Outcomes for Recurrent Mantle Cell Lymphoma post-BTK Inhibitor Therapy in Japan; an Administrative Database Study

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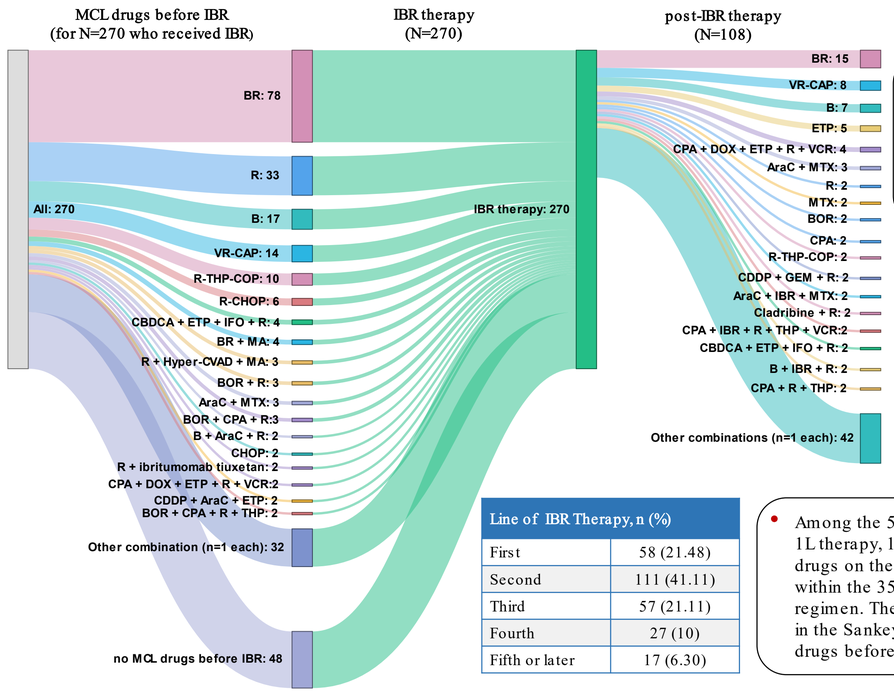
Background

- For patients with mantle cell lymphoma (MCL) there are currently no standard drug therapies after treatment with the covalent BTK inhibitor (BTKi), ibrutinib (IBR)
- The aim of this study was to investigate real-world treatment patterns and outcomes for patients with MCL following BTKi treatment in Japan

Methods

- This is a retrospective study using a hospital-sourced database (Medical Data Vision) that includes inpatient and outpatient claims and discharge summaries from ~25% of acute care hospitals in Japan
- **Patient selection:** MCL diagnosed in Dec. 2010 to Sep. 2019 (N=1,914) → received first MCL drug (index date) &age ≥20 years (N=1,374) → 171 excluded for MCL drugs before index date (170) and clinical trials after index date (1) → received first-line (1L) therapy starting on index date (N=1,203) → received IBR therapy (N=270)
- **MCL drug:** Antitumor drugs approved in Japan or listed in the Japanese Society of Hematology (JSH) or National Comprehensive Cancer Network (NCCN) guidelines for MCL. Regimens are defined as MCL drugs prescribed within 35 days from start of specific line of therapy
- **Analyses:** Baseline variables were evaluated within 90 days prior to start of therapy. Patients were followed from index date to end of available data for their antitumor treatments, other cares and outcomes

Treatments Before and After IBR Therapy



- Among 270 patients who received IBR therapy, 183 (68%) discontinued IBR and 108 (40%) subsequently received post-BTKi therapy
- These 108 of 183 (59%) patients received 60 unique antitumor drug combinations

Post-IBR Drug Combinations, n (%)	
B-based	29 (26.85)
BOR-based	20 (18.52)
AraC-based	14 (12.96)
Others	45 (41.67)

Line of IBR Therapy, n (%)	
First	58 (21.48)
Second	111 (41.11)
Third	57 (21.11)
Fourth	27 (10)
Fifth or later	17 (6.30)

- Among the 58 patients who received IBR as 1L therapy, 10 patients started other MCL drugs on the index date before receiving IBR within the 35-day period that defined the 1L regimen. These 10 patients were classified in the Sankey plot as those who had MCL drugs before IBR

Drug abbreviations: **AraC**, cytarabine; **B**, bendamustine; **BEAM**, carmustine, etoposide, cytarabine, melphalan; **BR**, bendamustine, rituximab; **BOR**, bortezomib; **CBDCA**, carboplatin; **CDDP**, cisplatin; **CHASER**, cyclophosphamide, cytarabine, dexamethasone, etoposide, rituximab; **CHOP**, cyclophosphamide, doxorubicin, vincristine, prednisolone; **COP**, cyclophosphamide, vincristine, prednisolone; **CPA**, cyclophosphamide; **DOX**, doxorubicin; **ETP**, etoposide; **GEM**, gemcitabine; **hyper-CVAD**, hyperfractionated cyclophosphamide, vincristine, doxorubicin, dexamethasone; **IBR**, ibrutinib; **ICE**, ifosfamide, carboplatin, etoposide. **IFO**, ifosfamide; **MA**, methotrexate, cytarabine; **MTX**, methotrexate; **R**, rituximab; **THP**, pirarubicin (tetrahydropyranyl-doxorubicin); **VCR**, vincristine; **VR-CAP**, bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisolone.

