Hematopoietic cell transplantation in inherited bone marrow failure syndromes

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Section editor: Fernando Barroso Duarte

Received: Sept. 10, 2025 • **Accepted:** Sept. 23, 2025

ABSTRACT

Inherited bone marrow failure syndromes (IBMFS) comprise a heterogeneous group of rare genetic disorders characterized by defective hematopoiesis, congenital anomalies, and a predisposition to clonal evolution and malignancies. Hematopoietic cell transplantation remains the only curative option for the hematologic manifestations of these disorders, although it does not correct congenital malformations or eliminate the long-term risk of non-hematopoietic cancers. This review summarized current evidence and transplantation strategies for major IBMFS, including Fanconi anemia, dyskeratosis congenita/telomere biology disorders, Diamond-Blackfan anemia, Shwachman-Diamond syndrome, congenital neutropenia, congenital amegakaryocytic thrombocytopenia, and other inherited thrombocytopenias. We discussed disease-specific transplant indications, donor selection, conditioning regimens, graft source preferences, and outcomes across different patient populations. Advances in reduced-intensity conditioning and post-transplant cyclophosphamide have expanded donor availability, improving survival even with alternative donors. Nevertheless, long-term challenges persist, such as increased risks of solid tumors, endocrine dysfunction, and organ toxicity, emphasizing the need for multidisciplinary care and lifelong surveillance. Optimal outcomes depend on timely referral to specialized centers, meticulous donor screening, and individualized transplant strategies tailored to the unique biology of each disorder.

Keywords: Hematopoietic Stem Cell Transplantation. Congenital Bone Marrow Failure Syndromes. Fanconi Anemia. Dyskeratosis Congenita. Anemia.

INTRODUCTION

Inherited bone marrow failure syndromes (IBMFS) are a heterogeneous group of rare genetic disorders characterized by the inadequate production of one or more hematopoietic lineages, resulting in cytopenias and an increased predisposition to malignancy[1,2]. They are associated with distinct biological mechanisms, such as defective DNA repair pathways in Fanconi anemia, telomere maintenance defects in dyskeratosis congenita, ribosomopathy in Shwachman-Diamond syndrome and Diamond Blackfan anemia, and functional

defect in thrombopoietin receptor in congenital amegakaryocytic thrombocytopenia. These disorders typically manifest in childhood, often associated with physical anomalies and systemic manifestations, as well as an increased risk of clonal evolution—myelodysplasia (MDS) and acute myeloid leukemia (AML)—and non-hematopoietic neoplasias, particularly gynecological and squamous cell carcinomas[2,3].

Hematopoietic cell transplantation (HCT) is an effective cure for the hematologic manifestations in IBMFS, but it does not cure the congenital malformations or reduce the long-term risk of non-hematopoietic cancers. In fact, HCT may increase the risk of malignancies.

It is essential to screen potential family donors for carrier status. Specialized centers are needed for managing these patients due to their higher susceptibility to toxicities and the need for tailored care throughout the transplant process[1,2,4–7].

FANCONI ANEMIA

Fanconi anemia, the most common IBMFS (incidence ~1:100,000–160,000 births), is typically an autosomal recessive genetic disorder affecting DNA repair, causing increased chromosomal breakage[8]. Clinical presentation varies; about 70% show congenital abnormalities, while others are diagnosed later due to pancytopenia, MDS, or malignancies. Bone marrow failure affects 90% by age 40, often in late childhood. Complications include AML, MDS, and solid tumors, particularly head and neck squamous cell carcinomas and gynecologic cancers. Due to genomic instability, Fanconi anemia patients are highly susceptible to alkylating agents and radiation toxicity, increasing the risks of severe mucositis and gastrointestinal complications, making HCT particularly challenging. However, HCT is the only curative treatment for the hematologic manifestations of Fanconi anemia, indicated for patients with severe cytopenias, high-risk cytogenetic abnormalities, or MDS/AML. Early transplantation—before transfusions, infections, or clonal evolution—leads to better outcomes.

Fanconi anemia patients face a 30–40% cumulative risk of myeloid malignancies by age 40, often linked to cytogenetics abnormalities (*e.g.*, 1q gain, monosomy 7/del(7q), 3q gain, RUNX1 mutations) guiding HCT urgency. Preventing MDS/AML is critical, as HCT outcomes are significantly worse when performed in active disease[9,10].

The ideal donor is a matched sibling (Table 1), and screening potential family donors is essential, as some may be asymptomatic carriers of Fanconi anemia. Transplant advances expanded donor options, especially in resource-limited settings. Post-transplant cyclophosphamide enabled successful, cost-effective haploidentical HCT with adapted protocols (Table 2)[9].

Bone marrow is the preferred graft source due to a lower risk of graft-*versus*-host disease (GVHD). Umbilical cord blood should only be considered for a matched related donor (MRD), while peripheral blood stem cells should be avoided due to the high risk of severe GVHD. Younger, healthier donors provide better outcomes due to superior cell quality and proliferation potential.

Table 1. Hematopoietic cell transplantation outcomes by donor type.

