Supplemental Digital Content, containing 3 tables. The Supplemental Digital Content was not copyedited by Archives of Pathology & Laboratory Medicine.

Supplemental Table 1. Summary of major differential diagnoses of pediatric MDS

Parameter	CDA	IBMFS	AA	MDS	Cytopenia with germline predisposition defects
Anemia	Moderate-severe	Variable	Moderate-severe	Variable	Variable
MCV	↑	nL - ↑	nL - ↑	nL - ↑	nL
Reticulocyte Count	↑	↓	↓	nL - ↓	Variable
Platelet count	nL	nL - ↓	nL - ↓	nL - ↓	Variable
Smear Findings	Anisopoikilocytosis, basophilic stippling, ↑ RDW	Variable	Variable	Variable; Anisopoikilocytosis	Variable
Hemolysis Markers	↑LDH and bilirubin	None	None	None	None
Known Genetics	CDAN1, C15orf41, SEC23B, KIF23, KLF1 GATA1	Variable germline mutations	Usually no cytogenetic abnormalities or germline/somatic mutations	Somatic mutations or abnormal cytogenetics	Variable germline mutations
Bone marrow Morphology	Erythroid hyperplasia, multinucleated erythroblasts; Chromatin bridges with binucleation or multinucleation	Variable hypocellularity and lineage hypoplasia; no overt dysplasia or increased blasts	Variable hypocellularity (e.g, severe AA <25%); variable lineage hypoplasia; no overt dysplasia or increased blasts	Variable cellularity; variable lineage dysplasia; some increased blasts with aberrant phenotype or none	Variable cellularity; no overt dysplasia or increased blasts

Inheritance pattern	Variable, differs by CDA subtype	Variable, differs by IBMFS type	Acquired	Acquired, generally	Variable, differs by subtype
Onset and Major Clinical Symptoms	Usually in neonatal or infantile period; other associated physical dysmorphism; HSM; jaundice; iron overload	Usually in neonatal or infantile period; other associated physical dysmorphism, differs by underlying IBMFS	Usually in childhood and adolescents; generally no other physical dysmorphism	Usually young children; no other dysmorphism	Usually in neonatal or infantile period; associated physical other dysmorphism, depending on underlying subtype
Therapy	Supportive: red blood cell transfusions HSCT in refractory cases	Supportive: Blood product transfusions Allo-HSCT in most cases	Supportive: Blood product transfusions Immunosuppressive therapy or Allo-HSCT	Supportive: Blood product transfusions Chemotherapy HSCT in most cases	Supportive: Blood product transfusions HSCT in most cases

Abbreviations: CDA, congenital dyserythropoietic anemia; IBMFS, inherited bone marrow failure syndromes; AA, aplastic anemia; MDS, myelodysplastic syndrome; MCV = mean corpuscular volume, nL = normal, HSM = hepatosplenomegaly; LDH = lactate dehydrogenase; RDW = red cell distribution width; Allo-HSCT = allogeneic hematopoietic stem cell transplant.

Supplemental Table 2. Revised International Prognostic Scoring System (R-IPSS)

Cytogenetics Classification		
Cytogenetic Risk Groups	**Cytogenetic Abnormalities**	**Prognostic Score Value**
Very Good	-Y; del(11q)	0
Good	Normal; del(5q); del(20q); del(12p)	1
Intermediate	del(7q); +8; +19; i(17q); any other single or double independent clones	2
Poor	-7; inv(3)/t(3q)/del(3q); double including -7/del(7q); complex: 3 abnormalities	3

Very Poor	Complex: >3 abnormalities	4
Clinical Features		
Clinical Variable	**Category**	**Prognostic Score Value**
Bone Marrow Blast Percentage	≤2%	0
	<2% to <5%	1
	5-10%	2
	>10%	3
Hemoglobin (g/dL)	≥10	0
	8 to <10	1
	<8	1.5
Platelet Count ($10^3/\mu L$)	≥100	0
	50 to <100	0.5
	<50	1
Absolute Neutrophil Count ($10^3/\mu L$)	≥0.8	0
	<0.8	0.5
Prognostic Risk Categories/Scores		
Risk Category	**Risk Score**	**Median Survival, years (95% CI)**
Very Low	≤1.5	8.8 (7.8-9.9)
Low	>1.5 to 3	5.3 (5.1-5.7)
Intermediate	>3 to 4.5	3 (2.7-3.3)
High	>4.5 to 6	1.6 (1.5-1.7)
Very High	>6	0.8 (0.7-0.8)

Obtained from the mds-foundation.org; CI = confidence interval.

