Submitted by: Audrey Demaree, PharmD, Senior Manager, Medical Affairs
Name: Lance Baldo, MD, Chief Medical Officer
Company/Organization: Adaptive Biotechnologies Corporation
Address: 1551 Eastlake Ave East, #200 Seattle, WA 98102
Phone: (206) 693-2224
Email: lbaldo@adaptivebiotech.com
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NCCN Guidelines Panel: Multiple Myeloma

On behalf of Adaptive Biotechnologies, we request that the NCCN Multiple Myeloma (MM) Guideline Panel review and consider the following modifications for the MM Guidelines.

Rationale

In 2018, the clonoSEQ® Assay was cleared by the FDA for the assessment of minimal residual disease (MRD) in the bone marrow of patients with MM and acute lymphoblastic leukemia.[1] clonoSEQ is the first and only test approved for MRD assessment in these malignancies. The FDA has publicly recognized the rigor of clonoSEQ validation[2] and has restated the need for a standardized MRD tool to aid in clinical management. To that end, the FDA published draft guidance for the use of MRD in hematologic malignancies to support drug development,[3] and this guidance follows three new drug labels that incorporate MRD data.

To ensure that all patient populations have access to most standardized and specific technology, Adaptive Biotechnologies has secured a positive coverage determination by Medicare[4] and will continue to pursue private payer coverage policies, thus removing a patient access barrier.

Because of clonoSEQ's FDA authorization and the publication of new clinical data, we believe it would be useful to update the Discussion section to include published data that demonstrate use of clonoSEQ in patients with MM.[5-11] Specifically, recent studies of next-generation sequencing (NGS) MRD in the frontline and relapsed/refractory populations have shown that patients who achieve MRD-negativity have the best outcomes (CASTOR, POLLUX, ALCYONE, MAIA, CASSIOPEIA).[8-11] Since 2019, 11 new manuscripts utilizing Adaptive's NGS MRD Assay have been published in Myeloma.

Requested Modifications (based off version 2.2020)

- Page 10 (MYEL-1): Adaptive had previously asked the panel to add in NGS assessment to this section. The guideline committee agreed and added: 'single nucleotide polymorphism (SNP) array on bone marrow, and/or next-generation sequencing (NGS) panel on bone marrow.' We would request further clarification that at baseline, a bone marrow sample should be taken or stored for subsequent NGS MRD assessment. This is separate and distinct from a genetic mutation assessment panel by NGS. An example from the Diagnostic Workup in the NCCN ALL Guidelines reads: 'baseline assessment of leukemic clone to facilitate subsequent MRD analysis'. We believe that this is an important distinction so that clinicians are aware that NGS MRD assessment includes the requirement for a baseline sample.

- Adaptive has received feedback from clinicians and payers that it is not clear within the Guidelines on when to assess MRD. The Guidelines (MYEL-E, page 3/3, footnote q) recommend that 'information on MRD after each treatment stage is recommended (post induction, high-dose therapy/ASTCT, consolidation, maintenance).' However, this recommendation is not widely found, based on feedback from clinicians and payers. The following requests relate to making this recommendation more prominent outside of this footnote. Note that previous guideline comments stated that MYEL-E cannot be updated as it is reprinted with permission from Elsevier, so modification elsewhere in the guidelines would be our recommendation.

- Page 12 (MYEL-E): Update the following section to call out MRD assessment (3rd bullet from bottom; suggested updates in red): Bone marrow aspirate and biopsy with FISH, SNP array, and NGS~~,~~ or multi-parameter flow cytometry for MRD assessment as clinically indicated. Alternatively, add bullet: 'Assess minimal residual disease (MRD) as indicated for prognosis after shared decision with patient' (as seen in MYEL-5).

- Page 13 (MYEL-4): Add bullet: 'Assess minimal residual disease (MRD) as indicated for prognosis after shared decision with patient' (as seen in MYEL-5).

- We would request that the Guideline Committee add a note within the Guidelines stating that MRD determination is recommended in the conduct of clinical trials and at the discretion of the health care provider for the clinical management of individual patients. As MYEL-E cannot be edited (per prior Guideline Meeting comments), we would defer to the committee on the best place to add this information.

- Discussion section: Update the discussion of use of MRD in patients with MM to reflect recent clinical trials using clonoSEQ.[5-12]

References

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4. CMS. Local Coverage Article: MolDX: Clonoseq® Assay for Assessment of Minimal Residual Disease (MRD) in Patients with Specific Lymphoid Malignancies (A56270). https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=56270&ver=5&Cntrctr=374&ContrVer=1&CntrctrSelected=374*1&DocType=Active&s=48&bc=AhAAAAIAgAAA&. Updated January 17, 2019. Accessed March 20, 2019.
5. Bahlis N, et al. *Leukemia.* 2020. doi: 10.1038/s41375-020-0711-6.
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