Supplementary Table 1. Clinical data of NCI IBMFS participants with an SDS-like phenotype.

	SDS-like
Number of Cases	**7**
Sex (Male:Female)	1.3:1
Median age at diagnosis in years (range)[a]	2.13 (1.03-3.23)
Vital Status (Alive, Deceased) **Disease-specific death** **Treatment-related death** **Malignant disease**	7, 0 - - -
Age at death in years, median (range)	-
All Hallmark SDS Features	0% (0/2)
Pancreatic Insufficiency	100% (3/3)
History of Neutropenia	66.6% (4/6)
Skeletal Dysplasia[b]	33.3% (1/3)
Hematologic Malignancy, MDS/AML (N)	No
MDS/AML Median age in years (range)	-
Frequent Cytogenetic Abnormalities of MDS/AML	-
Other Solid Cancer, Age at diagnosis, years	No
Immune Dysfunction[c]	17% (1/6)
Failure to Thrive	100% (3/3)
GI Symptoms[d]	100% (3/3)
Steatorrhea	100% (1/1)
Elevated Liver Transaminases	100% (1/1)
Malabsorption	100% (3/3)
Received Nutritional Assistance via Tube Feedings, Parental Nutrition (N)	1, 0
Developmental Delay/Learning Disabilities[e]	100% (1/1)
Microcephaly	0% (0/2)
Short Stature	100% (4/4)
Cardiac Abnormalities[f]	100% (1/1)
Dermatologic Findings[g]	100% (1/1)

[a]Date of SDS diagnosis was based on physician report, when available. Genetic testing report date confirmed the date of diagnosis if no earlier medical records were available.

[b]Skeletal dysplasia findings include severe thoracic dystrophy, metaphyseal dysostosis, scoliosis, short arms, short legs, small hands, other bony abnormalities in the extremities, or other rib cage/thoracic malformations.

[c]Immunodeficiency as defined in Methods.

[d]GI symptoms include a history of malabsorption, malnutrition, steatorrhea, gastroesophageal reflux disease (GERD), liver disease, liver steatosis, and/or liver cirrhosis.

[e]Psychodevelopmental findings include ADHD/ADD, speech delay, depression, anxiety, Asperger's syndrome, Bipolar disorder, PTSD, OCD, dyslexia, auditory processing disorder, sensory integration dysfunction, and anger issues.

[f]Cardiac abnormalities include ventricular septal defect, patent foramen ovale, atrial septal defect, patent ductus arteriosus, and other heart malformations (*e.g.*, cardiomegaly).

[g]Dermatologic findings include eczema, café au lait spots, hypopigmentation, hyperpigmentation, ichthyosis, petechiae, xerosis, ecchymosis, atopic dermatitis, subcutaneous lupus erythematosus, pityriasis alba, dermatofibroma, xanthelasma, psoriasis, hyperkeratosis, and keratosis pilaris.

Supplementary Table 2. Hematologic findings in NCI IBMFS SDS-like cohorts.

	SDS-like
Total Number	**7**
Neutropenia at Diagnosis	25% (1/4)
Median ANC at Diagnosis (cells/µL) (Range)	2400 (1390-6890)
Thrombocytopenic at Diagnosis	0% (0/4)
Median Platelet Count at Diagnosis (K/µL) (Range)	331 (237-383)
Anemic at Diagnosis	0% (0/2)
Median Hemoglobin at Diagnosis (g/dL) (Range)	11.7 (10.9-14.1)
Hypocellular for age at First BMBx	50% (2/4)
Median Cellularity at First Biopsy (Range)	63% (25-95%)
Cytogenetic Abnormalities of First Bone Marrow Aspirate	Del(20q) (N=2)
Hypocellular for age at Most Severe BMBx	75% (3/4)
Median Cellularity for Most Severe Biopsy (Range)	58% (25-75%)
Cytogenetic Abnormalities of Most Severe Bone Marrow Aspirate	Del(20q) (N=1)

Supplementary Table 3. Details on genetic testing performed on participants with SDS and an unknown genetic variant in the NCI IBMFS Cohort.