Donor type	Outcomes
Matched sibling donor	Five-year overall survival of 83–94%. Acute GVHD rates of 6–20%[11]
Matched unrelated donor	Five-year overall survival of 86%. Acute GVHD rates of 12–29%[11,12]
Haploidentical donor	Five-year OS of 82%. Acute GVHD rates of 35% with reduced-intensity conditioning and post-transplant cyclophosphamide[13]
Active myelodysplasia / acute myeloid leukemia	Three-year progression-free survival and OS of 53%[10]

Source: Elaborated by the authors. GVHD: graft-*versus*-host disease.

Table 2. Conditioning and graft-*versus*-host disease (GVHD) prophylaxis for hematopoietic cell transplantation in Fanconi anemia.

	Aplastic phase and matched sibling donor (MSD)
Conditioning	Cyclophosphamide 60 mg/kg (D-6, D-5, D-4, D-3). Mesna 160% of Cy dose, divided into five doses (0, 3, 6, 9, and 12 hours after Cy). Rabbit ATG 5-7.5 mg/kg (D-3, D-2, D-1) given to patients older than 10 years old and patients with other matched related donors.
GVHD prophylaxis	Cyclosporine 4 mg/kg per day between D-1 and D+100, with gradual tapering after that. Methotrexate (D+1 = 15 mg/m^2; D+3, +6 and +11 = 10 mg/m^2). Related cord blood unit: cyclosporine + methylprednisolone or mycophenolate mofetil
	Aplastic phase and matched unrelated donor (MUD)
Conditioning	Cyclophosphamide 60 mg/kg (D-6, D-5, D-4, D-3). Mesna 160% of Cy dose, divided into five doses (0, 3, 6, 9, and 12 hours after Cy). Fludarabine 150 mg/m^2 (D-6, D-5, D-4, D-3, D-2). Rabbit ATG 5-7.5 mg/kg (D-3, D-2, D-1).
GVHD prophylaxis	Cyclosporine 4 mg/kg per day between D-1 and D+180, with gradual tapering after that during two or three months. Methotrexate (D+1 = 15 mg/m^2; D+3, +6 and +11 = 10 mg/m^2).
	Aplastic phase and haploidentical donor
Conditioning	Alemtuzumab 0.66 mg/kg SC (D-7, D-6, D-5). Fludarabine 150 mg/m^2 (D-6, D-5, D-4, D-3, D-2). Total body irradiation 100 cGy at D-1.
GVHD prophylaxis	Post-transplant cyclophosphamide 50 mg/kg (D+3, D+4). Mesna 160% of Cy dose, divided into five doses (0, 3, 6, 9, and 12 hours after Cy). Cyclosporine 4 mg/kg per day between D+5 and D+180, with gradual tapering after that during two or three months. MMF intravenous 40–45 mg/kg per day between D+5 and D+90.
	Myelodysplastic phase or acute myeloid leukemia
< 10% of blasts in bone marrow	Use the recommended protocol for Fanconi anemia in aplastic phase.
≥ 10% of blasts in bone marrow	FLAG (Fludarabine 30 mg/m^2 daily D1-5 + Cytarabine 1,000 mg/m^2 twice daily D1-5 + G-CSF 5 mcg/kg daily D1-5) followed by the recommended Fanconi anemia protocol for the aplastic phase, starting 14 days after the initiation of chemotherapy. In protocols in which total body irradiation is not included in the conditioning regimen (MSD or MUD), add 200 cGy on D-1. It is important to initiate this scheme only with a confirmed transplant schedule.
GVHD prophylaxis	Cyclosporine 4 mg/kg per day between D-1 (if MSD or MUD) or D+5 (if haploidentical donor) and D+180, with gradual tapering after that during two or three months. Methotrexate: 15 mg/m^2 on D+1 and 10 mg/m^2 on days +3, +6 and +11 (if MSD or MUD). MMF intravenous 40–45 mg/kg per day between D+5 and D+60 (if haploidentical donor).

Source: Elaborated by the authors.

Important points are:

- Expert consultation is recommended for deciding on advanced-phase HCT timing and regimen;
- We strongly advise that advanced phase or haploidentical HCT should be performed exclusively at expert centers.

After HCT, Fanconi anemia patients require long-term monitoring due to complications from the disease and treatment. They face a significantly higher risk of head and neck squamous cell carcinoma, often diagnosed between the ages of 20–40, making early detection and prevention vital. Surveillance should include annual oral exams, endoscopic and colonoscopic screenings starting at age 18, annual endocrinological and hematological assessments, tracking issues like hypothyroidism, osteoporosis (50% by age 30), and organ toxicity, and avoiding alcohol and tobacco[13–16].

CONGENITAL DYSKERATOSIS/TELOMERE BIOLOGY DISORDERS

Telomere biology disorders are characterized by impaired telomere maintenance, resulting in very short telomeres and a wide spectrum of clinical manifestations. The classical presentation, known as congenital dyskeratosis, includes the mucocutaneous triad of dysplastic nails, oral leukoplakia, and lacy reticular skin pigmentation, which may be subtle or absent initially but progresses over time. Pediatric patients may also present severe phenotypes like Hoyeraal-Hreidarsson syndrome, Revesz syndrome, or Coats plus syndrome[17–19]. Beyond dermatological manifestations, congenital dyskeratosis are associated with systemic complications, including cytopenias, pulmonary fibrosis, and liver cirrhosis/fibrosis. Bone marrow failure and increased risks of MDS and AML are significant, especially in children and adolescents, requiring early intervention[17–19].

