-respond while on therapy, or progresses within 60 days of last therapy.
Biochemical Relapse	**One or more of the following indicators:** 1. Doubling of M – protein component in 2 consecutive measurements separated by < or= 2-months. 2. Increase in absolute level of serum M – protein by >or= 1gm/dl. 3. Increase in absolute level of urine M – protein by >or= 500mg/24hrs. 4. Increase in absolute level of involved FLC by >or= 20mg/dl (plus an abnormal FLC ratio in 2 consecutive measurements separated by < or= 2-months. ⁑ **Definite increase is defined as 50%(and at least 1 cm)increase as measured serially by the sum of the product of the cross diameter of measurable lesion.**

Progressive disease (PD)	Any one or more of the following: • Increase of 25% from lowest confirmed response value in any one or more of the following: ◦ Serum M-protein (absolute increase must be ≥5 g/L) and/or ◦ Urine M-protein (absolute increase must be ≥200 mg/24 hours) and/or ◦ In patients in whom the only measurable disease is by sFLC levels, the difference between involved and uninvolved sFLC levels (absolute increase must be >100 mg/L) ◦ If serum and urine M-protein are unmeasurable, and sFLCs are also unmeasurable, bone marrow plasma cell percentage (absolute % must be ≥10%) • Appearance of new lesions, ≥50% increase from nadir in SPD of >1 lesion, or a ≥50% increase in the longest diameter of a previous lesion >1 cm in short axis • ≥50% increase in circulating plasma cells (minimum of 200 cells per µL) if this is the only measure of disease

*Subsequent evaluations can be used to further specify the duration of negativity (e.g. MRD-negative at 5 years)
**Using EuroFlow standard operation procedure for MRD detection in MM, or validated equivalent method
***Presence of a clone defined as less than two identical sequencing reads obtained after DNA sequencing of bone marrow aspirates using the LymphoSIGHT platform or validated equivalent method

Note
- That all response categories require two consecutive assessments made at any time before the institution of any new therapy;
- For MRD there is no need for two consecutive assessments, but information on MRD after each treatment stage is recommended.
- All categories of response and MRD require no known evidence of progressive or new bone lesions if radiographic studies were performed.
- Radiographic studies are not required to satisfy these response requirements.
- Bone marrow assessments need not be confirmed.
- For PD, serum M-protein increases of ≥10 g/L are sufficient to define relapse if baseline M-protein is ≥50 g/L.

Newly diagnosed Multiple Myeloma/eligible BMT therapy guideline

TREATMENT

Supportive treatment:

- **Bone disease:**

All patients should receive bisphosphonate (zoledronic acid) for at least 2 years.

➢ Consider the dose adjusting according Cr. Cl.,

➢ If Crcl <30mml/hr then denosumab is indicating 120mg sc every 4 weeks.

➢ Dose every 3 month is acceptable

➢ Basal dental examination is recommended.

- **Hypercalcemia:**

Hydration, frusemide, bisphosphonate, steroid, calcitonin.

- **Hyperviscosity:**

Plasmapharesis plus treatment of myeloma.

- **Anemia:**

➢ Erythropoietin therapy s.c.

➢ Blood group and subgroup should be identifying before daratumumab therapy

- **Renal dysfunction:**

➢ Maintain good hydration.

➢ Dialysis(peritoneal or hemodialysis)/Consult the nephrologist

➢ Treatment of hypercalcemia

- **Hyperuraecaemia:**

allopurinol, rasburicase therapy

- **Coagulation and thrombosis:**

➢ Antiplatlets or anticoagulation is recommended for patients receiving thalidomide or linalidomide or pomalidomide and according the risk factor of thrombosis and orthopedic surgery.

- **Infection**

➢ Acyclovir tablets 400mgx2 or valaciclovir tab 500mg per day for those patients who are receiving bortizomib or daratumumab based regimen, continuous for 6months after last dose of therapy.

➢ prophylaxis for PCJ and anti fungal for those receiving high dose steroid.

- **Vaccination**

➢ Influenza vaccine/annual

➢ pneumococcal conjugate vaccine followed by pneumococcal polysaccharide vaccine one year later.

- **Chemotherapy induced sever neutropenia**

➢ GCSF

- **Radiotherapy:**

Low dose radiotherapy can be used as a palliative treatment for uncontrolled pain, impending pathological fracture or impending cord compression.

MULTIPLE MYELOMA PATIENTS ANDTHOSE WITH ELIGIABLE ASCT THERAPY

Early referral to BMT center for registration for AutoBMT after achieving the target response.

