



ASH Draft Recommendations for Aplastic Anemia

INTRODUCTION

American Society of Hematology (ASH) guidelines are based on a systematic review of available evidence. Through a structured process, a guideline panel makes judgments about the evidence and forms recommendations.

The public comment period occurs after recommendations are formed but before ASH organizational approval of the guidelines. Comments collected during the open comment period are provided to the guideline panel for review prior to finalizing the guidelines.

These draft recommendations are not final and therefore are not intended for use or citation.

To submit comments on the draft recommendations, please email guidelines@hematology.org. Evidence Profiles and Evidence to Decision Frameworks are available via links below. If you are unable to access these links, please email Natalie Martin at nmartin@hematology.org.

The public comment period for these draft recommendations is open until **May 5th, 2025.**

RECOMMENDATIONS

DEFINITIONS

- Paroxysmal Nocturnal Hemoglobinuria – PNH
- Anti-thymocyte globulin – ATG

Diagnosis evaluation tests

Paroxysmal Nocturnal Hemoglobinuria (PNH) Clone

- **Question 1:** *Should PNH clone testing vs. no test be used for patients under 20 years old with severe or very severe aplastic anemia?*
 - **Recommendation 1:** For individuals under 20 years old with severe or very severe aplastic anemia, the ASH guideline panel suggests PNH clone testing over no testing (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)
- **Question 2:** *Should PNH clone testing vs. no test be used for patients between 20 and 40 years old with severe or very severe aplastic anemia?*
 - **Recommendation 2:** For individuals between 20 and 40 years old with severe or very severe aplastic anemia, the ASH guideline panel suggests PNH clone testing over no testing (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)
- **Question 3:** *Should PNH clone testing vs. no test be used for patients over 40 years old with severe or very severe aplastic anemia?*
 - **Recommendation 3:** For individuals over 40 years old with severe or very severe aplastic anemia, the ASH guideline panel suggests PNH clone testing over no testing (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)
- **Question 4:** *Should PNH clone testing vs. no test be used for patients with severe or very severe aplastic anemia refractory to immunosuppressive therapy?*
 - **Recommendation 4:** For individuals with severe or very severe aplastic anemia refractory to immunosuppressive therapy, the ASH guideline panel suggests PNH clone testing over no testing (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)

Somatic Mutations

- **Question 5:** *Should somatic mutation testing vs. no test be used for patients under 20 years old with severe or very severe aplastic anemia?*

- **Recommendation 5.** For individuals under 20 years old with severe or very severe aplastic anemia, the ASH guideline panel suggests somatic mutations testing over no testing (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
- [Evidence Profile](#)
- [Evidence to Decision Framework](#)
- **Question 6:** *Should somatic mutation testing vs. no test be used for patients between 20 and 40 years old with severe or very severe aplastic anemia?*
 - **Recommendation 6.** For individuals between 20 and 40 years old with severe or very severe aplastic anemia, the ASH guideline panel suggests somatic mutations testing over no testing (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)
- **Question 7:** *Should somatic mutation testing vs. no test be used for patients over 40 years old with severe or very severe aplastic anemia?*
 - **Recommendation 7.** For individuals over 40 years old with severe or very severe aplastic anemia, the ASH guideline panel suggests somatic mutations testing over no testing (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)
- **Question 8:** *Should somatic mutation testing vs. no test be used for patients with severe or very severe aplastic anemia refractory to immunosuppressive therapy?*
 - **Recommendation 8.** For individuals with severe or very severe aplastic anemia refractory to immunosuppressive therapy, the ASH guideline panel suggests somatic mutations testing over no testing (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)

Telomere Length Testing

- **Question 9:** *Should telomere length testing vs. no test be used for patients under 20 years old with severe or very severe aplastic anemia?*
 - **Recommendation 9.** For individuals under 20 years old with severe or very severe aplastic anemia, the ASH guideline panel suggests conducting telomere length testing over no testing (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)

- [Evidence to Decision Framework](#)

- **Question 10:** *Should telomere length testing vs. no test be used for patients between 20 and 40 years old with severe or very severe aplastic anemia?*

- **Recommendation 10.** For individuals between 20 and 40 years old with severe or very severe aplastic anemia, the ASH guideline panel suggests conducting telomere length testing over no testing (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).

