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Positive Quality Intervention: clonoSEQ Next Generation Sequencing for Minimal Residual Disease Testing in Multiple Myeloma

Description: This document will discuss the utility of the clonoSEQ assay in patients with multiple myeloma by following patients during their treatment.

Background: In Fall 2016, the NCCN endorsed the full new International Myeloma Working Group (IMWG) response criteria, including MRD testing.[1,2] This was important news as it would lead to insurance reimbursement of this testing for patients. The majority of recent myeloma clinical trials including many of the anti-CD38 combination trials have incorporated MRD testing as part of their trial design.[3] Studies have shown that those patients who attain MRD negative status and maintain it are shown to have better outcomes regardless of how they attain it.[3] These outcomes have been measured in improved PFS and OS compared to MRD positive patients. As a result, MRD testing through clonoSEQ is becoming standard practice at leading cancer centers around the United States. As of this publication, clonoSEQ is FDA-cleared not only for multiple myeloma, but also for CLL and B-ALL. clonoSEQ is available for use in other lymphoid malignancies (including DLBCL) as a CLIA-validated test.[4]

PQI Process:

- A clonality ID sample is needed to identify the myeloma rearrangement; once the rearrangement is identified, this will be followed with future clonoSEQ MRD tests
- At the time of initial diagnosis, nearly all patients will be undergoing a bone marrow biopsy; the best time to check for a clonality ID is on a fresh Bone Marrow Aspirate (BMA) or smear slide during this process
    - In the event that a clonality ID sample was not collected and sent during this time, it can still be checked on the archived bone marrow aspirate, smear slides or clot sections
- MRD testing after each treatment stage is recommended for best achievable response:
    - Transplant Eligible
        - After induction therapy, prior to transplant
        - After stem cell transplant
        - After consolidation therapy (if needed)
        - During the maintenance period (recommendation at least every 12 months)
    - Transplant-Ineligible
        - After induction therapy
        - After consolidation therapy (if needed)
        - During the maintenance period (recommendation at least every 12 months)
- Access the **clonoSEQ Next Generation Sequencing for Minimum Residual Disease Testing in Chronic Lymphocytic Leukemia PQI** for sample ordersets

Patient-Centered Activities:

- Explain MRD testing to the patient:
    - We are attempting to detect myeloma cells that may be present in the body that are not able to be detected through standard sampling of the bone marrow or blood tests. The clonoSEQ assay is a very sensitive test and can detect a single cancer cell among a million normal cells. In scientific terms, a sample is deemed MRD-negative by an assay with a sensitivity of 10^{-6}
    - It is important to continue to monitor the MRD status on an outlined interval regardless of what

the test results are on the initial testing
    - Based on current literature, a negative MRD test does not mean that you can stop all cancer treatment; this decision will be best left to the treating physician
- Explain results to patients clearly, including how to interpret the test results
- Explain the data regarding MRD positive vs. negative status to patients
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. https://www.myeloma.org/blog/dr-duries/nccn-endorses-mrd-testing-what-does-mean-patients.
2. NCCN. (n.d.). Retrieved February 7, 2023, from https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf
3. Bal S. Assessment of measurable residual disease (MRD) in multiple myeloma: a review of the data. *Clin Adv Hem Oncol*. 2020;supp 1(1):3-10. https://pubmed.ncbi.nlm.nih.gov/33843860/.
4. clonoSEQ®. [technical summary]. Seattle, WA: Adaptive Biotechnologies; 2020.