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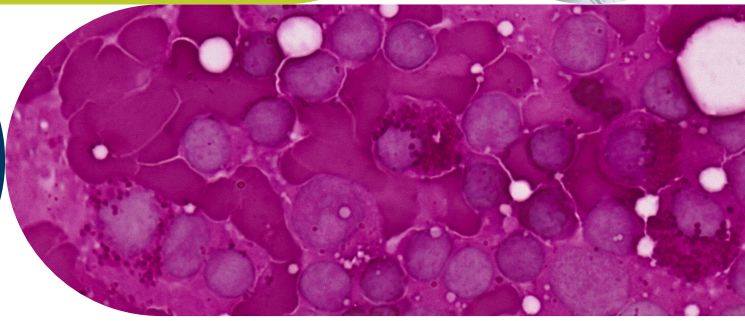
2024 CONSULTATION GUIDELINES

# Recommended Timing for Transplant Consultation



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American Society for Transplantation and Cellular Therapy (ASTCT)

# 2024 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.

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 the NMDP Registry℠ should be completed at diagnosis.

These guidelines were developed jointly by NMDP and the American Society for Transplantation and Cellular Therapy (ASTCT). The guidelines 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, 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

At NMDP, we believe each of us holds the key to curing blood cancers and disorders. As a global nonprofit leader in cell therapy, NMDP creates essential connections between researchers and supporters to inspire action and accelerate innovation to find life-saving cures. With the help of blood stem cell donors from the world's most diverse registry and our extensive network of transplant partners, physicians and caregivers, we're expanding access to treatment so that every patient can receive their life-saving cell therapy. NMDP. Find cures. Save lives.

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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 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]. Transplant consultation may be reasonable for favorable-risk AML patients with unusual or adverse co-mutations or cytogenetic alterations. Early referral for allogeneic HCT should also be considered for any patients in CR1 who are 60 years old or older; regardless of cytogenetic or genomic information.
- Antecedent hematological disease (e.g., myelodysplastic syndrome [MDS]), either based on prior clinical diagnosis or suggested by the presence of secondary-type somatic mutations on molecular testing
- 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 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 and referral to HCT consultation is recommended at diagnosis for all patients with:*

- 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 primary myelofibrosis (PMF) and essential thrombocythemia or polycythemia vera that has progressed to MF (secondary MF)

*High-resolution HLA typing and referral to HCT consultation is recommended at diagnosis for all patients with:*

- DIPSS or DIPSS Plus Intermediate-1 (INT-1) or higher
- MIPSS70/MIPSS 70 plus version 2.0 intermediate-risk or higher
- Cytopenic subtype
- Young age
- High-risk features including high-risk mutations (*ASXL1, TP53*), triple negative (lack of a driver mutation such as *JAK2, MPL* or *CALR*)
- Patients failing JAK inhibitor therapy

*HCT is recommended upfront for patients with:*

- DIPSS or DIPSS Plus Intermediate-2 (INT-2) and high-risk disease
- MIPSS70/MIPSS 70 plus version 2.0 high-risk disease
- Patients with DIPSS INT-1 or MIPSS70/MIPSS 70 plus version 2.0 intermediate-risk, cytopenic subtype, young age, high-risk features, including high-risk mutations (ASXL1, TP53), triple negative (lack of a driver mutation such as *JAK2, MPL*, or *CALR*) and those failing JAK inhibitor therapy should be considered for upfront HCT balancing patient preferences and clinical trial options

## Adult Leukemias and Myelodysplasia (continued)

### Chronic Lymphocytic Leukemia (CLL)

- Resistance or intolerance to BTK inhibitors and BCL2 inhibitors
- Ritcher's transformation

## Pediatric Acute 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 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 ≤39 years)

- Infant at diagnosis
  - unfavorable genetics
  - age <3 months with any WBC, or <6 months with WBC >300,000 at presentation or any infant with measurable (also known as minimal) residual disease (MRD)+ after consolidation
- Primary induction failure (M3 marrow) after achieving MRD negative status
- Presence of MRD after initial therapy; MRD ≥0.01% following consolidation (9–12 weeks from diagnosis)
- High/very high-risk CR1, including:
  - Philadelphia chromosome positive slow-TKI responders or with *IKZF1* deletions; Philadelphia-like if MRD+ at end of consolidation, or persistently detectable low level of molecular disease
  - *iAMP21* if MRD+ at end of consolidation
  - 11q23 rearrangement if MRD+ at end of consolidation
- First relapse with aim to transplant in CR2
- CR2 and beyond, if not previously evaluated, including:
  - all young adults in CR2
  - early relapse (≤36 months from diagnosis for medullary disease, ≤18 months from diagnosis for EMD)
  - MRD+ (>0.1% for medullary disease or equivalent for EMD) after re-induction (4–8 weeks from relapse)
  - T cell ALL
  - CR3 and beyond
- Chimeric antigen receptor therapy (CAR-T), including:
  - patients who receive CD19 4-1BB and achieve MRD negative CR if they have not already received HCT
  - patients who receive CD22 or other investigational therapies