- [Evidence Profile](#)

- [Evidence to Decision Framework](#)

- **Question 11:** *Should telomere length testing vs. no test be used for patients over 40 years old with severe or very severe aplastic anemia?*

- **Recommendation 11.** For individuals over 40 years old with severe or very severe aplastic anemia, the ASH guideline panel suggests conducting telomere length testing over no testing (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).

- [Evidence Profile](#)

- [Evidence to Decision Framework](#)

- **Question 12:** *Should telomere length testing vs. no test be used for patients with severe or very severe aplastic anemia refractory to immunosuppressive therapy?*

- **Recommendation 12.** For individuals with severe or very severe aplastic anemia refractory to immunosuppressive therapy, the ASH guideline panel suggests conducting telomere length testing over no testing (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).

- [Evidence Profile](#)

- [Evidence to Decision Framework](#)

Diagnosis Good Practice Statements

- In individuals with bone marrow failure, the ASH guideline panel considers it good practice to perform a bone marrow biopsy (ungraded good practice statement).
- In individuals with bone marrow failure, the ASH guideline panel considers it good practice to obtain a detailed history of exposures, medications, infections, and other potential acquired causes of aplastic anemia (ungraded good practice statement).
- In individuals with clinical features suggestive of a germline-inherited blood disorder (e.g., Fanconi anemia), the ASH guideline considers it good practice to perform germline genetic testing (ungraded good practice statement).
- In individuals with severe or very severe aplastic anemia who are eligible for stem cell transplantation, the ASH guideline panel considers it good practice to perform HLA testing as soon as possible (ungraded good practice statement).

Frontline Therapy

Hematopoietic cell transplant with a matched sibling donor vs. Immunosuppressive therapy

- **Question 13:** *Should hematopoietic cell transplant with a matched sibling donor vs. immunosuppressive therapy be used for patients under 20 years old with severe or very severe aplastic anemia?*
 - **Recommendation 13.** For individuals under 20 years old with severe or very severe aplastic anemia who have a matched sibling donor available, the ASH guideline panel suggests a hematopoietic cell transplant with a matched sibling donor over immunosuppressive therapy (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)
- **Question 14:** *Should hematopoietic cell transplant with a matched sibling donor vs. immunosuppressive therapy be used for patients between 20 and 40 years old with severe or very severe aplastic anemia?*
 - **Recommendation 14.** For individuals between 20 and 40 years old with severe or very severe aplastic anemia who have a matched sibling donor available, the ASH guideline panel suggests a hematopoietic cell transplant with a matched sibling donor over immunosuppressive therapy (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)
- **Question 15:** *Should hematopoietic cell transplant with a matched sibling donor vs. immunosuppressive therapy be used for patients over 40 years old with severe or very severe aplastic anemia?*
 - **Recommendation 15.** For individuals over 40 years old with severe or very severe aplastic anemia who have a matched sibling donor available, the ASH guideline panel suggests immunosuppressive therapy over hematopoietic cell transplant (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)

Hematopoietic cell transplant with a matched unrelated donor vs. Immunosuppressive therapy

- **Question 16:** *Should hematopoietic cell transplant with a matched unrelated donor vs. immunosuppressive therapy be used for patients under 20 years old with severe or very severe aplastic anemia?*
 - **Recommendation 16.** For individuals under 20 years old with severe or very severe aplastic anemia, the ASH guideline panel suggests either matched unrelated hematopoietic cell transplant or immunosuppressive therapy (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)
- **Question 17:** *Should hematopoietic cell transplant with a matched unrelated donor vs. immunosuppressive therapy be used for patients between 20 and 40 years old with severe or very severe aplastic anemia?*
 - **Recommendation 17.** For individuals between 20 and 40 years old with severe or very severe aplastic anemia, the ASH guideline panel suggests either matched unrelated hematopoietic cell transplant or immunosuppressive therapy (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)
- **Question 18:** *Should hematopoietic cell transplant with a matched unrelated donor vs. immunosuppressive therapy be used for patients over 40 years old with severe or very severe aplastic anemia?*
 - **Recommendation 18.** For individuals over 40 years old with severe or very severe aplastic anemia, the ASH guideline panel suggests immunosuppressive therapy over matched unrelated hematopoietic cell transplant (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)

