National Comprehensive Cancer Network®

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Tamara Syrek-Jensen, JD
Director, Coverage and Analysis Group
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD

RE: National Coverage Analysis: Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Myelodysplastic Syndromes (MDS)

Dear Ms. Syrek-Jensen:

The National Comprehensive Cancer Network® (NCCN®) appreciates the opportunity to comment on the Centers for Medicare and Medicaid Services (CMS) National Coverage Analysis: Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Myelodysplastic Syndromes (MDS). NCCN's mission is to improve and facilitate quality, effective, equitable, and accessible cancer care so all patients can live better lives. NCCN thanks CMS for opening this National Coverage Analysis and encourages CMS to consider covering HSCT for MDS without evidence development in clinical scenarios outlined by nationally recognized clinical practice guidelines. NCCN is pleased to provide information, recommendations, and resources as CMS considers this coverage analysis.

NCCN Background

As an alliance of 33 leading academic cancer centers in the United States that treat hundreds of thousands of patients with cancer annually, NCCN® is a developer of authoritative information regarding cancer prevention, screening, diagnosis, treatment, and supportive care that is widely used by clinical professionals and payers alike. The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a comprehensive set of guidelines detailing the sequential management decisions and interventions that currently apply to 97 percent of cancers affecting patients in the United States.

NCCN Guidelines® and Library of Compendia products help ensure access to appropriate care, clinical decision-making, and assessment of quality improvement initiatives. NCCN was recognized by CMS in 2016 and renewed in 2021 as a qualified Provider Led Entity (PLE) for the Medicare Appropriate Use Criteria (AUC) Program for the development of AUC and the establishment of policy and decision-making for diagnostic imaging in patients with cancer. NCCN Imaging Appropriate Use Criteria (NCCN Imaging AUC™) include information designed to support clinical decision-making around the use of imaging in patients with cancer and are based directly on the NCCN Guidelines®. NCCN Imaging AUC™ include recommendations pertaining to cancer screening, diagnosis, staging, treatment response assessment, follow-up, and surveillance. The NCCN Drugs & Biologics Compendium (NCCN Compendium®) has been recognized by CMS and clinical professionals in the commercial payer setting since 2008 as an evidence-based reference for establishment of coverage policy and coverage decisions regarding off-label use of anticancer and cancer-related medications. The NCCN Biomarkers Compendium® has been referenced as a coverage mechanism and source of evidence by local Medicare Administrative Contractors and serves as a resource for payers, providers, and health care entities navigating the rapidly changing evidence-base for

medically necessary biomarker testing in oncology. The NCCN Biomarkers Compendium® contains information derived directly from the NCCN Guidelines to support decision-making around the use of biomarker testing in patients with cancer. The NCCN Biomarkers Compendium is updated continuously in conjunction with the NCCN guidelines to stay evergreen.

NCCN imposes strict policies to shield the guidelines development processes from external influences. The "firewall" surrounding the NCCN Guidelines processes includes the following: financial support policies; panel participation and communication policies; guidelines disclosure policies; and policies regarding relationships to NCCN's other business development activities. The guidelines development is supported exclusively by the Member Institutions' dues and does not accept any form of industry or other external financial support for the guidelines development program. The NCCN Guidelines are updated at least annually in an evidence-based process integrated with the expert judgment of multidisciplinary panels of expert physicians from NCCN Member Institutions. The NCCN Guidelines are transparent, continuously updated, available free of charge online for non-commercial use, and are available through a multitude of health information technology (HIT) vendors.

NCCN Recommendations Regarding HCT for MDS

CMS received a request to reconsider the National Coverage Determination regarding HSCT for MDS, specifically coverage of allogeneic HSCT for beneficiaries with MDS. CMS has responded by opening a National Coverage Analysis (NCA) and notes the scope is only for coverage of allogeneic HSCT for beneficiaries with MDS absent a CED requirement. NCCN applauds CMS for reconsidering this service for coverage without evidence development. NCCN encourages CMS to cover HSCT for Medicare beneficiaries with MDS to ensure all Medicare beneficiaries can access optimal and appropriate cancer care. NCCN is pleased to provide information on NCCN Guideline recommendations related to the use of HCT for MDS and has also attached the most recent version of the NCCN Guidelines for Myelodysplastic Syndromes® as an appendix to this document.

