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Relapsed Refractory Multiple Myeloma: Treatment Approaches and Adverse Events

New therapeutic strategies and expert insights

Multiple myeloma is a cancer originating in plasma cells

It represents[1]:

~1% of all cancer cases

~10% of all hematological malignancies

Almost all patients with multiple myeloma experience relapse after first-line therapy

New drug agents have expanded the therapeutic armamentarium against relapsed/refractory multiple myeloma (RRMM)

Overview of established and emerging treatments

Established therapies

Immunomodulators such as thalidomide, lenalidomide, and pomalidomide[2]

Proteasome inhibitors such as bortezomib, carfilzomib, and ixazomib[3]

Monoclonal antibodies such as daratumumab, isatuximab, and elotuzumab[4]

Emerging therapies

Small molecules such as B-cell lymphoma 2 inhibitors and exportin-1 inhibitors (selinexor)

Antibody-drug conjugates (belantamab mafodotin)

T-cell redirected therapies
- Chimeric antigen receptor (CAR) T-cell therapy
- Bispecific antibodies

Each class of RRMM medication has different biological mechanisms, unique toxicity profiles, and therapy-related adverse events

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Goals of optimal RRMM therapy

- Deep response to therapy
- Improved survival
- Effective management of adverse events so that they do not compromise responses and survival outcomes

Carfilzomib, a next-generation proteasome inhibitor

- Produces significant response in patients with RRMM
- Can be used in combination with immunomodulatory drugs and monoclonal antibody drugs

Side effects associated with carfilzomib

Cardiotoxicity

- Patients commonly experience shortness of breath
- Cardiac toxicity manifesting as congestive heart failure is less common
- Reduction in muscular strength of the heart due to proteasome inhibition may be the underlying mechanism causing side effects
- Reduction in muscle strength can be reversed by discontinuing the drug

Start patients on a lower dose of the drug and then increase it progressively

Strategies for managing cardiotoxicity

- Give the infusions over a longer period of time in case of issues
- Ensure that blood pressure is well maintained at the time of treatment initiation
- Consider alternative drugs for at-risk patients (such as bortezomib)
- Screen patients for pre-existing cardiac problems to anticipate and prevent issues
  - Baseline echocardiogram
  - Assessment of cardiac functions
  - Cardiac biomarkers like N-terminal pro-B-type natriuretic peptide

Proactively monitor patients at risk of congestive heart failure (such as those with low ejection fraction)

Other side effects

- Renal toxicity
- Drug-induced fever
- Thrombotic microangiopathy

Groups at risk of adverse events

- Older patients
- Patients with pre-existing cardiac problems
- Patients with diabetes mellitus

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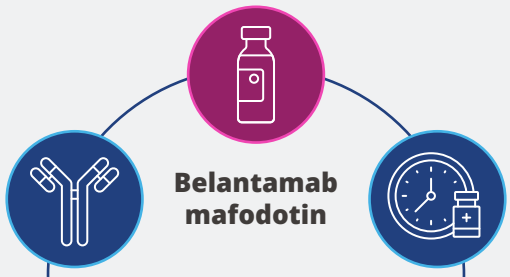
Combination therapy with pomalidomide + dexamethasone or bortezomib + dexamethasone has shown benefit in phase 3 trials



It is an antibody-drug conjugate

Belantamab mafodotin

It has high efficacy

Side effects associated with belantamab mafodotin

Ocular toxicity

Belantamab mafodotin may impact vision, especially at higher doses

However, since efficacy is high, treatment can be resumed after vision problem resolves

Other side effects

Ocular toxicity

Strategies for managing ocular toxicity

Start treatment with a low dose (2.5 mg/kg)

Administer drug once every eight weeks

Use low doses, especially in older patients

In case of issues, reduce the dose to 1.9 mg/kg

Optimize vision through requisite procedures such as cataract surgery before starting treatment

The drug is used in combination with bortezomib and dexamethasone

It is an inhibitor of nuclear export (selectively inhibits exportin-1)

Selinexor

Can be administered orally

Side effects associated with selinexor

Nausea

May affect patients' appetite

Needs to be monitored proactively

Strategies for managing nausea

Administer drugs once a week

Prevent nausea through prophylaxis (a combination of two antiemetic drugs)

Other side effects

Diarrhea – treat to manage

Neutropenia – more common in combination therapies involving pomalidomide and daratumumab

Vomiting

Fatigue

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CAR T-cell therapy

Groundbreaking therapy that targets specific antigens in cancer cells

Highly effective in treating hematologic malignancies

Side effects associated with CAR T-cell therapy

- Cytokine release syndrome (CRS)
- Neurological toxicity
- Heightened risk of infections

Ensure vaccination (for influenza, coronavirus disease, pneumococcal disease) before treatment

Strategies for managing CAR T-cell therapy side effects

- Suggest prophylaxis for CRS using interleukin-6 antibodies
- Administer intravenous immunoglobulin to prevent infections
- Monitor patients with CRS (in the intensive care unit if required)
- Screen patients for Cytomegalovirus (CMV), Epstein-Barr virus, pneumocystis pneumonia, etc. before treatment
- Provide supportive care therapy for CRS
- Prophylactic ganciclovir for CMV prevention is not a common practice; instead, patients are monitored and treated only upon significant viremia or disease signs

Prescribe medications for maintaining blood pressure if necessary

Key message

By proactively preventing adverse events and effectively managing side effects, clinicians can leverage emerging treatments to achieve substantial survival benefits for patients with RRMM

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