Real-World (RW) Treatment (tx) Patterns and Outcomes of 4216 Previously Untreated Mantle Cell Lymphoma (MCL) Patients (pts) in US Routine Clinical Practice

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Additional information can be viewed by accessing this link: https://www.oncologysciencehub.com/OncologyAM2021/ibrutinib/Martin/
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Background

- Mantle cell lymphoma (MCL) is a non-Hodgkin lymphoma associated with **heterogeneous biology and outcomes**\(^1\)

- Chemoimmunotherapy with or without autologous stem-cell transplantation (SCT) consolidation is currently a standard first-line (1L) treatment approach in younger patients with MCL, while bendamustine-rituximab (BR) and R-CHOP are standard in older patients. However, understanding of how clinical study findings are reflected in routine clinical practice is limited

- Here, we **retrospectively** characterized the real-world (RW) 1L MCL treatment patterns and outcomes in a **large cohort of patients treated in the US** as collected in a nationwide electronic health record (EHR)–derived de-identified database
Methods

- Retrospective study of adults with MCL in the US from January 2011 to January 2021, as captured in the nationwide Flatiron Health EHR-derived de-identified database\(^1\)-\(^3\)
  - Longitudinal database comprising de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction. Data originated from approximately 280 cancer clinics with 800 sites; most patients (87%) were treated in community oncology setting

- Inclusion criteria: confirmed MCL diagnosis (ICD-9-CM code 200.48 or ICD-10-CM code C83.1x); age ≥ 18 years at diagnosis; ≥ 2 clinic visit records

- Patient characteristics,\(^a\) treatment patterns, real-world time-to-next treatment (rwTTNT), and real-world overall survival (rwOS) were evaluated. rwTTNT and rwOS were evaluated using Kaplan-Meier methods
  - rwTTNT: time from start of 1L treatment to subsequent treatment or death, whichever comes first
  - rwOS: time from start of 1L treatment to death

- Multivariate analyses were performed to identify predictors of rwTTNT and rwOS, including the factors: age, ECOG PS, WBC, LDH/ULN ratio, blastoid/pleomorphic MCL, bulky disease,\(^b\) and use of R-maintenance

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\(^a\)As documented in the EHR. \(^b\)Bulky defined as per local oncologist.

ECOG PS, Eastern Cooperative Oncology Group performance status; ICD-CM, International Classification of Disease, Clinical Modification; LDH, lactate dehydrogenase; ULN, upper limit of normal; WBC, white blood cell count.

Patient Cohorts

Confirmed diagnosis of MCL in Flatiron Health database from January 2011 to January 2021 (N = 4216)

Patients with record of 1L MCL treatment (n = 3614)

Patients < 65 years:\n\[ n = 1274 \text{ (35.3\%)} \]

Patients ≥ 65 years:\n\[ n = 2340 \text{ (64.7\%)} \]

No record of 1L MCL treatments (n = 602)

*297 patients received SCT; includes allogenic (n = 8) and autologous (n = 287).

94 patients received SCT; includes allogenic (n = 1) and autologous (n = 93).
Patient Cohorts

Confirmed diagnosis of MCL in Flatiron Health database from January 2011 to January 2021 (N = 4216)

Patients with record of 1L MCL treatment (n = 3614)

Patients < 65 years: n = 1274 (35.3%)

Patients ≥ 65 years\(^a\): n = 2340 (64.7%)

Not considered eligible for SCT (n = 303)

“SCT-eligible” patients: n = 971

Did not receive SCT: n = 680

Received SCT\(^b\): n = 291

Given the potential for treatment response to impact the receipt of SCT in the real world, only patients < 65 years who were alive and did not initiate subsequent treatment within 6 months of starting the 1L treatment were considered “SCT-eligible.”

\(^a\)94 patients received SCT, includes allogenic (n = 1) and autologous (n = 93).

\(^b\)Includes allogenic (n = 7) and autologous (n = 282) SCT.

