Impact of novel therapies (NTs) on real-world (RW) clinical outcomes of patients (pts) with relapsed/refractory (R/R) mantle-cell lymphoma (MCL) by race/ethnicity and *TP53* mutation status

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Introduction: Treatments for R/R MCL have evolved with NTs, including BTK inhibitors (BTKis). Little is known about RW treatment patterns and clinical outcomes of pts with R/R MCL for chemoimmunotherapy (CIT) vs NTs among pts of different race/ethnicity. Data on RW testing and clinical outcomes of pts with R/R MCL harboring a *TP53* mutation are limited.

Methods: This retrospective cohort study included adult pts with R/R MCL who initiated second-line (2L) or third-line (3L) treatment on 1/1/2018 or later and were followed up until loss to follow-up, death, or data cut-off using US Flatiron Health electronic health record-derived de-identified databases. Median RW time to next treatment (mrwTTNT) and median RW overall survival (mrwOS) were estimated based on Kaplan–Meier analyses and adjusted for age and sex. CIT included any MCL treatment with chemotherapy + anti-CD20 antibody. NTs included BTKis, BCL2 inhibitors, lenalidomide, bortezomib, and CAR-T, or combinations.

Results: This study included 1,377 pts with R/R MCL who received 2L+ therapy. Of these, 1,028 (75%) were non-Latinx (NL)-White, 53 (4%) were NL-Black, 86 (6%) were Latinx, 108 (8%) were NL-Asian or other race, and 102 (7%) were of unknown/undocumented race. The overall 2L+ population had a median age of 71 y (range 63-78), were mostly male (74%), had a diagnosis of MCL not otherwise specified (NOS; 85%), and had stage IV disease (62%). Sixty-three percent had disease progression within 24 mo from first-line (1L) treatment (POD24) before starting 2L therapy. Relative to all pts, NL-Black and NL-Asian/other race pts had more variants of MCL (blastic, leukemic, pleomorphic) and higher Ki67% and lactose dehydrogenase (LDH) levels at 2L/3L index date. In contrast, Latinx pts had more MCL NOS (92%) and lower Ki67% and LDH levels at 2L index date. More NL-Black and unknown race pts had POD24 than did other races (70% and 76%, respectively).

Overall, the most common NTs used were BTKis. 1L treatments were bendamustine-rituximab (BR; 54%), R-CHOP (18%), and cytarabine-containing CIT (9.7%). The most common 2L treatments were BR (32%), acalabrutinib (31%), ibrutinib (21%), zanubrutinib (11%), and R-CHOP (11%). The most common 3L therapies were BR (34%), acalabrutinib (21%), zanubrutinib (12%), ibrutinib (10%), R-CHOP (9.2%), and brexucabtagene autoleucel (7.4%). Transplantation rates before 2L and CAR-T use in 3L was highest among White pts.

When assessing mrwTTNT and mrwOS by therapy in 2L, 766 pts (70%) received NTs and 333 (30%) received CIT. Among all pts, mrwTTNT (mo [95% CI]) was longer with 2L NT (11.9 [10.6, 14.5]) vs CIT (9.9 [8.1, 12.9]). NL-White, NL-Black, and NL-Asian/other race pts had longer mrwTTNT with NT (11.9 [10.5, 14.6], 12.9 [7.6, NR], and 14.6 [8.5, 21.4], respectively) vs CIT (9.9 [7.6, 12.9], 9.7 [3.0, NR], and 6.0 [3.2, 21.2]). Latinx pts had longer mrwTTNT with CIT (14.9 [11.8, NR]) vs NT (9.0 [3.8, 24.2]).

Among all pts, mrwOS (mo [95% CI]) was longer with 2L CIT (43.0 [34.1, 56.5]) vs NT (35.6 [29.9, 41.2]). White and Latinx pts had longer mrwOS with CIT (47.3 [33.9, NR] and NR [33.3, NR], respectively) vs NT (35.0 [28.8, 48.4] and 42.3 [31.0, NR]). Black and Asian/other race pts had longer mrwOS with NT (41.2 [32.8, NR] and 38.8 [23.5, NR], respectively) vs CIT (34.8 [9.7, NR] and 13.5 [8.3, NR]).

Among all 3L pts (n=364 on NTs, n=119 on CIT), mrwTTNT (mo [95% CI]) improved when using NTs (7.9 [6.8, 10.3]) vs CIT (4.4 [3.5, 6.9]). NTs demonstrated better mrwTTNT vs CIT in all

race/ethnic groups except Latinx pts. For all race/ethnic groups, mrwOS was improved with NTs (32.5 [24.7, 42.6]) vs CIT (19.5 [13.7, 47.3]).

Overall RW testing for *TP53* aberrations was limited, with 72 pts (5%) found to be positive for a *TP53* mutation. For pts with *TP53* mutations, mrwTTNT and mrwOS were longer for 2L NTs (3.3 [2.2, 6.4] and 18.3 [9.0, NR], respectively; n=42) vs CIT (3.0 [1.9, 7.6] and 15.0 [7.2, NR]; n=16).

Conclusions: High-risk features, treatment patterns, and clinical outcomes for NTs vs CIT in R/R MCL differed by race/ethnicity. Use of 2L+ NTs was associated with a trend towards improved mrwTTNT and mrwOS among NL-Black and NL-Asian/other race pts. NT use in 3L numerically improved mrwTTNT and mrwOS for most pts vs CIT. RW pts with *TP53* mutations had a poor prognosis and numerically improved outcomes with the use of 2L NT, although testing remains limited. Future research evaluating reasons for these differences and increased RW *TP53* testing is warranted.