2018 REFERRAL GUIDELINES

Recommended Timing for Transplant Consultation

Published jointly by the
National Marrow Donor Program®/Be The Match®
and the American Society for Blood and Marrow Transplantation

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2018 Recommended Timing for Transplant Consultation

Intent of guidelines

These guidelines identify appropriate timing of consultation for autologous or allogeneic hematopoietic cell transplantation (HCT) based on disease characteristics. Evaluation and coordination of the timing of HCT for eligible patients is determined in collaboration with the transplant center.

In many situations, early referral is a critical factor for optimal transplant outcomes. Likewise, delays in referral can reduce success rates for transplant because there may be a narrow window of opportunity to proceed to transplant and delays might preclude transplant altogether. Research data comparing outcomes by disease status can be found at **BeTheMatchClinical.org/HCTtiming**

If allogeneic transplant is a possibility, HLA typing of the patient (high resolution) and potential family donors should be completed at time of diagnosis, and if no matches are found, a preliminary unrelated donor search of the Be The Match Registry® should be done.

These 2018 guidelines were developed jointly by the National Marrow Donor Program® (NMDP®)/Be the Match® and the American Society for Blood and Marrow Transplantation (ASBMT), and are based on current clinical practice, medical literature, National Comprehensive Cancer Network® (NCCN®) Guidelines for the treatment of cancer and evidence-based reviews.

About the American Society for Blood and Marrow Transplantation (ASBMT)

The American Society for Blood and Marrow Transplantation (ASBMT) is an international professional membership association of more than 2,200 physicians, investigators and other health care professionals promoting blood and marrow transplantation, cellular therapy research, education, scholarly publication and clinical standards.

Learn more at ASBMT.org

ASBMT™ American Society for Blood and Marrow Transplantation

About the National Marrow Donor Program (NMDP)/Be The Match

We are the global leader in providing a cure to patients with life-threatening blood and marrow cancers like leukemia and lymphoma, as well as other diseases. We manage the world's largest registry of potential marrow donors and cord blood units, connect patients to their donor match for a life-saving marrow or umbilical cord blood transplant and educate health care professionals and patients. We conduct research through our research program, CIBMTR® (Center for International Blood and Marrow Transplant Research®), in collaboration with Medical College of Wisconsin.

Learn more at BeTheMatchClinical.org

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Adult Leukemias and Myelodysplasia
Acute Myeloid Leukemia (AML)
High-resolution HLA typing is recommended at diagnosis for all patients
Early after initial diagnosis, all patients with AML including: • Primary induction failure • Minimal residual disease after initial therapy • CR1 — except favorable risk AML [defined as: t(16;16), inv 16, or t(8;21) without *c-KIT* mutation; t(15;17); normal cytogenetics with *NPM1* or isolated biallelic *CEBPA* mutation and without *FLT3*-ITD] • Antecedent hematological disease (e.g., myelodysplastic syndromes (MDS)) • Treatment-related leukemia • First relapse • CR2 and beyond, if not previously evaluated
Acute Lymphoblastic Leukemia (ALL) (adult defined as ≥ 40 years)
High-resolution HLA typing is recommended at diagnosis for all patients
Early after initial diagnosis, all patients with ALL including: • Primary induction failure • Minimal residual disease after initial therapy • CR1 • First relapse • CR2 and beyond, if not previously evaluated
Myelodysplastic Syndromes (MDS)
High-resolution HLA typing is recommended at diagnosis for all patients
Any intermediate or high IPSS or IPSS-R score
Any MDS with poor prognostic features, including: • Treatment-related MDS • Refractory cytopenias • Adverse cytogenetics and molecular features • Transfusion dependence • Failure of hypomethylating agents or chemotherapy • Moderate to severe marrow fibrosis
Chronic Myeloid Leukemia (CML)
• Inadequate hematologic or cytogenetic response to tyrosine kinase inhibitor (TKI) therapies • Disease progression • Intolerance to TKI therapies
• Accelerated phase • Blast crisis (myeloid or lymphoid)
Myeloproliferative Neoplasms (MPN) (including BCR-ABL–negative myeloproliferative neoplasms, myelofibrosis and later stages of polycythemia vera and essential thrombocytosis)
Intermediate- or high-risk disease, including: • High-risk cytogenetics • Poor initial response or at progression
Chronic Lymphocytic Leukemia (CLL)
• High-risk cytogenetics or molecular features (e.g., del(11q) or del(17p); ZAP70, CD38 positivity; unmutated Ig VH mutational status, complex karyotype) • Poor initial response • Short initial remission • Chemotherapy- or targeted therapy-resistant • Richter's transformation

