**Module 3  
Clinical approaches for managing special patient subgroups and challenging cases**

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| **Chapters** | **Subchapters** |
| **Welcome** | Welcome |
| **Meet the expert** | Meet the expert |
| **Learning objectives** | Learning objectives |
| **Introduction** | Introduction |
| **Managing pediatric/adolescent patients with AA** | Introduction:AA in pediatric/adolescent patients |
| Following Luka’s case in practice |
| Platelet response to eltrombopag therapy |
| **Managing non-severe AA** | Introduction: non-severe AA |
| Non-severe AA case: Nadia |
| Non-severe AA case: Joanna |
| International treatment patterns in NSAA |
| Conclusion |
| **Managing pregnancy and AA** | Introduction:Pregnancy and AA |
| Post-partum care: Sasha |
| Maternal and fetal outcomes in pregnancy and AA |
| Conclusion |
| **Managing elderly patients with AA** | Introduction: elderly patients with AA |
| Managing elderly patients (> 60 years of age) |
| Recent insights and conclusion |
| **Case homepage** | Case homepage |
| **Conclusion** | Conclusion |
| **Thank you** | Thank you |

**Abbreviations**

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| **Abbreviation** | **Definition** |
| AML | Acute myeloid leukemia |
| ATG | Antithymocyte globulin |
| BMF | Bone marrow failure |
| BMAT | Bone marrow aspiration and trephine |
| BMT | Bone marrow transplant |
| BSC | Best supportive care |
| BSH | British Society for Haematology |
| CSA | Cyclosporine |
| EPAG | Eltrombopag |
| hATG | Horse antithymocyte globulin |
| IST | Immunosuppressive therapy |
| LDH | Lactate dehydrogenase |
| MDS | Myelodysplastic syndrome |
| MDT | Multidisciplinary team |
| MMF | Mycophenolate mofetil |
| NSAA | Non-severe aplastic anemia |
| PNH | Paroxysmal nocturnal hemoglobinuria |
| W+W | Watch and wait |

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| **Chapter: Welcome** | **Sub-chapter: Welcome** |
| **Text** | **Graphic/Animation/Video** |
| {Title}: **Welcome**  {1} Welcome to this interactive module on the clinical approaches for managing special patient subgroups and challenging cases. You’ll explore the latest approaches to treatment through expert insights, engaging videos, and international guidelines. Dive into real-world cases and actionable guidance to enhance your understanding and impact patient outcomes.  {2} This module will take approximately 15 minutes to complete.  When you see an underlined word, hover over it to learn more.  {footer} This activity is supported by an educational grant from Pfizer. The funder has had no input into the content. | [AA 2024 branding] |
| **Visual details** | |
| N/A | |
| **Interactivity/buttons** | |
| Add glossary entry for highlighted text as an example | |
| **References** | |
| N/A | |
| **Notes/Settings** | |
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| **Chapter: Meet the expert** | **Sub-chapter: Meet the expert** |
| **Text** | **Graphic/Animation/Video** |
| {Title}: Meet the expert  {Balloon Title}:Dr. Austin Kulasekararaj  {Balloon Subtitle} King’s College Hospital, London, UK  {Balloon text}: Dr. Austin Kulasekararaj is a consultant hematologist at King’s College Hospital (UK), specializing in aplastic anemia, bone marrow failure syndromes, PNH, MDS, and myeloid malignancies.  He is the lead of the King’s National PNH service and the national AA referral centre at King’s College Hospital (UK).  Dr. Austin Kulasekararaj holds positions in various professional organizations, including Secretary of the European Blood and Marrow Transplantation (EBMT) group Severe Aplastic Anaemia Working Party (SAAWP), Vice-Chair of the American Society of Hematology (ASH) Scientific Committee on Bone Marrow Failure, and Chair of the MDS Special Interest Group (SIG) of the British Society for Haematology (BSH). He is also an Associate Editor of the British Journal of Haematology and eJHaem, and an Editorial Board Member of Haematologica.  Dr. Kulasekararaj researches the molecular and immunological pathogenesis of MDS and AA, focusing on overlap disorders. He also coordinates several national and global clinical trials and is a scientific advisor for MDS UK and a member of the MDS National Cancer Research Network (NCRN) working group.  He has authored or co-authored over 200 articles in peer-reviewed journals and contributed to book chapters in major textbooks.  {Button 1 label} Disclosures  {Button 1 text} **Consulting/speaker (symposium/bureau):** Alexion/AstraZeneca, Amgen, Celgene/BMS, Pfizer, Novartis, Ra Pharma/UCB, Roche, SOBI, Janssen, Apellis, Agios, Biocryst, Geron, Regeneron  **Grants/research support:** Celgene/BMS and Novartis | [Austin picture]    [AK bio video] |
| **Visual details** | |
| {Title} headline 2  {Balloon} 7th option down under avatar option, large placeholder for medium on the left. Insert [Austin picture], as medium. {Balloon title} Headline 4, {Balloon text} paragraph. | |
| **Interactivity/buttons** | |
| Add glossary entry for PNH, BMF, MDS  Add {Button} underneath {Balloon} with disclosures. | |
| **References** | |
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| **Notes/Settings** | |
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| **Chapter: Learning objectives** | **Sub-chapter: Learning objectives** |
| **Text** | **Graphic/Animation/Video** |
| {Title} Learning objectives  {Text} After completing this module, you will be able to:   * Select and apply appropriate first-line and escalation treatment strategies for pediatric/adolescent patients with AA based on clinical presentation and treatment response * Differentiate appropriate management strategies for non-severe AA patients, ensuring timely intervention to prevent disease progression * Determine the safest and most effective management approach for pregnant patients with AA, balancing maternal and fetal risks * Optimize treatment decisions for elderly patients with AA by considering immunosuppressive therapy as the standard of care and assessing when to adjust therapy | Suggest PM to decide how to make this look visual |
| **Visual details** | |
| {Title} as headline  {text} top line paragraph, bullets as unordered list. | |
| **Interactivity/buttons** | |
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| **Chapter: Introduction** | **Sub-chapter: Introduction** |
| **Text** | **Graphic/Animation/Video** |
| {Title} Clinical approaches for managing special patient subgroups and challenging cases  {text 1} This case-based module will explore unique clinical strategies through the lens of a range of patient scenarios.  {text 2} To begin, click on a case below to reveal the button to proceed. You can complete the cases in any order or follow the linear path by clicking the button at the bottom of the page:  {Element 1: Managing pediatric/adolescent patients with AA}  {Element 2: Managing non-severe AA}  {Element 3: Managing pregnant patients with AA}  {Element 4: Managing elderly patients with AA} | [adolescent icon]    [non severe icon]    [pregnant icon]    [elderly icon] |
