

2019 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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2019 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.

The consideration for HCT primarily includes patient and disease characteristics, not age alone, as advances in HCT now permit older patients with selected comorbidities and good functional status to safely undergo HCT for curative intent with a relatively low and acceptable risk of non-relapse mortality. HCT consultations include risk-to-benefit considerations based on risk score assessments.

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 2019 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 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. Download the ASBMT Practice Guidelines app on iTunes or Google Play for up-to-date access to clinical calculators, practice guidelines, evidence-based reviews and position statements from the ASBMT Committee on Practice Guidelines.

Learn more at [ASBMT.org](https://www.asbmt.org)

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](https://www.bethematch.org)

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Adult Leukemias and Myelodysplasia	
Acute Myeloid Leukemia (AML)	
<i>High-resolution HLA typing is recommended at diagnosis for all patients</i>	
<p>Early after initial diagnosis, all patients with AML including:</p> <ul style="list-style-type: none"> • Primary induction failure • Minimal residual disease after initial therapy • CR1 – except favorable risk AML [defined as: t(16;16), inv16, or t(8;21) without c-<i>KIT</i> mutation; t(15;17); normal cytogenetics with <i>NPM1</i> or isolated biallelic <i>CEBPA</i> mutation and without <i>FLT3</i>-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)	
<i>High-resolution HLA typing is recommended at diagnosis for all patients</i>	
<p>Early after initial diagnosis, all patients with ALL including:</p> <ul style="list-style-type: none"> • Primary induction failure • Minimal residual disease after initial therapy • CR1 • First relapse • CR2 and beyond, if not previously evaluated 	
Myelodysplastic Syndromes (MDS)	
<i>High-resolution HLA typing is recommended at diagnosis for all patients</i>	
Any intermediate or high IPSS or IPSS-R score	
<p>Any MDS with poor prognostic features, including:</p> <ul style="list-style-type: none"> • 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)	
<ul style="list-style-type: none"> • Inadequate hematologic or cytogenetic/molecular response to tyrosine kinase inhibitor (TKI) therapies • Disease progression • Intolerance to TKI therapies 	
<ul style="list-style-type: none"> • Accelerated phase • Blast crisis (myeloid or lymphoid) 	
Myeloproliferative Neoplasms (MPN) (including <i>BCR-ABL</i> -negative myeloproliferative neoplasms and later stages of polycythemia vera and essential thrombocytosis)	
<i>High resolution HLA typing is recommended at diagnosis for all patients</i>	
<p>Intermediate- or high-risk disease, including:</p> <ul style="list-style-type: none"> • High-risk cytogenetics • Poor initial response or at progression 	

Adult Leukemias and Myelodysplasia (continued)

Myelofibrosis (MF)

- DIPSS Intermediate-2 (INT-2) and high risk disease
- DIPSS Intermediate-1 (INT-1) with low platelet counts, red blood cell transfusion dependent, complex cytogenetics
- High risk driver mutations (*ASXL1*, *EZH2*, *TET2*, *IDH1*, *IDH2*, *SRSF2*, and *TP53*) or triple negative (lack of a driver mutation such as *JAK2*, *MPL*, or *CALR*) should be considered in decision making

Chronic Lymphocytic Leukemia (CLL)

- Second or greater relapse following chemoimmunotherapy
- 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); inv16; 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 slow-TKI responders or with *IKZF1* deletions; 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

Pediatric Acute Leukemias and Myelodysplasia (continued)

Juvenile Myelomonocytic Leukemia (JMML)

- At diagnosis

Lymphomas

Non-Hodgkin Lymphoma

Follicular

- Poor response to initial treatment
- Initial remission duration <24 months
- First relapse
- Transformation to diffuse large B-cell lymphoma

Diffuse Large B-Cell

- Primary induction failure, including residual PET avid disease
- First relapse
- CR2 or subsequent remission
- Double or triple hit (*MYC* and *BCL-2* and/or *BCL-6*) - at diagnosis
- Primary CNS lymphoma at diagnosis

High Grade

- *C-myc* rearrangement at diagnosis
- Primary induction failure
- CR1
- First relapse
- CR2 or subsequent remission

Mantle Cell

- At diagnosis
- First relapse
- Bruton's tyrosine kinase (BTK) intolerant or resistant disease

Mature T-cell

- CR1
- First relapse

Other High-Risk Lymphomas

- At diagnosis

Hodgkin Lymphoma

- Primary induction failure
- First relapse
- CR2 or subsequent remission

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

Other Malignant Diseases (continued)

Ewing Family of Tumors

- Metastatic disease at diagnosis
- First relapse or CR2

Medulloblastoma

- First relapse or CR2

Multiple Myeloma

Multiple Myeloma

- At diagnosis
- At first progression

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

- Children with available matched sibling donor
- All patients 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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