While androgens can offer transient hematopoiesis improvement, HCT is the only cure for bone marrow failure. Although there is no consensus on the ideal conditioning regimen for congenital dyskeratosis, the current practice is fludarabine-based reduced intensity conditioning (RIC) (Table 3), minimizing radiation/alkylating agents to reduce late effects (organ damage, secondary malignancies), especially in children[20]. Despite improved results in the past decade due to RIC regimens, long-term survival remains poor due to disease progression (pulmonary and liver fibrosis and hepatopulmonary syndrome)[7,21].

Table 3. Conditioning and graft-*versus*-host disease (GVHD) prophylaxis for hematopoietic cell transplantation in dyskeratosis congenita.

	Matched related or unrelated donors
Conditioning	Cyclophosphamide 60 mg/kg (D-6, D-5, D-4, D-3) Mesna 160% of Cy dose, divided into five doses (0, 3, 6, 9, and 12 hours after Cy) Fludarabine 150 mg/m^2 (D-6, D-5, D-4, D-3, D-2) Rabbit ATG 5 mg/kg (D-3, D-2, D-1)
GVHD prophylaxis	Same as Fanconi anemia

Source: Elaborated by the authors.

A retrospective multicenter study of HCT outcomes in congenital dyskeratosis reported better outcomes in younger patients (≤ 20 years old) with a three-year overall survival of 72% compared to 43% in older patients (p = 0.017), with no significant difference in outcomes (overall survival and event free survival) between MRD and matched unrelated donor (MUD) recipients[22]. Recently, a Brazilian study with 29 Telomere biology disorders patients who underwent HCT reported one, five, and ten-year OS probabilities of 86.2, 60.3, and 44.2%, respectively, with a higher probability of better survival in MRD transplants compared to MUD. This cohort demonstrated a low probability of OS (less than 30% in 15 years) and EFS (less than 50% after the first year of transplant), suggesting that HCT should be considered on an individual basis, especially in the pediatric context, to balance risks and benefits[21].

HCT is indicated for aplastic phase, myelodysplasia, or acute leukemia. Ideally, transplant should precede the need for transfusions, serious infections, or clonal evolution. Besides prototypical dyskeratosis congenita, HCT is also recommended for severe aplasia with extremely short telomeres (<1%), even without classic dyskeratosis congenita symptoms[17,23].

DIAMOND-BLACKFAN ANEMIA

Diamond-Blackfan anemia is a rare inherited red cell aplasia caused by an intrinsic defect in erythropoietic progenitors, resulting in hereditary anemia that manifests in early infancy[24]. It should be considered in all children under 1 year old who present with macrocytic or normocytic anemia, reticulocytopenia, normal marrow cellularity, and reduced or absent marrow red cell precursors[24]. Diamond-Blackfan anemia is a cancer predisposition syndrome, increasing risk of hematological malignancies (MDS/AML), and solid tumors like osteosarcoma[25].

The therapeutic approach is based on chronic red blood cell transfusions used mainly in infants and patients refractory to corticosteroid therapy, which is considered first-line treatment, with an approximately 80% success rate[25]. However, due to the significant adverse effects of corticosteroids on the physical and neurocognitive development of younger children, their use should be restricted to patients older than 1. HCT, a potentially curative treatment for Diamond-Blackfan anemia, is indicated for patients who do not respond to first-line therapy[24,25], as detailed in Table 4. In 2020, data from the Brazilian group demonstrated a five-year OS of 70% (95% confidence interval—95%CI 57–85%) in pediatric patients with Diamond-Blackfan anemia transplanted in Brazil. Considering transplants performed with an MRD, the OS was 80% (95%CI 65–97%), while in patients who received a transplant from an MUD, the OS was 73% (95%CI 52–100%)[26]. Data from the European group recently demonstrated an excellent OS of 91% (95%CI 84–98%) in patients who received a transplant from an MRD and MUD with a median follow-up of 4.5 years[27].

Table 4. Indications for hematopoietic cell transplantation in Diamond-Blackfan anemia.

Indications
Patients unresponsive to corticosteroid therapy or those dependent on corticosteroids with doses greater than 0.3 mg/kg/day, or unacceptable steroid toxicity. Transfusion-dependence and/or alloimmunization. Pancytopenia or progression to acute leukemia or myelodysplastic syndrome.

Source: Elaborated by the authors.

The best results are obtained with an MRD and hematopoietic stem cells from bone marrow. Myeloablative busulfan-based conditioning regimens is currently recommended (Table 5)[24,25,27]. Transplantation should be carried out in patients under 10 years old, preferably before the age of 5. Busulfan dose should be myeloablative, weight-based, ideally using pharmacokinetics. GVHD prophylaxis for patients with compatible related or unrelated donors (bone marrow) should include cyclosporine and a short course of methotrexate[26].

Table 5. Conditioning and graft-*versus*-host disease (GVHD) prophylaxis for hematopoietic cell transplantation in Diamond-Blackfan anemia.

	Matched related or unrelated donors
Conditioning	Busulfan 16–20 mg/kg* (D-6, D-5, D-4, D-3). Fludarabine 160 mg/m^2 (D-6, D-5, D-4, D-3, D-2). Rabbit ATG 5 mg/kg (D-3, D-2, D-1).
GVHD prophylaxis	BM: cyclosporine + methotrexate (D+1: 15 mg/m^2; D+3, +6 and +11: 10 mg/m^2). Related cord blood unit: cyclosporine + methylprednisolone or mycophenolate mofetil.

