# REAL-WORLD TREATMENT PATTERNS AND COMPARATIVE EFFECTIVENESS OF BRUTON TYROSINE KINASE INHIBITORS IN PATIENTS WITH MANTLE CELL LYMPHOMA

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**Background:**
Bruton tyrosine kinase inhibitor (BTKi) therapies, approved for relapsed or refractory (R/R) mantle cell lymphoma (MCL), have not been comprehensively evaluated in real world populations.

**Aims:**
This study aimed to assess patient characteristics, treatment patterns and associated outcomes in real world BTKi-treated MCL patients.

**Methods:**
The retrospective multicenter chart review was conducted in the Cardinal Health Oncology Provider Extended Network. EMR data were extracted for eligible patients diagnosed with MCL who initiated any of the approved BTKi (ibrutinib, acalabrutinib, zanubrutinib) from 2018 to 2021; patients enrolled in trials were excluded. Index date was defined as the use of any of the BTKis. Patients were required to have 12-month pre-index for medical history, and from index to last follow-up or death. Descriptive analyses were conducted to assess demographic/clinical characteristics, MCL baseline features, BTKi treatment patterns, adverse events (AE), and response rates by BTKi. Multivariable logistic regression was performed to assess factors associated with response and AE.

**Results:**
The study cohort consisted of 300 MCL patients (59% male; 69% white); most (64%) patients were covered by Medicare, 34% had commercial insurance. BTKis were given mainly as monotherapy (93%) and in R/R setting (86%). Patients in zanubrutinib group were significantly older (n = 100, median age = 71, range = 50-91) than patients in ibrutinib (n = 100, median age = 69, range = 39-87) and acalabrutinib (n = 100, median age = 70, range = 51-86) groups. Significantly fewer patients in the zanubrutinib group had baseline Ann Arbor stage I-II (4%) than ibrutinib (10%) or acalabrutinib (13%), while more zanubrutinib patients had presence of B symptoms (67%) than ibrutinib (44%) or acalabrutinib (57%). Patients in the zanubrutinib group also had significantly less with ECOG of 3+ (4%) compared to ibrutinib (8%) or acalabrutinib (6%). At BTKi initiation, significantly more patients in zanubrutinib group (18%) had history of atrial fibrillation than ibrutinib (1%) or acalabrutinib (5%). BTKis were given mainly as second-line (86%) and as monotherapy (93%). Most patients were started at on-label BTKi dose. In zanu patients, 160 mg BID was more common (64%) than 320 mg QD (31%). Multivariable regression reported a significant association of age, gender, extranodal/splenic involvement, and timing of BTKi initiation with response and AE (Table).

**Conclusion:**
This study provides the first real world evidence on comparative effectiveness of ibrutinib, acalabrutinib, zanubrutinib in MCL patients. While patients treated with zanubrutinib were older and had more complex MCL baseline features at initiation, multivariable regression suggested a trend favoring zanubrutinib over ibrutinib or acalabrutinib for both response and AE. Frontline initiation of BTKi therapy was also associated with improved tolerability. Future real world studies are needed to discern long-term outcomes.

**Table.**

| | Response | AE |
|---|---|---|
| | Odds Ratio (95% CI) | |
| **BTKi** | | |
| Zanubrutinib | Reference | Reference |
| Ibrutinib | 0.75 (0.38, 1.47) | 1.17 (0.61, 2.24) |
| Acalabrutinib | 0.87 (0.45, 1.69) | 1.52 (0.80, 2.87) |
| **Age** | 0.54 (0.31, 0.96)* | 2.52 (1.43, 4.47)* |
| **Gender** | | |
| Male | Reference | Reference |
| Female | 0.91 (0.84, 0.98)* | 0.96 (0.92, 1.01) |
| **RACE** | | |
| White | Reference | Reference |
| Non-White | 1.11 (0.63, 1.94) | 1.44 (0.84, 2.46) |
| **Ann Arbor stage** | | |
| 2+ | Reference | Reference |
| 0/1 | 1.04 (0.57, 1.91) | 0.70 (0.40, 1.22) |
| **ECOG** | | |
| 2+ | Reference | Reference |
| 0/1 | 0.31 (0.07, 1.43) | 0.69 (0.27, 1.72) |
| **Splenic involvement** | | |
| Yes | Reference | Reference |
| No | 0.34 (0.19, 0.60)* | 0.49 (0.28, 0.86)* |
| **Extranodal disease involvement** | | |
| Yes | Reference | Reference |
| No | 0.33 (0.16, 0.68)* | 0.31 (0.14, 0.68)* |
| **BTKi line of therapy** | | |
| 2L+ | Reference | Reference |
| 1L | 0.73 (0.25, 2.16) | 0.26 (0.01, 0.70)* |

*P value <0.05