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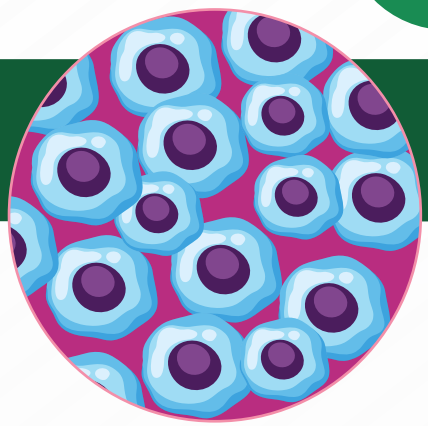
Emerging Treatment Approaches for Mantle Cell Lymphoma

Highlights from the European Hematology Association Congress 2024



Treatment of mantle cell lymphoma (MCL) depends on several factors, including disease presentation, stage, patient age, and comorbidities[1]

Common classification based on morphology and genetics

- Classical MCL
- Blastoid MCL
- Pleomorphic MCL (cancer progression due to *TP53* mutation and other oncogenic abnormalities)

Patients with a low tumor burden and without adverse mutations are spared immediate treatment. The treatment approach takes into account the stage, tumor burden, symptoms, and disease aggressiveness, which may include but is not limited to genetic factors. The "wait and watch" approach eliminates unnecessary side effects of treatment[2]

Patients with *TP53*, *NOTCH1*, and other oncogenic mutations are treated using high-dose cytarabine, with additional biological agents and anthracycline depending on the MCL international prognostic index (MIPI) score[2]

Real-world data from observational studies in the UK[3]

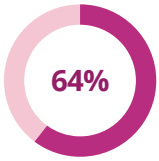
73 centers

588 patients

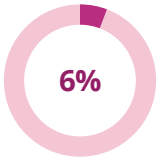
Patient factors associated with immediate treatment approach

- MIPI score
- Lactate dehydrogenase levels
- Nodal disease
- Ki-67 protein levels

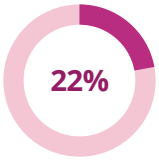
Percentage of patients in the "wait and watch" group who:



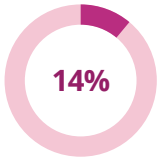
Proceeded to treatment eventually



Received treatment within 6 months of diagnosis



Remained under observation



Did not receive treatment until death

Phases of MCL treatment

Induction → Immunotherapy + chemotherapy → MCL remission

Maintenance → Maintenance therapy → Elimination of minimal residual disease

Benefits of maintenance treatment using rituximab[4]

Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) induction + Rituximab maintenance

- Progression-free survival (PFS)
- Overall survival (OS)
- Maintenance is safe beyond 2 years

Possible benefits of rituximab maintenance after first-line bendamustine and rituximab induction[5]

Bendamustine and rituximab induction + Rituximab maintenance

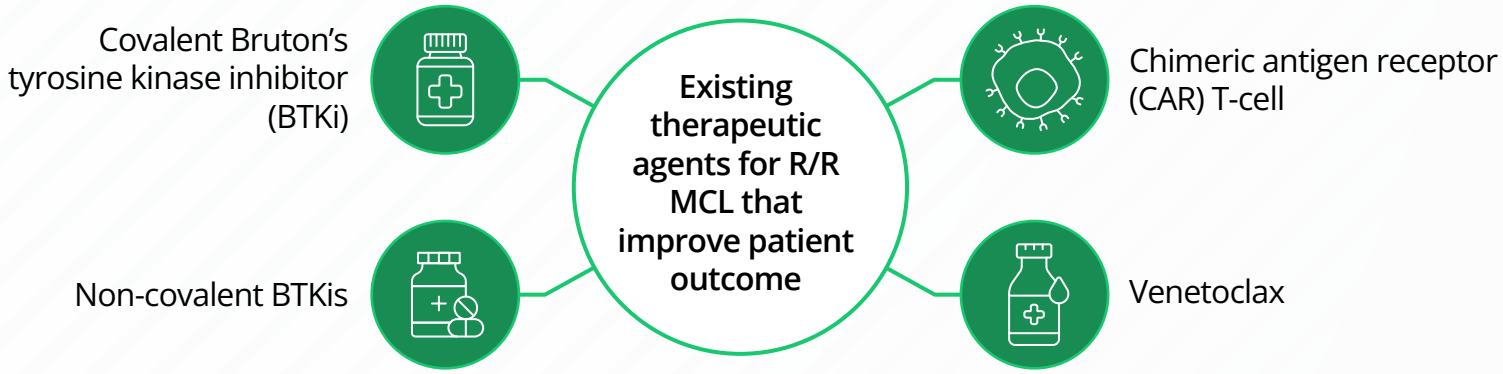
- Event-free survival
- OS

Effects of adding ibrutinib to immunochemotherapy induction[6]

- Survival benefits in younger patients
- Increased toxicity with autologous stem-cell transplantation

Maintenance therapy using rituximab may improve treatment outcomes for patients with MCL, while the addition of ibrutinib to induction therapy benefits only younger patients

Treatment outcomes for relapsed/refractory (R/R) MCL have improved greatly in the past decades[7]



Covalent BTKi therapy[6,8,9]

Advantages

- Well-tolerated in most patients
- Oral administration

Disadvantages

- Can result in cross-resistance when used with ibrutinib, zanubrutinib, and acalabrutinib
- Safety profiles differ as indicated by studies comparing zanubrutinib/acalabrutinib versus ibrutinib regimen

Patients with R/R MCL treated with ibrutinib have:[10]

Objective response rate:
66%

PFS:
12.8 months

OS:
25.0 months

Venetoclax (B-cell lymphoma 2 inhibitor) therapy[11]

Advantages

- Combinations with CD20 antibodies, BTKi, and venetoclax seem to be effective in *Tp53*-mutated MCL
- Can be used in combination with BTKi

Disadvantages

- The combination of venetoclax with BTKi does not show a clear OS benefit when considering all patients with R/R MCL, but there is a trend towards better OS with the combination therapy compared to BTKi alone in this specific subgroup
- Large cohort studies needed to confirm efficacy

Screening patients with R/R MCL for *TP53* mutation status is a key step in treatment design[12,13]

Benefits of ibrutinib (BTKi) and venetoclax combinational therapy for *TP53* + R/R MCL[12,13]

- Higher complete remission rates
- Durable remission

Advantages of bispecifics over CAR-T therapy

- Administration is convenient for patients
- Lower risk of cytokine release syndrome

Bispecifics currently approved for R/R that diffuse large B-cell lymphoma include:

- Glofitamab
- Epcoritamab

Benefits of glofitamab monotherapy in patients with heavily pretreated R/R MCL[14]

Overall response rate:
85.0%

Complete responses:
78.3%

A wider array of treatment options for R/R MCL has made therapy more tailored to:[15]

Patient risk tolerance

Comorbidities

Patient age

Patient's convenience and access to care

The development of new therapeutic agents and combination therapies has made the treatment of R/R MCL more tailored to the patient, significantly improving outcomes

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