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Results: 1L MCL Treatment Pattern by Year

- Cytarabine-containing regimens were used in 30.5% of patients < 65 years
- BR was the most used treatment, including 28% of patients < 65 years and 49% in those ≥ 65 years
- Increasing trend of BR use over time across both age groups, whereas R-CHOP use decreased over time and use of cytarabine-containing regimens did not change notably over time

![Graph showing treatment patterns for patients < 65 years (n = 1265) and ≥ 65 years (n = 2329)]

\*Others\* (among 3614 treated patients) includes: 9.5% targeted agents (eg, bortezomib, lenalidomide, BTKi, Bcl-2); 7.8% immunotherapy only; 4.7% clinical trial drug; 2.4% chemo only; additional 1.8% of other types of chemoimmunotherapy.
Results: Baseline Demographics by Treatment Types

In patients with documented 1L MCL treatment (N = 3614):
- Median age: 69.4 years
- 87% treated in a community setting
- In patients with complete data: 35.7% high-risk MIPI, 11.8% ECOG PS ≥ 2

Treatments:
- Patients treated with cytarabine-containing regimens or SCT compared with those treated with R-CHOP or BR were:
  - Younger
  - Less likely to be treated in the community
  - Patients treated with cytarabine regimens were more likely to have blastoid/pleomorphic morphology but also low-risk MIPI score
- 11% of patients received SCT
- 23.1% of patients received R-maintenance

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### Patient Characteristics

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Overall (N = 3614)</th>
<th>R-CHOP (n = 636)</th>
<th>BR (n = 1502)</th>
<th>Cytarabine-Containing (n = 514)</th>
<th>SCT (n = 391)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), years</td>
<td>69.4 (27.7-84.6)</td>
<td>66.3 (35.1-83.4)</td>
<td>72.7 (41.0-84.6)</td>
<td>60.1 (27.7-83.7)</td>
<td>59.6 (34.0-77.9)</td>
</tr>
<tr>
<td>≥ 65, n (%)</td>
<td>2340 (64.7)</td>
<td>356 (56.0)</td>
<td>1147 (76.4)</td>
<td>125 (24.3)</td>
<td>94 (24.0)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>2584 (71.5)</td>
<td>497 (78.1)</td>
<td>1034 (68.8)</td>
<td>395 (76.8)</td>
<td>309 (79.0)</td>
</tr>
<tr>
<td>Community setting, n (%)</td>
<td>3130 (86.6)</td>
<td>570 (89.6)</td>
<td>1360 (90.5)</td>
<td>392 (76.3)</td>
<td>321 (82.1)</td>
</tr>
<tr>
<td>Blastoid/pleomorphic, n (%)</td>
<td>361 (10.0)</td>
<td>79 (12.4)</td>
<td>105 (7.0)</td>
<td>103 (20.0)</td>
<td>47 (12.0)</td>
</tr>
<tr>
<td>LDH/ULN: ≥ 1.00, n/N (%)</td>
<td>508/1631 (31.1)</td>
<td>78/239 (32.6)</td>
<td>232/764 (30.4)</td>
<td>75/194 (38.7)</td>
<td>56/171 (32.7)</td>
</tr>
<tr>
<td>WBC: ≥ 10 × 10⁹/L, n/N (%)</td>
<td>696/2075 (33.5)</td>
<td>110/340 (32.4)</td>
<td>305/926 (32.9)</td>
<td>81/240 (33.8)</td>
<td>59/222 (26.6)</td>
</tr>
<tr>
<td>Bulky disease, n (%)</td>
<td>511/3501 (14.6)</td>
<td>99/620 (16.0)</td>
<td>223/1474 (15.1)</td>
<td>98/504 (19.4)</td>
<td>59/385 (15.3)</td>
</tr>
<tr>
<td>ECOG PS ≥ 2, n (%)</td>
<td>184/1558 (11.8)</td>
<td>23/233 (9.9)</td>
<td>94/735 (12.8)</td>
<td>7/172 (4.1)</td>
<td>4/162 (2.5)</td>
</tr>
<tr>
<td>MIPI score group, n</td>
<td>820</td>
<td>118</td>
<td>379</td>
<td>89</td>
<td>78</td>
</tr>
</tbody>
</table>
  - High risk, n (%) | 293 (35.7) | 43 (36.4) | 131 (34.6) | 20 (22.5) | 8 (10.3) |
  - Intermediate risk, n (%) | 326 (39.8) | 53 (44.9) | 164 (43.3) | 29 (32.6) | 31 (39.7) |
  - Low risk, n (%) | 201 (24.5) | 22 (18.6) | 84 (22.2) | 40 (44.9) | 39 (50.0) |