Consideration of allogeneic HCT is included as a Category 2A recommendation for select patients with lower-risk disease after disease progression or after no response or intolerance to other recommended therapy. Patients with International Prognostic Scoring System (IPSS) Intermediate-1, International Prognostic Scoring System-Revised (IPSS-R) Intermediate, and WHO-Based Prognostic Scoring System (WPSS) Intermediate risk MDS with severe cytopenias would also be considered candidates for HCT. NCCN Guidelines note that matched sibling, unrelated donor, or alternative (haploidentical or cord blood when appropriate) donor, including standard and reduced-intensity preparative approaches, may be considered.

For patients who have a higher-risk of disease progression and are eligible for transplant, allogeneic HCT from the most suitable stem cell donor (HLA-matched sibling or unrelated donor, HLA-haploidentical family member or cord blood) is included as a Category 2A recommendation. **NCCN guidelines emphasize that early referral for transplant evaluation is recommended to allow moving to transplant efficiently**. Pre-transplant debulking therapy to reduce marrow blasts to <5% with the goal of reducing post-transplant relapse is recommended, although the optimum strategy (azacitidine, decitabine, induction-type chemotherapy) has not been determined. NCCN Guidelines note that reducing the disease burden pre-

transplant is particularly important in patients who will receive a reduced-intensity conditioning regimen.[1] At some centers, failure to achieve <5% blasts with cytoreduction should not preclude from proceeding to transplant, as these patients appeared to derive survival benefit from transplant.[2,3] Strategies for patients with specific mutations are under investigation. Patients with TP53 mutations, particularly biallelic, have a poor prognosis even with transplantation. These cases should be discussed with a physician who has expertise in HCT and patients should be enrolled in a clinical trial whenever possible.

For patients who experience a disease relapse after initial HCT or whose disease did not respond to treatment, NCCN Guidelines include as Category 2A consideration of a second allogeneic HCT. NCCN Guidelines specifically note that physicians should consider a second transplant or donor lymphocyte infusion immuno-based therapy for appropriate patients who had a prolonged remission after first transplant.

NCCN also feels it's important to note that age alone should not be an exclusionary factor for allogenic HCT. In a prospective allogeneic transplant trial using nonmyeloablative conditioning, 372 patients between ages 60 and 75 years with hematologic malignancies (AML, MDS, chronic lymphocytic leukemia, lymphoma, and multiple myeloma) were shown to have no association between age and non-relapse mortality, overall survival, and progression free survival.[4] The study supports the use of comorbidities and disease status, rather than age alone, as criteria for determining the eligibility of patients for allogeneic HCT. Further information can be found in the NCCN Guidelines for Myelodysplastic Syndromes® which are included as an appendix. Additionally, these guidelines are continuously updated and the most up to date version can always be found online at www.nccn.org.

In sum, NCCN thanks CMS for reconsidering coverage of this critical intervention. NCCN supports coverage of HSCT for MDS without evidence development as outlined within nationally recognized clinical practice guidelines and supported by the literature. NCCN appreciates the opportunity to comment on the CMS National Coverage Analysis: Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Myelodysplastic Syndromes (MDS). NCCN is happy to serve as a resource and looks forward to working together to advance access to equitable, high-quality cancer care.

Sincerely,

Peter L. Greenberg, MD
Panel Chair
NCCN Guidelines for Myelodysplastic Syndromes

Robert W. Carlson, MD
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National Comprehensive Cancer Network

[1] Festuccia M, et al. Biol Blood Marrow Transplant 2016;22:1227-1233

[2] Nakamura R, et al. J Clin Oncol 2021;39:3328-3339.

[3] Schroeder T, et al. Biol Blood Marrow Transplant 2019:25;1550-1559

[4] Sorror ML, et al. JAMA 2011;306:1874-1883.