Supplemental Table 3. Published HCT Studies in recent large cohort Pediatric MDS

Study	Number of Patients	Ages, Years	Type of HCT Donor and Source	Conditioning	Last Follow Up, Median (Range)	HCT Outcomes	Notes

Shaw *et al.* (2010)[1] Dates: 1993-2006	1625 (N=161 with MDS)	<1-17	MRD, MMRD, MUD, MMUD Source: BM	MAC Ppx: CSA/tacrolimus +/- MTX	2-177 months	-OS: at 3-year -MRD: 61% -MMRD: 51% -URD: 50% -DFS: at 3-year -MRD: 54% -MMRD: 44% -URD: 43% -aGVHD (>-II): at 100-days -MRD: 29% -MMRD: 56% -URD: 45% -cGVHD: at 1-year -MRD: 15% -MMRD: 30% -URD: 33% -Relapse Rate: at 3-year -MRD: 36% -MMRD: 29% -URD: 32% -TRM: at 3-year -MRD: 10% -MMRD: 27% -URD: 24%	-Compared outcomes of HSCT for malignant hematologic disease based on donor type -HSCT outcomes were superior in the MRD vs URD and MMRD groups: higher OS and DFS as well as less TRM, aGVHD, cGVHD
Strahm *et al.* (2011)[2] Dates: January 1998-May 2007	97	1-18.2	MRD, MUD, MMRD, MMUD Source: BM (69), PBSC (28)	MAC: BU-Mel-Cy +/-ATF or Campath PPx: CSA OR CSA+MTX	5.2 years (1-10.9 years)	-OS: 63% at 5-years -EFS: 41% -aGVHD: 46% -cGVHD: 37% -TRM: 21% -CIR: 21% at 5-years	-HCT cohort included those with advanced MDS: RAEB (N=53), RAEB-T (N=29), MDS-AML (N=15) -N=24 (25%) of patients received pre-HCT induction chemotherapy -Blast percentage at HSCT and pre-HSCT

							chemotherapy did not significantly affect EFS -Age ≥12 years old at HSCT, interval between diagnosis and HSCT >4 months, and aGVHD and extensive cGVHD were associated with increased TRM.
Boztug *et al.* (2016)[3] Dates: January 2005-July 2010	193 (N=40 with MDS/MPN)	0.4-18	MRD, MMRD, MUD Source: BM (97), PBSC (72), CB (23), and BM + CB (1)	MAC: Treo-Flu-TT OR Treo-Cy OR Treo-Flu-Mel Ppx: CSA +/- MTX	NR	-OS: 54% at 3-years -EFS: 45% at 3-years -aGVHD: 50% -cGVHD: 24% -TRM: 14%	-Cohort included patients with ALL, AML, MDS/MPN, and other types of leukemia or lymphoma -Evaluated treosulfan-based conditioning in a cohort undergoing second or third HCT, pre-HCT organ dysfunction, and/or advanced stage of disease -Patients undergoing 2nd/3rd HSCT did not have higher rate of early transplant-associated toxicity or GVHD occurrence compared to patients following first HSCT -Disease status at time of HSCT influenced OS and EFS outcomes—worse for those not in remission

Teyssier *et al.* (2022)[4] Dates: March 2015-February 2019	141 (N=7 with MDS)	0.38-34.58	UCB (single or double)	MAC: Flu-TBI-Cy OR BU-Cy OR Etoposide-TBI OR Bu-Flu-TT OR Flu-Bu	NR	-OS: 72% at 2-years -DFS: 59% at 2-years -aGVHD: 66.4% -cGVHD: 19.8% -TRM: 7.8% -Relapsed Rate: 31.2%	-Cohort: Patients with ALL, AML, or MDS -Results are reported for the whole cohort -Authors compared results of this study to their prior randomized control trial; not included in this table

Abbreviations: N= Number, HSCT= hematopoietic stem cell transplant, JMML = Juvenile Leukemia, MRD = Matched-Related Donor, MMRD: Mis-matched Related Donor, MUD = Matched-Unrelated Donor, MMUD = Mismatched Unrelated Donor, UCB = Unrelated cord blood, BM = Bone marrow, PBSC = Peripheral blood stem cells, CB = Cord Blood, MAC = Myeloablative conditioning, NMA: Non-myeloablative conditioning, RIC: Reduced-intensity Conditioning, Bu = Busulfan, Cy = cyclophosphamide, TBI = Total body irradiation, Flu = fludarabine, ATG = Anti-thymocyte globulin, Mel = Melphalan, TT = Thiotepa, AraC = Cytarabine, Ppx = prophylaxis, CSA = cyclosporine, OS = Overall survival, DFS = Disease free survival, NRM = Non-relapse mortality, aGVHD = acute Graft versus host disease, cGVHD = chronic GVHD, CIR = Cumulative Incidence of Relapse

Supplemental reference:

1. Shaw PJ, Kan F, Woo Ahn K, et al. Outcomes of pediatric bone marrow transplantation for leukemia and myelodysplasia using matched sibling, mismatched related, or matched unrelated donors. *Blood.* 2010;116(19):4007-4015.
2. Strahm B, Nollke P, Zecca M, et al. Hematopoietic stem cell transplantation for advanced myelodysplastic syndrome in children: results of the EWOG-MDS 98 study. *Leukemia.* 2011;25(3):455-462.
3. Boztug H, Sykora KW, Slatter M, et al. European Society for Blood and Marrow Transplantation Analysis of Treosulfan Conditioning Before Hematopoietic Stem Cell Transplantation in Children and Adolescents With Hematological Malignancies. *Pediatr Blood Cancer.* 2016;63(1):139-148.
4. Teyssier AC, Michel G, Jubert C, et al. Unrelated Cord Blood Transplantation in Children, Adolescents, and Young Adults with Acute Leukemia or Myelodysplastic Syndrome: A Retrospective Comparative Study from the French Society for Bone Marrow Transplantation and Cellular Therapy Between Real-World Data and Previously Reported Results of a Randomized Clinical Trial. *Transplant Cell Ther.* 2022;28(11):780 e781-780 e787.