- Induction therapy for 4-6cycles.
- Assessment after 2-4cycles.
- Follow by mobilization of stem cell and autologous bone marrow transplant.
- Consolidation with 2-4cycles of same induction regimen after 3months of autologous BMT.
- Maintenance therapy indefinitely.

Type of induction therapy

Eligible bone marrow transplant myeloma patients:

- Bortizomib + Linalidomide+ Dexamethasone(VRD), (prefered protocol for high risk group). ((Not approved by MOH for intermediate and low risk)).
- Bortizomib + Thalidomide + dexamethasone(VTD)
- Bortizomib+Cyclophosphamide+dexamethasone(VCD).
- Bortizomib+Doxorubicine+dexamethasone(PAD), (specially with plasmacytoma)
- Bortizomib + dexamethasone(VD)
- KRD (high risk group as an early access program)

Protocol therapy:

- ➢ For 4-6 cycles every 21 days.
- ➢ Bortizomib vial 1.3mg/m2, s.c. for day 1,4,8 &11 with 10 days off treatment once weekly(1,8,15,22,28) after 2cycles is an option also.
- ➢ Thalidomide 50-100mg/day p.o. continuously.
- ➢ Cyclophosphamide tab. 500mg PO. Day 1, 8, 15.
- ➢ Carfizomib vial 20mg/m2 testing dose, then 70mg/m2 week 1,8,15.
- ➢ Dexamethasone is 40 mg/day PO. on days 1-4 or with each dose of Velcade day 1 and 2 of each 21 day cycle for the first 4 cycles of therapy.
- ➢ Liposomal Doxorubicin vial 30mg/m2, D 4.
- ➢ Linalidomide 25 mg/day p.o. as a single capsule on days 1 through 14/21, repeated 28 day cycles.

Note:

- ○ Intravenous dexamethasone ampule can be taken orally after the meal instead of intravenous intake.
- ○ Dose of steroid may be reduction to the 20mg per dose in patients with steroid complication.
- ○ Bortizomib doses may be reduction to 1mg/m2 and 0.7mg/m2 if there is neuropathy complication.

Maintenance therapy:

- ➢ Lenalidomide tablet 10mg once daily for 21-28 days or,
- ➢ Thalidomide tablet 50mg once daily or,
- ➢ Bortizomib vial 1.3mg/m2 sc.every 2weeks∓ lenalidomide(high risk group).

Solitary plasmacytoma

- Solitary osseous :

Involved field radiotherapy.

Follow up every 3 months.

- Extraosseous plasmacytoma:

Involved field radiotherapy.

Follow up every 3 months.

Follow up by:CBC, RFT, S.Ca++, β2 microglobuline, FLC assay, urine protein electrophoresis, urine immunofixation, S. immunofixation electrophoresis, bone scan annually, bone marrow biopsy as clinically indicated.

Smoldering myeloma

**** Follow the SLiM criteria

- No need treatment.
- Observation at 3-6 months interval.
- If progression occur, treat as active myeloma.
- Follow up by:CBC, RFT, S.Ca++, β2 microglobuline, FLC assay, urine protein electrophoresis, urine immunofixation, S. immunofixation electrophoresis, bone scan annually, bone marrow biopsy as clinically indicated.

Hematological adverse effect

Dose adjustment recommendations for the treatment of frail patients

Frail patients: treatment algorithm

Risk Factors
Age over 75(65)years
Mild to moderate or severe frailty: Help needed for household and personal care
Co morbidity and organ dysfunction Cardiac, pulmonary, hepatic, renal

Dose level - 0……no risk factor

Dose level -1……at least one risk factor

Dose level -2……at least one risk factor plus any grade 3-4

elderly patien

Agent	Dose level 0	Dose level -1	Dose level- 2
Bortizomib	1.3mg/m2twice/week Day1,4, 8, 11/3week	1.3mg/m2 once/week Day 1,8, 15, 22/5 weeks	1.0mg/m2 once/week Day 1,8, 15, 22/5 weeks
Thalidomide	100mg/day	50mg/day	50mg/day
lenalidomide	25mg/day, day1-21/4weeks	15mg/day, day1-21/4weeks	10mg/day, day1-21/4weeks
dexamthasone	40mg/day Day1,8, 15, 22 /4week	20mg/day Day1,8, 15, 22 /4week	10mg/day Day1,8, 15, 22 /4week
melphalan	0.25mg/kg Day1-4/4-6weeks	0.18mg/kg Day1-4/4-6weeks	0.13mg/kg Day1-4/4-6weeks
prednesolone	50mg/day	25mg/day	12.5mg/day
cyclophosphamide	100mg/day Day1-21/weeks	50mg/day Day1-21/4weeks	50mg/day Day1-21/4weeks

Newly diagnosed Multiple Myeloma/

Non eligible BMT therapy guideline

Definition

Who are Non-eligible

- Age > 65years
- Poor performance status/frial patient (ECOG, CCI)
- Presence of comorbidity disease.

http://www.myelomacomorbidityindex.org/en_calc.html.