Hematopoietic cell transplant with a haploidentical donor vs. Immunosuppressive therapy

- **Question 19:** *Should hematopoietic cell transplant with a haploidentical donor vs. immunosuppressive therapy be used for patients under 20 years old with severe or very severe aplastic anemia?*
 - **Recommendation 19.** For individuals under 20 years of age with severe or very severe aplastic anemia, the ASH guideline panel suggests immunosuppressive therapy over

haploidentical hematopoietic cell transplant (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).

- [Evidence Profile](#)
- [Evidence to Decision Framework](#)

- **Question 20:** *Should hematopoietic cell transplant with a haploidentical donor vs. immunosuppressive therapy be used for patients between 20 and 40 years old with severe or very severe aplastic anemia?*
- **Recommendation 20.** For individuals between 20 and 40 years of age with severe or very severe aplastic anemia, the ASH guideline panel suggests immunosuppressive therapy over haploidentical hematopoietic cell transplant (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)
- **Question 21:** *Should hematopoietic cell transplant with a haploidentical donor vs. immunosuppressive therapy be used for patients over 40 years old with severe or very severe aplastic anemia?*
- **Recommendation 21.** For individuals over 40 years of age with severe or very severe aplastic anemia, the ASH guideline panel suggests immunosuppressive therapy over haploidentical hematopoietic cell transplant (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)

Second line therapy

Refractory

- **Question 22:** *Should hematopoietic cell transplant vs. second anti-thymocyte globulin- (ATG) based therapy be used for patients under 40 years old with severe or very severe aplastic anemia with no response to an initial course of immunosuppressive therapy?*
- **Recommendation 22.** For individuals under 40 years old with severe or very severe aplastic anemia with no response to an initial course of immunosuppressive therapy, the ASH guideline panel suggests hematopoietic cell transplant over second ATG-based therapy (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)

- **Question 23:** *Should hematopoietic cell transplant vs. second ATG-based therapy be used for patients between 40 and 60 years old with severe or very severe aplastic anemia with no response to an initial course of immunosuppressive therapy?*
 - **Recommendation 23.** For individuals between 40 and 60 years old with severe or very severe aplastic anemia and no response to an initial course of immunosuppressive therapy, the ASH guideline panel suggests hematopoietic cell transplant over second ATG-based therapy (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)
- **Question 24:** *Should hematopoietic cell transplant vs. second ATG-based therapy be used for patients over 60 years old with severe or very severe aplastic anemia with no response to an initial course of immunosuppressive therapy?*
 - **Recommendation 24.** For individuals over 60 years old with severe or very severe aplastic anemia and no response to an initial course of immunosuppressive therapy, the ASH guideline panel suggests either hematopoietic cell transplant or a second ATG-based therapy (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)

Relapse

- **Question 25:** *Should hematopoietic cell transplant vs. second ATG-based therapy be used for patients under 40 years old with severe or very severe aplastic anemia who respond to a first course of immunosuppressive therapy but subsequently relapse?*
 - **Recommendation 25.** For individuals under 40 years old with severe or very severe aplastic anemia who respond to a first course of immunosuppressive therapy but subsequently relapse, the ASH guideline panel suggests either hematopoietic cell transplant or a second-ATG based therapy (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)
- **Question 26:** *Should hematopoietic cell transplant vs. second ATG-based therapy be used for patients between 40 and 60 years old with severe or very severe aplastic anemia who respond to a first course of immunosuppressive therapy but subsequently relapse?*
 - **Recommendation 26.** For individuals between 40 and 60 years old with severe or very severe aplastic anemia who respond to a first course of immunosuppressive therapy but subsequently relapse, the ASH guideline panel suggests either hematopoietic cell

transplant or a second ATG-based therapy (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).