Source: Elaborated by the authors. *Busulfan dose should be myeloablative, weight-based, and ideally guided by pharmacokinetic monitoring.

SHWACHMAN-DIAMOND SYNDROME

Shwachman-Diamond syndrome is a rare autosomal recessive ribosomopathy caused by SBDS gene mutations, essential for ribosome biogenesis. It is characterized by exocrine pancreatic insufficiency, metaphyseal dysostosis, and bone marrow dysfunction, with severe hematologic complication risk[28,29]. Clinically, Shwachman-Diamond syndrome presents in infancy with failure to thrive, recurrent infections, and malabsorption due to pancreatic insufficiency, leading to nutritional deficiencies. Skeletal abnormalities include short stature and rib cage deformities. Hematologic complications range from neutropenia to pancytopenia, with significant clonal progression risk. Diagnosis relies on genetic testing for SBDS mutations, complemented by bone marrow and pancreatic function assessments[29].

HCT, a potentially curative treatment for SDS, is indicated for patients with progressive cytopenias or pancytopenia, transfusion dependence, or MDS/AML progression. No consensus exists on optimal Shwachman-Diamond syndrome conditioning, but the best results were obtained in patients receiving a reduced-intensity conditioning regimen using a MRD or MUD[28]. Outcomes for bone marrow failure show

a five-year survival rate of 72%, whereas patients with MDS/AML face a significantly poorer prognosis, with only 15% surviving beyond five years[29]. Donor selection is crucial, with MRD preferred, and reduced-intensity conditioning (Table 6) recommended to minimize toxicity[28]. Long-term monitoring is essential due to transplant-related complications and inherent malignancy risk[30].

Table 6. Conditioning and graft-*versus*-host disease (GVHD) prophylaxis for hematopoietic cell transplantation in Shwachman-Diamond syndrome.

	Matched related or unrelated donors
Conditioning	Cyclophosphamide 120 mg/kg (D-6, D-5). Mesna 160% of Cy dose, divided into five doses (0, 3, 6, 9, and 12 hours after Cy). Fludarabine 150 mg/m^2 (D-6, D-5, D-4, D-3, D-2). Rabbit ATG 5 mg/kg (D-3, D-2, D-1).
GVHD prophylaxis	Cyclosporine + methotrexate (D+1: 15 mg/m^2; D+3, +6 and +11: 10 mg/m^2) or mycophenolate mofetil 40–45 mg/kg/day.

Source: Elaborated by the authors.

CONGENITAL NEUTROPENIA

Congenital neutropenia is a rare disorder characterized by persistently low absolute neutrophil count, typically below 500 cells/µL, due to a maturation arrest of myelopoiesis in the bone marrow, leading to recurrent and severe bacterial and fungal infections[31]. The condition is associated with several germline mutations, with ELANE mutations accounting for 50–60% of cases. Other genetic syndromes, such as GATA2 deficiency, Shwachman-Diamond syndrome, Chediak-Higashi syndrome, and Griscelli syndrome, can also present with chronic neutropenia[31].

The standard treatment for severe congenital neutropenia is continuous granulocyte-colony stimulating factor (G-CSF) therapy[31]. The primary goal is to maintain ANC levels above 1,000 cells/µL, which is typically achievable with G-CSF doses of 3–5 µg/kg/day. Patients requiring doses of 10–15 µg/kg/day are defined as poor responders, while those requiring > 20 µg/kg/day are considered non-responders[32]. Beyond the risk of life-threatening sepsis, congenital neutropenia also carries a significant long-term risk of progression to MDS/AML, particularly in poor responders to G-CSF[31]. HCT is the only curative treatment currently available and should be offered to patients who are poor or non-responders to G-CSF or those who develop AML/MDS[31,32]. For children under 10 years old with a healthy MRD, HCT may be considered even for good responders[32,33]. According to EBMT guidelines, a myeloablative conditioning regimen is recommended[32]. A busulfan-based regimen resulted in excellent outcomes, with a 93% survival rate for fully matched donors—related or unrelated—and 75% for mismatched[31]. Data with alternative donors are limited but suggest favorable outcomes[34,35].

CONGENITAL AMEGAKARYOCYTIC THROMBOCYTOPENIA AND OTHER INHERITED THROMBOCYTOPENIAS

Congenital amegakaryocytic thrombocytopenia (CAMT) is a rare inherited disorder characterized by severe thrombocytopenia from birth, progressing to bone marrow failure[36]. It is mainly caused by mutations in the c-MPL gene, with rare cases linked to THPO mutations[37]. Blood smear shows normal size platelets, and bone marrow analysis typically reveals absent megakaryocytes[38,39]. Somatic malformations are not common in CAMT, and there is not a clear relationship with clonal progression[37].

The only curative therapy is HCT, and the ideal moment to perform it is before a high transfusion burden and progression to severe aplastic anemia[39,40]. However, patients with THPO mutations do not benefit from HCT and should be treated with thrombopoietin receptor agonists[38]. HCT with a healthy MRD using bone marrow is the best option of treatment[41], but unrelated and haploidentical donors are also acceptable choices[31–33]. Other congenital thrombocytopenias may also require HCT in specific cases as Wiskott-Aldrich syndrome. Severe forms of Bernard-Soulier syndrome, an autosomal recessive disorder with large dysfunctional platelets, may also warrant HCT when significant bleeding occurs.

