Real-world (RW) treatment patterns and comparative effectiveness of Bruton tyrosine kinase inhibitors (BTKi) in patients (pts) with mantle cell lymphoma (MCL)

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Background: BTKi therapies, approved for relapsed or refractory (R/R) MCL, have not been comprehensively evaluated in RW populations. This study aimed to assess patient characteristics, treatment patterns and associated outcomes in RW BTKi-treated MCL pts.

Methods: The retrospective multicenter chart review was conducted in the Cardinal Health Oncology Provider Extended Network. EMR data were extracted for eligible pts diagnosed with MCL who initiated any of the approved BTKi (ibrutinib [ibr], acalabrutinib [acal], zanubrutinib [zanu]) from 2018 to 2021; pts enrolled in trials were excluded. Index date was defined as the use of any of the BTKis. Pts were followed 12-mo 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 pts (59% male; 69% white); most (64%) pts were covered by Medicare, 34% had commercial insurance. BTKis were given mainly as monotherapy (93%) and in R/R setting (86%). Pts in zanu group were significantly older (n = 100, median age = 71, range = 50-91) than pts in ibr (n = 100, median age = 69, range = 39-87) and acal (n = 100, median age = 70, range = 51-86) groups. Significantly fewer pts in the zanu group had baseline Ann Arbor stage I-II (4%) than ibr (10%) or acal (13%), while more zanu pts had presence of B symptoms (67%) than ibr (44%) or acal (57%). Pts in the zanu group also had significantly less with ECOG of 3+ (4%) compared to ibr (8%) or acal (6%). At BTKi initiation, significantly more pts in zanu group (18%) had history of atrial fibrillation than ibr (1%) or acal (5%). Multivariable regression reported a significant association of age, gender, extranodal/splenic involvement, and timing of BTKi initiation with response and AE (**Table**).

Conclusions: This study provides the first RW evidence on comparative effectiveness of ibr, acal, zanu in MCL pts. While pts treated with zanu were older and had more complex MCL baseline features at initiation, multivariable regression

suggested a trend favoring zanu over ibr or acal for both response and AE. Frontline initiation of BTKi therapy was also associated with improved tolerability. Future RW studies are needed to discern long-term outcomes.

	Response	**AE**
	Odds Ratio (95% Confidence Int	
Ibr vs zanu	0.75 (0.38, 1.47)	1.17 (0.61, 2
Acal vs zanu	0.87 (0.45, 1.69)	1.52 (0.80, 2
Age	0.54 (0.31, 0.96)	2.52 (1.43, 4
Female vs male	0.91 (0.84, 0.98)	0.96 (0.92, 1
Splenic involvement (N vs Y)	0.34 (0.19, 0.60)	0.49 (0.28, 0
Extranodal disease involvement (N vs Y)	0.33 (0.16, 0.68)	0.31 (0.14, 0
1L vs 2L+	0.73 (0.25, 2.16)	0.26 (0.01, 0