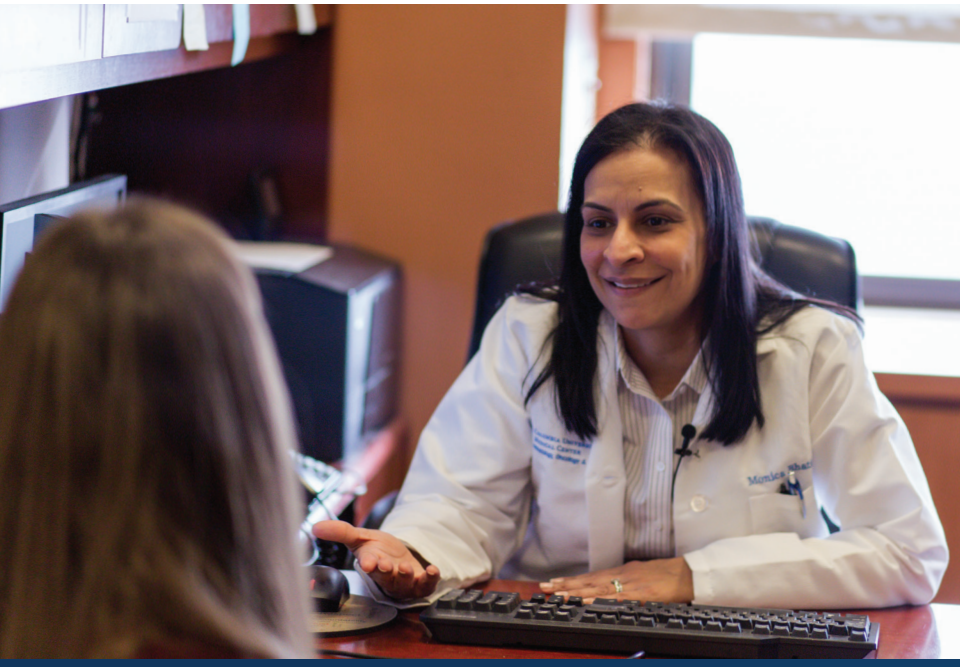
2022 CONSULTATION GUIDELINES

Recommended Timing for Transplant Consultation



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2022 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 includes patient and disease characteristics. HCT consultations include risk-to-benefit consideration based on risk score assessments. Advances in HCT 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, thus age alone is not a contraindication for HCT.

Early referral is a critical factor for optimal transplant outcomes. In many situations, there may be a narrow window of opportunity to proceed to transplant and delays might preclude transplant or impair transplant outcomes. Research data comparing outcomes by disease status can be found at BeTheMatchClinical.org/HCTtiming

If allogeneic transplant is potentially indicated, high resolution HLA typing of the patient and potential family donors should be performed and a preliminary unrelated donor search of NMDP℠ should be completed at diagnosis.

These 2022 guidelines were developed jointly by NMDP and the American Society for Transplant and Cellular Therapy (ASTCT), 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 Transplant and Cellular Therapy (ASTCT)

The American Society for Transplantation and Cellular Therapy (ASTCT), formerly known as the American Society for Blood and Marrow Transplantation, is a professional society of more than 2,200 health care professionals and scientists from over 45 countries who are dedicated to improving the application and success of blood and marrow transplantation and related cellular therapies. ASTCT strives to be the leading organization promoting research, education and clinical practice to deliver the best, comprehensive care. Download the ASTCT 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 ASTCT Committee on Practice Guidelines. For more information, please visit ASTCT.org.

About NMDP

NMDP has more than 30 years' experience operating the world's largest registry of unrelated adult donors and cord blood units. NMDP advances the science of transplantation through our research program, the CIBMTR® (Center for International Blood and Marrow Transplant Research®) in collaboration with Medical College of Wisconsin.