Additionally, thrombocytopenias associated with mutations in MECOM, HOXA1, ETV6, and RUNX1 carry a risk of bone marrow failure or clonal evolution, making HCT a preventive option in selected cases[41]. Conditioning regimens typically include myeloablative busulfan and fludarabine, which have demonstrated favorable outcomes (Table 7). If the patient develops severe aplastic anemia, the conditioning regimen should be like that used for sAA. Reduced-intensity conditioning has also been associated with positive results[40,42–44]. MRD is the preferred choice, but alternative donors, such as unrelated matched donors, are also viable, though associated with a higher risk of complications, including GVHD[40,42,43].

Table 7. Conditioning and graft-*versus*-host disease (GVHD) prophylaxis for hematopoietic cell transplantation in congenital amegakaryocytic thrombocytopenia.

Conditioning	
Matched related donor	Busulfan 16–20 mg/kg* (D-6, D-5, D-4, D-3). Fludarabine 160 mg/m^2 (D-6, D-5, D-4, D-3, D-2).
Matched unrelated donor	Busulfan 16–20 mg/kg* (D-6, D-5, D-4, D-3). Fludarabine 160 mg/m^2 (D-6, D-5, D-4, D-3, D-2). Rabbit ATG 5 mg/kg (D-3, D-2, D-1).
GVHD prophylaxis	
	Bone marrow: cyclosporine + methotrexate (D+1: 15 mg/m^2; D+3, +6 and +11: 10 mg/m^2). Related cord blood unit: cyclosporine + methylprednisolone or mycophenolate mofetil.

Source: Elaborated by the authors. *Busulfan dose should be myeloablative, weight-based, and ideally guided by pharmacokinetic monitoring.

CONCLUSION

HCT is currently the only curative treatment for the hematologic complications associated with various IBMFS.

All family donors must undergo thorough screening before being considered as potential donors. Patients and families should be informed that HCT corrects only the hematologic manifestations of the disease.

Long-term follow-up is essential to monitor for late effects of both the transplant and the underlying genetic disorder.

Iron overload should be managed aggressively.

Patients with telomere biology disorders may experience disease progression, including pulmonary and liver fibrosis, as well as vascular complications.

Particular attention should be paid to the increased cancer risk in all IBMFS patients, especially in Fanconi anemia, Diamond-Blackfan anemia, and dyskeratosis congenita.

CONFLICT OF INTEREST

Nothing to declare.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable.

AUTHORS' CONTRIBUTIONS

Substantive scientific and intellectual contributions to the study: Loth G, Darrigo LG, Sousa AM, Antunes AA and Vieira AK. **Conception and design:** Loth G. **Analysis and interpretation of data:** Loth G, Darrigo LG, Sousa AM, Antunes AA and Vieira AK. **Manuscript writing:** Loth G, Darrigo LG, Sousa AM, Antunes AA and Vieira AK. **Final approval:** Loth G.

FUNDING

Not applicable.

ACKNOWLEDGMENTS

The authors would like to thank the Pediatric Hematology and Oncology team of the Brazilian Society of Pediatrics for their valuable contributions to the preparation of this manuscript.

REFERENCES

1. Alter BP. Inherited bone marrow failure syndromes: considerations pre- and posttransplant. Blood. 2017 3;130(21):2257–64. https://doi.org/10.1182/blood-2017-05-781799
2. Dokal I, Tummala H, Vulliamy T. Inherited bone marrow failure in the pediatric patient. Blood. 2022;140(6):556–70. https://doi.org/10.1182/blood.2020006481
3. Bluteau O, Sebert M, Leblanc T, Peffault de Latour R, Quentin S, Lainey E, Hernandez L, Dalle JH, Sicre de Fontbrune F, Lengline E, Itzykson R, Clappier E, Boissel N, Vasquez N, Da Costa M, Masliah-Planchon J, Cuccuini W, Raimbault A, De Jaegere L, Adès L, Fenaux P, Maury S, Schmitt C, Muller M, Domenech C, Blin N, Bruno B, Pellier I, Hunault M, Blanche S, Petit A, Leverger G, Michel G, Bertrand Y, Baruchel A, Socié G, Soulier J. A landscape of germ line mutations in a cohort of inherited bone marrow failure patients. Blood. 2018;131(7):717–32. https://doi.org/10.1182/blood-2017-09-806489
4. Bonfim C. Special pre- and posttransplant considerations in inherited bone marrow failure and hematopoietic malignancy predisposition syndromes. Hematology. 2020;2020(1):107–14. https://doi.org/10.1182/hematology.2020000095
5. Sakaguchi H, Yoshida N. Recent advances in hematopoietic cell transplantation for inherited bone marrow failure syndromes. Int J Hematol. 2022;116(1):16–27. https://doi.org/10.1007/s12185-022-03362-4
6. Alter BP, Giri N, Savage SA, Rosenberg PS. Cancer in the National Cancer Institute inherited bone marrow failure syndrome cohort after fifteen years of follow-up. Haematologica. 2018;103(1):30–9. https://doi.org/10.3324/haematol.2017.178111
7. Calado RT, Clé DV. Treatment of inherited bone marrow failure syndromes beyond transplantation. Hematology. 2017;2017(1):96–101. https://doi.org/10.1182/asheducation-2017.1.96
8. Peake JD, Noguchi E. Fanconi anemia: current insights regarding epidemiology, cancer, and DNA repair. Hum Genet. 2022;141(12):1811–36. https://doi.org/10.1007/s00439-022-02462-9
9. Dufour C, Pierri F. Modern management of Fanconi anemia. Hematology. 2022;2022(1):649–57. https://doi.org/10.1182/hematology.2022000393
10. Debureaux PE, Sicre de Fontbrune F, Bonfim C, Dalle JH, Buchbinder N, Bertrand Y, Renard C, Forcade E, Fernandes J, Talbot A, Pasquini R, Soulier J, Leblanc T, Socie G, Peffault de Latour R. FLAG-sequential regimen followed by bone marrow transplantation for myelodysplastic syndrome or acute leukemia in patients with Fanconi anemia: a Franco-Brazilian study. Bone Marrow Transplant. 2021;56(1):285–8. https://doi.org/10.1038/s41409-020-0994-2
11. Lum SH, Eikema DJ, Piepenbroek B, Wynn RF, Samarasinghe S, Dalissier A, Kalwak K, Ayas M, Hamladji RM, Yesilipek A, Dalle JH, Uckan-Cetinkaya D, Bierings M, Kupesiz A, Halahleh K, Skorobogatova E, Öztürk G, Faraci M, Renard C, Evans P, Corbacioglu S, Locatelli F, Dufour C, Risitano A, Peffault de Latour R. Outcomes of hematopoietic stem cell transplantation in 813 pediatric patients with Fanconi anemia. Blood. 2024;144(12):1329–42. https://doi.org/10.1182/blood.2023022751

