| Regimen                              | Number (%) |
|-------------------------------------|------------|
|                                      | N=121      |
|                                      |            |
| **First-line therapy regimen**      |            |
| R-CHOP                              | 61 (50.4%) |
| Alternating R-CHOP/R-DHAP           | 27 (22.3%) |
| CHOP                                | 11 (9.1%)  |
| R-HyperCVAD                         | 6 (5.0%)   |
| Rituximab + lenalidomide            | 3 (2.5%)   |
| others                              | 13 (10.7%) |
| **Most recent front-line therapy regimen** |            |
| R-CHOP                              | 38 (31.4%) |
| Alternating R-CHOP/R-DHAP           | 20 (16.5%) |
| Rituximab + lenalidomide            | 8 (6.6%)   |
| CHOP                                | 4 (3.3%)   |
| VR-CAP                              | 4 (3.3%)   |
| others                              | 47 (38.8%) |

Data are shown as number (%). The sum of some percentages may not equal 100% because of rounding. R-CHOP, rituximab + cyclophosphamide, vincristine, doxorubicin, prednisone; R-CHOP/R-DHAP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone/rituximab, dexamethasone, cytarabine, platinum; CHOP, cyclophosphamide, vincristine, doxorubicin, prednisone; R-HyperCVAD, cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine) + rituximab; VR-CAP, bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone.
Table S2. The ibrutinib-containing regimens in combination therapy group.

| Regimen                                      | Number (%) | N=53 |
|----------------------------------------------|------------|------|
| **Chemotherapy-free regimen**                |            |      |
| Ibrutinib + rituximab                        | 32 (60.4%) |      |
| Ibrutinib + rituximab + lenalidomide        | 10 (18.9%) |      |
| Ibrutinib + lenalidomide                    | 2 (3.8%)   |      |
| Ibrutinib + rituximab + bortezomib          | 1 (1.9%)   |      |
| **Ibrutinib-containing chemotherapy regimen** | 8 (15.1%)  |      |
| Ibrutinib + bendamustine                    | 2 (3.8%)   |      |
| Ibrutinib + bendamustine + rituximab        | 2 (3.8%)   |      |
| Ibrutinib + rituximab + chemotherapy        | 4 (7.6%)   |      |

Data are shown as number (%). The sum of some percentages may not equal 100% because of rounding.
Table S3. Subsequent therapy after ibrutinib failure.

| Regimen                        | Monotherapy group (N=42) | Combination therapy group (N=17) |
|--------------------------------|--------------------------|----------------------------------|
| Bendamustine + rituximab       | 6 (14.3%)                | 3 (17.6%)                        |
| Chemotherapy                   | 11 (26.2%)               | 7 (41.2%)                        |
| BTKi-based regimens            | 6 (14.3%)                | 2 (11.8%)                        |
| Lenalidomide ± rituximab       | 2 (4.8%)                 | 1 (5.9%)                         |
| Others                         | 3 (9.5%)                 | 1 (5.9%)                         |
| Unknown                        | 13 (31.0%)               | 3 (17.6%)                        |

Data are shown as number (%). The sum of some percentages may not equal 100% because of rounding. BTKi, Bruton tyrosine kinase inhibitor.
Table S4. Relationship of ibrutinib dose and electrocardiogram abnormality.

| Ibrutinib dose | Electrocardiogram abnormality | Total |
|----------------|-------------------------------|-------|
|                | Yes (percentage) | No (percentage) |     |
| 560mg/d        | 10 (12.2%)          | 72 (87.8%)      | 82   |
| < 560mg/d      | 5 (21.7%)           | 18 (78.3%)      | 23   |
| Total          | 15                  | 90              | 105  |

Data are shown as number (%).
Table S5. Cross-trial comparison of observational studies in R/R MCL patients treated with ibrutinib monotherapy.

| References      | Study design          | Sample size | Median age (range), years | Lines of previous therapy (median [range]) | ORR (%) | CR (%) | Median PFS (months) | Median OS (months) |
|-----------------|-----------------------|-------------|---------------------------|-------------------------------------------|---------|--------|--------------------|--------------------|
| Current study   | Retrospective         | 68          | 63 (34-81)                | 1 (1-7)                                   | 60.3    | 16.2   | 18.5               | 28.2               |
| Broccoli et al. | Retrospective         | 77          | 65 (35-81)                | 3 (1-10)                                  | 36.4    | 18.2   | 12.9               | 16                 |
| Epperla et al.  | Retrospective         | 97          | 63 (39–87)                | 2 (1-8)                                   | 65      | 33     | 15                 | 22                 |
| McCulloch et al.| Retrospective         | 211         | 73 (33–96)                | 1                                         | 69      | 27     | 17.8               | 23.9               |
| Tucker et al.   | Retrospective         | 65          | 67 (48–90)                | 2 (1–6)                                   | NA      | NA     | 12                 | 18.5               |
| Yi et al.       | Retrospective         | 88          | 71 (42-92)                | 1 (1-6)                                   | 64.8    | NA     | 30.8               | Not reached         |
| Jeon et al.     | Retrospective         | 33          | 65 (40-79)                | 2 (1–4)                                   | 64      | 15     | 27.4               | 35.1               |
| Janssens et al. | Retrospective         | 71          | 74 (47-88)                | 1 (50.7%)                                 | 93      | 32     | 22.3               | 39.4               |
| Slama et al.    | Retrospective and prospective | 106 | 74 (49-88)                | 1 (38.7%)                                 | 76.4    | NA     | 20.0               | 29.8               |

R/R, relapsed and refractory; MCL, mantle cell lymphoma; ORR, objective response rate; CR, complete remission; PFS, progression-free survival; OS, overall survival; NA, not available.
214 R/R MCL patients initiated salvage therapy between Aug 2017 and Dec 2020

137 patients received ibrutinib-based treatment

130 patients had no prior BTKi exposure and not in clinical trials

121 patients with medical records of response assessment after treatment

68 patients received ibrutinib monotherapy

53 patients received ibrutinib-based combination therapy

Figure S1. Flow diagram of the case selection process. R/R, relapsed/refractory; MCL, mantle cell lymphoma; BTKi, Bruton tyrosine kinase inhibitor.
### Figure S2

| Pathway                        | Gene          | Alterations |
|-------------------------------|---------------|-------------|
| **NF-κB signaling pathway**   | ATM, NFKB1E, RUNX1T1 | 61.9% 14.3% 9.5% |
| **Epigenetic regulation**     | KMT2D, ARID1A | 38.1% 4.8%  |
| **Apoptosis/Cell cycle**      | NSD2, CCND1, TERT, TP53, BCL2, BIRC3, RB1, TRAF2 | 28.6% 14.3% 14.3% 9.5% 9.5% 9.5% 9.5% 9.5% 9.5% 4.8% |
| **Transcriptional regulation**| SMARCA4        | 23.8%       |
| **B cell receptor signaling pathway** | CARD11, MALT1 | 9.5% 9.5% |
| **Others**                    | IDH1, MAP3K1, NRAS, ABCB1, ARHGAP26, CALR, ARID2, BRAF, CBLB | 9.5% 9.5% 9.5% 9.5% 4.8% 4.8% 4.8% 4.8% 4.8% 4.8% |

**CASE** 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Figure S2. Progression-free survival of patients with or without (A) BCL2/MALT1 mutation, and (B) CARD11 mutation. Log-rank $P$ values are shown.