AEs/Supportive Care

	IBR Therapy (N=270)	Post-IBR Therapy (N=108)
Adverse events, n (%)		
Antiinfectives &infection in same month	69 (25.56)	29 (26.85)
Atrial fibrillation and flutter	26 (9.63)	5 (4.63)
Gastrointestinal hemorrhage	18 (6.67)	5 (4.63)
GCSF with FN in same month	3 (1.11)	14 (12.96)
Intracerebral hemorrhage	1 (0.37)	0
Supportive care, n (%)		
Antiinfectives	87 (32.22)	56 (51.85)
Arrhythmia procedures	0	1 (0.93)
Blood transfusions	40 (14.81)	42 (38.89)
Drugs for arrhythmia	75 (27.78)	27 (25)
Emergent hospital admission	46 (17.04)	6 (5.56)
Oral anticoagulants	19 (7.04)	4 (3.70)
Radiotherapy	11 (4.07)	9 (8.33)

Abbreviations: FN, febrile neutropenia; GCSF, granulocyte colony-stimulating factor; IBR, ibrutinib; AEs, adverse events.

Limitations

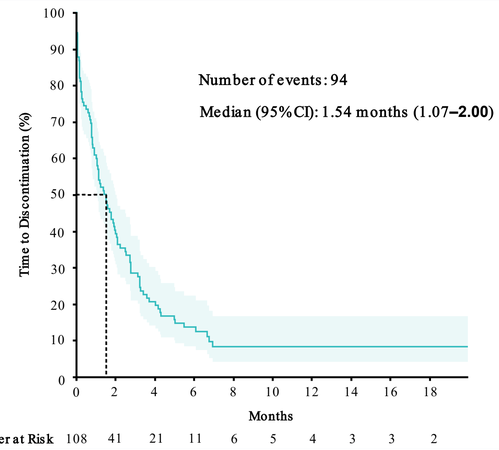
- The MDV database does not track a patient across multiple hospitals. Therefore, patient treatment information may be lost or only partially described
- Deaths are captured only from hospitalizations and therefore the mortality data may be incomplete
- Treatment lines and regimens were defined using the prespecified rule. Therefore, some patients may be misclassified regarding their intended prescribed regimen

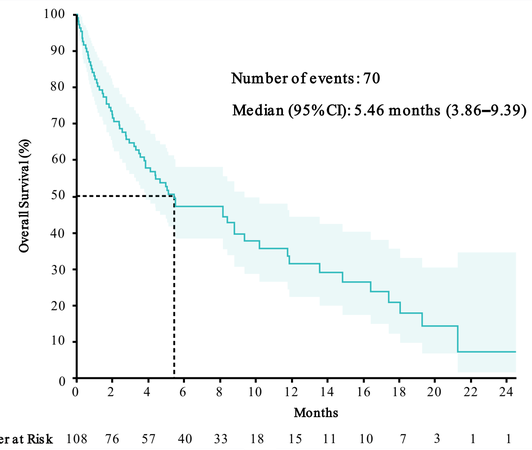
Patient Characteristics

Characteristic at baseline	Overall Population (N = 1,203)	Post-IBR Therapy (N = 108)
Age at index date, mean years (SD)	71 (10.48)	75 (7.30)
Sex, n (%)		
Male	893 (74.23)	83 (76.85)
Female	310 (25.77)	25 (23.15)
Any metastasis, n (%)	128 (10.64)	13 (12.04)
Bone or bone marrow metastasis, n (%)	79 (6.57)	8 (7.41)
CCI, mean (SD)	2.27 (1.37)	3.19 (1.49)
BMI, mean (SD)[a]	22.63 (3.40)	22.73 (3.77)
Total ADL independence, n (%)[b]		
Independent	880 (86.53)	68 (79.07)
Dependent	137 (13.47)	18 (20.93)

[a]Results were available only from discharge summaries for 1,053 patients in the overall population and 89 post-IBR therapy patients. [b]Results were available only from discharge summaries for 1,017 patients in the overall population and 86 post-IBR therapy patients. Abbreviations: ADL, activities of daily living; BMI, body mass index; CCI, Charlson Comorbidities Index; SD, standard deviation.

Time to Discontinuation and Overall Survival Post-IBR Therapy





Conclusions

- After completing IBR therapy, patients received subsequent antitumor therapy which was highly diverse because of lack of established standard of care
- Patients who received post-IBR therapy were in poor health status, experienced frequent adverse events and needed supportive care, indicating high disease and treatment burden
- After IBR therapy, patients experienced extremely poor outcomes (median time to treatment discontinuation of 1.5 months, median overall survival of 5.5 months) with currently available therapy options
- The development of safe and effective targeted therapy after BTKi is needed to improve the otherwise dismal outcomes of these patients

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