

Chinese Society of Hematology clinical practice guidelines for the comprehensive management of allogeneic hematopoietic stem cell transplantation in patients with severe aplastic anemia

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Abstract

Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a potentially curative treatment for severe aplastic anemia (SAA). In China, the number of SAA patients undergoing allo-HSCT has risen considerably. However, owing to variations in clinical practices between China and other countries, certain aspects of transplantation demonstrate unique and distinct characteristics. To address these unique challenges and standardize clinical practice, we developed evidence-based guidelines tailored to the management of Chinese SAA patients undergoing allo-HSCT.

Methods: This clinical practice guideline was developed using the Evidence to Decision framework and the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system to formulate evidence-based recommendations. In instances where high-quality evidence was lacking, the Delphi method was used to integrate expert opinions. The guidelines adhere to the Appraisal of Guidelines for Research and Evaluation II (AGREE II) framework and the Reporting Items for Practice Guidelines in Health Care (RIGHT) statement to ensure methodological rigor and transparency.

Results: The guidelines present 32 recommendations encompassing key aspects of allo-HSCT for SAA, including patient eligibility criteria, donor and graft selection, pretransplant assessment, conditioning strategies, graft-versus-host disease prophylaxis, early management of posttransplant complications, and long-term follow-up. These recommendations are based on the latest clinical evidence and expert consensus, offering a structured approach to optimize transplantation outcomes.

Conclusions: These guidelines establish standardized protocols to enhance allo-HSCT management for SAA in China by integrating current evidence and expert consensus. Its widespread adoption is expected to improve donor selection strategies, conditioning regimen applications, posttransplant care, and long-term patient outcomes. Ultimately, these recommendations aim to increase the quality of patient care, improve survival rates, and contribute to the advancement of national health care standards.

Keywords: Allogeneic hematopoietic stem cell transplantation; Severe aplastic anemia; Guideline; Graft-versus-host disease prophylaxis

Introduction

Aplastic anemia (AA) is a rare and heterogeneous disease characterized by pancytopenia with reduced bone marrow (BM) cellularity in the absence of abnormal infiltration or BM fibrosis.^[1] In Asian populations, the incidence of AA is two to three times greater than that in Western countries, reaching 3.0 to 5.0 cases per million.^[2–5] Epidemiological studies estimate the annual incidence of AA in China to be 7.4 per million, with severe aplastic anemia (SAA) accounting for 1.4 per million.^[6]

In recent years, allogeneic hematopoietic stem cell transplantation (allo-HSCT) has significantly improved survival outcomes for patients with SAA.^[7–10] China has witnessed a rapid increase in the number of SAA patients undergoing allo-HSCT,^[11] facilitating the progressive realization of universal donor availability. Currently, among patients with SAA receiving allo-HSCT in China, 56% undergo haploidentical donor (HID) transplantation, 23% receive matched sibling donor (MSD) transplantation, 17% receive unrelated donor (URD) transplantation, and 4% receive cord blood (CB) transplantation.^[11]

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Owing to the differences between China and Western countries in the practice of allo-HSCT, the monitoring, prevention, and treatment of Chinese patients after allo-HSCT cannot be entirely managed according to the current recommendations in Western countries. Currently, China has reached a consensus on the management of leukemia patients.^[12] However, existing international guidelines on SAA management incorporate limited clinical data from Chinese patients.^[1,13–17] Similarly, owing to differences in transplantation practices, such as indications, donor selection strategies, and conditioning regimens, direct adoption of Western recommendations may not be entirely applicable in China. Given China's large patient population and extensive clinical experience with allo-HSCT, its transplantation strategies have the potential to inform global practices.

This guideline establishes evidence-based recommendations tailored to the unique clinical landscape in China, incorporating the latest scientific evidence, particularly from Chinese studies. This guideline is intended for hematologists involved in the administration of allo-HSCT for patients with SAA and includes 32 graded recommendations outlining key aspects of transplantation management. These recommendations are based on multiple factors, such as age and human leukocyte antigen (HLA) matching ([Figure 1]; the specific recommendations are presented in Table 1).

Guideline Development Group

The guideline development group (GDG) consists of 33 experts from the Chinese Society of Hematology specializing in HSCT and/or immunosuppressive therapy (IST) for SAA. These experts represent 25 institutions across China. Conflicts of interest were documented and evaluated in accordance with the principles outlined by the Guidelines International Network. All the GDG members declare that they have no financial or intellectual conflicts of interest and are fully eligible to participate in the guideline

development process. These guidelines have been organized by the Stem Cell Application Group, Chinese Society of Hematology, and Chinese Medical Association.

Guideline Development Process

The development of these guidelines followed a structured, evidence-based approach. The process began with GDG members identifying key clinical questions requiring guidance, particularly those relevant to allo-HSCT in patients with SAA. Afterward, a literature search was conducted using PubMed and Google Scholar between October 2024 and May 2025 without date or language limits. The paper retrieval strategy and the criteria for including and excluding literature are detailed in the Supplementary Material, <http://links.lww.com/CM9/C704>. Recommendations were formulated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework, which categorizes the quality of evidence as high, moderate, or low and classifies recommendations as strong or weak; the specific criteria are presented in Table 2.^[13,18] When sufficient evidence was unavailable, expert consensus was sought. A structured voting process using a 9-point Likert scale was implemented, where 1–3 indicated disagreement, 3.01–6.99 indicated partial consensus, and 7–9 indicated agreement.^[19] Recommendations were accepted if at least 50% of the voting experts supported them, with fewer than 20% opposing. Those achieving $\geq 70\%$ agreement were designated as strong recommendations, whereas those with lower agreement were classified as weak recommendations.^[20] The voting on the guideline recommendations was conducted using the Delphi method. If consensus was not reached in the initial voting round, contentious recommendations were revised iteratively based on expert feedback, followed by a second round of voting to achieve agreement.

The complete guideline report underwent external peer review by independent guideline methodologists and clinicians who were not involved in its development. The

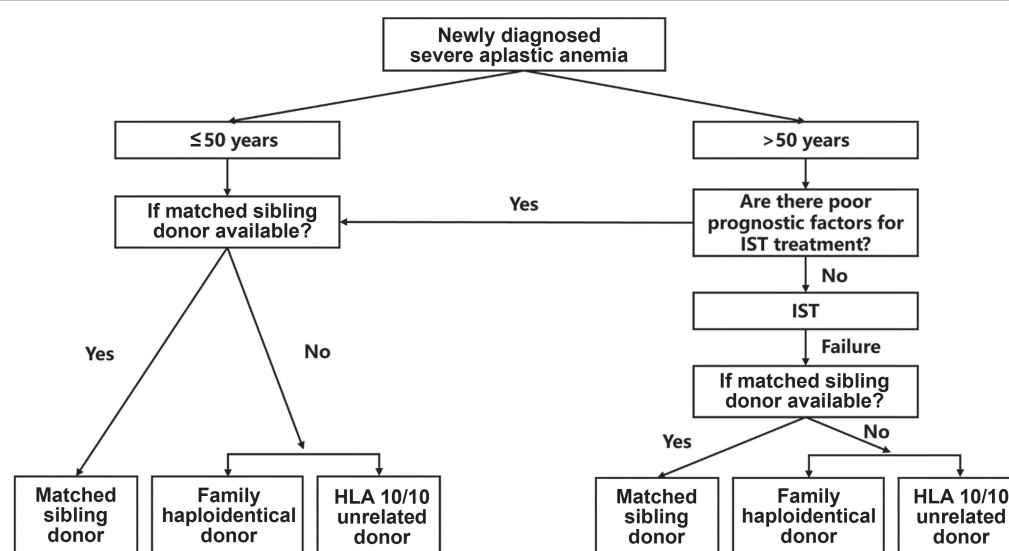


Figure 1: Treatment of acquired severe aplastic anemia. HLA: Human leukocyte antigen; IST: Immunosuppressive therapy.

Table 1: Summary and strength of the recommendations.