### Myelodysplastic Syndromes (MDS)

- At diagnosis for all subtypes

### Juvenile Myelomonocytic Leukemia (JMML)

- At diagnosis

## Lymphomas

### Non-Hodgkin Lymphoma

#### Follicular (FL)

- Poor response to initial treatment
- Initial remission duration <24 months
- At relapse (CAR or alloHCT can be offered to patients with multiple relapsed FL)
- Transformation to diffuse large B-cell lymphoma

## Lymphomas (continued)

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

### Mature T-cell and NK Cell Lymphomas
- At diagnosis or CR1
- At relapse

### Other High-Risk Lymphomas
- At diagnosis

### Hodgkin Lymphoma
- Primary refractory disease
- First or subsequent relapse
- Brentuximab vedotin and check point inhibitor refractory and/or intolerant disease (for alloHCT)

## Other Malignant Diseases

### Germ Cell Tumors
High-dose therapy with autologous stem cell support may be considered for patients with:
- Non-germinomatous germ cell tumors (NGGCTs) for refractory disease post induction chemotherapy as long as the patient has chemo-responsive disease and does not have bulky residual tumor
- Germinoma or NGGCT, if the patient has chemo-responsive disease to reinduction chemotherapy and does not have bulky residual tumor

### Neuroblastoma
- INRGSS L2 at diagnosis
  - *MYCN* amplification
  - age >18 months with unfavorable histology and segmental chromosome aberration
- INRGSS stage M at diagnosis:
  - *MYCN* amplification
  - age >18 months at diagnosis
  - age 12–18 months with unfavorable histology, segmental chromosome aberrations, or diploid DNA content

### Ewing Family of Tumors
- Metastatic disease at diagnosis
- First relapse or CR2

### Medulloblastoma
High-dose therapy with autologous stem cell support may be considered standard therapy for several infant (younger than 3 years of age) embryonal tumors as first line, including:
- Medulloblastoma
- Atypical teratoid rhabdoid tumor (AT/RT)
- Embryonal tumor with multilayered rosettes (ETMR)
- Primitive neuroectodermal/embryonal tumors, not otherwise specified (NOS)

High-dose therapy with autologous stem cell support may be considered at relapse for patients with:
- Embryonal tumors as long as the patient has chemoresponsive disease to re-induction chemotherapy and does not have bulky residual disease

## Plasma Cell Disorders

### Multiple Myeloma
- At diagnosis
- At progression and/or relapse

### Light Chain Amyloidosis
- At diagnosis
- At progression and/or relapse

### POEMS Syndrome (Osteosclerotic Myeloma)
- At diagnosis

## 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
- Adrenoleukodystrophy (ALD): following the diagnosis of the cerebral form of ALD

### Hemoglobinopathies

Sickle Cell Disease
- Children (especially under age 13) with available matched sibling donors
- 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
  - Abnormal transcranial Doppler (TCD) velocity of ≥ 200 cm/sec or > 185 cm/sec with intracranial vasculopathy
  - Frequent episodes of acute chest syndrome or severe vaso-occulusive pain crises or combination of both in the preceding 2–3 years
  - Regular red blood cell transfusions to prevent sickle cell disease complications
  - Tricuspid value regurgitant jet (TRJ) velocity ≥2.7 m/sec (mainly in adults)
  - Chronic pain ≥6 months (leg ulcers, avascular necrosis)

Transfusion-Dependent Thalassemias
- At diagnosis

### Hemophagocytic Lymphohistiocytosis (HLH)
- At diagnosis

### Severe Aplastic Anemia
- At diagnosis

### Other Marrow Failure Diseases
Including Diamond-Blackfan anemia, Shwachman-Diamond syndrome, Fanconi anemia, Dyskeratosis Congenita and others
- Diamond-Blackfan Anemia: continued transfusion dependent anemia following a course of steroid therapy, development of significant infections, MDS/AML
- Shwachman-Diamond syndrome, Fanconi anemia, Dyskeratosis Congentia and others: development of cytopenias, transfusion dependence, or significant infections; high-risk cytopenic clones, high-risk somatic mutation patterns; MDS/AML

### 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).