*As documented in the EHR. **Bulky defined as per local oncologist.
**rwTTNT and rwOS for Patients With Documented 1L MCL Treatment**

- In patients with documented 1L MCL treatment (N = 3614), median follow-up was 45.5 months (range, 0.033-119.4); median rwTTNT was 24 months (95% CI, 21.9-26.2)
  - Median rwTTNT: 28 months (95% CI, 24.4-34.5) in patients < 65 years and 22.3 months (95% CI, 20.7-24.5) in patients ≥ 65 years

<table>
<thead>
<tr>
<th></th>
<th>Overall (N = 3614)</th>
<th>&lt; 65 Years (n = 1274)</th>
<th>≥ 65 Years (n = 2340)</th>
</tr>
</thead>
<tbody>
<tr>
<td>36-month rwTTNT, % (95% CI)</td>
<td>41 (39-43)</td>
<td>46 (43-49)</td>
<td>38 (36-41)</td>
</tr>
</tbody>
</table>

rwTTNT is defined as time from start of 1L treatment to subsequent treatment or death, whichever comes first; rwOS is defined as time from start of 1L treatment to death.

CI, confidence interval.
Predictors of rwTTNT and rwOS in 1L MCL

Multivariate analysis showed:

- Older age and high-risk disease features were associated with worse outcome in the RW

- Use of R-maintenance\(^a\) appeared to be associated with superior outcomes

### rwTTNT

<table>
<thead>
<tr>
<th>Variables (MVA)</th>
<th>HR</th>
<th>95% CI</th>
<th>(p) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: (\geq 65) years vs &lt; 65 years</td>
<td>1.29</td>
<td>1.18-1.41</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ECOG PS: (\geq 2) vs 0-1</td>
<td>1.69</td>
<td>1.40-2.04</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LDH/ULN: (\geq 1) vs &lt; 1</td>
<td>1.47</td>
<td>1.28-1.68</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>WBC group: (\geq 10 \times 10^9/L) vs &lt; (10 \times 10^9/L)</td>
<td>1.32</td>
<td>1.17-1.49</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Blastoïd/pleomorphic MCL: Yes vs No</td>
<td>1.62</td>
<td>1.43-1.85</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Bulky disease(^b): Yes vs No</td>
<td>1.26</td>
<td>1.11-1.42</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Rituximab maintenance: No vs Yes</td>
<td>3.32</td>
<td>2.95-3.73</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

### rwOS

<table>
<thead>
<tr>
<th>Variables (MVA)</th>
<th>HR</th>
<th>95% CI</th>
<th>(p) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: (\geq 65) years vs &lt; 65 years</td>
<td>2.07</td>
<td>1.82-2.35</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ECOG PS: (\geq 2) vs 0-1</td>
<td>2.43</td>
<td>1.96-3.00</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LDH/ULN: (\geq 1) vs &lt; 1</td>
<td>1.60</td>
<td>1.35-1.89</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>WBC group: (\geq 10 \times 10^9/L) vs &lt; (10 \times 10^9/L)</td>
<td>1.55</td>
<td>1.34-1.79</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Blastoïd/pleomorphic MCL: Yes vs No</td>
<td>1.74</td>
<td>1.49-2.03</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Bulky disease(^b): Yes vs No</td>
<td>1.22</td>
<td>1.05-1.42</td>
<td>0.009</td>
</tr>
<tr>
<td>Rituximab maintenance: No vs Yes</td>
<td>2.49</td>
<td>2.15-2.89</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