Recommendations	Strength of recommendation
Part 1. Indications and timing of allo-HSCT for SAA	
Patients with newly diagnosed SAA	
Recommendation 1.1: Allo-HSCT is recommended as the first-line treatment for newly diagnosed pediatric and adult patients under 50 years old with SAA or vSAA.	Strong recommendation, moderate-quality evidence
Recommendation 1.2: For patients with poor prognostic factors, including those who are expected to respond poorly to IST treatment and those with vSAA, infection, hemorrhagic complications, or high-risk clonal evolution, allo-HSCT can still be considered as a first-line treatment option even if they are over 50 years old.	Strong recommendation, strength of consensus 8.04
Second-line treatment for patients with SAA	
Recommendation 1.3: Allo-HSCT is recommended as a second-line treatment for patients with relapsed/refractory SAA.	Strong recommendation, moderate-quality evidence
Recommendation 1.4: Early transplant evaluation should be performed for patients who fail to achieve a response after at least 4 months of IST.	Strong recommendation, strength of consensus 7.71
Recommendation 1.5: If the patient can benefit from second-line allo-HSCT and if the patient's physical status is eligible for transplantation, the patient may be recommended for allo-HSCT with no further age restrictions. Age alone should not be a limiting factor for second-line allo-HSCT. If a comprehensive pretransplant evaluation confirms that a patient is physically fit for transplantation and may benefit from the procedure, allo-HSCT should be considered, regardless of age.	Strong recommendation, strength of consensus 7.75
Special considerations for unique patient populations	
Recommendation 1.6: Patients with non-SAA who later progress to SAA are considered for allo-HSCT as a first-line treatment option.	Strong recommendation, moderate-quality evidence
Recommendation 1.7: The treatment principles for patients with HAAA align with those for patients with acquired SAA, and allo-HSCT should be considered accordingly.	Strong recommendation, moderate-quality evidence
Recommendation 1.8: Patients with BMF/PNH may benefit from allo-HSCT.	Strong recommendation, moderate-quality evidence
Part 2. Donor selection	
Recommendation 2.1: HLA typing should be performed at diagnosis for all patients and their family members. If available, an MSD is the preferred graft source for allo-HSCT. In the absence of an MSD, alternative donor options, including HIDs and MUDs, should be evaluated on the basis of institutional expertise, disease urgency, and patient preference. If an unmatched donor is under consideration, DSA testing is recommended.	Strong recommendation, moderate-quality evidence
Recommendation 2.2: In patients who present with life-threatening complications, such as severe or high-risk infections, fatal bleeding, or other critical conditions requiring urgent transplantation, a related donor should be prioritized.	Strong recommendation, strength of consensus 8.11
Recommendation 2.3: MUDs or HIDs should be prioritized over UCB.	Strong recommendation, moderate-quality evidence
Recommendation 2.4: Optimal donor selection should adhere to high-resolution HLA typing, with a preference for 10/10 HLA-matched related or URDs (HLA-A, -B, -C, -DRB1, -DQB1). MMUDs with a 9/10 HLA match should not be considered equivalent to MUD; however, MMUDs may be considered an alternative in cases where no fully matched donors are available.	Strong recommendation, moderate-quality evidence
Part 3. Pretransplant workup	
Pretransplant evaluation	
Recommendation 3.1: All patients being considered for allo-HSCT should undergo a comprehensive risk-benefit assessment comparing allo-HSCT with IST ± TPO-RA to guide first-line treatment decisions.	Strong recommendation, strength of consensus 8.07
Recommendation 3.2: Patients should undergo a thorough reevaluation before transplantation to confirm the diagnosis of SAA and rule out IBMF or other secondary etiologies. Recommended investigations include BM biopsy, cytogenetics, FISH analysis, flow cytometry, NGS, and chromosome breakage testing.	Strong recommendation, strength of consensus 8.68
Recommendation 3.3: Patient comorbidities and physical status must be assessed before allo-HSCT.	Strong recommendation, moderate-quality evidence
Recommendation 3.4: Iron overload should be evaluated using SF level, and where available, noninvasive imaging techniques such as MRI (T2* or R2*) should be used to assess cardiac and hepatic iron burden.	Strong recommendation, moderate-quality evidence
Recommendation 3.5: Iron chelation therapy is recommended for patients with SF levels >1000 ng/mL; however, allo-HSCT should not be delayed solely for iron chelation.	Strong recommendation, moderate-quality evidence
Recommendation 3.6: Patients of reproductive age who wish to preserve fertility should consult an obstetrician-gynecologist before undergoing allo-HSCT, provided their clinical condition allows.	Strong recommendation, strength of consensus 8.43
Recommendation 3.7: For patients with SAA, consultation with a psychologist prior to allo-HSCT is encouraged if needed. Psychological consultation is encouraged for patients with psychological disorders before undergoing allo-HSCT.	Strong recommendation, strength of consensus 8.21
Part 4. The conditioning regimen for patients receiving allo-HSCT	
Recommendation 4.1: For MRD and MUD-HSCT, CyATG ± Bu consisting of a full dose of cyclophosphamide (Cy, 200 mg/kg) and rabbit anti-human thymocyte globulin (rATG, 10–12.5 mg/kg) is recommended. In high-risk patients, e.g., those with a long medical history, a history of significant hemorrhagic complications, or evidence of cardiotoxicity, FAC ± Bu consisting of fludarabine (Flu, 120–200 mg/m ²), a decreased dose of Cy (100–200 mg/kg) and rATG (10–12.5 mg/kg) is recommended.	Strong recommendation, moderate-quality evidence
Recommendation 4.2: For SAA patients undergoing HID-HSCT, a BCA regimen consisting of 6.4 mg/kg Bu, 200 mg/kg Cy, and 10 mg/kg rATG is recommended. For patients with medical comorbidities, heavy pretreatment, or advanced age, the BFCA regimen—consisting of Bu (6.4 mg/kg), Flu (120–150 mg/kg), and reduced doses of Cy (80–120 mg/kg) and rATG (7.5–10 mg/kg)—is recommended.	Strong recommendation, moderate-quality evidence

(continued)

Table 1
(continued)

Recommendations	Strength of recommendation
Recommendation 4.3: Currently, the optimal conditioning regimen for CBT requires further investigation.	Strong recommendation, strength of consensus 8.03
Part 5. The graft type for patients undergoing allo-HSCT	
Recommendation 5.1: PBSCs with or without BM are recommended for MSD-HSCT.	Strong recommendation, strength of consensus 7.43
Recommendation 5.2: PBSCs are mostly accepted in MUD-HSCT.	Strong recommendation, strength of consensus 8.21
Recommendation 5.3: Both PBSCs alone and PBSCs combined with BM are equally recommended for HID-HSCT.	Strong recommendation, strength of consensus 7.11
Part 6. aGvHD prophylaxis	
Recommendation 6.1: CsA combined with short term MTX and MMF is recommended as standard prophylaxis in allo-HSCT, BMT, and PBST.	Strong recommendation, moderate-quality evidence
Recommendation 6.2: For CBT recipients, a combination of CsA and MMF is recommended, and the addition of low dose rATG may further prevent GvHD.	Strong recommendation, strength of consensus 7.45
Part 7. Follow-up and management of early post-transplant issues	
Recommendation 7.1: Long-term chimerism monitoring is essential for posttransplant care. Chimerism evaluations are recommended monthly for the first 3 months, then every 3 months from months 3–12, and every 6 months thereafter using BM or peripheral blood mononuclear cells. The frequency may be adjusted based on blood counts and the degree of mixed chimerism.	Strong recommendation, strength of consensus 8.24
Recommendation 7.2: When mixed chimerism occurs, close monitoring is recommended to ensure appropriate immunosuppressant levels while tracking blood counts and donor cell proportions, interventions should also be taken when necessary.	Strong recommendation, strength of consensus 8.03
Recommendation 7.3: In cases of PGF, administration of hematopoietic growth factors (such as G-CSF and TPO-RA), infusion of additional selected donor CD34+ stem cells or MSCs, and secondary allo-HSCT may be considered.	Strong recommendation, strength of consensus 8.12
Recommendation 7.4: In case of GF, therapeutic options include G-CSF administration, boosting with selected donor CD34+ stem cell, and secondary allo-HSCT with the same or a different donor.	Strong recommendation, low-quality evidence
Part 8. Long-term follow-up	
Recommendation: Long-term posttransplant follow-up is essential to monitor transplant-related complications and overall patient health. Posttransplant monitoring should involve multidisciplinary evaluations of the cardiovascular, pulmonary, thyroid, and skeletal systems, fertility preservation assessments, surveillance for secondary malignancies, and assessment of QoL.	Strong recommendation, strength of consensus 8.71

aGvHD: Acute graft-versus-host-disease; allo-HSCT: Allogeneic hematopoietic stem cell transplantation; BCA: Busulfan, cyclophosphamide, and rabbit anti-human thymocyte globulin; BFCA: Busulfan, fludarabine, a decreased dose of cyclophosphamide, and rabbit anti-human thymocyte globulin; BM: Bone marrow; BMF/PNH: Bone marrow failure-associated paroxysmal nocturnal hemoglobinuria; BMT: Bone marrow transplant; Bu: Busulfan; CBT: Cord blood transplantation; CsA: Cyclosporine; Cy: Cyclophosphamide; CyATG: Cytotoxic anti-thymocyte globulin; DSA: Donor-specific anti-HLA antibody; FAC: Fludarabine, a decreased dose of cyclophosphamide and rabbit anti-human thymocyte globulin; FISH: Fluorescence in situ hybridization; Flu: Fludarabine; G-CSF: Granulocyte colony-stimulating factor; GF: Graft failure; GvHD: Graft-versus-host-disease; HAAA: Hepatitis-associated aplastic anemia; HID: Haploidentical donor; HLA: Human leukocyte antigen; HSCT: Hematopoietic stem cell transplantation; IBMF: Inherited bone marrow failure; IST: Immunosuppressive therapy; MMF: Mycophenolate mofetil; MMUD: Mismatched unrelated-donor; MRD: Matched related donor; MRI: Magnetic resonance imaging; MSC: Mesenchymal stem cell; MSD: Matched sibling donor; MTX: Methotrexate; MUD: Matched unrelated-donor; NGS: Next-generation sequencing; PBSC: Peripheral blood stem cell; PBST: Peripheral blood stem cell transplantation; PGF: Primary graft failure; QoL: Quality of life; rATG: Rabbit anti-human thymocyte globulin; SAA: Severe aplastic anemia; SF: Serum ferritin; TPO-RA: Thrombopoietin receptor agonist; UCB: Unrelated cord blood; URD: Unrelated donor; vSAA: Very severe aplastic anemia.

Table 2: Grading recommendations.

Items	Definitions
Recommendation	
1A	Strong recommendation, high-quality evidence
1B	Strong recommendation, moderate-quality evidence
1C	Strong recommendation, low-quality evidence
2A	Weak recommendation, high-quality evidence
2B	Weak recommendation, moderate-quality evidence
2C	Weak recommendation, low-quality evidence
Quality of evidence	
A (High quality)	Robustly designed RCTs
B (Moderate quality)	RCTs with limitations; large-scale, multiple, or methodologically robust observational studies
C (Low quality)	Limited observational studies, small case series, or expert consensus in the absence of substantial empirical data

RCT: Randomized controlled trial.

feedback was systematically reviewed, and relevant modifications were integrated to enhance the scientific rigor and applicability of the guidelines. To ensure methodological quality, the guidelines were developed in accordance with the Appraisal of Guidelines for Research and Evaluation II (AGREE II) framework and adhered to the Reporting Items for Practice Guidelines in Health Care (RIGHT) statement for structured and transparent reporting.^[21,22]

Recommendations and Evidence Profile

Part 1. Indications and timing of allo-HSCT for SAA

Patients with newly diagnosed SAA

Clinical question 1.1: How should first-line treatment options be selected for newly diagnosed pediatric and adult (under 50 years old) patients with SAA/very severe aplastic anemia (vSAA)?