12. Cancio M, Troullioud Lucas AG, Bierings M, Klein E, de Witte MA, Smiers FJ, Bresters D, Boelens JJ, Smetsers SE. Predictors of outcomes in hematopoietic cell transplantation for Fanconi anemia. Bone Marrow Transplant. 2024;59(1):34–40. https://doi.org/10.1038/s41409-023-02121-1

13. Bonfim C, Nichele S, Loth G, Funke VAM, Nabhan SK, Pillonetto DV, Lima ACM, Pasquini R. Transplantation for Fanconi anaemia: lessons learned from Brazil. The Lancet Haematology. 2022;9(3):e228–36. https://doi.org/10.1016/s2352-3026(22)00032-1

14. Bonfim C, Ribeiro L, Nichele S, Bitencourt M, Loth G, Koliski A, Funke VAM, Pilonetto DV, Pereira NF, Flowers MED, Velleuer E, Dietrich R, Fasth A, Torres-Pereira CC, Pedruzzi P, Eapen M, Pasquini R. Long-term survival, organ function, and malignancy after hematopoietic stem cell transplantation for Fanconi anemia. Biol Blood Marrow Transplant. 2016;22(7):1257–63. https://doi.org/10.1016/j.bbmt.2016.03.007

15. Shimamura A, Alter BP. Pathophysiology and management of inherited bone marrow failure syndromes. Blood Rev. 2010;24(3):101–22. https://doi.org/10.1016/j.blre.2010.03.002

16. MacMillan ML, DeFor TE, Young JA, Dusenbery KE, Blazar BR, Slungaard A, Zierhut H, Weisdorf DJ, Wagner JE. Alternative donor hematopoietic cell transplantation for Fanconi anemia. Blood. 2015;125(24):3798–804. https://doi.org/10.1182/blood-2015-02-626002

17. Agarwal S. Evaluation and management of hematopoietic failure in dyskeratosis congenita. Hematol Oncol Clin North Am. 2018;32(4):669–85. https://doi.org/10.1016/j.hoc.2018.04.003

18. Savage SA. Dyskeratosis congenita and telomere biology disorders. Hematology Am Soc Hematol Educ Program. 2022;2022(1):637–48. https://doi.org/10.1182/hematology.2022000394

19. Niewisch MR, Giri N, McReynolds LJ, Alsaggaf R, Bhala S, Alter BP, Savage SA. Disease progression and clinical outcomes in telomere biology disorders. Blood. 2022;139(12):1807–19. https://doi.org/10.1182/blood.2021013523

20. Bhoopalan SV, Wlodarski M, Reiss U, Triplett B, Sharma A. Reduced-intensity conditioning–based hematopoietic cell transplantation for dyskeratosis congenita: Single-center experience and literature review. Pediatr Blood Cancer. 2021;68(10):e29177. https://doi.org/10.1002/pbc.29177

21. Nichele S, Bonfim C, Junior LGD, Loth G, Kuwahara C, Trennephol J, Funke VAM, Marinho DE, Koliski A, Rodrigues AM, Mousquer RTG, Fasth A, Lima ACM, Calado RT, Pasquini R. Hematopoietic cell transplantation for telomere biology diseases: A retrospective single-center cohort study. Eur J Haematol. 2023;111(3):423–31. https://doi.org/10.1111/ejh.14023