Pediatric Acute Leukemias and Myelodysplasia
Acute Myeloid Leukemia (AML)
High-resolution HLA typing is recommended at diagnosis for all patients
Early after initial diagnosis, all patients with AML including: • Age <2 years at diagnosis • Primary induction failure • Minimal residual disease after initial therapy • CR1 — except favorable risk AML [defined as: t(16;16); inv 16; t(8;21); t(15;17); normal cytogenetics with *NPM1* or isolated biallelic *CEBPA* mutation and without *FLT3*-ITD] • Monosomy 5 or 7 • Treatment-related leukemia • First relapse • CR2 and beyond, if not previously evaluated
Acute Lymphoblastic Leukemia (ALL) (age <15 years)
• Infant at diagnosis • Primary induction failure • Presence of minimal residual disease after initial therapy • High/very high risk CR1 including: - Philadelphia chromosome positive or Philadelphia-like - iAMP21 - 11q23 rearrangement • First relapse • CR2 and beyond, if not previously evaluated
Acute Lymphoblastic Leukemia (ALL) (adolescent and young adults age 15-39 years)
High-resolution HLA typing is recommended at diagnosis for all patients
• Primary induction failure • Presence of minimal residual disease after initial therapy • High/very high-risk CR1 including: - Philadelphia chromosome positive or Philadelphia-like - iAMP21 - 11q23 rearrangement - B-cell with poor-risk cytogenetics • First relapse • CR2 and beyond, if not previously evaluated
Myelodysplastic Syndromes (MDS)
• At diagnosis for all subtypes
Juvenile Myelomonocytic Leukemia (JMML)
• At diagnosis

For HCT outcomes data: BeTheMatchClinical.org/outcomes

Lymphomas

Non-Hodgkin Lymphoma

Follicular
- Poor response to initial treatment
- Initial remission duration <12 months
- First relapse
- Transformation to diffuse large B-cell lymphoma

Diffuse Large B-Cell
- Primary induction failure
- CR1 for patients with PET positivity
- First relapse
- CR2 or subsequent remission
- Double or triple hit (MYC and BCL-2 and/or BCL-6) – at diagnosis

High Grade
- Primary induction failure
- CR1
- First relapse
- CR2 or subsequent remission

Mantle Cell
- At diagnosis

Other High-Risk Lymphomas
- At diagnosis

Hodgkin Lymphoma

- Primary induction failure
- At first or subsequent relapse
- CR2 or subsequent remission

Multiple Myeloma

Multiple Myeloma

- At diagnosis
- At first progression

Other Malignant Diseases

Germ Cell Tumors

- Poor initial response
- Short initial remission

Neuroblastoma

- INSS stage 2 or 3 at diagnosis
  - MYCN amplification (>4x above reference)
- INSS stage 4 at diagnosis
  - MYCN amplification (>4x above reference)
  - age >18 months at diagnosis
  - age 12-18 months with unfavorable characteristics
- Metastatic disease at diagnosis
- Progressive disease while on therapy or relapsed disease

Ewing Family of Tumors

- Metastatic disease at diagnosis
- First relapse or CR2

Medulloblastoma

- First relapse or CR2

Non-Malignant Disorders
Immune Deficiency Diseases (including severe combined immunodeficiency syndromes, Wiskott-Aldrich syndrome, Omenn syndrome, X-linked lymphoproliferative syndrome, severe congenital neutropenia and others)
• At diagnosis or if detected on newborn screening
Inherited Metabolic Disorders (including Hurler syndrome, adrenoleukodystrophy, and others)
• At diagnosis or if detected on newborn screening
Hemoglobinopathies
Sickle Cell Disease • With aggressive course (stroke, end-organ complications, frequent pain crises)
Transfusion-Dependent Thalassemias • At diagnosis
Hemophagocytic Lymphohistiocytosis (HLH)
• At diagnosis
Severe Aplastic Anemia and Other Marrow Failure Syndromes (including Fanconi anemia, Diamond-Blackfan anemia, Shwachman-Diamond syndrome and others)
• At diagnosis

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