Table 3: The conditioning regimen for SAA.				
Conditioning regimen	Bu or TBI	Drugs	Dose (total)	Donor type
CyATG-based	–	Cy	200 mg/kg	MRD/MUD
		rATG	10.0–12.5 mg/kg	
		Bu	6.4 mg/kg	
		Cy	160 mg/kg	
		rATG	10 mg/kg	
FAC-based*	–	Flu	120–200 mg/m ²	MRD/MUD
		Cy	100–200 mg/kg	
		rATG	10.0–12.5 mg/kg	
		Bu	6.4 mg/kg	
		Flu	120–200 mg/m ²	
	+ Bu	Cy	80–150 mg/kg	MUD
		rATG	10.0–12.5 mg/kg	
		TBI	2–4 Gy	
		Flu	120–200 mg/m ²	
		Cy	80–150 mg/kg	
BCA	N/A	rATG	10.0–12.5 mg/kg	HID
		Bu	6.4 mg/kg	
		Cy	200 mg/kg	
		rATG	10 mg/kg	
BFCA†	N/A	Bu	6.4 mg/kg	HID
		Flu	120–150 mg/kg	
		Cy	80–120 mg/kg	
		rATG	7.5–10.0 mg/kg	

*For patients with high-risk clinical features—including a long medical history, history of significant hemorrhagic complications, or evidence of cardiotoxicity. †For those with medical comorbidities or heavily pretreated or older patients. – For patients without addition of Bu or TBI; BCA: Bu, Cy and rATG; BFCA: Bu, Flu, Cy and rATG; Bu: Busulfan; Cy: Cyclophosphamide; FAC: Flu, Cy and rATG; Flu: Fludarabine; HID: Haploidentical donor; MRD: Matched related donor; MUD: Matched unrelated donor; N/A: Not applicable; rATG: Rabbit anti-thymocyte globulin; SAA: Severe aplastic anemia; TBI: Total body irradiation.

Recommendation 1.1: Allo-HSCT is recommended as the first-line treatment for newly diagnosed pediatric and adult patients under 50 years old with SAA or vSAA (Strong recommendation, moderate-quality evidence).

A multicenter, prospective study by Liu *et al*^[7] demonstrated that among patients under 40 years of age with SAA or vSAA, first-line matched related donor (MRD) HSCT resulted in superior three-year failure-free survival (FFS) compared with IST. Prior international guidelines and expert consensus also recommend allo-HSCT as the preferred first-line treatment for patients younger than 40 years of age.^[1,23] Owing to its demonstrated benefits in hematologic recovery, survival, and quality of life (QoL), recent studies have evaluated the role of first-line allo-HSCT in patients older than 40 years of age with SAA/vSAA. Evidence suggests that patients aged 40–50 years may achieve favorable long-term outcomes with first-line allo-HSCT, supporting its consideration in this population.^[10,24,25]

Clinical question 1.2: When should allo-HSCT be considered a first-line treatment for patients older than 50 years of age?

Recommendation 1.2: For patients with poor prognostic factors, including those who are expected to respond poorly to IST treatment and those with vSAA, infection, hemorrhagic complications, or high-risk clonal evolution,

allo-HSCT can still be considered as a first-line treatment option even if they are over 50 years old (Strong recommendation, strength of consensus 8.04).

Existing evidence on first-line allo-HSCT for SAA/vSAA patients in China focuses primarily on individuals under 50 years of age. However, for patients older than 50 years of age, first-line allo-HSCT remains a viable option if IST is expected to have poor efficacy. Prognostic indicators of IST failure include significant telomere shortening, adverse genetic mutations (*ASXL1*, *TP53*, *RUNX1*, and *DNMT3A*), uncontrolled active infections, and progression from non-SAA to SAA.^[23] Real-world studies indicate that patients with vSAA frequently exhibit poor responses to IST and that vSAA is an independent risk factor for poor survival outcomes.^[26] Liu *et al*^[27] developed and validated an early death risk score model for patients with vSAA receiving first-line IST. This model revealed that high-risk vSAA cases are significantly associated with early mortality. The results of this study suggest that in these high-risk patients with vSAA, alternative-donor HSCT may yield better outcomes than IST, even in the absence of an HLA-matched donor. In addition, clonal evolution remains a major long-term concern for SAA patients treated with IST. Patients older than 50 years of age with a high risk of clonal evolution should be considered for first-line allo-HSCT.^[28] For patients who present with severe hemorrhagic complications, first-line

allo-HSCT should also be considered, regardless of age. Although studies on bleeding-related indications for allo-HSCT in China are currently limited, expanding eligibility beyond the conventional 50-year age limit may improve overall survival (OS) and long-term outcomes.

Second-line treatment for patients with SAA

Clinical question 1.3: When should allo-HSCT be considered a second-line treatment option?

Recommendation 1.3: Allo-HSCT is recommended as a second-line treatment for patients with relapsed/refractory SAA (Strong recommendation, moderate-quality evidence).

Patients with SAA receiving IST may develop relapsed or refractory disease, necessitating alternative treatment approaches. Relapsed SAA is defined as the recurrence of pancytopenia meeting the criteria for SAA after initial hematologic recovery.^[29] Refractory SAA is characterized by the failure to achieve transfusion independence or persistently meeting SAA diagnostic criteria in blood counts and BM findings after 4–6 months of IST.^[30] Since the outcomes of second-line allo-HSCT are superior to those of repeated IST, timely identification of suitable candidates is essential. A retrospective study by Zhang *et al*^[31] compared the long-term efficacy of second-line allo-HSCT (including MSD, matched unrelated-donor [MUD], and HID) *vs.* repeated IST. Compared with patients who underwent repeated IST, patients who underwent second-line allo-HSCT exhibited higher rates of hematologic recovery at 3, 6, and 12 months and significantly improved FFS.^[31] Pediatric patients who underwent allo-HSCT also had superior OS and FFS.^[31] A multicenter prospective study by Xu *et al*^[29] specifically evaluated the long-term outcomes of second-line HID HSCT in patients with relapsed/refractory SAA. The study reported a 93.4% rate of complete hematopoietic recovery, with estimated 9-year OS and FFS rates of 85.4% and 84.0%, respectively.^[29] In addition, the posttransplant QoL significantly improved, with 74.0% of pediatric patients and 72.9% of adult patients successfully returning to school or work at the last follow-up.^[29] When no matched MSDs are available, a retrospective analysis by Zhao *et al*^[32] revealed that for 40- to 50-year-old patients with relapsed/refractory SAA, the outcomes in terms of FFS, OS, and graft-versus-host disease-free survival (GRFS) did not significantly differ between offspring donors and MUD for second-line allo-HSCT. This suggests that for patients undergoing second-line allo-HSCT, when there is a significant delay in identifying a suitable MUD, the option of using younger offspring as alternative donors should be considered. With respect to the selection of different donors for patients with SAA over 50 years old, a study by Xu *et al*^[33] revealed that there was no significant difference in 3-year OS among patients who underwent allo-HSCT from MSDs, HIDs, and URDs (100.0% *vs.* 71.8% *vs.* 60.0%, $P = 0.053$). This indicates that patients over the age of 50 years can still achieve good survival outcomes through allo-HSCT.

Clinical question 1.4: When should second-line allo-HSCT be initiated for patients who do not respond to IST?

Recommendation 1.4: Early transplant evaluation should be performed for patients who fail to achieve a response after at least 4 months of IST (Strong recommendation, strength of consensus 7.71).

The response to anti-thymocyte globulin (ATG)-based IST typically becomes evident within 3–4 months.^[1] Given the risks associated with prolonged IST, including infections, hemorrhagic complications, drug-related toxicity, and clonal evolution, previous guidelines have recommended proceeding with allo-HSCT if no hematologic response is observed within this timeframe and if a matched donor is available.^[13] These guidelines emphasize early preparation for second-line allo-HSCT if no response is observed after at least 4 months of IST.

Clinical question 1.5: Should second-line allo-HSCT be restricted to patients under 60 years of age?

Recommendation 1.5: If the patient can benefit from second-line allo-HSCT and if the patient's physical status is eligible for transplantation, the patient may be recommended for allo-HSCT with no further age restrictions. Age alone should not be a limiting factor for second-line allo-HSCT. If a comprehensive pretransplant evaluation confirms that a patient is physically fit for transplantation and may benefit from the procedure, allo-HSCT should be considered, regardless of age (Strong recommendation, strength of consensus 7.75).

As second-line allo-HSCT has demonstrated superior efficacy over repeated IST, appropriate patient selection is crucial. If a patient is deemed medically fit based on a comprehensive pretransplant assessment, second-line allo-HSCT should be considered regardless of age. Therefore, age should not be the sole criterion for transplant eligibility, which may enable more relapsed/refractory SAA patients to receive effective treatment.

Special considerations for unique patient populations

Clinical question 1.6: Are patients with non-SAA who later progress to SAA considered for allo-HSCT?

Recommendation 1.6: Patients with non-SAA who later progress to SAA are considered for allo-HSCT as a first-line treatment option (Strong recommendation, moderate-quality evidence).