| **Visual details** | |
| {title} header, {text 1} paragraph underneath small margin to previous element, {text 2} block quotation underneath none margin to previous element. | |
| **Interactivity/buttons** | |
| Add Elements 1-4 {content selection} underneath block quotation, small margin to previous element, centre aligned.  {Element 1} add button “Click to continue to case”, centre-aligned, internal link to first page of chapter ‘Managing pediatric/adolescent patients with AA’  {Element 2} add button “Click to continue to case”, centre-aligned, internal link to first page of chapter ‘Managing non-severe AA’  {Element 3} add button “Click to continue to case”, centre-aligned, internal link to first page of chapter ‘Managing pregnant patients with AA’  {Element 4} add button “Click to continue to case”, centre-aligned, internal link to first page of chapter ‘Managing elderly patients with AA | |
| **References** | |
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| **Chapter:** Managing pediatric/adolescent patients with AA | **Sub-chapter:** Introduction: AA in **p**ediatric/adolescent patients |
| **Text** | **Graphic/Animation/Video** |
| {Title} Pediatric/adolescent patient case: Luka  {text 1} Managing aplastic anemia (AA) in pediatric and adolescent patients requires a highly individualized approach, and is dependent both on local guidance and approvals, as demonstrated by the complexity of decision-making in this case.  Luka initially presented with acute hepatitis, leading to abnormal liver function. His condition worsened, requiring ITU admission. Post-discharge, his liver function stabilized, but he developed pancytopenia, indicating **hepatitis-associated aplastic anemia (HAAA).** He was readmitted with recurrent sepsis, prompting a bone marrow analysis.  {Question text} After hearing from Austin and reading through the details in the case infographic, how would you proceed with treatment?   |  |  |  | | --- | --- | --- | | **Answers (correct answer in green)** | **Answer Related Positive Feedback** | **Answer Related Negative Feedback** | | Horse ATG + cyclosporine | Correct! This approach is recommended in absence of a suitably matched transplant donor. |  | | Cyclosporine only |  | That’s not quite right. The combination of horse ATG + cyclosporine has been shown to be more beneficial than cyclosporine alone. | | Unrelated donor transplant |  | That’s not quite right. There is no readily available matched donor, immunosuppressive therapy should be considered until one becomes available. | | Haploidentical donor transplant |  | That’s not quite right. There is no readily available matched donor, immunosuppressive therapy should be considered until one becomes available. |   PREASSESSMENT DO NOT SHOW  Solution: For pediatric/adolescent patients like Luka, horse ATG + cyclosporine should be considered as first-line in the absence of a suitably matched transplant donor. Depending on local guidance and approvals, eltrombopag may be added in a stepwise approach if there is a lack of, or inadequate response. | [AK ped case intro]  [luka case]      **{Caption} Luka’s case details.** AST, Aspartate aminotransferase; FBC, Full blood count; HLA, Human leukocyte antigen; ITU, Intensive therapy unit; PNH, Paroxysmal nocturnal hemoglobinuria. Note: profile image created with Microsoft Image Creator.  [luka investigations]    **{Caption}** **Investigations made to come to a diagnosis of acute hepatitis.** CMV, Cytomegalovirus; EBV, Epstein-Barr virus; FBC, Full blood count; Hep A-E, Hepatitis A-E; HHV, Human herpes virus; HSV, Herpes simplex virus; Parvo, Parvovirus.  [Luka bloods, BMAT, liver]    {Caption} **Results from Luka’s most recent blood, BMAT and liver examinations. \***BSHcriteria for SAA: Marrow cellularity <25% (or 25%–50% with <30% residual hematopoietic cells), plus at least two of: (a) neutrophil count <0.5 × 109/L; (b) platelet count <20 × 109/L; (c) reticulocyte count <60 × 109/L (using an automated reticulocyte count). BMAT, Bone marrow aspiration and trephine; BSH, British Society for Haematology; DEB, Diepoxybutane; Hb, Hemoglobin; WCC, White cell count. |
| **Visual details** | |
| {Title} header 3 with {text 1} underneath  Add {medium} with [luka case], add another next to it with [AK ped case intro]. Add {hotpsot} in the red next to ‘Diagnosis: Acute hepatitis’ and insert [luka investigations] in popup. Add {hotpsot} in the red next to ‘ITU admission’ and insert [Luka bloods, BMAT, liver] in popup. | |
| **Interactivity/buttons** | |
| Add glossary entry for BMAT, BSH, SAA | |
| **References** | |
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| **Chapter:** Managing pediatric/adolescent patients with AA | **Sub-chapter:** Following Luka’s case in practice |
| **Text** | **Graphic/Animation/Video** |
| {Title} Following Luka’s case in practice  {Text} In this case, it was decided to start Luka on immunosuppressive therapy in the absence of a matched related BMT donor.  Luka experienced multiple hospital readmissions due to recurrent episodes of neutropenic sepsis:  {Question text} Considering all the information about Luka’s patient journey, what would be the next best course of action?     |  |  |  | | --- | --- | --- | | **Answers (correct answer in green)** | **Answer Related Positive Feedback** | **Answer Related Negative Feedback** | | Haploidentical transplant |  | That’s not quite right. Unless there is a readily available matched related donor, addition of eltrombopag should be considered first (if available). | | Second course of ATG (horse or rabbit) |  | That’s not quite right. Addition of eltrombopag to hATG + cyclosporine has shown benefits in pediatric/adolescent patients (if available). | | Matched unrelated donor transplant |  | That’s not quite right. Unless there is a readily available matched related donor, addition of eltrombopag should be considered first (if available). | | Add eltrombopag (if available) | Correct! Eltrombopag can be added to this treatment as the response is not adequate. |  |   Solution: For pediatric/adolescent patients like Luka, in absence of a matched related donor, addition of eltrombopag to the standard of care IST regimen of horse ATG + cyclosporine should be considered upon inadequate response to hATG + cyclosporine alone. | [luka progression]  **{Caption} Luka’s progression.** ATG, Antithymocyte globulin; |
| **Visual details** | |
| {Title} header 3  Underneath {text}, add {medium} with [luka progression]  Add non-assessment question below | |
| **Interactivity/buttons** | |
| Add glossary for BMT | |
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| **Chapter:** Managing pediatric/adolescent patients with AA | **Sub-chapter:** Platelet response to eltrombopag therapy |
| **Text** | **Graphic/Animation/Video** |