- [Evidence Profile](#)
- [Evidence to Decision Framework](#)

➤ **Question 27:** *Should hematopoietic cell transplant vs. second ATG-based therapy be used for patients over 60 years old with severe or very severe aplastic anemia who respond to a first course of immunosuppressive therapy but subsequently relapse?*

- **Recommendation 27.** For individuals over 60 years old with severe or very severe aplastic anemia who respond to a first course of immunosuppressive therapy but subsequently relapse, the ASH guideline panel suggests a second ATG-based therapy over hematopoietic cell transplant (conditional recommendation, based on very-low certainty evidence of the effects ⊕○○○).

- [Evidence Profile](#)
- [Evidence to Decision Framework](#)

Timing of second line of treatment

➤ **Question 28:** *Should a second line of treatment be done before six months vs. after six months be used in patients with severe aplastic anemia without response to immunosuppressive therapy?*

- **Recommendation 28.** In individuals with severe aplastic anemia who do not respond to immunosuppressive therapy, the ASH guideline panel suggests initiating a second-line treatment no later than six months of follow-up (conditional recommendation based on very low certainty evidence of the effects ⊕○○○).

- [Evidence Profile](#)
- [Evidence to Decision Framework](#)

➤ **Question 29:** *Should a second line of treatment be done before six months vs. after six months be used in patients with very severe aplastic anemia without response to immunosuppressive therapy?*

- **Recommendation 29.** In individuals with very severe aplastic anemia who do not respond to immunosuppressive therapy, the ASH guideline panel suggests initiating a second-line treatment as soon as it becomes clear the patient is not responding to immunosuppressive therapy, and no later than six months of follow-up (conditional recommendation based on very low certainty evidence of the effects ⊕○○○).

- [Evidence Profile](#)
- [Evidence to Decision Framework](#)

Medical Management

Antimicrobial prophylaxis

- **Question 30:** *Should mold-active antifungal prophylaxis in addition to immunosuppressive therapy vs. immunosuppressive therapy alone be used for individuals with aplastic anemia with a neutrophil count below 500 per μL ?*
 - **Recommendation 30.** In individuals with aplastic anemia with a neutrophil count below 500 per μL , the ASH guideline panel suggests mold-active antifungal prophylaxis in addition to immunosuppressive therapy (conditional recommendation based on very-low certainty evidence of the effects $\oplus\bigcirc\bigcirc\bigcirc$).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)
- **Question 31:** *Should antibacterial prophylaxis in addition to immunosuppressive therapy vs. immunosuppressive therapy alone be used for individuals with aplastic anemia with a neutrophil count below 500 per μL ?*
 - **Recommendation 31.** In individuals with aplastic anemia with a neutrophil count below 500 per μL , the ASH guideline panel suggests antibacterial prophylaxis in addition to immunosuppressive therapy (conditional recommendation based on very-low certainty evidence of the effects $\oplus\bigcirc\bigcirc\bigcirc$).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)

Eltrombopag

- **Question 32:** *Should eltrombopag in addition to immunosuppressive therapy vs. immunosuppressive therapy alone be used for adults with severe or very severe aplastic anemia?*
 - **Recommendation 32.** In adults with severe or very severe aplastic anemia undergoing immunosuppressive therapy, the ASH guideline panel suggests the addition of eltrombopag to immunosuppressive therapy (conditional recommendation, based on low certainty evidence of the effects $\oplus\oplus\bigcirc\bigcirc$).
 - [Evidence Profile](#)
 - [Evidence to Decision Framework](#)
- **Question 33:** *Should eltrombopag in addition to immunosuppressive therapy vs. immunosuppressive therapy alone be used for children with severe or very severe aplastic anemia?*
 - **Recommendation 33.** In children with severe or very severe aplastic anemia undergoing immunosuppressive therapy, the ASH guideline panel suggests the addition of



eltrombopag to the immunosuppressive therapy (conditional recommendation, based on low certainty evidence of the effects ⊕⊕○○).

- [Evidence Profile](#)
- [Evidence to Decision Framework](#)