NCI ID	PacBio	Exome	NGS	aCGH	External Genetic Testing	Samples Status
NCI 21-1						No samples
NCI 37-1						No samples
NCI 37-2						No samples
NCI 42-1	X	X		X		
NCI 46-1		X			X	
NCI 104-1	X	X	X	X	X	
NCI 104-2	X	X	X	X	X	
NCI 178-1	X	X	X	X	X	
NCI 190-1					X	No samples
NCI 205-1	X	X	X	X	X	
NCI 337-1	X	X		X	X	
NCI 337-2	X	X		X		
NCI 466-1						Yes, awaiting testing
NCI 480-1		X			X	
NCI 554-1					X	Yes, awaiting testing

Supplementary Table 4. Phenotypes of SDS reported from five cohorts in comparison with the NCI IBMFS cohort.[5,35-39]

	NCI IBMFS Cohort SDS	NCI IBMFS Cohort SDS-like	North American SDS Registry[5]	Italian SDS Registry[35]	French National Cohort of SDS Patients[36]	Greek SDS Registry[37]	Japanese SDS Cohort[39]
Number of Participants with SDS (N)	47	7	37	121	102	11	24
Sex (Male:Female)	0.74:1	1.3:1	1.85:1	1.33:1	1.32:1	0.83:1	1.67:1
Median age at diagnosis	1.78 years	2.13 years	3.5 years	1.3 years	0.55 years	1.3 years	1.6 years
Method of SDS Diagnosis	Genetic Testing: 68% Symptomatic: 100%	Genetic testing: 0% Symptomatic: 100%	Genetic testing: 100% Symptomatic: 51%	Genetic testing and symptomatic: 100%	Genetic testing and symptomatic: 100%	Genetic testing and symptomatic: 100%	Genetic testing and symptomatic (18/21, 85.7%)
Neutropenia (ANC < 1500 cells/uL)	100% (45/45)	66.6% (4/6)	81% (30/37)	59.9%, cumulative incidence	100% (102/102)	100%	73.7% at diagnosis
Pancreatic Insufficiency	95.3% (41/43)	100% (3/3)	100% (17/17)	76.8% (93/121)	100% (102/102)	64%	75% (18/24)
Bony abnormalities	80.6% (29/36)	33.3% (1/3)	38% (14/37)	50.4%	8.8% (9/102)	64%	-
Anemia	15% (6/40), at diagnosis	0% (0/2), at diagnosis	16% (6/37)	20.2%, cumulative incidence	12.7% (13/102), at diagnosis	27%	4.5% (1/24)
Thrombocytopenia	19% (8/42), at diagnosis	0% (0/4), at diagnosis	27% (10/37)	66.8%, cumulative incidence	10.8% (11/102), at diagnosis	36%	-
Notable Bone Marrow Biopsy Findings	66.6% (20/30) hypocellular most severe BMBx; Del(7q) (N=1), Del(20q) (N=8), Isochromosome(Xp10)/+(Xp22) (N=1), Mono 7/Del(20q) (N=1),	75% (3/4) hypocellular most severe BMBx; Del(20q) (N=1)	100% hypocellular (32/32); Cytogentic abnormalities (N=7); Del(20q) (N=5)	49% cytogentic abnormalities; Most common, i(7)(q10) or del(20)(q)	Non-MDS/AML: Cytogenetic abnormalities (N=10); Del(20q)=5, Isochromosome 7 (N=3)	2 with cytogenetic abnormalities; i(7)(q10) and del(X)(q24→qter)	-

	Isochromosome 7 (N=2)						
GCSF Usage	N=12	N=1	-	19%	16.7% (17/102)	18%	-
Severe GI Symptoms (Diarrhea, Steatorrhea, etc.)	85.7% (36/42)	100% (3/3)	58% (21/37)	-	18.6% (19/102)	-	73.9% at diagnosis
Elevated liver function tests	88.9% (16/18)	100% (1/1)	41% (15/37)	61.9% (75/121)	-	55%	36.4% (8/24)
Required Nutritional Assistance	Tube feedings (N=12); TPN (N=2)	Tube feedings (N=1)	-	-	18.6% (19/102)	55%	MCT (5/24, 20.8%); IV LCT (1/24, 4.2%)
Short Stature	90% (27/30)	100% (4/4)	-	60.3% (73/121)	58.8% (60/102)	82%	4.5% (1/24)
Cardiac Abnormalities	43.5% (10/23)	100% (1/1)	19% (7/37)	-	11.8% (12/102)	27%	-
Developmental Delay/Failure to Thrive	58.8% (20/34)	100% (1/1)	73% (27/37)	50%	34% (25/73)	36%	Developmental delay, 15.4% (2/13); FTT, 50.5% (11/24)
Hematologic Malignancy	3 MDS/2 AML	None	2 MDS	10 MDS/AML	4 MDS/8 AML	N=2; (1) Malignant definitive severe cytopenia and (1) clonal bone marrow cytogenetics	1 AML/1 MDS