| {Title} Platelet response to eltrombopag therapy  {Text} Eltrombopag (EPAG) was added to Luka’s IST regimen (hATG and CSA) after an inadequate response.  {box} EPAG was not approved in the UK as first line therapy in pediatric patients at the time of this case but was approved as a bridge to allograft in the absence of response. **Please check your local guidance and approvals before considering addition of EPAG to IST in pediatric cases.**  {text 2} After two rounds of positive treatment response and subsequent discontinuation, the decision was made to initiate a BMT with a haploidentical donor.  {conclusion text}  Pediatric/adolescent patients with AA require a highly individualized approach to monitoring and careful consideration of treatment strategy.  {Question text} After hearing from Austin and reading through the details in the case infographic, how would you proceed with treatment?   |  |  |  | | --- | --- | --- | | **Answers (correct answer in green)** | **Answer Related Positive Feedback** | **Answer Related Negative Feedback** | | Horse ATG + cyclosporine | Correct! This approach is recommended in absence of a suitably matched transplant donor. |  | | Cyclosporine only |  | That’s not quite right. The combination of horse ATG + cyclosporine has been shown to be more beneficial than cyclosporine alone. | | Unrelated donor transplant |  | That’s not quite right. There is no readily available matched donor, immunosuppressive therapy should be considered until one becomes available. | | Haploidentical donor transplant |  | That’s not quite right. There is no readily available matched donor, immunosuppressive therapy should be considered until one becomes available. |   PREASSESSMENT DO NOT SHOW  Solution: For pediatric/adolescent patients like Luka, horse ATG + cyclosporine should be considered as first-line in the absence of a suitably matched transplant donor. Depending on local guidance and approvals, eltrombopag may be added in a stepwise approach if there is a lack of, or inadequate response.  {Expansion box element 1 text} Click here to see Luka’s case details again | [luka platelet response]    **{Caption} Luka’s platelet response to eltrombopag therapy.** Upon EPAG initiation, platelet counts normalize, allowing for reduction and discontinuation after one year. Luka is readmitted shortly after with wet purpura and severe thrombocytopenia. Platelets normalize again with EPAG reinitiation, but discontinuation after 3 months results in severe thrombocytopenia.  luka case]      **{Caption} Luka’s case details.** AST, Aspartate aminotransferase; FBC, Full blood count; HLA, Human leukocyte antigen; ITU, Intensive therapy unit; PNH, Paroxysmal nocturnal hemoglobinuria. Note: profile image created with Microsoft Image Creator  [luka investigations]    **{Caption}** **Investigations made to come to a diagnosis of acute hepatitis.** CMV, Cytomegalovirus; EBV, Epstein-Barr virus; FBC, Full blood count; Hep A-E, Hepatitis A-E; HHV, Human herpes virus; HSV, Herpes simplex virus; Parvo, Parvovirus.  [Luka bloods, BMAT, liver]    {Caption} **Results from Luka’s most recent blood, BMAT and liver examinations**. **\***BSHcriteria for SAA: Marrow cellularity <25% (or 25%–50% with <30% residual hematopoietic cells), plus at least two of: (a) neutrophil count <0.5 × 109/L; (b) platelet count <20 × 109/L; (c) reticulocyte count <60 × 109/L (using an automated reticulocyte count). BMAT, Bone marrow aspiration and trephine; BSH, British Society for Haematology; DEB, Diepoxybutane; Hb, Hemoglobin; WCC, White cell count.  [Austin Luka treatment justification] |
| **Visual details** | |
| {Title} header 3  Underneath {text}, add {medium} with [luka progression], with {text 2} underneath {section divider}  {conclusion text}  Add post assessment question after  Add {expansion box} underneath question with {element 1 text} for element 1, right-aligned. In {element 2}, add{medium} with [luka case]. Add {hotpsot} in the red next to ‘Diagnosis: Acute hepatitis’ and insert [luka investigations] in popup. Add {hotpsot} in the red next to ‘ITU admission’ and insert [Luka bloods, BMAT, liver] in popup. | |
| **Interactivity/buttons** | |
| Add glossary for BSH, BMT, IST, hATG, CSA, EPAG, SAA | |
| **References** | |
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| **Chapter:** Managing non-severe AA | **Sub-chapter:** Introduction: non-severe AA |
| **Text** | **Graphic/Animation/Video** |
| {Title} Introduction: non-severe AA  {Question text} Which non-severe AA patient has the most favorable overall prognosis based on their characteristics and history?   |  |  |  | | --- | --- | --- | | **Answers (correct answer in green)** | **Answer Related Positive Feedback** | **Answer Related Negative Feedback** | | Very low neutrophil count at diagnosis, transfusion-dependent, no PNH clone, nonresponsive to treatment. |  | That’s not quite right. This patient has the risk factors of low neutrophil count at diagnosis, nonresponse to treatment, and the absence of a PNH clone may contribute to worse outcomes for this patient. | | Relatively high neutrophil count at diagnosis, achieved trilineage response at 6 months, PNH clone present at diagnosis. | Correct! This patient has both protective factors and importantly does not possess any risk factors. |  | | Relatively high neutrophil count at diagnosis, somatic mutations detected, partial response to treatment, no PNH clone. |  | That’s not quite right. This patient has the risk factor of partial response to treatment, and the absence of a PNH clone may contribute to worse outcomes for this patient. | | Relatively high neutrophil count at diagnosis, no PNH clone, persistent cytopenias, requires intermittent transfusions. |  | That’s not quite right. Although this patient had a relatively high neutrophil count at diagnosis, the absence of a PNH clone and transfusion-dependence may contribute to worse outcomes for this patient. |   PREASSESSMENT DO NOT SHOW  Solution: Presence of a PNH clone and relatively high neutrophil counts at diagnosis, as well as achieving trilineage response at 6 months are strong protective factors, indicating the most favorable overall response. Presence of somatic mutations, transfusion-dependence, and lack of treatment response are all risk factors for worse overall survival of patients with NSAA. |  |
| **Visual details** | |
| {Title} header 3  Add question below | |
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| **Chapter:** Managing non-severe AA | **Sub-chapter:** Non-severe AA case: Nadia |
| **Text** | **Graphic/Animation/Video** |
