LymphomaHub

MCL

Long-term follow-up of ^{90}Y ibritumomab tiuxetan consolidation in MCL patients

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Immunochemotherapy followed by consolidation with autologous stem cell transplantation (ASCT) and/or rituximab maintenance is the current standard of care for patients with mantle cell lymphoma (MCL). However, this approach is not a feasible option for some patients, such as the elderly or unfit patients with comorbidities.

On 9 April , Wojciech Jurczak from Jagiellonian University Medical College, Krakow, PL, and colleagues, published in *Leukemia & Lymphoma* an 8-year follow-up of a phase II trial on behalf of the Polish Lymphoma Research Group.

This multicenter, prospective phase II study investigated whether radioimmunotherapy consolidation with ^{90}Y ibritumomab tiuxetan (RIT) is an efficient treatment for patients with MCL, who are ineligible to receive high-dose chemotherapy. The primary endpoints of the study were complete response (CR) rates after consolidation with the ^{90}Y-labeled anti-CD20 monoclonal antibody, and the feasibility of the regimen. Secondary endpoints included progression-free survival (PFS), and overall survival (OS).

Study design & baseline characteristics

- N = 46 patients with advanced MCL chemosensitive to first or second line chemotherapy, and not eligible for ASCT

Total number of patients	N = 46
Median patient age	60 (30–78) years
Male gender	70% (n = 32)
Advanced disease clinical stage (IV)	85% (n = 39)
Extranodal disease	87% (n = 40)
Bone marrow involvement	41% (n = 19)

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Elevated lactate dehydrogenase (LDH)	71% (n = 33)
MCL International Prognostic Index (MIPI)	5.8 (range, 4–7)
Low risk	39% (n = 18)
Intermediate risk	32.6% (n = 15)
High risk	28.4% (n = 13)

- Treatment plan:
  - Induction chemotherapy regimens:
    - Cyclophosphamide, vincristine, and prednisone (CVP): C, 750 mg/m^2; V, 1.4 mg/m^2 (maximum 2 mg); P, 60–100 mg on Days 1–5
    - Cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP): C, 750 mg/m^2; H, 50 mg/m^2; O, 1.4 mg/m^2 (maximum 2 mg); P, 60–100mg on Days 1–5
    - Fludarabine and cyclophosphamide (FC): F, 25 mg/m^2; C, 250 mg/m^2 on Days 1–3
    - FC plus mithoxanthrone (FCM): F, 25 mg/m^2; C, 250 mg/m^2 on Days 1–3 and M, 12.5 mg/m^2 on Day 1
    - Rituximab (R; 375 mg/m^2) was not regarded a standard of care at the time so it was given depending on availability on Day 1 of every cycle in 58.5% of patients. No patient was given R maintenance
  - RIT: Patients responding to induction therapy were consolidated with RIT 3–5 weeks after the last chemotherapy cycle
    - RIT: Two doses of 250 mg/m^2 of R administered seven days and 24 hours prior to the intravenous injection of the ^{90}Y-labeled ibritumomab tiuxetan at a dose of 0.4 mCi/kg for patients with normal platelet count and 0.3 mCi/kg for those with platelet count between 100.,000 and 150,000 cells/mm^3. Maximum dose was 32.0 mCi
  - Treatment assessments were performed at baseline, after the third chemotherapy cycle, before RIT and six weeks after RIT completion
- Median observation (range): 4.6 (0.4–12) years

Key findings

- Patients receiving induction chemotherapy as first-line (n = 34):
  - FCM/FC ± R: n = 20 patients
  - CHOP/CVP ± R: n = 14 patients
- Response rates from both induction treatments:

- CR: 41% (n = 14)
- Partial response (PR): 59% (n = 20)

- In this population, RIT consolidation improved CR rates from 41% to 91%

- Patients receiving induction chemotherapy as second-line (n = 12):
  - FCM/FC ± R: n = 1
  - CHOP/CVP ± R: n = 11
- Response rates from both induction treatments:
  - CR: 17% (n = 2)
  - PR: 83% (n = 10)
- In this population, RIT consolidation improved CR rates from 17% to 75%

- All consolidated patients (first- and second-line treatments; n = 46):
  - Response rates from both induction treatments:
    - CR: 35% (n = 16)
    - PR: 65% (n = 30)
  - Median PFS of patients consolidated after first-line therapy: 3.3 years
  - Median PFS of patients after chemosensitive relapse: 1.8 years
    - Comparison: $P < 0.05$
  - Median OS of patients consolidated after first-line therapy: 6.5 years
  - Median OS of patients after chemosensitive relapse: 2.2 years
    - Comparison: $P < 0.05$
  - Median PFS of patients achieving CR after first-line therapy and RIT: 5.8 years

Safety

- Deaths during the course of the study: n = 26
  - Due to early complications: 4.3% (n = 2)
  - Due to developing myelodysplastic syndrome: 10.8% (n = 5)
  - Due to MCL relapse or progression: 38% (n = 16)
- The entire protocol was well-tolerated
- Most common adverse events (AEs):
  - Bone marrow toxicity in the form of cytopenias:
    - Grade 1–2: 43% (n = 19)
    - Grade 3–4: 34% (n = 15)

- Grade 3–4 thrombocytopenia and leukopenia were more frequent in patients treated with fludarabine-based regimens ($P < 0.05$)
- Non-life threatening infections occurred in 48% of patients (n = 22) following RIT

Conclusions

- RIT seemed to be a feasible regimen for elderly or unfit patients with comorbidities, who are ineligible for high-dose chemotherapy and ASCT consolidation
- In this population, RIT consolidation following induction chemotherapy appears to confer durable responses and good PFS
- The regimen had a manageable toxicity profile but was worse after fludarabine-based regimens

References

1. Jurczak W. *et al.* Consolidation with 90Y ibritumomab tiuxetan radioimmunotherapy in mantle cell lymphoma patients ineligible for high dose therapy: results of the phase II multicentre Polish Lymphoma Research Group trial, after 8-year long follow-up. *Leuk Lymphoma*. 2019 Apr 9:1-8. DOI: 10.1080/10428194.2019.1602261 [Epub ahead of print].