

**A. Diagnostic Criteria Multiple Myeloma**

## DIAGNOSIS OF MULTIPLE MYELOMA

## Major criteria:

1. plasmacytoma (tissue biopsy)
2. > 30% plasma cells in bone marrow
3. monoclonal serum M-protein IgG > 35 g/l; IgA >20 g/l, or urine M-protein >1 g/24 hrs in the absence of amyloidosis

## Minor criteria:

- a. plasma cells in bone marrow > 10% but ≤ 30%
- b. monoclonal serum M-protein IgG ≤ 35 g/l, IgA ≤ 20 g/l, urine M-protein ≤ 1 g/24 hrs
- c. lytic bone lesions
- d. normal IgG <6 g/l or IgM <0.5 g/l or IgA <0.2 g/l

Multiple Myeloma is diagnosed in case one of the following combinations of criteria is present:

1 + b **or** 1 + c **or** 1 + d

2 + b **or** 2 + c **or** 2 + d

3 + a **or** 3 + c **or** 3 + d

a + b + c **or** a + b + d

## STAGING OF MULTIPLE MYELOMA

**Staging according to Salmon & Durie criteria**

<u>Stage I</u>	<u>Low Tumor Mass – all of the following:</u>  Hemoglobin > 6.2 mmol/l Ca <sup>2+</sup> < 2.65 mmol/l * IgG < 50 g/l IgA < 30 g/l Urine M-protein < 4 g/24 hrs Normal skeletal assessment or solitary plasmacytoma
<u>Stage II</u>	<u>Intermediate Tumor Mass:</u>  Patients who qualify for neither Stage I nor III
<u>Stage III</u>	<u>High Tumor Mass – Any one of the following:</u>  Hemoglobin < 5.3 mmol/l Ca <sup>2+</sup> > 2.65 mmol/l * IgG > 70 g/l IgA > 50 g/l Urine M-protein > 12 g/24 hrs ≥ 3 lytic bone lesions on skeletal survey (bone scans are not acceptable)
A	Normal renal function (creatinin < 177 µmol/l)
B	Renal insufficiency (creatinin ≥ 177 µmol/l)

\* Correct the serum Ca<sup>2+</sup> by adding 0.02 mmol/l for every g/l albumin below 40 g/l

**Staging according to ISS criteria**

Stage I: Serum  $\beta_2$ -microglobulin < 3.5 mg/l AND  
Serum albumin  $\geq$  3.5 g/dl ( $\geq$  35 g/l)

Stage II: Patients who qualify for neither Stage I nor III

Stage III: Serum  $\beta_2$ -microglobulin  $\geq$  5.5 mg/l

## B. Response Criteria for Multiple Myeloma

Based on EBMT, IBMTR and ABMT criteria (British J. Haemat. 102: 1115-1123, 1998)

Complete response (CR) requires *all* of the following:

1. Absence of the original monoclonal paraprotein (M-Protein) in serum and (10 x concentrated) urine by immunofixation, maintained for at least 6 weeks.
2. < 5% plasma cells in a representative bone marrow aspirate or otherwise in a bone marrow biopsy. Only in patients with non-secretory myeloma, bone marrow investigation must be repeated after an interval of 6 weeks to confirm CR.
3. No increase in size or number of lytic bone lesions (development of compression fractures does not exclude CR)
4. Disappearance of any soft tissue plasmacytoma.

Patients in whom some, but not all, criteria for CR are fulfilled are classified as PR or VGPR, providing the remaining criteria satisfy the requirements for PR/VGPR. This includes patients in whom routine electrophoresis is negative but in whom immunofixation has not been performed.

Very good partial response (VGPR) requires all of the following:

1. Meeting the criteria for partial response but show a 90% reduction of serum M-protein concentration for at least 6 weeks.

Partial response (PR) requires *all* of the following:

1.  $\geq 50\%$  reduction of serum M-protein concentration maintained for at least 6 weeks.
2. Reduction in 24 hrs urine M-protein either by  $\geq 90\%$  or to < 200 mg, maintained for at least 6 weeks.
3. In patients with non-secretory myeloma,  $\geq 50\%$  reduction in plasma cells in a representative bone marrow aspirate, or otherwise bone marrow biopsy, maintained for at least 6 weeks.
4.  $\geq 50\%$  reduction in size of soft tissue plasmacytoma.
5. No increase in size or number of lytic bone lesions (development of compression fractures does not exclude PR).

Patients in whom some, but not all, criteria for PR are fulfilled are classified as MR, providing the remaining criteria satisfy the requirements for PR.

Minimal response (MR) requires *all* of the following:

1.  $\geq 25\%$  reduction of serum M-protein concentration maintained for at least 6 weeks.
2.  $\geq 50\%$  reduction in 24 hrs urine M-protein, maintained for at least 6 weeks.
3. In patients with non-secretory myeloma,  $\geq 25\%$  reduction in plasma cells in a representative bone marrow aspirate, or otherwise bone marrow biopsy, maintained for at least 6 weeks.
4.  $\geq 25\%$  reduction in size of soft tissue plasmacytoma.
5. No increase in size or number of lytic bone lesions (development of compression fractures does not exclude MR).

No change (NC)

1. Not meeting the criteria of either minimal response or progressive disease.

Progressive disease (for patients without prior response) requires one or more of the following:

1.  $> 25\%$  increase in serum M-protein level, which must also be an absolute increase of at least 5 g/l and confirmed at least once.
2.  $> 25\%$  increase in 24 hrs urine M-protein, which must also be an absolute increase of at least 200 mg/24 hrs and confirmed at least once.
3.  $> 25\%$  increase in plasma cells in a representative bone marrow aspirate or bone marrow biopsy
4. Definite increase in the size of existing bone lesions or soft tissue plasmacytomas.
5. Development of new bone lesions or soft tissue plasmacytomas (development of compression fractures does not exclude continued response and may not indicate progression).
6. Development of hypercalcaemia (corrected serum calcium  $> 2.80$  mmol/l) not attributable to any other cause.

Plateau

1. Stable values (within 25% above or below value at the time response is assessed) maintained for at least 3 months.

Relapse from CR requires at least one of the following:

1. Reappearance of serum or urine M-protein on immunofixation or routine electrophoresis, confirmed by at least one further investigation and excluding oligoclonal immune reconstitution.
2.  $\geq 5\%$  plasma cells in a representative bone marrow aspirate or bone marrow biopsy
3. Development of new lytic bone lesions or soft tissue plasmacytomas or definite increase in the size of residual bone lesions (development of compression fractures does not exclude continued response and may not indicate relapse).

4. Development of hypercalcaemia (corrected serum calcium > 2.80 mmol/l) not attributable to any other cause.

*Progression after PR / MR* requires one or more of the following:

1. > 25% increase in serum M-protein level compared to nadir, which must also be an absolute increase of at least 5 g/l and confirmed at least once.
2. > 25% increase in 24 hrs urine M-protein compared to nadir, which must also be an absolute increase of at least 200 mg/24 hrs and confirmed at least once.
3. > 25% increase in plasma cells in a representative bone marrow aspirate or bone marrow biopsy compared to nadir.
4. Definite increase in the size of existing bone lesions or soft tissue plasmacytomas.
5. Development of new bone lesions or soft tissue plasmacytomas (development of compression fractures does not exclude continued response and may not indicate progression).
6. Development of hypercalcaemia (corrected serum calcium > 2.80 mmol/l) not attributable to any other cause.