| {Title} Non-severe AA case: Nadia  {text 1} Nadia has been diagnosed with acquired non-severe aplastic anemia (NSAA):  {Question text} After reviewing the case infographic, rank the following treatment approaches by appropriateness:   |  |  |  | | --- | --- | --- | | **Answers (correct answer in green)** | **Answer Related Positive Feedback** | **Answer Related Negative Feedback** | | Watch and wait |  |  | | Cyclosporin monotherapy |  |  | | Cyclosporin + eltrombopag |  |  | | hATG + cyclosporin + eltrombopag |  |  | | Matched sibling donor bone marrow transplant |  |  |   Solution: See Austin’s explanation of his treatment approach in Nadia’s case below | [Nadia case]    **{Caption} Nadia’s case details.** \*BSH guidelines classify NSAA as not fulfilling the criteria for SAA. Criteria for SAA: Marrow cellularity <25% (or 25%–50% with <30% residual hematopoietic cells), plus at least two of: (a) neutrophil count <0.5 × 109/L; (b) platelet count <20 × 109/L; (c) reticulocyte count <60 × 109/L (using an automated reticulocyte count). BSH, British Society of Hematology; CMV, Cytomegalovirus; Hb, Hemoglobin; HLA, Human leukocyte antigen; IU/L, International units per litre; LDH, Lactate dehydrogenase; MDS, Myelodysplastic syndrome; NGS, Next-generation sequencing; NR, Normal range; PNH, Paroxysmal nocturnal hemoglobinuria; WCC, White cell count. Note: profile image created with Microsoft Image Creator.  [AK nadia case justification] |
| **Visual details** | |
| {Title} header 3  Add {medium} with [Nadia case]  Add question below | |
| **Interactivity/buttons** | |
| Add glossary for BSH, NSAA, SAA | |
| **References** | |
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| **Chapter:** Managing non-severe AA | **Sub-chapter:** Non-severe AA case: Joanna |
| **Text** | **Graphic/Animation/Video** |
| {Title} Non-severe AA case: Joanna  {text 1} Joanna’s history, presenting complaint, and the results of subsequent investigations suggested a diagnosis of NSAA:  {element 1: Watch and wait (W+W)}   * {text} **Duration:** 1 year * **Outcome:** Monitoring without active treatment   {element 2: Cyclosporin (CSA)}   * {text} **Start:** After 1 year of W+W * **Outcome:** Treatment stopped due to side effects   {element 3: Mycophenolate mofetil (MMF)}   * {text} **Duration:** 3 months * **Outcome:** No response to treatment   {element 4: Antithymocyte Globulin (ATG) and CSA)}   * {text} **Start:** After MMF treatment * **Outcome:** Developed serum sickness leading to hospital admission   {element 5: 6-month follow-up)}   * {text} **Outcome:** Bleeding phenotype improved and blood counts appear to be stabilizing, but significant health anxiety persists. | [Joanna case]    **{Caption} Joanna’s case details.** \*BSH guidelines classify NSAA as not fulfilling the criteria for SAA. Criteria for SAA: Marrow cellularity <25% (or 25%–50% with <30% residual hematopoietic cells), plus at least two of: (a) neutrophil count <0.5 × 109/L; (b) platelet count <20 × 109/L; (c) reticulocyte count <60 × 109/L (using an automated reticulocyte count). BSH, British Society of Hematology; Hb, Hemoglobin; NGS, Next-generation sequencing; PNH, Paroxysmal nocturnal hemoglobinuria; WCC, White cell count. Note: profile image created with Microsoft Image Creator.  [Joanna 6mo bloods]    **{Caption} Joanna’s blood counts after treatment.** \*BSH guidelines classify NSAA as not fulfilling the criteria for SAA. Criteria for SAA: Marrow cellularity <25% (or 25%–50% with <30% residual hematopoietic cells), plus at least two of: (a) neutrophil count <0.5 × 109/L; (b) platelet count <20 × 109/L; (c) reticulocyte count <60 × 109/L (using an automated reticulocyte count). BSH, British Society of Hematology; Hb, Hemoglobin; WCC, White cell count.  [Austin\_Joanna treatment justification] |
| **Visual details** | |
| {Title} header 3  Add {medium} with [Joanna case]  Add {text 1} with {timeline} underneath for {elements 1-5}  {element 5} add video [Joanna 6mo bloods] | |
| **Interactivity/buttons** | |
| Add glossary for NSAA, W+W, MMF, BSH, SAA | |
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| **Chapter:** Managing non-severe AA | **Sub-chapter:** International treatment patterns in NSAA |
| **Text** | **Graphic/Animation/Video** |
| {Title} International treatment patterns in NSAA  {text} A recent international observational study on NSAA treatment patterns has identified key factors influencing response rates, survival outcomes, and the impact of different therapeutic approaches.  {element 1: Response assessment}  {title} Key findings on treatment response:  {text}   * **1/3 of patients** with mild cytopenias and transfusion independence could be **monitored without treatment** * **CSA** alone or in combination (ATG or EPAG) improves hematological parameters and survival   **Response rates are similar** across treatment options:  {box}   * **EPAG may enhance response** – more patients achieved response at 12 months * **Trilineage response** is a strong predictor of long-term survival   {element 2: Clonal evolution}  {title} Genetic & disease progression insights:  {text}   * **No genetic differences** between cytopenia groups, or between treated vs. untreated patients * **Clonal evolution (progression to MDS/AML) was not linked** to clinical/hematologic features at diagnosis or EPAG treatment   {box}  Progression rates were similar between treated and untreated patients:  {element 3: Key factors affecting survival}  {title} Genetic & disease progression insights  {text} Overall survival of patients with NSAA is dependent on certain **protective** and **risk** factors: | [NSAA treatment response charts]    {Caption} **Response rates across treatment options for NSAA.** ATG, Antithymocyte globulin; CSA, Cyclosporine; EPAG, Eltrombopag; OR, Overall response. Adapted from Fattizzo B, et al. *Leukemia* 2023;37(12):2479–2485.  [Clonal evolution]    {Caption} **Rates of clonal evolution of NSAA.** Cumulative incidence of MDS/AML and PNH in patients with NSAA. 8% evolved to MDS or AML and 9% developed hemolytic PNH after more than 3 years from initial diagnosis. PNH, Paroxysmal nocturnal hemoglobinuria. Adapted from Fattizzo B, et al. *Leukemia* 2023;37(12):2479–2485.  [protective factors]    {Caption} PNH, Paroxysmal nocturnal hemoglobinuria.  [risk factors]    [NSAA factors affecting response\_PNH]    {Caption} **Overall survival in patients with NSAA divided by presence of PNH clone**. Adapted from Fattizzo B, et al. *Leukemia* 2023;37(12):2479–2485.  [NSAA factors affecting response\_NGS somatic mutations]    {Caption} **Overall survival in patients with NSAA divided by presence of mutations by next generation sequencing**. Adapted from Fattizzo B, et al. *Leukemia* 2023;37(12):2479–2485.  [NSAA factors affecting response\_response trilineage]    {Caption} **Overall survival in patients with NSAA divided by response to treatment**. Adapted from Fattizzo B, et al. *Leukemia* 2023;37(12):2479–2485.  [NSAA factors affecting response\_Transfusions 1]    **{Caption} Overall survival in patients with NSAA divided by need for platelet transfusions.** Adapted from Fattizzo B, et al. *Leukemia* 2023;37(12):2479–2485.  [NSAA factors affecting response\_Transfusions 2]    **Overall survival in patients with NSAA divided by red blood cell transfusion.** Adapted from Fattizzo B, et al. *Leukemia* 2023;37(12):2479–2485. |
| **Visual details** | |