22. Fioredda F, Iacobelli S, Korthof ET, Knol C, van Biezen A, Bresters D, Veys P, Yoshimi A, Fagioli F, Mats B, Zecca M, Faraci M, Miano M, Arcuri L, Maschan M, O'Brien T, Diaz MA, Sevilla J, Smith O, Peffault de Latour R, de la Fuente J, Or R, Van Lint MT, Tolar J, Aljurf M, Fisher A, Skorobogatova EV, Diaz de Heredia C, Risitano A, Dalle JH, Sedláček P, Ghavamzadeh A, Dufour C. Outcome of haematopoietic stem cell transplantation in dyskeratosis congenita. Br J Haematol. 2018;183(1):110–8. https://doi.org/10.1111/bjh.15495

23. Rolles B, Tometten M, Meyer R, Kirschner M, Beier F, Brümmendorf TH. Inherited telomere biology disorders: pathophysiology, clinical presentation, diagnostics, and treatment. Transfus Med Hemother. 2024;51(5):292–309. https://doi.org/10.1159/000540109

24. Costa L, Leblanc T, Mohandas N. Diamond-Blackfan anemia. Blood. 2020;136(11):1262–73. https://doi.org/10.1182/blood.2019000947

25. Wlodarski MW, Vlachos A, Farrar JE, Da Costa LM, Kattamis A, Dianzani I, Belendez C, Unal S, Tamary H, Pasauliene R, Pospisilova D, de la Fuente J, Iskander D, Wolfe L, Liu JM, Shimamura A, Albrecht K, Lausen B, Bechensteen AG, Tedgard U, Puzik A, Quarello P, Ramenghi U, Bartels M, Hengartner H, Farah RA, Al Saleh M, Hamidieh AA, Yang W, Ito E, Kook H, Ovsyannikova G, Kager L, Gleizes PE, Dalle JH, Strahm B, Niemeyer CM, Lipton JM, Leblanc TM; international Diamond-Blackfan anaemia syndrome guideline panel. Diagnosis, treatment, and surveillance of Diamond-Blackfan anaemia syndrome: international consensus statement. Lancet Haematol. 2024;11(5):e368–e382. https://doi.org/10.1016/S2352-3026(24)00063-2

26. Darrigo LG Junior, Loth G, Kuwahara C, Vieira A, Colturato V, Rodrigues AL, Arcuri L, Fernandes J, Macedo A, Tavares R, Gomes A, Ribeiro L, Seber A, Zecchin V, de Souza M, Calixto R, Pasquini R, Flowers M, Rocha V, Bonfim C. Hematopoietic cell transplantation for Diamond Blackfan anemia: A report from the Pediatric Group of the Brazilian Bone Marrow Transplantation Society. Eur J Haematol. 2020;105(4):426–33. https://doi.org/10.1111/ejh.13463

27. Strahm B, Loewecke F, Niemeyer CM, Albert M, Ansari M, Bader P, Bertrand Y, Burkhardt B, Da Costa LM, Ferster A, Fischer A, Güngör T, Gruhn B, Hainmann I, Kapp F, Lang P, Müller I, Schulz A, Szvetnik A, Wlodarski M, Noellke P, Leblanc T, Dalle JH. Favorable outcomes of hematopoietic stem cell transplantation in children and adolescents with Diamond-Blackfan anemia. Blood Adv. 2020;4(8):1760–9. https://doi.org/10.1182/bloodadvances.2019001210

28. Cesaro S, Donadieu J, Cipolli M, Dalle JH, Styczynski J, Masetti R, Strahm B, Mauro M, Alseraihy A, Aljurf M, Dufour C, de la Tour RP. Stem cell transplantation in patients affected by Shwachman-Diamond Syndrome: Expert Consensus and Recommendations From the EBMT Severe Aplastic Anaemia Working Party. Transplant Cell Ther. 2022;28(10):637–49. https://doi.org/10.1016/j.jtct.2022.07.010

29. Myers KC, Furutani E, Weller E, Siegele B, Galvin A, Arsenault V, Alter BP, Boulad F, Bueso-Ramos C, Burroughs L, Castillo P, Connelly J, Davies SM, DiNardo CD, Hanif I, Ho RH, Karras N, Manalang M, McReynolds LJ, Nakano TA, Nalepa G, Norkin M, Oberley MJ, Orgel E, Pastore YD, Rosenthal J, Walkovich K, Larson J, Malsch M, Elghetany MT, Fleming MD, Shimamura A. Clinical features and outcomes of patients with Shwachman-Diamond syndrome and myelodysplastic syndrome or acute myeloid leukaemia: a multicentre, retrospective, cohort study. Lancet Haematol. 2020;7(3):e238–46. https://doi.org/10.1016/S2352-3026(19)30206-6

30. Cesaro S, Pillon M, Sauer M, Smiers F, Faraci M, de Heredia CD, Wynn R, Greil J, Locatelli F, Veys P, Uyttebroeck A, Ljungman P, Chevalier P, Ansari M, Badell I, Güngör T, Salim R, Tischer J, Tecchio C, Russell N, Chybicka A, Styczynski J, Krivan G, Smith O, Stein J, Afanasyev B, Pochon C, Menconi MC, Bosman P, Mauro M, Tridello G, de Latour RP, Dufour C. Long-term outcome after allogeneic hematopoietic stem cell transplantation for Shwachman-Diamond syndrome: a retrospective analysis and a review of the literature by the Severe Aplastic Anemia Working Party of the European Society for Blood and Marrow Transplantation (SAAWP-EBMT). Bone Marrow Transplant. 2020;55(9):1796–809. https://doi.org/10.1038/s41409-020-0863-z. Epub 2020 Mar 19. Erratum in: Bone Marrow Transplant. 2020;55(9):1884. https://doi.org/10.1038/s41409-020-0901-x

