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LETTER TO THE EDITOR

Successful retreatment with 3-week rituximab-bendamustine with high-dose dexamethasone in patients with relapsed/refractory mantle cell lymphoma

Wolfgang Lamm[1] · Barbara Kiesewetter[1] · Hannah Puhr[1] · Werner Dolak[2] · Marius E. Mayerhöfer[3] · Markus Raderer[1]

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Dear Editor,

Mantle cell lymphoma (MCL) is an aggressive subtype of B cell non-Hodgkin's lymphoma (NHL) which accounts for approximately 6% of all NHLs [1]. Roughly 5% of patients suffer from the more aggressive blastic variant MCL [2].

Bendamustine in combination with rituximab (RB) has shown promising results in different phase III trials in elderly patients unfit for high-dose chemotherapy in different kinds of lymphomas, including MCL with response rates of approximately 86–93% [3–6].

Bendamustine in relapsed/refractory lymphomas including MCL also showed promising results [7]. RB retreatment, however, has never been investigated before. In view of this, we have performed a retrospective single-center analysis to evaluate the clinical efficacy and safety of RB retreatment in patients with MCL.

Seven patients were retreated with RB (Table 1), which was given on a 3-week basis along with dexamethasone. The median age was 81 years (range 65–83). Additional patients' characteristics and disease-related features are summarized in Table 1. According to the MIPI risk group, one patient was at low risk, two patients had intermediate risk, and the remaining four patients were at high risk, when RB was given for the first time. Five patients achieved a complete remission, whereas one patient each achieved partial remission or stable disease. The median number of cycles for initial therapy was 6, and the median time from end of first RB initiation until retreatment with RB was 33.7 months (range 12.4–152.8). At retreatment, the most common MIPI stage was high risk (86%). Five patients (71%) again achieved a complete remission. All patients consented to treatment according to institutional guidelines and all patients had consented to anonymized assessment and analysis of data and outcome of therapy.

Rituximab was administered at 375 mg/m^2 on day 1 of each cycle; bendamustine was given at 90-mg/m^2 dose on days 2 and 3. Dexamethasone was given orally at a daily dose of 40 mg on days 1–4 of each treatment cycle and treatment was repeated every 3 weeks. Patients were restaged every three cycles and then every 3 months afterwards until progression using conventional CT scans.

At the time of analysis, 5/7 patients are still alive. After a median follow-up of 79.1 months, a median OS of 98.8 months (range 56.5–152.8) was found.

Tolerance was excellent, with most of the toxicities being grades 1 and 2. The most frequent hematological adverse events during first administration were anemia (67%) and leukopenia (57%). Frequent grade 3 and 4 hematological toxicities were only observed during retreatment and consisted of leukopenia and anemia, each one person.

To the best of our knowledge, this is the first report of RB retreatment in patients with MCL. Retreatment with RB was excellently tolerated with few side effects. Our investigations are in line with other phase III trials in the front-line setting, as mentioned before [3–6]. When compared to RB treatment in the relapsed/refractory setting, RB was more effective when compared to other regimens [7, 8].

Taken together, our data show that RB retreatment is an active regimen with excellent tolerance in elderly patients with MCL, with a surprisingly low incidence of side effects.

✉ Wolfgang Lamm
wolfgang.lamm@meduniwien.ac.at

[1] Department of Medicine I, Clinical Division of Oncology, Medical University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria

[2] Department of Medicine III, Clinical Division of Gastroenterology and Hepatology, Medical University of Vienna, Vienna, Austria

[3] Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna, Vienna, Austria

Table 1 Patient characteristics

Sex/age	Histology	Stage 1	MIPI 1	R-Benda 1 (months)	Response 1	Time from first until second R-Benda (months)	Therapies between first R-Benda and reinduction	Stage 2	MIPI 2	R-Benda 2 (months)	Response 2	Status	OS
f/83	Common type	2a	Low risk	5.23	CR	152.8	R-Thal	2a	Intermediate risk	5.5	CR	Alive	226.12
m/78	Common type	4b	High risk	5.56	CR	35.6	RADOX, Imbruvica	4a	High risk	7.0	CR	Alive	98.9
m/82	Common type	4a	High risk	4.28	PR	33.7	R-CHOP	4b	High risk	4.7	CR	Alive	79.1
m/81	Common type	4b	High risk	5.03	CR	24.9	Rituximab maintenance	4b	High risk	7.2	CR	Alive	106.1
m/82	Common type	2a	High risk	7.57	SD	27.9	Imbruvica	4a	High risk	5.3	SD	Dead	50.6
m/75	Common type	2a	Intermediate risk	3.98	CR	12.4	R-CHOP	4b	High risk	5.0	PR	Dead	39.7
w/65	Common type	4a	Intermediate risk	4.87	CR	40.5	No therapy	4a	High risk	4.6	CR	Alive	54.3

MIPI, Mantle Cell Lymphoma International Prognostic Index; *CR*, complete remission; *PR*, partial remission; *SD*, stable disease; *R-CHOP*, rituximab, cyclophosphamide, doxorubicine, vincristine, prednisone; *R-Thal*, rituximab, thalidomide; *R-BENDA*, rituximab, bendamustine; *T*, thalidomide; *RADOX*, rituximab; *ArA-C*, oxaliplatin

Compliance with ethical standards All authors gave their informed consent for this study.

Conflict of interest The authors declare that they have no conflict of interest.

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