| {title} header 3 with {text} underneath  {element 1} add {title} header 3 with {text} underneath. Under {text}, add {medium} with [NSAA charts]. Add {box} under charts.  {element 2} add {title} header 3 with {text} underneath, add {medium} next to or under with [CumI MDS PNH in NSAA]. Under {text}, add {box} under charts with text and {medium} with [clonal evolution].  {element 3} add {title} header 3 with {text} underneath. Add {carousel} underneath:  {carousel element 1} add {medium} with [protective factors]. Add {hotspot text} directly under ‘presence of PNH clones at diagnosis’ icon, with text “Click to view data”, anchor top centre, do not show icon. In popup, add {medium} with [NSAA factors affecting response\_PNH]. Add another {hotspot text} with the same settings directly under ‘Achieving a trilineage response  at 6 months’ with [NSAA factors affecting response\_response trilineage]  {carousel element 2} add {medium} with [risk factors]. Add another {hotspot text} with the same settings directly under ‘presence of somatic mutations’ with [NSAA factors affecting response\_NGS somatic mutation]. Add another {hotspot text} with the same settings directly under ‘Requirement for tranfusions’ with 2 {mediums} [NSAA factors affecting response\_transfusions 1] and [NSAA factors affecting response\_transfusions 1]. Add another {hotspot text} with the same settings directly under ‘lack of treatment response’ with [NSAA factors affecting response\_response trilineage]. | |
| **Interactivity/buttons** | |
| {elements 1-3} tabs.  Add glossary for NSAA, ATG, CSA, PNH, MDS, AML, EPAG  Add button at the bottom of the page “References” with references linked | |
| **References** | |
| [Fattizzo B, et al. *Leukemia* 2023;37(12):2479–2485.](https://pmc.ncbi.nlm.nih.gov/articles/PMC10681892/) | |
| **Notes/Settings** | |
| Do not show learning objective or chapter number.  Note bold words | |

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| **Chapter:** Managing non-severe AA | **Sub-chapter:** Conclusion |
| **Text** | **Graphic/Animation/Video** |
| {Title} Conclusion  {text} Treatment of NSAA should be focused on preventing progression and careful consideration of patient characteristics.  {Question text} After reviewing this section, does your answer change for the following question? Which non-severe AA patient has the most favorable overall prognosis based on their characteristics and history?   |  |  |  | | --- | --- | --- | | **Answers (correct answer in green)** | **Answer Related Positive Feedback** | **Answer Related Negative Feedback** | | Very low neutrophil count at diagnosis, transfusion-dependent, no PNH clone, nonresponsive to treatment. |  | That’s not quite right. This patient has the risk factors of low neutrophil count at diagnosis, nonresponse to treatment, and the absence of a PNH clone may contribute to worse outcomes for this patient. | | Relatively high neutrophil count at diagnosis, achieved trilineage response at 6 months, PNH clone present at diagnosis. | Correct! This patient has both protective factors and importantly does not possess any risk factors. |  | | Relatively high neutrophil count at diagnosis, somatic mutations detected, partial response to treatment, no PNH clone. |  | That’s not quite right. This patient has the risk factor of partial response to treatment, and the absence of a PNH clone may contribute to worse outcomes for this patient. | | Relatively high neutrophil count at diagnosis, no PNH clone, persistent cytopenias, requires intermittent transfusions. |  | That’s not quite right. Although this patient had a relatively high neutrophil count at diagnosis, the absence of a PNH clone and transfusion-dependence may contribute to worse outcomes for this patient. |   Solution: Presence of a PNH clone and relatively high neutrophil counts at diagnosis, as well as achieving trilineage response at 6 months are strong protective factors, indicating the most favorable overall response. Presence of somatic mutations, transfusion-dependence, and lack of treatment response are all risk factors for worse overall survival of patients with NSAA. |  |
| **Visual details** | |
| {Title} header 3 add underneath {text}, Add question below | |
| **Interactivity/buttons** | |
| Add {button} at bottom of page “Click here to view cases”, internal link to Case homepage chapter  Add glossary for NSAA | |
| **References** | |
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| **Notes/Settings** | |
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| **Chapter:** Managing pregnancy and AA | **Sub-chapter:** Introduction:Pregnancy and AA |
| **Text** | **Graphic/Animation/Video** |
| {Title} Pregnancy and AA case: Sasha  {text 1} Managing AA in a patient who is pregnant requires close monitoring and an MDT approach between hematologists and obstetricians.  Sasha was diagnosed with polyarticular juvenile rheumatoid arthritis at the age of 15 and has undergone a range of pharmacologic and surgical treatment for her condition. Intermittent, mild thrombocytopenia was detected almost a decade after her diagnosis, and after falling pregnant, experiences progressive cytopenia in all blood cell lineages. Her BMAT indicates a diagnosis of aplastic anemia.  {Question text} After hearing from Austin and reading through the details in the case infographic, how would you proceed with treatment?     |  |  |  | | --- | --- | --- | | **Answers (correct answer in green)** | **Answer Related Positive Feedback** | **Answer Related Negative Feedback** | | Immediately look for a matched related bone marrow transplant donor. |  | That’s not quite right. Bone marrow transplant would not be appropriate during pregnancy. | | Cyclosporin monotherapy |  | That’s not quite right. There may be possible complications with side effects of CSA. | | Initiate supportive care of weekly red cell and platelet transfusions | Correct! Continuing the best supportive care for Sasha with careful monitoring would be the best approach in this case. |  | | Horse antithymocyte globulin + cyclosporin + eltrombopag |  | That’s not quite right. Careful consideration is needed with this approach due to potential fetal effects. |   DO NOT SHOW PREASSESSMENT  Solution: Bone marrow transplantation should only be considered before pregnancy or postpartum, and side effects and fetal effects from immunosuppressive therapy should be heavily considered before initiating during pregnancy. Optimized supportive care in the form of weekly red cell and platelet transfusions should be continued with the hope that cytopenias remit post-delivery. | [AK Sasha case intro]  [Sasha case]    **{Caption} Sasha’s case details.** BM, Bone marrow; IOL, induction of labor; MGP, Matrix Gla protein; MTX, Methotrexate; PNH, paroxysmal nocturnal hematoglubinuria; RTX, Rituximab; SNP, single nucleotide polymorphism; TCR, T-cell receptor. Note: profile image created with Microsoft Image Creator. |
| **Visual details** | |
| {Title} header 3  Add {medium} with [Nadia case] | |
| **Interactivity/buttons** | |