31. Skokowa J, Dale DC, Touw IP, Zeidler C, Welte K. Severe congenital neutropenias. Nat Rev Dis Primers. 2017;3:17032. https://doi.org/10.1038/nrdp.2017.32

32. Sureda A, Corbacioglu S, Greco R, Kröger N, Carreras E, editores. The EBMT Handbook: Hematopoietic Cell Transplantation and Cellular Therapies. Cham: Springer International; 2024. https://doi.org/10.1007/978-3-031-44080-9

33. Connelly JA, Choi SW, Levine JE. Hematopoietic stem cell transplantation for severe congenital neutropenia. Curr Opin Hematol. 2012;19(1):44–51. https://doi.org/10.1097/moh.0b013e32834da96e

34. Giardino S, Eikema DJ, Piepenbroek B, Algeri M, Ayas M, Faraci M, Tbakhi A, Zecca M, Essa M, Neven B, Bertrand Y, Kharya G, Bykova T, Lawson S, Petrini M, Mohseny A, Rialland F, James B, Colita A, Fahd M, Cesaro S, Schulz A, Kleinschmidt K, Kałwak K, Corbacioglu S, Dufour C, Risitano A, de Latour RP. HLA-haploidentical stem cell transplantation in children with inherited bone marrow failure syndromes: A retrospective analysis on behalf of EBMT severe aplastic Anemia and pediatric diseases working parties. Am J Hematol. 2024;99(6):1066–76. https://doi.org/10.1002/ajh.27293

35. Oved JH, Gibson NM, Venella K, Elgarten CW, Wray L, Warren JT, Olson TS. Reduced toxicity matched sibling bone marrow transplant results in excellent outcomes for severe congenital neutropenia. Front Immunol. 2024;15:1369243. https://doi.org/10.3389/fimmu.2024.1369243

36. Ballmaier M, Germeshausen M. Advances in the understanding of congenital amegakaryocytic thrombocytopenia. Br J Haematol. 2009;146(1):3–16. https://doi.org/10.1111/j.1365-2141.2009.07706.x

37. Germeshausen M, Ballmaier M. CAMT-MPL: congenital amegakaryocytic thrombocytopenia caused by MPL mutations - heterogeneity of a monogenic disorder - a comprehensive analysis of 56 patients. Haematologica. 2021;106(9):2439–48. https://doi.org/10.3324/haematol.2020.257972

38. Germeshausen M, Ballmaier M. Congenital amegakaryocytic thrombocytopenia - Not a single disease. Best Pract Res Clin Haematol. 2021;34(2):101286. https://doi.org/10.1016/j.beha.2021.101286

39. Geddis AE. Congenital amegakaryocytic thrombocytopenia. Pediatr Blood Cancer. 2011;57(2):199–203. https://doi.org/10.1002/pbc.22927

40. Aldebert C, Fahd M, Galimard JE, Ghemlas IA, Zecca M, Silva J, Mohseny A, Kupesiz A, Hamladji RM, Miranda N, Güngör T, Wynn RF, Merli P, Sundin M, Faraci M, Diaz-de-Heredia C, Burkhardt B, Bordon V, Angoso M, Bader P, Ifversen M, Herrera Arroyo C, Maximova N, Riesco S, Stein J, Dalissier A, Locatelli F, Kalwak K, Dalle JH, Corbacioglu S. Outcomes of patients undergoing allogeneic haematopoietic stem cell transplantation for congenital amegakaryocytic thrombocytopenia; a study on behalf of the PDWP of the EBMT. Bone Marrow Transplant. 2024;59(12):1717–25. https://doi.org/10.1038/s41409-024-02416-x

41. Pecci A, Balduini CL. Inherited thrombocytopenias: an updated guide for clinicians. Blood Rev. 2021;48:100784. https://doi.org/10.1016/j.blre.2020.100784

42. Cancio M, Hebert K, Kim S, Aljurf M, Olson T, Anderson E, Burroughs L, Vatsayan A, Myers K, Hashem H, Hanna R, Horn B, Prestidge T, Boelens JJ, Boulad F, Eapen M. Outcomes in hematopoietic stem cell transplantation for congenital amegakaryocytic thrombocytopenia. Transplant Cell Ther. 2022;28(2):101.e1–e6. https://doi.org/10.1016/j.jtct.2021.10.009

43. Consensus Guidelines for pediatric hematopoietic stem cell transplantation from Brazilian Society for Blood and Marrow Transplantation and Cellular Therapy. JBMTCT. 2021;2(4). https://doi.org/10.46765/2675-374X.2021v2n4

44. Loth G, Dumke CCK, Muratori RR, Pelegrina PD, Peixoto CMA, Bach JLM, Nichele S, Trennepohl JP, Koliski A, Mousquer RTG, Rodrigues AM, Marchesini R, Feitosa MK, Pilonetto DV, Gouvea L, Benini FML, Pirolli ES, Tutumi RAF, Lima ACM, Pasquini R, Bonfim C. Haematopoietic cell transplantation for 106 infants and preschoolers with acquired and inherited bone marrow failures. Br J Haematol. 2024;205(6):2387–402. https://doi.org/10.1111/bjh.19831