For more information, please visit 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

HCT consultation should take place early after initial diagnosis for all patients with AML, including:

- Primary induction failure
- Measurable (also known as minimal) residual disease after initial therapy
- CR1 – except favorable risk AML [defined as:t(8;21)(q22;q22.1); RUNX1-RUNX1T1, inv(16)(p13.1q22) or t(16;16)(p13.1;q22); CBFB-MYH11, mutated NPM1 without FLT3-ITD, biallelic mutated]. Early referral for allogeneic HCT should also be considered for any AML patients in CR1 who are 60 years or older; regardless of cytogenetic or genomic information.
- 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

HCT consultation should take place early after initial diagnosis for all patients with ALL, including:

- Primary induction failure
- Measurable (also known as 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/molecular response to tyrosine kinase inhibitor (TKI) therapies
- Disease progression
- Intolerance to TKI therapies

- Accelerated phase
- Blast crisis (myeloid or lymphoid)
- T315I mutation

Myeloproliferative Neoplasms (MPN) (including BCR-ABL–negative myeloproliferative neoplasms and later stages of polycythemia vera and essential thrombocytosis)

High-resolution HLA typing is recommended at diagnosis for all patients

Intermediate- or high-risk disease, including:

- High-risk cytogenetics
- Poor initial response or at progression

Myelofibrosis (MF)

- DIPSS Intermediate-2 (INT-2) and high risk disease
- DIPSS Intermediate-1 (INT-1) with low platelet counts, refractory, red blood cell transfusion dependent, circulating blast cells > 2%, 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

Adult Leukemias and Myelodysplasia (continued)

Chronic Lymphocytic Leukemia (CLL)

- Resistance or intolerance to BTK inhibitors and/or BCL2 inhibitors

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
- Measurable (also known as minimal) residual disease after initial therapy
- CR1 — except favorable risk AML [defined as:t(8;21)(q22;q22.1); RUNX1-RUNX1T1, inv(16)(p13.1q22) or t(16;16)(p13.1;q22); CBFB-MYH11, mutated NPM1 without FLT3-ITD or with FLT3-ITD^{low}, biallelic mutated CEBPA]
- 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
  - unfavorable genetics
  - age < 3 months with any WBC, or < 6 months with WBC > 300,000 at presentation
- Primary induction failure
- Presence of measurable (also known as 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
- Chimeric Antigen Receptor Therapy (CAR-T)

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 measurable (also known 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

Plasma Cell Disorders

Multiple Myeloma

- At diagnosis
- At progression and/or relapse

Light Chain Amyloidosis

- At diagnosis
- At progression and/or relapse

Plasma Cell Disorders (continued)

POEMS Syndrome (Osteosclerotic Myeloma)

- 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 PIF or first relapse

High Grade B-Cell
- MYC and BCL-2 and/or BCL-6 rearrangements
- 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 relapse

Other Malignant Diseases

Germ Cell Tumors

- Poor initial response
- Short initial relapse

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

- Children with available matched sibling donor
- All patients with aggressive course (stroke, end-organ complications, frequent pain crises)
- All patients with an alternative donor option and any of the following:
  - Stroke or silent cerebral infarct or cognitive impairment > 24 hours
  - ≥ 2 episodes of acute chest syndrome/2 year period [or] 'recurrent' acute chest syndrome'
  - Regular red blood cell transfusion therapy (8 or more per year)
  - Tricuspid value regurgitant jet (TRJ) velocity ≥ 2.7 m/sec
  - Chronic pain ≥ 6 months (leg ulcers, avascular necrosis)
  - Abnormal transcranial Doppler (TCD) velocity of ≥ 200 cm/sec or > 185 cm/sec with intracranial vasculopathy
  - Silent cerebral infarct
  - ≥ 3 severe vaso-occlusive pain crises per 2-year period

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

Systemic Sclerosis

- At diagnosis or with diffuse disease, with increasing skin tightness score (modified Rodnan skin score, [mRSS]) and evidence of decrease (< 80%) in % predicted pulmonary function tests: forced vital capacity (FVC) and/or diffusion capacity (DLCO)

Multiple Sclerosis (MS)

- After MS relapse, with ≥ 2 relapse episodes in past 3 years, while on disease modifying therapy. Refer patient prior to progression of severe disability: patient must be able to walk 100 meters (with unilateral assistance: cane, crutch or brace)

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