Although most patients meet the SAA criteria at diagnosis, some initially present with non-SAA and later progress to SAA, necessitating reassessment of treatment strategies. A retrospective study by Liu *et al*^[34] compared treatment outcomes in three groups of patients: patients who were diagnosed with SAA at onset and were treated with first-line IST, those who progressed from non-SAA to SAA and received first-line IST, and those who progressed from non-SAA to SAA and received first-line allo-HSCT. Among patients who progressed from non-SAA to SAA, a significantly greater percentage of those in the allo-HSCT group achieved normal hematologic parameters at 6 months than those in the IST group.^[34] Furthermore, compared with the IST group, the allo-HSCT group had a

significantly higher estimated 5-year FFS rate and a lower relapse rate.^[34] These findings suggest that IST has limited efficacy in this patient population, whereas allo-HSCT may offer superior long-term outcomes.^[34]

Clinical question 1.7: Should patients with hepatitis-associated aplastic anemia (HAAA) undergo allo-HSCT?

Recommendation 1.7: The treatment principles for patients with HAAA align with those for patients with acquired SAA, and allo-HSCT should be considered accordingly (Strong recommendation, moderate-quality evidence).

HAAA is a rare subtype of aplastic anemia, and its optimal management has been evaluated in several studies. A study by Li *et al*^[35] compared outcomes between 30 patients with HAAA and 90 non-HAAA patients, all of whom underwent allo-HSCT. No significant differences were observed between the two groups in terms of estimated 5-year OS, graft-versus-host-disease (GvHD)-free failure-free survival (GFFS), engraftment success, rates of severe infections, cytomegalovirus (CMV) and Epstein-Barr virus (EBV) viremia, or incidence of acute and chronic GvHD (cGvHD).^[35] In addition, when stratified by donor type, patients with HAAA who received MSD or HID transplants had comparable survival rates, transplant-related mortality (TRM), and GvHD incidence.^[35] Similarly, a study by Ma *et al*^[36] revealed no significant differences in neutrophil engraftment time, 3-year OS, or liver event-free survival (EFS) rates between patients with HAAA and non-HAAA patients who underwent HID HSCT. These findings indicate that allo-HSCT is a viable and effective treatment option for HAAA.

Clinical question 1.8: Should patients with bone marrow failure-associated paroxysmal nocturnal hemoglobinuria (BMF/PNH) receive allo-HSCT?

Recommendation 1.8: Patients with BMF/PNH may benefit from allo-HSCT (Strong recommendation, moderate-quality evidence).

Allo-HSCT remains the only potentially curative therapy for PNH.^[37] A retrospective analysis compared outcomes in patients with BMF/PNH and classic PNH (cPNH) following allo-HSCT.^[37] This study revealed no significant difference in three-year OS between the BMF/PNH and cPNH groups and a significant reduction in PNH clone frequency following allo-HSCT.^[37] In addition, a study by Liu *et al*^[38] compared allo-HSCT outcomes between Chinese patients with PNH and those with paroxysmal nocturnal hemoglobinuria-aplastic anemia (PNH-AA) syndrome. Myeloid and platelet engraftment occurred more rapidly in the PNH group, and no significant differences were observed in 3-year OS, GFFS, or the incidence of acute GvHD (aGvHD) and cGvHD between the PNH and PNH-AA groups. These findings suggest that allo-HSCT is effective at reducing PNH clone burden and offers comparable survival outcomes in patients with BMF/PNH.

In addition to patients with SAA, treatment principles for SAA can also be applied to transfusion-dependent non-SAA patients.

Part 2. Donor selection

Clinical question 2.1: How should appropriate allo-HSCT donors be selected for newly diagnosed pediatric and adult patients under 50 years old?

Recommendation 2.1: HLA typing should be performed at diagnosis for all patients and their family members. If available, an MSD is the preferred graft source for allo-HSCT. In the absence of an MSD, alternative donor options, including HIDs and MUDs, should be evaluated based on institutional expertise, disease urgency, and patient preference. If an unmatched donor is under consideration, donor-specific anti-HLA antibody (DSA) testing is recommended (Strong recommendation, moderate-quality evidence).

International guidelines, including the British Society for Haematology Guideline (2024), the North American Pediatric Aplastic Anemia Consortium (NAPAAAC) Recommendations (2024), the Italian Association of Pediatric Hematology and Oncology (AIEOP) Guideline (2024), the American Society for Transplantation and Cellular Therapy Guidelines (2024), and the American Society of Hematology Consensus (2024), consistently identify MSD HSCT as the first-line treatment for SAA.^[1,14-17] In addition, studies in Chinese patients with SAA/vSAA have confirmed the superior therapeutic efficacy of MSD-HSCT compared with IST.^[7] Therefore, HLA typing should be performed at diagnosis for all patients and their family members, and if an MSD is identified, the MSD should be prioritized as the first-line donor choice.

A study by Shin *et al*^[39] compared the outcomes of adult SAA patients receiving allo-HSCT from MSD *vs.* URD. Although OS was significantly greater for MSD HSCT than for mismatched unrelated-donor (MMUD) HSCT, OS rates were comparable between MSD and MUD HSCT. In pediatric patients with SAA, first-line URD HSCT resulted in a 2-year EFS rate comparable to that of MSD HSCT and superior to that of IST.^[40] These findings suggest that in the absence of an MSD, MUD transplantation represents a viable first-line alternative.

In China, it is difficult for patients with SAA to obtain an MSD. Moreover, finding a MUD in the BM transplantation registry requires a long waiting period, which increases the difficulty for patients to access MUDs. Nowadays, HID HSCT is widely applied in China. Multiple studies have evaluated the efficacy of HID in SAA/vSAA patients.^[24,31,41] Wu *et al*^[25] reported that even among patients with vSAA with an absolute neutrophil count (ANC) of 0, HID HSCT resulted in significantly higher OS and complete response rates than IST did.^[25] Moreover, for patients with SAA, compared with IST, HID was associated with significantly higher 8-year FFS (83.7% *vs.* 38.5%) and a greater proportion of patients who achieved hematologic recovery (83.1% *vs.* 38.2%), and there was also a trend toward higher 8-year OS (83.7% *vs.* 75.6%) in HID than in IST.^[42] In a retrospective study by Xu *et al*,^[43] the cumulative incidence of myeloid and platelet engraftment was comparable between first-line HID and MSD HSCT at 97.75% *vs.* 97.10% and 96.63% *vs.* 95.65%,

respectively. The cumulative incidence of aGvHD was higher in HID patients than in MSD patients. However, the three-year incidence of extensive cGvHD was similar between the two groups (3.4% *vs.* 0.0%, $P = 0.426$). In another long-term study, the 9-year OS (87.1% *vs.* 89.3%) and FFS (86.5% *vs.* 88.1%) were comparable between HID and MSD. In terms of QoL after transplantation, no significant differences were found between HID and MSD either in children or adults.^[8] With respect to 40- to 50-year-old patients with SAA, relevant studies in China have also compared MSDs and HIDs. The findings of Xu *et al*^[44] revealed that the incidence of GvHD, as well as survival outcomes, was comparable between the HID and MSD groups. These data support HID as a first-line alternative in patients lacking an MSD, including patients aged 40–50 years.

Direct head-to-head comparisons between HID and MUD in the Chinese population remain limited. Recommendations for prospective studies or registry-based comparative effectiveness analyses are warranted.

When mismatched donor transplantation is considered, DSA levels are critical, as high DSA titers increase the risk of graft failure (GF) and reduce survival in patients who have undergone HLA-mismatched allo-HSCT.^[45] Yoshihara *et al*^[46] demonstrated that among patients who underwent HID HSCT, a pretransplantation DSA median fluorescence intensity (MFI) >5000 was an independent predictor of GF. Furthermore, a prospective study by Chang *et al*^[47] revealed that DSAs with an MFI $\geq 10,000$ were significantly associated with primary graft rejection (GR), whereas an MFI ≥ 2000 correlated with poor graft function. On the basis of this evidence, DSA testing is strongly recommended when mismatched donor HSCT is considered to optimize donor selection and mitigate transplant-related risks. The specific management principles may refer to those applied in transplantation for hematologic malignancies. Previous expert consensus recommended that for HSCT candidates with hematologic malignancies, the order of selection for DSA-negative HID should be as follows: Children, siblings, fathers, mothers, and collateral relatives.^[48] However, for patients with SAA, similar survival outcomes were observed when the donors were fathers, mothers, siblings, or children, while maternal donors had a higher incidence of cGvHD.^[49] In addition, ABO blood type compatibility between the donor and recipient does not impact survival outcomes, but minor ABO incompatibility can affect the incidence of grade III–IV aGvHD.^[50,51]

Clinical question 2.2: How should first-line treatment options be selected for patients with urgent clinical conditions?

Recommendation 2.2: In patients who present with life-threatening complications, such as severe or high-risk infections, fatal bleeding, or other critical conditions requiring urgent transplantation, a related donor should be prioritized (Strong recommendation, strength of consensus 8.11).

For patients with SAA/vSAA who experience life-threatening complications, such as severe infections, a high risk of sepsis, or critical bleeding, allo-HSCT should be initiated

as soon as possible. Studies have shown that allo-HSCT can still be beneficial for survival when infections are controllable before transplantation.^[52–54] Related donors, including MSDs and HIDs, are typically more accessible, whereas URD identification and matching require additional time, which may not be feasible in urgent cases. Given the need for rapid donor availability, MSDs and HIDs should be prioritized for patients requiring urgent transplantation.

Clinical question 2.3: When should unrelated cord blood transplantation (UCBT) be considered?

Recommendation 2.3: MUDs or HIDs should be prioritized over UCB (Strong recommendation, moderate-quality evidence).

Lu *et al*^[55] conducted a single-center retrospective analysis involving 240 pediatric patients with SAA to compare outcomes among different HSCT donor sources.^[55] UCBT was associated with significantly higher rates of GF, including primary graft failure and secondary graft failure (SGF), than MUD and HID HSCT were. In addition, UCBT resulted in lower rates of platelet engraftment within 180 days post-HSCT, with prolonged platelet recovery times.^[55] Furthermore, compared with MUD and HID HSCT recipients, UCBT recipients had lower 3-year FFS and GRFS rates.^[55] Given these findings, UCBT should be considered a lower-priority option when MUD or HID HSCT is available. However, further data collection or inclusion in national registries should be encouraged.

