Table 10. Comprehensive long-term surveillance in children and adults with DBA syndrome

Clinical scenario	Surveillance recommendations
HEMATOLOGY	
Any patient (including therapy-independent) Monitor changes in blood counts (Hb, other blood lineages): viral infection, drug induced, MDS/AML	• CBC and reticulocyte count at regular intervals (once yearly if therapy-independent) • Bone marrow aspirate if: more severe anemia without explanation, unexpected reticulocytosis, worsening of neutropenia or thrombocytopenia, abnormal cells

Patient receiving steroids
 	
Monitor efficacy (Hb and reticulocyte count) and treatment toxicity (see also **Table 7**)
 	
Involve endocrinology
	• CBC every ~3-4 months in stable patients
	• LFTs, creatinine, vitamin D levels regularly
	• Vitamin D and calcium supplementation as needed
	• Proton pump inhibitors (or H2 antagonists) during initial high dose prednisone therapy, or when symptomatic
	• Disclose that estrogen-containing oral contraceptives might weaken steroid effect
	• Steroid toxicity requires repeat endocrine evaluation
	  ○ At least yearly testing for diabetes/ metabolic syndrome, bone health (densitometry scan), eye exam (cataract exclusion)
	  ○ Bisphosphonates as therapy option in patients with significant osteoporosis
	  ○ Joint/bone pain must be investigated being mindful of steroid-induced avascular necrosis and risk of osteogenic sarcoma (MRI may be warranted)

Patients on transfusions and chelation
 	
Monitor efficacy (nadir Hb before transfusion) and toxicity (see also **Table 6 and 8**)
 	
Patients with poor iron balance
	• Before every transfusion: CBC with reticulocyte counts, RBC antibodies (if possible)
	• Ferritin and transferrin saturation trend (i.e., every 1-3 months before transfusion)
	• Routine transaminases, creatinine, electrolytes (phosphate if on DFX) virus serology (hepatitis B/C)
	• Annual MRI evaluation or more often according to iron status:
	  ○ Liver iron content (LIC) by T2* or R2
	  ○ Heart iron by T2*
	• Echocardiography, ECG evaluation every 1 to 3 years according to iron status. Consider Holter monitor for patients with cardiac iron overload. Intensify chelation; consider DFP
	• Pancreas and pituary glands: specific endocrine tests: fructosamine (instead of HbA1c in transfused patients), TSH, PTH
	• Growth hormone replacement when indicated
	• Consultation for medically assisted reproduction
	• Dose adjustments and combination of two chelators are frequently required, emphasize importance of medication adherence, facilitate networking with patient groups

Patients on DFO Monitor for toxicity: hearing loss, osteopenia, renal lithiasis	• Bone densitometry (every 1 to 3 years) • Regular audiogram and eye exam (at least annually or more often with dose changes) • Regular renal ultrasound surveillance • Higher risk of toxicity is present in patients with low ferritin

Patients on DFX: monitor for toxicity: renal (glomerular or tubular damage including Fanconi syndrome), hepatic toxicity, transaminitis, gastrointestinal issues	• Frequent evaluation of liver and kidney parameters. Patients with toxicity: decrease dose • Regular renal ultrasound surveillance • Audiogram and eye exam (yearly) • Higher risk of toxicity is possibly present in patients with low ferritin
Patients on DFP: screening for neutropenia/agranulocytosis	• Weekly CBC at treatment initiation and during any fever episode, monitor counts often and discontinue DFP for any sign of unusual or progressive neutropenia • Patient information & education (drug passport for emergencies with established plan)
For transplanted patients	• Standard surveillance recommendations. • Higher cancer risk in DBA syndrome patients must be taken into account
IMMUNOLOGY / INFECTIONS	
Hypogammaglobulinemia, Lymphopenia, recurrent infections	• Ig G, A, M levels and lymphocyte subsets (regularly if indicated) • Antibody responses, discuss immunizations and immunoglobulin treatment • For severe T-cell lymphopenia: consider pneumocystis jirovecii pneumonia prophylaxis • Additional prophylaxis and diagnostics according to local standard
Transfusion-related pathogens	• Virus testing at least once yearly (hepatitis B/C, HIV)
Vaccinations	• No restrictions on vaccines: Hepatitis B vaccine especially in patients receiving transfusions; live vaccines: first dose ideally before start prednisone, following doses after steroid reduction. • Patient with significant hypogammaglobulinemia: measure specific vaccine antibody titers
ONCOLOGY	
Solid tumors, MDS/AML	• Patient education, healthy lifestyle (avoid smoking, alcohol, toxins, unprotected sun exposure) • HPV vaccination • Patient adherence to screening procedures as in the general population • Colonoscopy beginning age 20 years, every 5 years or more often if clinically indicated • Bone marrow analysis: consider as baseline in adolescents/ young adults before transitioning to adult care, otherwise in any patient with significant unexplained cytopenia or rise in reticulocytes • Unexplained joint/bone pain: risk of osteogenic sarcoma (low threshold for x-ray / imaging)
FAMILY PLANNING, PREGNANCY	
Genetic risk (transmission)	• Patient education and genetic counselling • Discuss medically assisted reproduction for individuals asking for prenatal or pre-implantation diagnostics (according to national legal regulations)
Pregnancies in DBA syndrome: high risk obstetric care required	• Intensification of chelation prior planned pregnancy to optimize iron balance • Blood support frequently needed to maintain Hb >10.0-10.5 g/dL during pregnancy • Screening for fetal anemia • Detailed recommendations reviewed elsewhere (reference 136)