| Add glossary for MDT, BMAT | |
| **References** | |
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| **Chapter:** Managing pregnancy and AA | **Sub-chapter:** Sasha:post-partum care |
| **Text** | **Graphic/Animation/Video** |
| {Title} 4 months post-partum  {text1} Sasha delivered her baby, but unfortunately, she is still suffering from AA.  {text2} After blood tests and BMAT examination, concerns about PNH arose, leading to further investigations:  {text 3} From PNH test results it is clear Sasha has an expanding PNH clone population which requires imminent management, however, her most recent blood test shows she is **severely thrombocytopenic (platelet count <10 x 109/L)**  {Element 1} {box} {text} 4 months post-partum, ATG/CSA was initiated  {Element 2} {text} Three months after treatment initiation, Sasha’s blood counts are improving and her dependence on transfusion decreases, however, her bilirubin/LDH levels combined with additional symptoms are still affecting her.  {Element 3} {title}National PNH MDT meeting  {text} Sasha’s case was put forward and discussed in a national PNH MDT meeting:   1. Sasha was commenced on ravulizumab based on exceptional criteria 2. Sasha’s **blood counts normalized,** and she became **symptom-free** | [Sasha 4mo postpartum]    **{Caption} Sasha’s blood counts and BMAT results 4 months after birth of her child.** Sasha’s blood counts and BMAT examination results indicate no improvement in aplastic anemia and prompts concern about progression to PNH. **\***BSHcriteria for SAA: Marrow cellularity <25% (or 25%–50% with <30% residual hematopoietic cells), plus at least two of: (a) neutrophil count <0.5 × 109/L; (b) platelet count <20 × 109/L; (c) reticulocyte count <60 × 109/L (using an automated reticulocyte count). BMAT, Bone marrow aspirate trephine; Hb, hemoglobin, WCC, White cell count.  [Sasha PNH]    **{Caption} Sasha’s PNH testing results 4 months after birth of her child.** Both bilirubin and LDH levels were found to be high. Granulocytes are shown to increase in PNH clone population over time; just over half of Sasha’s leukocytes are PNH clones.BMAT, Bone marrow aspirate trephine; Hb, hemoglobin; WCC, White cell count.  [sasha 3 mo post ATG]    {caption}**Sasha’s blood counts are improving with ATG/CSA immunotherapy, but her bilirubin/LDH levels are not ideal, and additional symptoms are still affecting her. \***BSHcriteria for SAA: Marrow cellularity <25% (or 25%–50% with <30% residual hematopoietic cells), plus at least two of: (a) neutrophil count <0.5 × 109/L; (b) platelet count <20 × 109/L; (c) reticulocyte count <60 × 109/L (using an automated reticulocyte count).BSH, British Society for Haematology;Hb, hemoglobin; LDH, Lactate dehydrogenase; ULN, Upper limit of normal; WCC, White cell count  [Austin Sasha ATG/CSA justification] |
| **Visual details** | |
| {Title} header 3, then {text 1}.  Add {medium} with [Sasha 4mo postpartum]  Add {text2} underneath, then add {medium} below with [Sasha PNH]  Add {text 3} underneath, add {medium} with [Austin Sasha ATG/CSA justification]  {element 1} ensure box stands out so we know she has new treatment  {element 2} Add {text} with {medium} below, add [sasha 3 mo post ATG]  {element 3} Add {title} with numbered list below {text} | |
| **Interactivity/buttons** | |
| {Elements 1-3} expansion box  Add glossary for LDH, CSA, ATG, PNH, MDT, BMAT, BSH, SAA | |
| **References** | |
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| **Chapter:** Managing pregnancy and AA | **Sub-chapter:** Maternal and fetal outcomes in pregnancy and AA |
| **Text** | **Graphic/Animation/Video** |
| {Title} Maternal and fetal outcomes in pregnancy and AA  {text1} A recent single-center retrospective cohort study examined 70 pregnancies in 50 women over 25 years who experienced:   * Relapse of known AA * *De novo* occurrence of BMF during pregnancy | [pregnancy in AA study]    **Key findings, risk factors, and outcomes of pregnant patients with AA or *de novo* occurrence of BMF during pregnancy.** Adapted from Bortolotti M, et al. *Am J Hematol* 2024;99(8):1674–1650. |
| **Visual details** | |
| {Title} header 3, then {text 1}.  Add {medium} with [pregnancy in AA study] | |
| **Interactivity/buttons** | |
| Add ‘references’ button bottom left of section  Add glossary for BMF | |
| **References** | |
| [Bortolotti M, et al. *Am J Hematol* 2024;99(8):1674–1650.](https://onlinelibrary.wiley.com/doi/10.1002/ajh.27372) | |
| **Notes/Settings** | |
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| **Chapter:** Managing pregnancy and AA | **Sub-chapter:** Conclusion |
| **Text** | **Graphic/Animation/Video** |
| {Title} Conclusion  {text1} **Conclusion**  Effective management of pregnant patients with AA requires close MDT collaboration.  Key aspects include:   * **Supportive Care**: Ensure transfusions and address reversible factors. * **Cyclosporine A (CSA)**: Safe to start or continue but monitor for side effects. * **PNH Clone Monitoring**:   + **>10%**: Prophylactic low molecular weight heparin (LMWH)   + **>20%**: Eculizumab, continued for at least 3 months postpartum   These measures are vital for optimizing maternal and fetal outcomes.  {Question text} Considering the previous information, would you alter your treatment approach for Sasha?     |  |  |  | | --- | --- | --- | | **Answers (correct answer in green)** | **Answer Related Positive Feedback** | **Answer Related Negative Feedback** | | Immediately look for a matched related bone marrow transplant donor. |  | That’s not quite right. Bone marrow transplant would not be appropriate during pregnancy. | | Cyclosporin monotherapy |  | That’s not quite right. There may be possible complications with side effects of CSA. | | Initiate supportive care of weekly red cell and platelet transfusions | Correct! Continuing the best supportive care for Sasha with careful monitoring would be the best approach in this case. |  | | Horse antithymocyte globulin + cyclosporin + eltrombopag |  | That’s not quite right. Careful consideration is needed with this approach due to potential fetal effects. |   Solution: Bone marrow transplantation should only be considered before pregnancy or postpartum, and side effects and fetal effects from immunosuppressive therapy should be heavily considered before initiating during pregnancy. Optimized supportive care in the form of weekly red cell and platelet transfusions should be continued with the hope that cytopenias remit post-delivery. | [Sasha case]  A screenshot of a computer  AI-generated content may be incorrect.  **{Caption} Sasha’s case details.** BM, Bone marrow; IOL, induction of labor; MGP, Matrix Gla protein; MTX, Methotrexate; PNH, paroxysmal nocturnal hematoglubinuria; RTX, Rituximab; SNP, single nucleotide polymorphism; TCR, T-cell receptor. Note: profile image created with Microsoft Image Creator.  [AK pregnancy conclusion] |
| **Visual details** | |
| {Title} header 3, then {text 1}.  Add {medium} with [Nadia case] | |