Clinical question 2.4: When should MMUDs be considered?

Recommendation 2.4: Optimal donor selection should adhere to high-resolution HLA typing, with a preference for 10/10 HLA-matched related or URDs (HLA-A, -B, -C, -DRB1, -DQB1). MMUDs with a 9/10 HLA match should not be considered equivalent to MUD; however, MMUDs may be considered an alternative in cases where no fully matched donors are available (Strong recommendation, moderate-quality evidence).

Current guidelines establish high-resolution 10/10 HLA matching as the optimal standard for donor selection, whether related or unrelated.^[1] For allo-HSCT, ideal donor matching should include high-resolution typing at HLA-A, -B, and -C (class I) and at HLA-DRB1 and -DQB1 (class II) to minimize transplant-related risks. When a fully matched donor is unavailable, MMUD transplantation (9/10 HLA match) may be considered; however, it is associated with an increased risk of complications. A multicenter retrospective study by Wu *et al*^[56] compared MMUD (9/10 HLA-matched) HSCT to MUD HSCT and IST in SAA treatment. Compared with MUD HSCT, MMUD HSCT was associated with a significantly greater incidence of grade II–III aGvHD. Given these findings, MMUD HSCT should be considered only when MUD or HID are unavailable, as it is associated with an increased risk of GvHD and other transplant-related complications.

Part 3. Pretransplant workup

Pretransplant evaluation

Clinical question 3.1: Should response to IST and HSCT outcomes be preestimated before treatment initiation?

Recommendation 3.1: All patients considered for allo-HSCT should undergo a comprehensive risk-benefit assessment comparing allo-HSCT with IST $\pm$ thrombopoietin receptor agonist (TPO-RA) to guide first-line treatment decisions (Strong recommendation, strength of consensus 8.07).

Previous guidelines have identified several prognostic factors influencing the response to IST $\pm$ TPO-RA in SAA patients.^[23] In addition, Liu *et al*^[27] developed and validated an early death risk score model to predict the outcomes of first-line IST treatment in patients with vSAA. This model enables early prognostic assessment of IST treatment and assists in determining whether IST or allo-HSCT is the most suitable first-line approach. For patients with SAA/vSAA, pretreatment evaluation should incorporate prognostic models and validated risk stratification tools to compare first-line IST $\pm$ TPO-RA treatment with allo-HSCT. This individualized approach ensures optimal treatment selection on the basis of disease severity and patient-specific risk factors.

Clinical question 3.2: Is reevaluation necessary before transplantation in patients with SAA?

Recommendation 3.2: Patients should undergo a thorough reevaluation before transplantation to confirm the diagnosis of SAA and rule out inherited bone marrow failure (IBMF) or other secondary etiologies. Recommended investigations include BM biopsy, cytogenetics, fluorescence in situ hybridization (FISH) analysis, flow cytometry, next-generation sequencing, and chromosome breakage testing (Strong recommendation, strength of consensus 8.68).

A precise diagnosis of SAA is crucial for selecting the most appropriate therapeutic strategy. Because SAA is a diagnosis of exclusion, comprehensive clinical evaluation and laboratory testing are needed.^[16] Following initial diagnosis, further examinations should be conducted to differentiate SAA from unrecognized IBMF with germline mutations and other secondary BM failure disorders. On the basis of recommendations from previous guidelines and clinical practice experience,^[16,17] we propose a standardized diagnostic approach that includes BM biopsy, cytogenetic analysis, FISH analysis, flow cytometry, next-generation sequencing, and chromosome breakage testing.

Clinical question 3.3: Should comorbidities be assessed before allo-HSCT?

Recommendation 3.3: Patients' comorbidities and physical status must be assessed before allo-HSCT (Strong recommendation, moderate-quality evidence).

Comorbidities and overall physical condition are key determinants of allo-HSCT outcomes. Several studies

have identified risk factors associated with increased treatment-related mortality (TRM) and adverse posttransplant survival. In the study by Xu *et al*,^[57] for patients with SAA who underwent HID HSCT, a longer time from diagnosis to transplantation, poor performance status as assessed by the Eastern Cooperative Oncology Group (ECOG) scale, and a higher hematopoietic cell transplantation-specific comorbidity index (HCT-CI) score were all independent risk factors for worse TRM according to the final multivariate model. Similarly, a multicenter retrospective cohort study by Zhang *et al*^[10] assessed SAA patients who received MSD or URD HSCT. Poor ECOG performance status (score ≥ 2) was the only independent predictor of adverse transplant outcomes. Given the association between comorbidities and TRM, comprehensive pretransplant evaluation is critical for risk stratification and treatment optimization. Standardized assessment tools such as the HCT-CI and ECOG performance status score should be routinely used to assess transplant eligibility and guide clinical decision-making.

Clinical question 3.4: How should iron overload be assessed before allo-HSCT?

Recommendation 3.4: Iron overload should be evaluated using serum ferritin (SF) levels, and where available, noninvasive imaging techniques such as MRI (T2* or R2*) should be used to assess cardiac and hepatic iron burden (Strong recommendation, moderate-quality evidence).

Owing to the frequent need for extensive red blood cell transfusions, patients with SAA are at high risk for iron overload, which can negatively impact allo-HSCT outcomes.^[58] Iron overload may have a negative effect on the outcomes of allo-HSCT. A study by Zhang *et al*^[58] defined high SF levels as an SF concentration ≥ 1000 ng/mL and evaluated the association between pretransplant iron burden and survival outcomes in SAA patients undergoing HSCT. In patients who underwent early transplantation (within 2 months of diagnosis), elevated SF levels were significantly associated with increased mortality.^[58] Elevated SF is also correlated with an increased incidence of bloodstream infections.^[58] Among patients receiving long-term pretransplant treatment, higher SF levels were linked to prolonged red blood cell transfusion dependence posttransplant.^[58] Therefore, SF levels should be routinely assessed before transplantation to evaluate iron overload. In addition, previous guidelines recommend incorporating noninvasive imaging techniques such as T2* or R2* MRI to assess iron deposition in the heart and liver.^[1,15,23] Where available, these imaging techniques should be incorporated into routine pretransplant evaluations to improve risk assessment. A separate study by Pan *et al*^[59] further demonstrated that patients with pretransplant iron overload (SF >1000 ng/mL) had significantly lower 1-year and three-year OS rates and higher TRM at 180 days and 1 year.

Clinical question 3.5: Is iron chelation (IC) therapy required before allo-HSCT in patients with iron overload?

Recommendation 3.5: IC therapy is recommended for patients with SF concentrations >1000 ng/mL; however,

allo-HSCT should not be delayed solely for IC (Strong recommendation, moderate-quality evidence).

In SAA patients with iron overload, Pan *et al*^[59] evaluated whether pretransplant IC therapy could improve the outcomes of allo-HSCT. In this study, SAA patients with iron overload underwent IC therapy before transplantation.^[59] Patients were classified into two groups on the basis of chelation success: the IC-successful group (SF ≤ 1000 ng/mL) and the IC-failure group (SF > 1000 ng/mL).^[59] Compared with the IC-failure group, the IC-successful group had significantly higher 1-year and 3-year OS rates, whereas 180-day and 1-year TRM rates were significantly lower.^[59] Although this study revealed improved transplant outcomes in patients with reduced SF levels, it did not establish a direct causal relationship between IC therapy and enhanced survival following allo-HSCT. Given these findings, IC therapy may be considered for patients with SF concentrations > 1000 ng/mL; however, allo-HSCT should not be postponed solely to achieve target SF levels.

Clinical question 3.6: Should patients with reproductive concerns consult an obstetrician-gynecologist before allo-HSCT?

Recommendation 3.6: Patients of reproductive age who wish to preserve fertility should consult an obstetrician-gynecologist before undergoing allo-HSCT, provided that their clinical condition allows (Strong recommendation, strength of consensus 8.43).

Most conditioning regimens for allo-HSCT lead to irreversible gonadal damage, resulting in premature ovarian insufficiency in females and impaired spermatogenesis in males.^[60] To optimize fertility preservation, patients of reproductive age should receive pretransplant counseling with an obstetrician-gynecologist or reproductive specialist. Depending on their clinical status, fertility preservation options should be discussed.

Clinical question 3.7: Should patients with psychological disorders be referred to a psychologist before allo-HSCT?

Recommendation 3.7: Patients with SAA are encouraged to consult a psychologist prior to allo-HSCT if needed. Psychological consultation is encouraged for patients with psychological disorders before they undergo allo-HSCT (Strong recommendation, strength of consensus 8.21).

SAA not only affects physical health but also has a substantial psychological impact, contributing to anxiety, depression, and emotional distress.^[15] These psychological challenges can influence treatment adherence, posttransplant recovery, and overall QoL. Given these concerns, patients experiencing psychological distress should be referred for specialized psychological evaluation and intervention.

Part 4. Conditioning regimen for patients receiving allo-HSCT

Appropriate immunosuppressive strategies can help prevent the development of GvHD and improve the

prognosis of patients.^[61] Rabbit anti-human thymocyte globulin (rATG) is a commonly used approach for the *in vivo* depletion of T cells, aiming to mitigate the development of GvHD in patients undergoing HLA-matched or HLA-mismatched allo-HCT.^[62] As recommended by the “Guidelines for the Diagnosis and Management of Aplastic Anemia in China (2022)” and “The Consensus from The Chinese Society of Hematology on Indications, Conditioning Regimens and Donor Selection for Allogeneic Hematopoietic Stem Cell Transplantation: 2021 Update”, rATG is recommended as part of the conditioning regimen for MSD, MUD, and HID-HSCT for SAA patients.^[23,48]

Clinical question 4.1: What is the recommended conditioning regimen for patients undergoing MRD or MUD-HSCT?

