

E8. REFRACTORY / RELAPSED MULTIPLE MYELOMA - STANDARD AND CLINICAL TRIAL THERAPY

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Multiple myeloma (MM) is by definition a chronic disease that usually requires more than one regimen. So the second line treatment is necessary in most cases of multiple myeloma.

In practice, we meet two groups of patients with MM who require second-line therapy:

- MM refractory - nonresponsive disease, or progression within 60 days after the last treatment

- MM relapsed - the disease progresses to more than 60 days after first line therapy and require treatment

First-line treatment is standardized in therapeutic protocols, and usually include strengthening auto / allo stem cell transplant (SCT) to eligible patients. But complete answer does not exceed 20%.

International treatment guidelines recommendations (ESMO) are usually vague and general practitioner needs explicit customized recommendations.

In this context, second-line therapy in myeloma refractory / relapsed should be assessed and customized according to the time of relapse, the associated comorbidities, including post-induction complications and eligibility for stem cell transplantation.

Recommended therapeutic guidelines mention the possibility of using the initial therapy in case of relapse in distance, especially new molecules (thalidomide, bortezomib, lenalidomide) in combination.

An example of the second-line treatment protocols is shown in the HOVON guidelines which recommended retreatment if relapse occurred more than 1 year and at least VGPR type response (very good partial response). Otherwise, the combination of bortezomib in 11 cycles or lenalidomide until progression.

A more detailed guide is in the NCCN guidelines, which direct second-line therapy in stages, depending on eligibility for transplantation, the response to previous therapy, comorbidities.

Selection regimens must be a rational process based on patient characteristics.

Patient selection is based on:

- patient characteristics, cytogenetics, FISH, flow (NCCN)

- Renal function
- performance score
- preexisting peripheral neuropathy
- cytopenia, anemia, and gastrointestinal toxicity may limit treatment

Supportive treatment is also an important aspect in the treatment of patients with multiple myeloma.

The combinations available are different for refractory / relapsed MM:

- Bortezomib
- Bortezomib / dexamethasone
- Bortezomib / liposomal doxorubicin
- Bortezomib / thalidomide / dexamethasone
- Cyclophosphamide / bortezomib

dexamethasone

- Dexamethasone / cyclophosphamide / etoposide / cisplatin (DCEP)

- Dexamethasone / thalidomide / cisplatin / doxorubicin / cyclophosphamide / etoposide (DT PACE) ± bortezomib (VTDPACE)

- High-dose cyclophosphamide
- thalidomide / dexamethasone
- Melphalan / Prednisone
- Melphalan / Prednisone / Thalidomide
- Bortezomib / Melphalan / Prednisone /

Thalidomide

- Vincristine / Adriablastine / Dexamethasone (VAD)
- Auto / allo SCT

Besides the combination with established drugs, clinical trials are an important option that allows access to certain therapies. The actual use of lenalidomide is possible in most clinical trials with the introduction of new drugs: carfilzomib, elotuzumab, pomalidomide, bendamustine, vorinostat, Tanespimycin, etc..

In conclusion, lenalidomide and bortezomib regimens are effective in relapsed / refractory myeloma, and using weekly bortezomib decreases the risk of discontinuation. Also, the combination of thalidomide in refractory myeloma combinations should be supplemented with the increasing number of drugs in combination. Clinical trials are recommended as the first option for eligible patients. Stem cell transplantation should be reviewed in all patients with relapsed multiple myeloma.