July 6, 2023

Tamara Syrek Jensen, JD
Director, Coverage & Analysis Group
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Re:National coverage analysis for Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Myelodysplastic Syndromes (MDS)

Dear Ms. Syrek Jensen:

On behalf of the American Society of Hematology (ASH), the American Society for Transplantation and Cellular Therapy (ASTCT), the National Marrow Donor Program (NMDP), the Center for International Blood and Marrow Transplant Research (CIBMTR), and the Blood and Marrow Transplant Clinical Trials Network (BMT CTN), thank you for initiating the national coverage analysis for Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Myelodysplastic Syndromes (MDS) in response to our reconsideration request submitted October 12, 2021.

As the Centers for Medicare & Medicaid Services (CMS) develops the proposed decision memo on this topic, we respectfully request that the clinical studies and scientific evidence outlined in these comments be considered to support the coverage of HSCT for individuals with MDS without the coverage with evidence development (CED) requirement. This evidence includes the studies outlined in our original reconsideration request as well as recent studies and guidelines that have been published in the interim.

Allogeneic HSCT remains the only curative therapy for patients with MDS, a group of blood disorders in which the bone marrow does not produce enough healthy, functioning blood cells. MDS primarily impacts older adults: the median age at diagnosis is 70 years, making Medicare coverage for HSCT essential for patients to have access to this life-saving treatment.

Summary of the Evidence in Support of Removing the CED Requirement
We understand the agency will undertake a comprehensive literature review as a part of the NCA process. In the following sections of our letter, we have provided a synopsis of studies that support coverage of allogeneic HSCT for MDS without the CED requirement.

Summary of Biologic Assignment Trial of Reduced-Intensity Hematopoietic Cell Transplantation Based on Donor Availability in Patients 50-75 Years of Age with Advanced Myelodysplastic Syndrome[1]

Allogeneic HSCT, widely used in younger MDS patients, is the only curative therapy for MDS. While transplantation outcomes among selected older patients with MDS are similar to younger patients with MDS, early transplantation for older patients is infrequently offered since the relative benefits of HSCT over non-HSCT therapy have not been well defined in this patient group. The goal of this

[1] Nakamura R, Saber W, Martens MJ, et al. Biologic Assignment Trial of Reduced-Intensity Hematopoietic Cell Transplantation Based on Donor Availability in Patients 50-75 Years of Age with Advanced Myelodysplastic Syndrome. J Clin Onc 2021.

multi-center, biologic assignment study performed by the BMT CTN in older individuals with high risk MDS was to define the benefit of HSCT over non-HSCT therapy. Specifically, the study compared allogeneic HSCT with DNA hypomethylating therapy or best supportive care in individuals aged 50-75 years with advanced MDS.

To summarize, the study found that overall survival and leukemia-free survival were significantly improved for individuals who had a suitably matched donor in comparison with those who did not have a donor. Half of subjects with a donor were alive 3 years after trial entry compared to one-quarter when a donor was unavailable.

Biologic assignment was to the donor, or no donor group based on the identification of a suitable, HLA-matched related or unrelated donor within 90 days of trial entry. Subjects with an identified donor were expected to undergo transplantation within 6 months, while those without a suitable donor were expected to receive DNA hypomethylating therapy or best supportive care. The primary endpoint of the study was a point comparison of adjusted overall survival at 3 years from study registration. Secondary endpoints included leukemia-free survival at 3 years from study registration, quality of life measured at 6 timepoints, and a cost-effectiveness comparison. Additionally, pre-specified as-treated analyses were performed, analyzing only subjects who received their biologically assigned therapy.

Three hundred eighty-four subjects in total were accrued at 34 participating centers, with enrollment ending at the end of 2018, when sufficient subjects had been accrued to the no donor arm. Of the 384 subjects, a suitable donor was identified in 260 while no donor was found for 124. Seven subjects died during the 90-day search window and were included in the no donor arm. The donor and no donor arms were well balanced for age, gender, duration of MDS, disease risk and response to prior DNA hypomethylating therapy.

At three years from trial enrollment, overall survival was significantly higher in the donor vs. no donor

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haploidentical family donors. We believe it is appropriate to provide coverage for patients with MDS agnostic of the donor source, which is consistent with the statements in the current practice guidelines from the ASTCT and NCCN.

In conclusion, ASH, ASTCT, NMDP, CIBMTR, and BMT CTN submit this comment letter to support full coverage of allogeneic HSCT for individuals with myelodysplastic syndromes and the removal of the CED requirement currently tied to coverage for HSCT for individuals with MDS. Additionally, we have provided all published evidence in support of this recommendation in Appendix A.

Thank you for your consideration of our comments. Should you have any questions or require more information, please contact Suzanne Leous, American Society of Hematology's Chief Policy Officer, at sleous@hematology.org or 202-292-0258.

Sincerely,

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Appendix A: Literature outlining clinical evidence which supports eliminating the CED requirement