Recommendation 4.1: For MRD and MUD-HSCT, CyATG $\pm$ busulfan (Bu) consisting of a full dose of cyclophosphamide (Cy, 200 mg/kg) and rabbit anti-human thymocyte globulin (rATG, 10.0–12.5 mg/kg) is recommended. In high-risk patients, e.g., those with a long medical history, a history of significant hemorrhagic complications, or evidence of cardiotoxicity, Flu, rATG and Cy(FAC) $\pm$ Bu consisting of fludarabine (Flu, 120–200 mg/m²), a decreased dose of cyclophosphamide (Cy) (100–200 mg/kg), and rATG (10.0–12.5 mg/kg) is recommended (Strong recommendation, moderate-quality evidence).

Patients with SAA who undergo upfront MRD or MUD-HSCT are typically administered either the CyATG regimen or the FAC regimen. Data from the Chinese Bone Marrow Transplantation Registry (CBMTR) revealed that in MRD-HSCT patients, the median time to myeloid engraftment was 11 days (range, 8–19 days), with cumulative incidences of grade III–IV aGvHD within 100 days of HSCT and cGvHD of 1.5% and 4.4%, respectively.^[43] Furthermore, the estimated 3-year OS rate was 91.3%, whereas the estimated 3-year FFS rate reached 89.8%. A retrospective multicenter study demonstrated that for patients aged 40 years and older, the median time to neutrophil recovery was 12 days (range, 8–21 days) in MSD patients and 12 days (range, 9–22 days) in MUD patients. Notably, no cases of grade III–IV 3–4 aGvHD were observed. The incidence of cGvHD was 2.9% in the MSD group and 27.3% in the MUD group.^[10] In addition, for patients older than 50 years who received the CyATG, FAC, or Bu with FCA (BFCA) regimens, the 3-year overall survival was 100%.^[33]

Previous studies have reported that full-dose Cy is associated with cardiotoxicity and hemorrhagic cystitis, typically with a dose-dependent toxicity profile.^[63–65] On the basis of clinical experience in China, the FAC regimen may be a preferable alternative for CyATG-intolerant patients, particularly high-risk or elderly individuals. Two early phase 2 studies conducted in Korean pediatric and young adult populations evaluated FAC-based regimens for unrelated donor transplants. In 2010, Kang *et al*^[66] reported that the FAC regimen (Flu 120 mg/m², Cy 200 mg/kg, and rATG 7.5 mg/kg) achieved 100% engraftment success. However, TRM was high, with an overall survival

of 67.9%; all deaths were treatment related. Given the toxicity of Cy, in 2016 Kang *et al*^[67] reported a modified FAC regimen with a reduced Cy dosage (Flu 200 mg/m², Cy 120 mg/kg, and rATG 7.5 mg/kg), which resulted in improved outcomes regardless of whether patients received BM or peripheral blood stem cells (PBSCs) transplantation, with an OS rate of 96.6% and an EFS rate of 67.9%. These findings indicate that for Asian patients under 30 years old, the reduced-dose Cy (120 mg/kg) FAC regimen may be more suitable because of its improved safety profile.

However, a retrospective 10-year follow-up study revealed that for patients receiving PBSC transplantation from URD, the Bu-containing CyATG regimen (Bu 6.4 mg/kg, Cy 200 mg/kg, and rATG 10 mg/kg) offered superior outcomes relative to the FAC regimen (Flu 120 mg/m², Cy 160 mg/kg, and rATG 10 mg/kg), including improved OS/FFS and reduced Epstein-Barr virus infection, suggesting that the Bu-containing CyATG regimen may be the preferred choice for SAA patients undergoing URD HSCT, especially for those older than 30 years.^[68] However, it is important to note that Bu in the BCA regimen exhibits marked gonadotoxicity and may substantially elevate the risk of infertility following transplantation. Further prospective clinical trials are needed to verify the efficacy of FAC and BCA in MUD.

MRD and MUD HSCT have relatively high incidences of mixed chimerism, at 20.29% and 35.71%, respectively. Notably, the incidence of mixed chimerism was significantly greater in patients who did not receive Bu as part of their conditioning regimen. Furthermore, compared with donor chimerism, mixed chimerism was linked to a significantly lower incidence of grade II-IV aGVHD but higher rates of secondary GR and poorer OS.^[69] Thus, the addition of Bu may be necessary to reduce the incidence of mixed chimerism, and such clinical research in this area is ongoing (No. NCT06069180).

Reproductive health is a critical consideration when selecting a conditioning regimen for patients undergoing allo-HSCT. In Chinese female patients who underwent allo-HSCT, factors such as age at transplantation and the use of total body irradiation or Bu were identified as key determinants influencing the development of primary ovarian insufficiency.^[70] In a retrospective study by Borgmann-Staudt *et al*^[71], TBI was associated with gonadotoxic effects in males, whereas Bu treatment emerged as the primary treatment-related risk factor for infertility in females. In addition, initiating treatment after the age of 13 was found to further increase the risk of infertility. Given these reproductive considerations, for patients with fertility needs, fertility preservation should be considered before using BU. Some research centers in China have adopted modified FAC-based conditioning strategies with TBI (2–4 Gy on day 1) instead of Bu.^[72,73] For patients receiving TBI, local shielding of the genitals should also be carried out during the irradiation process.

An early comparative study of TBI-containing *vs.* TBI-free FAC conditioning regimen (analyzing patients from the European Society for Blood and Marrow Transplantation

database) demonstrated comparable OS between the two groups. Notably, when stratified by median age, compared with older patients, pediatric patients (<13 years) receiving the FAC regimen had significantly superior survival (87% *vs.* 60%). By comparison, the survival rates of the total body irradiation-containing FAC cohort (median age 27 years) were consistent across all age groups (79% *vs.* 78%). In addition, the incidence of cGVHD was significantly higher in the TBI-containing arm (50% *vs.* 27% in the FAC-only group).^[74] Furthermore, a retrospective study comparing conditioning regimens in pediatric SAA patients from China undergoing allo-HSCT revealed that while the time to neutrophil engraftment and 28-day survival rates were comparable between the Bu-FAC and FAC-only groups, the Bu-FAC regimen resulted in superior platelet engraftment rates ($P = 0.044$) and significantly reduced GF (0% *vs.* 20%, $P = 0.004$). The incidence of both severe (grade II-IV/III-IV) aGVHD and cGVHD was similar between the groups, as were the 3-year OS and FFS.^[75]

Clinical questions 4.2: What conditioning regimen is recommended for HID-HSCT?

Recommendation 4.2: For SAA patients undergoing HID-HSCT, a BCA regimen consisting of 6.4 mg/kg Bu, 200 mg/kg Cy, and 10 mg/kg rATG is recommended. For patients with medical comorbidities, heavy pretreatment, or advanced age, the BFCA regimen—consisting of Bu (6.4 mg/kg), Flu (120–150 mg/kg), and reduced doses of Cy (80–120 mg/kg) and rATG (7.5–10.0 mg/kg)—is recommended.

The BCA protocol is most commonly used in China for HID-HSCT.^[42,48] Patients receiving HID-HSCT with the BCA regimen had a median time for myeloid engraftment of 13 days (range, 10–21 days) and platelet recovery of 17.5 days (range, 7–101 days), with a cumulative incidence of grade III-IV aGVHD of 6%, moderate-severe cGVHD of 2.5% and 6.9% at 1 and 3 years, respectively, and both a 3-year OS and FFS of 83.5% after a median follow-up of 21.1 months.^[76] The BCA regimen is also suitable for relapsed/refractory patients with SAA, with estimated 9-year OS and FFS of 85.4% and 84.0%, respectively.^[29]

Full-dose Cy-containing regimens may face regimen-associated toxicity, such as hemorrhagic cystitis, sinusoidal obstruction syndrome, or infection. Flu is an effective immunosuppressant, and the addition of Flu with a reduction in Cy levels can reduce regimen-associated toxicity levels.^[77] Older age, a longer interval from diagnosis to transplantation, poor performance status as assessed by the ECOG, and a higher hematopoietic cell transplantation-specific comorbidity index (HCT-CI) were identified as independent risk factors for increased TRM in SAA patients undergoing HID-HSCT.^[57,78] Patients in the high-risk group were characterized by a prolonged interval from AA diagnosis to HSCT (≥ 12 months), worse performance status (ECOG score 2–3), and a greater comorbidity burden (HCT-CI score ≥ 1) before HSCT.^[57] Among high-risk patients (those with ≥ 2 risk factors for survival) receiving HID-HSCT, the BFCA regimen was associated with better outcomes than the BCA regimen.^[79]

Clinical questions 4.3: What is the conditioning regimen for patients undergoing cord blood transplant (CBT)?

Recommendation 4.3: Currently, the optimal conditioning regimen for CBT needs further investigation (Strong recommendation, strength of consensus 8.03).

Research on CBT is limited and is primarily restricted to single-center retrospective studies. Although FAC-based regimens are commonly used, the optimal conditioning regimen and dosage remains variable. A single-center study employing a regimen of Cy (100 mg/kg), rATG (12.5 mg/kg), and Flu (180 mg/m²), neutrophil engraftment was achieved in 10 cases (76.29%) with a median recovery time of 19 days (range, 15–40 days), while platelet engraftment occurred in 7 patients (53.8%) with a median recovery time of 32 days (range, 22–80 days). The cumulative incidence of grade II–IV aGVHD was 38.5%. After a median follow-up of 61 months, 6 patients survived, with predicted 5-year OS and GFFS rates of 42.9% ± 13.2% and 14.3% ± 9.4%, respectively.^[80] Recently, a case series on pediatric SAA patients treated with the BFCA regimen and receiving a single unrelated CB unit revealed that the median durations for granulocyte and platelet engraftment were 15 days and 26 days, respectively. Detailed conditioning regimen and drug dose were summarized in Table 3.^[81]

Part 5. The graft type for patients undergoing allo-HSCT

Clinical questions 5.1: What type of graft should SAA patients undergoing MSD, MUD or HID-HSCT choose?

