Real-World Minimal Residual Disease (MRD) Assessment and Trends Using clonoSEQ® in Acute Lymphoblastic Leukemia and Multiple Myeloma

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BACKGROUND
With advances in the care of lymphoid cancers, there has been a recognized need for better measures of response. As a result, the assessment of minimal residual disease (MRD) has increasingly been incorporated into routine patient management.1

MRD assessment is now recommended within several lymphoid cancer NCCN guidelines, including multiple myeloma (MM), acute lymphoblastic leukemia (ALL), and chronic lymphocytic leukemia (CLL).2,3

The clonoSEQ® Assay (NGS MRD Assay, Adaptive Biotechnologies; Seattle, WA) is currently the only FDA authorized MRD test for ALL and MM.

While MRD findings are commonly reported within clinical trials, there has to date been a limited ability to understand patient MRD testing patterns and response levels in the real-world care setting.

Adaptive’s database provides a unique perspective on how MRD is being incorporated into guideline-supported care in the US.

OBJECTIVE
In this retrospective analysis, we examined Adaptive’s internal database to analyze Clonality and MRD results in patients with MM and ALL.

METHODS
NGS MRD ASSAY
The NGS-MRD Assay uses multiplex polymerase chain reaction (PCR) and NGS to identify, characterize, and monitor unique patient tumor burden.

Immunglobulin (Ig) V (IgV), J (IgJ), and T cell receptor gamma (TCR-γ) sequences are assessed in DNA extracted from high disease burden diagnostic (ID) and calibration samples with no trackable sequence identified were categorized as Polyclonal (MRD tracking not enabled; Table 1).

Clonality (ID) clonality assessment were included in the MRD analysis.

RESULTS

Clonality Test Results by Indication

<table>
<thead>
<tr>
<th>Number of Patients</th>
<th>ALL</th>
<th>MM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>809</td>
<td>1,541</td>
<td>2,344</td>
<td></td>
</tr>
<tr>
<td>174</td>
<td>582</td>
<td>756</td>
<td></td>
</tr>
<tr>
<td>731</td>
<td>1,407</td>
<td>2,138</td>
<td></td>
</tr>
</tbody>
</table>

| Calibrated Rate | 90.0% | 91.3% | 91.2% |

MRD ASSOCIATION

MRD results from patients that ‘Calibrated’ during the Clonality (ID) test and who ordered an MRD test between January 2018 and October 2019 were analyzed (N=1,223).

The age distribution of patients with MRD testing performed (MM median age = 65, ALL median age = 25) was generally consistent with epidemiologic data (Table 2).

*The (I)calibrated state patient cohort is different from the MRD patient cohort as a patient could have ordered an ID Test prior to 2018 or could have an ID Test but no MRD test.

PATIENT POPULATION
- The population analyzed included a de-identified internal dataset of our NGS-MRD assay data from January 2018 to October 2019.
- Patients who had a trackable DNA sequence identified in a baseline (ID) clonality assessment were included in the MRD analysis.
- Clonality assessment, demographics and deepest level of MRD response were evaluated.

Table 2. Demographics of patients with MRD tests by condition, within the analysis population

<table>
<thead>
<tr>
<th>ALL</th>
<th>MM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>299 (42%)</td>
<td>551 (40%)</td>
</tr>
<tr>
<td>Male</td>
<td>405 (58%)</td>
<td>818 (60%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>0-17</th>
<th>18-34</th>
<th>35-64</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>266 (38%)</td>
<td>164 (23%)</td>
<td>213 (30%)</td>
<td>643</td>
<td></td>
</tr>
<tr>
<td>71 (11%)</td>
<td>171 (26%)</td>
<td>673 (49%)</td>
<td>955</td>
<td></td>
</tr>
<tr>
<td>690 (50%)</td>
<td>603 (42%)</td>
<td>534 (37%)</td>
<td>1,827</td>
<td></td>
</tr>
</tbody>
</table>

MRD < 10%
- 61 (9%) of ALL and MM patients achieved even deeper response, with MRD levels below 10%.

MRD < 0.1%
- 20 patients with 30.6% of MM patients achieved even deeper response, with MRD levels below 0.1%.

CONCLUSIONS
- Adaptive’s NGS-MRD Assay can identify trackable DNA sequences in most (91.2%) ALL and MM patients using the Clonality (ID) Test.
- Of the 2,073 patients assessed for MRD, many patients achieved deep levels of MRD negativity (<10%).

This real-world analysis of a standardized MRD assessment method reflects the adoption of NGS MRD assessment in routine patient management, consistent with NCCN guidelines.

The ability for NGS to assess response across a continuum of relevant MRD threshold levels is recommended in guidelines and is an important consideration for applying MRD testing in clinical practice.

Given the association between MRD levels and long-term outcomes demonstrated across clinical trials and meta-analyses in lymphoid cancers, the ability to capture and report patient MRD values in a quantitative and standardized assay in a large real-world population presents important opportunities for understanding lymphoid cancer population health and performing comparative effectiveness and other RWE studies.2-8

REFERENCES

AUTHOR DISCLOSURES
AD, AH, BE, LWL: Adaptive Biotechnologies (Employment, Equity Ownership)

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