Goal of treatment

Should be achievement of best QOL and depth of remission

Initial Treatment

- **See supportive therapy**
- **Fit, intermediate group patient**
  - Triplet : VRD,VCD,VTD,VMP,
  - Doublet: RD,VD,
- **Frial patient**
  - Triplet : VMP,VTD,VCD,MPT
  - Doublet : Rd,VD,

Duration of treatment

- VMP for 9 cycles, VD, VTD, MPT, VCD & VRD 4-6cycles, Rd for 18months or till progression.
- Maintenance until disease progression, or unacceptable toxicity.

Maintenance

- Rd or R alone until disease progression
- Lenalidomide with or without velcade for high risk group.

Relapsed/Refractory Multiple Myeloma

When to consider re-treatment

- Need to consider biochemical vs symptomatic relapse
  - ➢ Patients with asymptomatic rise in M-protein can be observed to determine the rate of rise and nature of relapse
  - ➢ Caveat: Patients with known aggressive or high-risk disease should be considered for salvage, even in the setting of biochemical relapse
- If relapse occurs > 6 months after completion of the initial primary therapy, patients may be retreated with the same primary regimen.
- Several new regimens were included as options for the treatment of R/R MM.

Factors in selecting treatment for relapsed/refractory myeloma

- **Disease-related factors**
  - ➢ Duration of response to initial therapy
  - ➢ High-risk vs low-risk status
  - ➢ Biochemical disease progression, or symptomatic?
- **Treatment-related factors**
  - ➢ Previous therapy exposure (relapsed or refractory)
  - ➢ Toxicity of regimen (combination vs single agent)
  - ➢ Mode of administration (eg, oral or IV)
  - ➢ Previous SCT
- **Patient-related factors**
  - ➢ comorbidity
  - ➢ performance status
  - ➢ Age
  - ➢ pre-existing toxicity

Treating Indolent, Slow-Growing Myeloma in First Relapse

IMiD -Based Salvage	PI- Based Salvage	Transplant - Based Salvage
• Initial treatment with Bortizomib • Underlying peripheral neuropathy	• Initial treatment with IMiD • Previous Bortizomib therapy but good or long response • Renal dysfunction	• Transplant not part of initial therapy • Long remission post -Transplant

Treatment Relapsed / Refractory Multiple Myeloma

Carfilzomib based salvage	Pomalidomide based salvage	Other salvage
• Intolerance or resistant to Bortizomib • Dexamethasone-sparing treatment as part of combination • Intolerance to IMiD	• Lenalidomide refractory • Refractory to standard dose PI • Patient with del (17)	• Refractory to pomalidomide & carfilzomib • Monoclonal antibody candidate

Treatment Aggressive Myeloma with Rapid Relapsed

- ➢ Likely combination therapy
- ➢ Do Not wait for symptomatic Relapse

Chemotherapy- Based Salvage	Chemotherapy Novel agents	Transplant Based Salvage
• DDCEP vs DT- PACE • Oral vs. i.v chemotherapy • performance status of patient plays an important role.	Combination of linalidomide/Bortizomib & other chemotherapy	• Likely to be short lived • Rapid disease control • Reconstitute marrow

New Agents and Regimens Approved for RRMM

Preferred Regimen:

- VRD (Velcade, Revlimid, Dexa); Approved by MOH
- KD (Carfilzomib weekly, Dexa); by early access progrom/MOH
- DVD(Daratumomab,Velcade,Dexa);by early access progrom/MOH
- DRD(Daratumomab, Revlimid ,Dexa);by early access progrom/MOH .
- Pomalidomide/Dexa; by early access progrom/MOH.
- PCD(Pomalidomide/Cyclophosohamide/Dexamethason) by early access progrom/MOH.

Other recommended regimen

- ➢ BVD (Bendamustine/Bortizomib/dexamethasone)
- ➢ BRD(Bendamustine/Revlimid/dexamethasone)
- ➢ Bendamustine/liposomal doxo/Dexamethasone

- VCD (Velcade, Cyclophosphamide,Dexa)
- KCD (Carfilzomib ,Cyclophosphamide,Dexa)
- VD (Velcade, ,Dexa)
- Poma/bortizomib/Dexa