Recommendation 5.1: PBSCs with or without BM are recommended for MSD-HSCT (Strong recommendation, strength of consensus 7.43).

For MSD-HSCT, BM is the preferred source of stem cells. When syngeneic donors are available, hematopoietic stem cells derived from peripheral blood (PB) can be used. In China, a single stem cell source, either PB or BM, accounts for 72% of MSD transplants, with PB comprising 98% of these cases.^[82] The remaining 28% of MSD transplants use multiple stem cell sources, predominantly BM+PB combinations. A meta-analysis revealed that after 2010, PBSC and BM transplants resulted in comparable 3-year OS, GvHD risk, TRM, and GF rates.^[83]

In accordance with the European Working Group on Severe Aplastic Anemia consensus on HSCT for aplastic anemia,^[84] BM is the preferred stem cell source, with unmanipulated BM ideally containing $>3.5 \times 10^8$ nucleated cells (NCs)/kg. For patients aged 35–50 years with *de novo* SAA or vSAA, a combination of BM and PBSCs has been used. In this approach, the target absolute NCs counts from both the BM and PB are $\geq 5 \times 10^8$ /kg, with CD34⁺ cells counts reaching $\geq 2 \times 10^6$ /kg of the recipient's weight.^[85]

Recommendation 5.2: PBSCs are generally accepted in MUD-HSCT (Strong recommendation, strength of consensus 8.21).

Although BM remains the preferred stem cell source, PBSCs are often the only available option. In China, nearly all MUD-HSCTs (97%) use PB as the stem cell source.^[82] A retrospective study by the Viva-Asia Blood and Marrow Transplantation Group revealed that PBSCs were much more common and that the mean NCs dose was $7.52 \pm 3.28 \times 10^8$ /kg, with CD34⁺ cells doses averaging $4.10 \pm 2.24 \times 10^6$ /kg.^[86] The target absolute NCs counts for unmanipulated BM was $>3.5 \times 10^8$ /kg, whereas for unmanipulated PBSCs, the target were $>4 \times 10^6$ CD34⁺ cells/kg but $<10 \times 10^6$ CD34⁺ cells/kg.^[84]

Recommendation 5.3: Both PBSCs alone and PBSCs combined with BM are equally recommended for HID-HSCT (Strong recommendation, strength of consensus 7.11).

In China, more than 60% of allo-HSCTs are from HIDs, and the use of multiple stem cell sources, primarily BM plus PBSCs, has become a distinctive feature of HID-HSCTs.^[82] Data from the Chinese Blood and Marrow Transplantation Registry Group indicate that PB has become the predominant source of stem cells, accounting for 77% of HID transplants.^[87]

Patients receive granulocyte colony-stimulating factor (G-CSF)-primed BM combined with PBSCs, targeting $\geq 5 \times 10^8$ NCs/kg and $\geq 2 \times 10^6$ CD34⁺ cells/kg based on recipient weight. In a retrospective multicenter study by Jiang *et al*,^[88] the graft types for upfront and salvage HID-HSCTs included PBSCs±BM or PBSCs±BM+CB. The target CD34⁺ cells dose was $\geq 2.5 \times 10^6$ /kg, with mononuclear cells not exceeding 10×10^8 NCs/kg. For patients with relapsed/refractory SAA, the recommended BM collection target was 4×10^8 NCs/kg of ideal body weight, with a minimum of 2.5×10^8 NCs/kg required for successful engraftment and outcomes.^[89]

Part 6. aGvHD prophylaxis

Clinical questions 6: What is the preferred aGvHD prophylaxis regimen for patients with SAA?

Recommendation 6.1: Cyclosporine (CsA) combined with short-term methotrexate (MTX) and mycophenolate mofetil (MMF) is recommended as the standard prophylaxis in allo-HSCT, bone marrow transplantation, and peripheral blood stem cell transplantation (Strong recommendation, moderate-quality evidence).

Recommendation 6.2: For CBT recipients, a combination of CsA and MMF is recommended, and the addition of low-dose rATG may further prevent GvHD (Strong recommendation, strength of consensus 7.45).

For HID-HSCT, the G-CSF/ATG-based “Beijing protocol” can promote haploidentical engraftment and reduce the incidence of GvHD, and CsA with short-term MTX and MMF for GvHD prophylaxis is recommended following the BCA regimen.^[90] An early retrospective study indicated that patients receiving the “Beijing protocol” achieved a median time for myeloid and platelet engraftment of 12 and 18 days, respectively, with a cumulative platelet engraftment incidence of 84.21%, a cumulative

grade II–IV aGvHD incidence of 42.1%, a cGvHD incidence of 56.2%, and an OS rate of 64.6%, with a median follow-up of 746 days for surviving patients.^[91] In a further multicenter prospective study comparing 89 cases of HID-HSCT with 69 cases of MSD-HSCT, the median time for myeloid engraftment were similar between the two groups at 12 and 11 days, with cumulative myeloid engraftment rates of 97.8% and 97.1%, respectively, while the incidence of grade II–IV aGvHD was 30.3% *vs.* 1.5%, that of grade III–IV aGvHD was 10.1% *vs.* 1.5%, and that of cGvHD was 30.6% *vs.* 4.4%.^[43]

There are only a few studies on post-transplant cyclophosphamide in China, and the application of modified post-transplant cyclophosphamide currently represents only a small-scale clinical exploration in HID-HSCT^[43] and MUD-HSCT.^[72,73] The mPTCy regimen was typically used following the FAC-based conditioning regimen.^[72,73,92]

Part 7. Follow-up and management of early posttransplantation issues

After HSCT, immune reconstitution occurs sequentially, with neutrophils recovering first (days 14–30), followed by natural killer cells (days 30–100), T cells (approximately days 100), and finally B cells, which may take up to 1–2 years.^[93] Neutrophil engraftment is typically defined as the first of three consecutive days with an ANC exceeding $0.5 \times 10^9/L$. Platelet engraftment is defined as a platelet counts greater than $20 \times 10^9/L$ and is sustained for at least 7 days without platelet transfusion.^[85]

At the time of neutrophil engraftment, donor chimerism is assessed using short tandem repeat analysis. For gender-mismatched HSCT, X/Y FISH can be used for chimerism analysis.^[94] Donor chimerism is defined as >95% donor cells, mixed chimerism as 5–95% recipient cells, and GF as <5% donor cells at any time after HSCT.^[95] The incidence of mixed chimerism is 1.93% in HID transplants, 20.29% in MRD transplants, and 35.71% in MUD transplants, and the incidence of mixed chimerism is significantly greater in patients who do not receive Bu in the conditioning regimen.^[69] Mixed chimerism tends to occur three months post-HSCT, and the chimeric status after transplantation is typically a dynamic process. Therefore, regular follow-up is necessary to monitor chimerism in SAA patients after HSCT. If a decrease in peripheral blood cell counts is observed, a chimerism evaluation should be performed at any time.^[95]

Clinical questions 7: How should engraftment be monitored following allo-HSCT, and how should chimerism, PGF, and GF be managed?

Recommendation 7.1: Long-term chimerism monitoring is essential for posttransplant care. Chimerism evaluations are recommended monthly for the first 3 months, then every 3 months from months 3–12, and every 6 months thereafter using BM or peripheral blood mononuclear cells. The frequency may be adjusted on the basis of blood counts and the degree of mixed chimerism (Strong recommendation, strength of consensus 8.24).

Recommendation 7.2: When mixed chimerism occurs, close monitoring is recommended to ensure appropriate immunosuppressant levels while tracking blood counts and donor cells proportions, interventions should also be taken when necessary (Strong recommendation, strength of consensus 8.03).

The serum concentrations of CsA and tacrolimus should be maintained within the ranges of 150–250 ng/mL and 7–12 µg/L, respectively. If the amount of recipient DNA spontaneously decreases over time, routine follow-up is recommended until full chimerism is established.

Short-term use of glucocorticoids or mycophenolic acid may be considered within the first three months to enhance immunosuppression in cases of persistent mixed chimerism. If mixed chimerism remains stable without progression, routine follow-up is recommended.

Currently, data on stable mixed chimerism are limited. A study comparing long-term stable mixed chimerism patients and full-donor chimerism patients following HSCT for nonmalignant diseases revealed no difference in infection rates over a median follow-up of 10 years. However, shortly after transplantation, the incidence of bloodstream infections was higher in the donor chimerism group. Although mixed chimerism and donor chimerism patients exhibited similar hematopoietic cell subsets, mixed chimerism patients had higher platelet counts and an increased frequency of potential natural killer T cells (CD56⁺CD8⁺ and CD94⁺CD8⁺ T cells). Overall, patients with long-term stable mixed chimerism remained in good health and appeared immunologically comparable to patients with donor chimerism, suggesting tolerance between the donor- and recipient-derived hematopoietic systems.^[96]

If the percentage of donor cells progressively decreases along with cytopenia, donor stem cell infusion can be considered when stem cells from donor peripheral blood are available. Cytopenia is defined as persistent hematologic abnormalities unresponsive to therapeutic interventions, with sustained reductions in neutrophil counts ($<0.5 \times 10^9/L$), platelet levels ($<20 \times 10^9/L$), and hemoglobin concentrations (<60 g/L) despite at least 2 weeks of appropriate treatment, including G-CSF, transfusions, or other standard therapies. Following donor stem cells infusion, the cells should be monitored closely for a minimum of 2 months. Repeated donor stem cells infusion or a second transplantation should be considered if cytopenia persists.^[95]

Recommendation 7.3: In cases of PGF, the administration of hematopoietic growth factors (such as G-CSF and thrombopoietin receptor agonist), the infusion of additional selected donor CD34⁺ stem cells or mesenchymal stem cells (MSCs), and secondary allo-HSCT may be considered (Strong recommendation, strength of consensus 8.12).