| **Interactivity/buttons** | |
| Add {button} at the bottom of page “Click here to view cases”, internal link to Case homepage chapter  Add glossary for MDT, PNH, | |
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| **Chapter:** Managing elderly patients with AA | **Sub-chapter:** Introduction: elderly patients with AA |
| **Text** | **Graphic/Animation/Video** |
| {Title} Introduction: elderly patient case  {text1} 83-year-old male, Lee, was diagnosed with **severe AA in the context of hematuria**. He required weekly transfusions and was initiated on CSA + EPAG. Within 9 months, he became transfusion independent, and EPAG was discontinued while continuing CSA.  {Question text} After hearing from Austin and reading through the details in the case infographic, how would you proceed?   |  |  |  | | --- | --- | --- | | **Answers (correct answer in green)** | **Answer Related Positive Feedback** | **Answer Related Negative Feedback** | | Initiate ATG |  | That’s not quite right. IST is the standard of care for elderly patients, and as eltrombopag was recently discontinued, it’s best to reinitiate. | | Continue cyclosporin monotherapy |  | That’s not quite right. As eltrombopag was recently discontinued, it’s best to reinitiate. | | Watch and wait |  | That’s not quite right. IST is the standard of care for elderly patients, and as eltrombopag was recently discontinued, it’s best to reinitiate. | | Reinitiate eltrombopag | Correct! IST is the standard of care for elderly patients, and the removal of eltrombopag caused the drop in platelet levels. |  | | Add androgen (e.g., danazol 200 mg BID for 3–6 months) |  | That’s not quite right. As eltrombopag was recently discontinued, it’s best to reinitiate before considering addition of androgens. |   PREASSESSMENT DO NOT SHOW IN PREASSESSMENT  Solution:  IST is the standard of care for elderly patients, and as eltrombopag was recently discontinued, it’s best to reinitiate it to see if platelet levels are restored. The addition of androgens (such as danazol) or ATG should be considered if reinitiation of eltrombopag does not improve the patient’s condition. | [AK elderly intro]  [Elderly case\_history]      **{Caption} Lee’s history, investigations and current status.** CSA, Cyclosporine; EPAG, Eltrombopag. Note: profile image created with Microsoft Image Creator.  [Elderly case\_at diagnosis]    **{Caption} Blood, BMAT, and PNH test results at diagnosis of AA. \***BSHcriteria for SAA: Marrow cellularity <25% (or 25%–50% with <30% residual hematopoietic cells), plus at least two of: (a) neutrophil count <0.5 × 109/L; (b) platelet count <20 × 109/L; (c) reticulocyte count <60 × 109/L (using an automated reticulocyte count). BMAT, Bone marrow aspirate trephine; Hb, hemoglobin, WCC, White cell count. BSH, British Society for Haematology; Hb, Hemoglobin; MDS, Myelodysplastic syndrome; MGP; Matrix gla protein; PNH, Paroxysmal nocturnal hemoglobinuria**;** WCC, White cell count.  [Elderly case\_ Feb 2023]    **{Caption} Blood test results upon discontinuation of EPAG. \***BSHcriteria for SAA: Marrow cellularity <25% (or 25%–50% with <30% residual hematopoietic cells), plus at least two of: (a) neutrophil count <0.5 × 109/L; (b) platelet count <20 × 109/L; (c) reticulocyte count <60 × 109/L (using an automated reticulocyte count). BMAT, Bone marrow aspirate trephine; Hb, hemoglobin, WCC, White cell count. BSH, British Society for Haematology; CSA, Cyclosporine; EPAG, Eltrombopag; Hb, Hemoglobin; WCC, White cell count. |
| **Visual details** | |
| {Title} header 3, then {text 1}.  Add {media section} underneath, with [Elderly case\_history]. Add {hotspot} in the red space next to diagnosis, in popup add {medium} [Elderly case\_at diagnosis]. Add {hotspot} in the red space next to current status box, in popup add {medium} [Elderly case\_ Feb 2023].  Add question underneath | |
| **Interactivity/buttons** | |
| Add hotspots on media section as above.  Add glossary for CSA, EPAG, BMAT, PNH, BSH, SAA | |
| **References** | |
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| **Chapter:** Managing elderly patients with AA | **Sub-chapter:** Managing elderly patients (> 60 years of age) |
| **Text** | **Graphic/Animation/Video** |
| {Title} Managing elderly patients (> 60 years of age)  {Box} **IST is the standard of care for elderly patients with AA**   * **Main issues**: Treatment toxicity and burden   {Flipcard 1 side 1} **Treatment choice**  {Flipcard 1 side 2}  Several factors should be considered in your treatment choice   * Individualized assessment of fitness * Rapidity of response required * Patient choice   {Flipcard 2 side 1} **Treatment options**  {Flipcard 2 side 2}   * ATG + CSA * CSA * Oxymetholone or danazol * Alemtuzumab * BSC | [choice]    [options] |
| **Visual details** | |
| {Title} header 3, then {box} with attention icon.  Add [choice] under header for {Flipcard 1 side 1}  Add [options] under header for {Flipcard 2 side 1} | |
| **Interactivity/buttons** | |
| Add hotspots on media section as above. Add glossary for IST, ATG, CSA, BSC | |
| **References** | |
| [Fattizo B, et al. *Am J Hematol* 2025;100(4): 584–591.](https://onlinelibrary.wiley.com/doi/full/10.1002/ajh.27611) | |
| **Notes/Settings** | |
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| **Chapter:** Managing elderly patients with AA | **Sub-chapter:** Recent insights and conclusion |
| **Text** | **Graphic/Animation/Video** |
| {title} Recent insights  {tabs element 1: Treatment algorithm for elderly patients} {tabs element 2: When to use androgens}  {text} A retrospective study of 274 patients across 82 centers on the current use of androgens in BMF disorders found:   * **Limited efficacy:** Only 6% achieved complete remission * **Best use case:** Improved failure-free survival when used **after** second-line treatments * **Toxicity:** Manageable but includes liver and endocrine effects * **Current role:** Now a third-line option, mainly for patients ineligible for immunosuppressive therapy or transplant   {Question text} Taking this into account, would you change your approach to Lee’s treatment (revisit case details below)?   |  |  |  | | --- | --- | --- | | **Answers (correct answer in green)** | **Answer Related Positive Feedback** | **Answer Related Negative Feedback** | | Initiate ATG |  | That’s not quite right. IST is the standard of care for elderly patients, and as eltrombopag was recently discontinued, it’s best to reinitiate. | | Continue cyclosporin monotherapy |  | That’s not quite right. As eltrombopag was recently discontinued, it’s best to reinitiate. | | Watch and wait |  | That’s not quite right. IST is the standard of care for elderly patients, and as eltrombopag was recently discontinued, it’s best to reinitiate. | | Reinitiate eltrombopag | Correct! IST is the standard of care for elderly patients, and the removal of eltrombopag caused the drop in platelet levels. |  | | Add androgen (E.g., danazol 200 mg BID for 3–6 months) |  | That’s not quite right. As eltrombopag was recently discontinued, it’s best to reinitiate before considering addition of androgens. |   Solution:  IST is the standard of care for elderly patients, and as eltrombopag was recently discontinued, it’s best to reinitiate it to see if platelet levels are restored. The addition of androgens (such as danazol) or ATG should be considered if reinitiation of eltrombopag does not improve the patient’s condition.  {Expansion box element 1 text} Click here to see Lee’s case details again | [treatment algorithm for elderly]    **{Caption}** Treatment algorithm for the management of non-severe, severe/very severe aplastic anemia (NSAA, SAA/VSAA) elderly patients. ATG, Anti-thymocyte globulin; BSC, Best supportive care; CYA, Cyclosporine A; EPAG, Eltrombopag; NR, No response; R, Response. Adapted from Fattizo B, et al. *Am J Hematol* 2025;100(4): 584–591.  [androgen treatment]    **Clinical outcomes of androgen treatment in acquired bone marrow failure patients.** (A) Response rates of patients with acquired disorders. PR: Partial remission; CR: Complete remission; SD: Stable disease; N: Total number of patients with complete information for the analysis of response (at 3 months and 6 months after androgen start). Percentages show response rate. Kaplan-Meyer estimates of (B) overall survival (OS), (C) transplant-free survival (TFS), and (D) failure-free survival (FFS).  Diagrams adapted from Pagliuca, et al. *Haematologica* 2024;109(3):765–776.  [Austin elderly intro]  [Elderly case\_history]    **{Caption} Lee’s history, investigations and current status.** CSA, Cyclosporine; EPAG, Eltrombopag. Note: profile image created with Microsoft Image Creator.  [Elderly case\_at diagnosis]    **{Caption} Blood, BMAT, and PNH test results at diagnosis of AA. \***BSHcriteria for SAA: Marrow cellularity <25% (or 25%–50% with <30% residual hematopoietic cells), plus at least two of: (a) neutrophil count <0.5 × 109/L; (b) platelet count <20 × 109/L; (c) reticulocyte count <60 × 109/L (using an automated reticulocyte count). BMAT, Bone marrow aspirate trephine; Hb, hemoglobin, WCC, White cell count. BSH, British Society for Haematology; Hb, Hemoglobin; MDS, Myelodysplastic syndrome; MGP; Matrix gla protein; PNH, Paroxysmal nocturnal hemoglobinuria**;** WCC, White cell count.  [Elderly case\_ Feb 2023]    **{Caption} Blood test results upon discontinuation of EPAG. \***BSHcriteria for SAA: Marrow cellularity <25% (or 25%–50% with <30% residual hematopoietic cells), plus at least two of: (a) neutrophil count <0.5 × 109/L; (b) platelet count <20 × 109/L; (c) reticulocyte count <60 × 109/L (using an automated reticulocyte count). BMAT, Bone marrow aspirate trephine; Hb, hemoglobin, WCC, White cell count. BSH, British Society for Haematology; CSA, Cyclosporine; EPAG, Eltrombopag; Hb, Hemoglobin; WCC, White cell count.  [AK elderly case conclusions] |
| **Visual details** | |
| Add {medium} in {tabs element 1} with [treatment algorithm for elderly]  Add {text} then {medium} in tabs element 2 with [androgen treatment]  Add question underneath tabs  Add {expansion box} underneath question with {element 1 text} for element 1, right aligned. In {element 2}, add [Elderly case\_history]. Add {hotspot} in the red space next to diagnosis, in popup add {medium} [Elderly case\_at diagnosis]. Add {hotspot} in the red space next to current status box, in popup add {medium} [Elderly case\_ Feb 2023].  Add question underneath | |
| **Interactivity/buttons** | |
| {Tabs} {Question}  {expansion box} Add hotspots on media section as above.  Add glossary for BMAT, PNH, EPAG, BSH, SAA | |
| **References** | |
| [Fattizzo B, et al. *Am J Hematol* 2025;100(4):584–591.](https://onlinelibrary.wiley.com/doi/full/10.1002/ajh.27611)  [Pagliuca, et al.](https://haematologica.org/article/view/11088) *[Haematologica](https://haematologica.org/article/view/11088)* [2024;109(3):765–776.](https://haematologica.org/article/view/11088) | |
| **Notes/Settings** | |
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| **Chapter:** Case homepage | **Sub-chapter: Case homepage** |
| **Text** | **Graphic/Animation/Video** |
| {Title} Clinical approaches for managing special patient subgroups and challenging cases  {text 2} To continue, click on a case below to reveal the button to proceed. You can complete the cases in any order or follow the linear path by clicking the button at the bottom of the page:  {Element 1: Managing pediatric/adolescent patients with AA}  {Element 2: Managing non-severe AA}  {Element 3: Managing pregnant patients with AA}  {Element 4: Managing elderly patients with AA} | [adolescent icon]  A red line drawing of a child and child  AI-generated content may be incorrect.  [non severe icon]  A red thermometer on a black background  AI-generated content may be incorrect.  [pregnant icon]  A red line drawing of a pregnant person  AI-generated content may be incorrect.  [elderly icon]  A red line drawing of two people  AI-generated content may be incorrect. |
| **Visual details** | |
| {title} header, {text 1} paragraph underneath small margin to previous element, {text 2} block quotation underneath none margin to previous element. | |
| **Interactivity/buttons** | |
| Add Elements 1-4 {content selection} underneath block quotation, small margin to previous element, centre aligned.  {Element 1} add button “Click to continue to case”, centre-aligned, internal link to first page of chapter ‘Managing pediatric/adolescent patients with AA’  {Element 2} add button “Click to continue to case”, centre-aligned, internal link to first page of chapter ‘Managing non-severe AA’  {Element 3} add button “Click to continue to case”, centre-aligned, internal link to first page of chapter ‘Managing pregnant patients with AA’  {Element 4} add button “Click to continue to case”, centre-aligned, internal link to first page of chapter ‘Managing elderly patients with AA | |
| **References** | |
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| **Chapter:** Conclusion | **Sub-chapter:** Conclusion |
| **Text** | **Graphic/Animation/Video** |
| {Title} Conclusion  {text 1}   * Effective management of special patient subgroups and challenging cases in AA requires a **multidisciplinary, patient-centered approach** * **Tailored interventions** are essential for pediatric/adolescent, pregnant, elderly, and non-severe cases * **Collaborative care and vigilant monitoring** help ensure optimal treatment outcomes * **Flexibility and individualization** in treatment plans are key to addressing each patient’s unique clinical context * Thoughtful **adaptation of strategies** enhances overall care quality and patient outcomes | [AK conclusion and thankyou] |
| **Visual details** | |
| {title} header, {text 1} paragraph underneath small margin to previous element, {text 2} block quotation underneath none margin to previous element. | |
| **Interactivity/buttons** | |
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