\(^a\)The analysis on R-maintenance was based on patients who received/did not receive R-maintenance (with no adjustments). A more detailed analysis to be presented at EHA 2021 (EP785). \(^b\)Bulky defined as per local oncologist.

rwTTNT is defined as time from start of 1L treatment to subsequent treatment or death, whichever comes first; rwOS is defined as time from start of 1L treatment to death.

HR, hazard ratio; MVA, multivariate analysis.
rwTTNT and rwOS for Patients < 65 Years by SCT Status in 1L MCL

- In patients < 65 years, without any adjustments to the analysis, SCT was associated with improved 36-month rwTTNT (63% [95% CI, 58-70]) compared with those who did not receive SCT (40% [95% CI, 37-43]); median rwTTNT was reached at 18.9 (95% CI, 15.1-24.4) months for those who did not receive SCT.

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**rwTTNT and rwOS for Patients < 65 Years by SCT Status in 1L MCL**

- In the “SCT-eligible” cohort (N = 971), 36-month rwTTNT was comparable for patients with SCT (65 [95%CI 59-71]) compared with those who did not receive SCT (59% [95% CI, 55-64])

rwTTNT and rwOS for Patients < 65 Years by SCT Status in 1L MCL

<table>
<thead>
<tr>
<th>36-Month rwTTNT, % (95% CI)</th>
<th>Age &lt; 65 Years at 1L Treatment (n = 1274)</th>
<th>Age &lt; 65 Years and “SCT-Eligible” (n = 971)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received SCT</td>
<td>63 (58-70)</td>
<td>65 (59-71)</td>
</tr>
<tr>
<td>Did not receive SCT</td>
<td>40 (37-43)</td>
<td>59 (55-64)</td>
</tr>
<tr>
<td>Log-rank test p value</td>
<td>&lt; 0.001</td>
<td>0.082</td>
</tr>
</tbody>
</table>

- Given the potential for treatment response to impact the receipt of SCT in the real world, only patients < 65 years who were alive and did not initiate subsequent treatment within 6 months of starting the 1L treatment were considered “SCT-eligible.”

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rwTTNT and rwOS for Patients ≥ 65 Years Without SCT in 1L MCL

- In patients ≥ 65 years who did not receive SCT, median rwTTNT was 21.7 months (95% CI, 19.2-23.5)
Limitations of Analyses

- Retrospective analysis
- Missing data in baseline characteristics. Available data were contingent on documentation practices and on continuity of treatment within the clinics originating the database
- Tumor response and disease progression data were not available to evaluate overall response rate or progression-free survival
- Intention for choosing treatments (eg, transplantation or maintenance) was not captured in the database
Conclusions: RW Treatment Patterns and Outcomes of 4216 Previously Untreated MCL Patients in US Routine Clinical Practice

- In this large RW cohort of patients with MCL treated primarily in community-based US practices, BR was the most commonly used 1L treatment. There appeared to be some discrepancy between actual patterns of care and recommendations based on clinical trials
  - In patients < 65 years, only 30.5% received a cytarabine-containing regimen; 23.3% underwent SCT
  - In patients ≥ 65 years, ~ 65% received BR or R-CHOP

- Median rwTTNT was 28 months in patients < 65 years and 22.3 months in patients ≥ 65 years, which appeared worse than what has been reported with standard therapies in this population
  - Older age and high-risk disease features were predictive of worse outcome in the RW, while R-maintenance appeared to be associated with better outcomes

- Among SCT-eligible patients, there was no clear rwTTNT or rwOS benefit associated with receipt of SCT

- These data highlight the need to develop treatment regimens that can be delivered effectively in routine and community practices, and treatments may not need to be centered around SCT intent in young patients

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