PGF is characterized by persistent cytopenia despite full donor chimerism and is assessed through the evaluation of posttransplant blood counts relative to predefined cytopenic thresholds; however, the definition of PGF varies

across different studies.^[97,98] The current international definition of PGF is primarily based on the number of affected cytopenic lineages; the thresholds for thrombocytopenia, neutropenia, and anemia; the minimum duration of cytopenia; and the time point after HSCT from which blood counts are included for cytopenia. The three most commonly used clinical definitions are comprehensively detailed in Müskens' investigation.^[97] Risk factors for the occurrence of PGF are a low dose of CD34⁺ cells in the graft, cytomegalovirus infection, GvHD, the presence of donor-specific antibodies, and iron overload. There is neither consensus nor guidelines on how to reduce the risk or manage this condition.

When PGF occurs, the treatment aims to resolve the inadequate production of leukocytes, thrombocytes, and erythrocytes.^[99] The most commonly used treatment options include growth factors (such as G-CSF and TPO-RA), infusion of a donor-derived stem cells boost, and secondary allo-HSCT.^[100,101]

A selected-donor CD34⁺ stem cells boost is an effective treatment for patients who develop PGF after allo-HSCT without rejection and in the absence of active bacterial or fungal infection, as it can enhance overall graft function without the need for additional preparative chemotherapy.^[102–104] In addition, a prospective multicenter trial reported that a single intravenous injection infusion of BM-derived MSCs from third-party donors improved hematological function in patients with PGF after allo-HSCT;^[101] within 90 days post-MSCs infusion, 53% of patients exhibited improved cytopenia in at least one cell type, and 37% achieved a complete hematological response.

Recommendation 7.4: In cases of GF, therapeutic options include G-CSF administration, boosting with selected donor CD34⁺ stem cells, and secondary allo-HSCT with the same or a different donor (Strong recommendation, low-quality evidence).

If GF occurs, there is no established standard approach, and no single drug or strategy has been definitively proven superior to manage failure. G-CSF therapy to support BM is recommended if it is not already initiated as part of the treatment protocol of the transplant center. If patients do not achieve hematological recovery by day 28 post-HSCT, infusion of cryopreserved autologous stem cells or a second transplant using related or unrelated donors can be considered.^[99,104] In a large multicenter study of second transplantations for GF in China, 70.6% of patients used a different donor, whereas the remaining 29.4% of patients retained the initial donor.^[105] Compared with second transplantation with the same donor, changing to a different donor was related to improved neutrophil (92.4% *vs.* 71.4%) and platelet engraftment (76.9% *vs.* 51.8%), reduced 1-year TRM (34.8% *vs.* 56.3%), and superior OS (61.9% *vs.* 42.7%).

Part 8. Long-term follow-up

Clinical questions 8.1: How should long-term follow-up be conducted after allo-HSCT?

Recommendation 8.1: Long-term posttransplant follow-up is essential to monitor transplant-related complications and overall patient health. Posttransplant monitoring should involve multidisciplinary evaluations of cardiovascular, pulmonary, thyroid, and skeletal systems; fertility preservation assessments; surveillance for secondary malignancies; and assessments of QoL (Strong recommendation, strength of consensus 8.71).

Patients with SAA undergoing allo-HSCT hope to achieve long-term survival. However, data on the long-term chronic health risks among Chinese SAA allo-HSCT survivors have not been reported. A study by Sun *et al*^[106] analyzed 1022 HSCT survivors and 309 sibling controls and revealed that 66% of the survivors had at least one chronic condition and that 18% reported severe or life-threatening conditions, whereas 39% and 8% of the siblings reported severe or life-threatening conditions, respectively. The 10-year cumulative incidence of any chronic health condition among survivors was 59%, whereas the incidence of severe/life-threatening conditions or death from chronic conditions reached 35%. HSCT survivors were twice as likely as siblings were to develop chronic conditions and 3.5 times more likely to experience severe/life-threatening conditions. Those with cGvHD had a 4.7-fold increased risk of severe or life-threatening conditions. A retrospective analysis of childhood allogeneic BMT revealed that compared with siblings, two-year survivors have a greater risk of CTCAE 5.0 grade 3–4 chronic health conditions, highlighting the need for long-term follow-up.^[107] Detailed follow-up recommendations and frequencies can be found in the “Chinese Expert Consensus on the Management of Long-Term Complications after Hematopoietic Stem Cell Transplantation (2023 edition)”.

Discussion

Allo-HSCT is a curative treatment for patients with SAA, either as an upfront or salvage therapy. In China, the number of patients undergoing allo-HSCT has increased annually, reaching 14,947 cases in 2023. Among these, patients with SAA accounted for 13% of all transplants. HID transplants constitute the majority of allo-HSCTs (66%).^[87] Although guidelines for the diagnosis and management of SAA exist, specific guidelines for the comprehensive management of allo-HSCT for SAA are needed to suit the current transplantation landscape in China. Therefore, these guidelines have been developed on the basis of the latest clinical research to address the clinical practice for SAA patients undergoing allo-HSCT in China.

On the basis of recent clinical practice in China, upfront allo-HSCT is recommended for newly diagnosed pediatric and adult patients under 40 years of age, as well as for those aged 40–50 years with SAA or vSAA. MRD can be used as a first-line treatment option. When a MRD is unavailable, MUD and HID-HSCT can be considered. However, there are currently insufficient data to compare MUD-HSCT and HID-HSCT in the Chinese population. A comparative study by the SAAWP EBMT revealed that for patients with SAA lacking an MSD, MUDs are the

preferable alternative donor option. The choice between MMUD and HID remains uncertain and requires further exploration.^[108] The broad availability of donors for HID significantly increases the likelihood of identifying suitable donors for patients with SAA who are in urgent need of transplantation and those without an MSD. Following HID transplantation, patients not only achieve prolonged disease-free survival but also experience significant improvements in their long-term QoL. The risk of transplantation-related complications can be mitigated through optimized conditioning regimens, such as reduced-intensity protocols. HID transplantation is also characterized by high engraftment success rates and rapid restoration of hematopoietic function.^[109] Consequently, in China, HID has emerged not only as an essential therapeutic option for patients with SAA but also as a hallmark of breakthroughs and advancements in the field of HSCT.

The conditioning regimen consists of immunosuppressive and myelosuppressive agents. The combination and intensity of the regimens are determined by the genetic disparity between the donor and recipient, the risk of rejection, and age-related complications. The CyATG-based regimen is the most commonly used conditioning regimen for SAA patients undergoing MRD and MUD. An FAC-based regimen is considered for high-risk patients in clinical practice. The addition of Bu may reduce the incidence of mixed chimerism in patients undergoing MRD and MUD; however, further clinical trials are warranted. In Chinese clinical practice, the BCA regimen serves as a standard conditioning approach. For patients with medical comorbidities, such as those who are heavily pretreated or older patients, Flu is added to reduce the dose of Cy, thereby minimizing toxicity while maintaining effectiveness.

According to the latest Chinese Blood and Marrow Transplantation Registry data (2022–2023), grafts of PBSCs alone have been used in a significantly increasing number of HSCTs in China.^[87] PBSC allografts contain greater numbers of CD34⁺ cells, are easier to collect from donors without the need for BM harvesting, and have faster engraftment, which is more likely to be sustained. However, PBSC allografts are associated with an increased incidence of cGvHD.^[110] Recent studies have shown comparable outcomes between adult acute myeloid leukemia patients who underwent HID HSCT and those who received PB alone or BM + PB.^[111] With respect to non-malignant hematological disorders, the incidence of GR was significantly lower in B-thalassemia major patients who received PBSC than in those who received BM.^[112] Recently, CB has also been widely used. The addition of CB to PBSC ± BM for upfront and salvage HID-HSCT patients revealed that the incidence of II-IV aGvHD was lower than that in the PBSC ± BM group.^[88] With the addition of unrelated CB to HID-HSCT compared with HID-HSCT alone, the 5-year GvHD-free and failure-free survival rates were similar; however, the 5-year OS was more favorable in the CB-added HID-HSCT group than in the HID-HSCT group, as was transplantation-related mortality.^[113] These findings indicate that the addition of unrelated CB helps reduce the occurrence of GvHD and improves prognosis.

In Chinese clinical practice, the most commonly used regimen for aGvHD prophylaxis in allo-HSCT recipients is the combination of calcineurin inhibitors and MTX. This same regimen is also recommended by both the AIEOP guidelines for pediatric patients receiving ATG^[15] and the Consensus Statement of the Indian Academy of Pediatrics.^[114] More clinical research is needed on mPT-Cy-based regimens for aGvHD prophylaxis in China. In addition to calcineurin inhibitor-based prophylaxis and the mPTCy regimen, posttransplant ATG is reported as a form of GvHD prophylaxis. A report from the EBMT Acute Leukemia Working Party revealed that ATG alone is less effective than PTCy is, but the combination of PTCy and ATG is superior to monotherapy.^[115]

In conclusion, the guidelines have been revised to align with the current standards of care and the latest evidence available for HSCT in China. The complexity of transplant decisions and the rarity of SAA often result in a scarcity of randomized, prospective controlled trials for many conditions. Nonetheless, regularly updated recommendations are essential to incorporate the latest advancements and enhance patient outcomes in the context of HSCT. By continuously integrating cutting-edge developments, these guidelines aim to provide a comprehensive framework for optimizing care and improving the prognosis for patients undergoing HSCT.

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Conflicts of interest

None.

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