Response criteria for multiple myeloma

In multiple myeloma (MM), the majority of patients will inevitably relapse. However, over the past few years, the introduction of novel therapies has enabled achievement of progressively higher complete response (CR) rates.

- Until relatively recently, there was no consistent definition of CR and, therefore, it was difficult to compare the effectiveness of different treatments for MM.
- As MM treatments become more effective, appropriately sensitive response criteria have become essential to assess treatment effectiveness and to guide when treatment should be stopped or started (Table 1).
- The level of response to treatment is linked to outcome measures such as progression-free survival (PFS) and overall survival.

The better the response to treatment, the better the prognosis for the patient.

Table 1. The 2011 International Myeloma Working Group (IMWG) response criteria for MM and efficacy endpoints measured in time.

<table>
<thead>
<tr>
<th>IMWG response criteria</th>
<th>Efficacy endpoints measured in time</th>
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</thead>
<tbody>
<tr>
<td>Molecular CR</td>
<td>Time to progression (TTP)</td>
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<tr>
<td>Immunophenotypic CR</td>
<td>PFS</td>
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<td>Stringent complete response (sCR)</td>
<td>Event-free survival (EFS)</td>
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<td>CR</td>
<td>Disease-free survival (DFS)</td>
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<td>Very good partial response (VGPR)</td>
<td>Duration of response (DOR)</td>
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<td>Partial response (PR)</td>
<td>Overall survival (OS)</td>
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<td>Minimal response (MR)</td>
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<td>Stable disease (SD)</td>
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<td>Progressive disease (PD)</td>
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Moving towards more stringent criteria

Since 1997, improvements in techniques for assessing disease status have led to the development of more stringent response criteria (Figure 1).

- IMWG uniform criteria are now the standard criteria for assessment of response.
- Techniques that have enabled the prediction of significantly inferior survival among CR patients with MM include:
  - Multiparameter flow cytometry (MFC)
  - Polymerase chain reaction (PCR)
  - Next-generation sequencing (NGS)
  - Positron emission tomography/computed tomography (PET/CT)
Multiple myeloma response criteria – guiding patient management

Response criteria – role in patient management

High quality response criteria can help to guide patient management, providing:

• More reliable assessment of the quality of response to treatment
• More accurate methods to measure the efficacy of different treatment approaches
• More rigorous comparisons between treatment strategies are possible
• More accurate determination of inadequate responses, allowing changes to treatment strategies
• Improved accuracy in detection/prediction of relapse

If patients achieve a greater depth of response following treatment they are more likely to have better outcomes (Figure 2). However, the drive to achieve greater depth of response than CR should be balanced against the potential for treatment toxicity, particularly in elderly patients and those with indolent disease that will be slow to progress.

Reaching down to the molecular level

New techniques now allow for the detection of minimal residual disease (MRD) the persistence of small numbers of residual myeloma cells during or following treatment. The presence of this small number of myeloma cells can lead to relapse, even in patients with CR.

• Patients without signs of residual disease are described as MRD-negative and these patients are likely to have the greatest duration of response to treatment (Figure 3)

Summary points

• Developments in diagnostic techniques have allowed or more stringent definition of response criteria
• Achieving a greater depth of response can improve long-term outcomes and delay disease progression
• The individual patient circumstances, rate of disease progression, and risk of toxicity versus benefit should be evaluated when considering treatment strategies
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References


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