Optimizing Transfusion Support for Patients with Myelodysplastic Syndrome

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Disclosure

• Presenter: Dr. Yulia Lin
• Relationships with commercial interests: None
Case Study

- 72 M with myelodysplastic syndrome (MDS) and severe anemia, not responding to treatment
- The hematologist asks.....
  - Are there transfusion guidelines for outpatients?
  - Any blood bank testing or measures that I need to order to help my patient?
Objectives

At the end of the presentation, attendees will be able to:

• Compare the approach to transfusion in patients with MDS with the approach to transfusion in hospitalized patients
• Explain the quality of life considerations for transfusion in patients with MDS
• Discuss the potential complications of transfusion in patients with MDS, their prevention and their management
What is MDS?

- Myeloid neoplasm
- Clonal proliferation
- Abnormal (dys) formation (plasis) of hematopoietic stem cells (myelo)
- Ineffective hematopoiesis, cytopenias, risk of evolution to AML
- Incidence 4-5 per 100,000 persons per year (likely underestimated)
- Median age: 70 years

Cazzola et al. NEJM 2020;383:1358-74
MDS and Transfusion Burden

• 2\textsuperscript{nd} leading indication for transfusion amongst hematologic diseases and \(\sim 7.2\%\) of transfused pts

• Most patients with MDS become transfusion-dependent
  – 2311 pts in 1\textsuperscript{st} 4 yrs after diagnosis (Swedish study)

<table>
<thead>
<tr>
<th>IPSS-R</th>
<th>RBCs in 1\textsuperscript{st} 4 y</th>
<th>PLTs in 1\textsuperscript{st} 4 y</th>
<th>Cost ($USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low</td>
<td>25</td>
<td>4</td>
<td>$8,805</td>
</tr>
<tr>
<td>High risk</td>
<td>171</td>
<td>66</td>
<td>$80,106</td>
</tr>
</tbody>
</table>

(Note: RBC unit $169 USD)

Zhao et al. Vox Sanguinis 2020 Nov 18; epub ahead of print
Impact of Transfusion on MDS

- Transfusion dependence associated with worse outcomes
  - ↓ overall survival
  - ↑ progression to AML
  - ↑ non-leukemic death (infection, bleeding, CV events)
  - ↑ cost of illness, medical costs (hospitalization, ER visit ~ 3x higher)
  - ↓ quality of life: physical, emotional and social domains

Braga Lemos et al. Eur J Haematol 2021; Epub ahead of print (Systematic Review)
Hiwase et al. AJH 2017;92:508-14
Transfusion & MDS

- Iron toxicity: cardiac toxicity, infections (impaired CD4, CD8 T cells), oxidative stress
- Transfusion: iron, microvesicles, inflammatory mediator
- Transfusion reactions

Kaphan et al. Blood Reviews 2020;41:100649
Are there transfusion guidelines for outpatients with MDS?
<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Restrictive Events</th>
<th>Total</th>
<th>Liberal Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laine 2017</td>
<td>0</td>
<td>40</td>
<td>0</td>
<td>40</td>
<td>Not estimable</td>
<td></td>
</tr>
<tr>
<td>Lotke 1999</td>
<td>0</td>
<td>62</td>
<td>0</td>
<td>65</td>
<td>Not estimable</td>
<td></td>
</tr>
<tr>
<td>Blair 1986</td>
<td>0</td>
<td>26</td>
<td>2</td>
<td>24</td>
<td>0.2%</td>
<td>0.19 [0.01, 3.67]</td>
</tr>
<tr>
<td>Foss 2009</td>
<td>5</td>
<td>60</td>
<td>0</td>
<td>60</td>
<td>0.3%</td>
<td>11.00 [0.62, 194.63]</td>
</tr>
<tr>
<td>Carson 1998</td>
<td>1</td>
<td>42</td>
<td>1</td>
<td>42</td>
<td>0.3%</td>
<td>1.00 [0.06, 15.47]</td>
</tr>
<tr>
<td>DeZern 2016</td>
<td>1</td>
<td>59</td>
<td>2</td>
<td>30</td>
<td>0.4%</td>
<td>0.25 [0.02, 2.69]</td>
</tr>
<tr>
<td>Weber 2008</td>
<td>1</td>
<td>29</td>
<td>2</td>
<td>31</td>
<td>0.4%</td>
<td>0.53 [0.05, 5.58]</td>
</tr>
<tr>
<td>Cooper 2011</td>
<td>2</td>
<td>23</td>
<td>1</td>
<td>21</td>
<td>0.4%</td>
<td>1.83 [0.18, 18.70]</td>
</tr>
<tr>
<td>Carson 2013</td>
<td>7</td>
<td>55</td>
<td>1</td>
<td>55</td>
<td>0.5%</td>
<td>7.00 [0.89, 55.01]</td>
</tr>
<tr>
<td>Parker 2013</td>
<td>5</td>
<td>100</td>
<td>3</td>
<td>100</td>
<td>1.1%</td>
<td>1.67 [0.41, 6.79]</td>
</tr>
<tr>
<td>Bush 1997</td>
<td>4</td>
<td>50</td>
<td>4</td>
<td>49</td>
<td>1.2%</td>
<td>0.98 [0.26, 3.70]</td>
</tr>
<tr>
<td>Hébert 1995</td>
<td>8</td>
<td>33</td>
<td>9</td>
<td>36</td>
<td>2.7%</td>
<td>0.97 [0.42, 2.22]</td>
</tr>
<tr>
<td>de Almeida 2015</td>
<td>23</td>
<td>101</td>
<td>8</td>
<td>97</td>
<td>3.2%</td>
<td>2.76 [1.30, 5.87]</td>
</tr>
<tr>
<td>Lacroix 2007</td>
<td>14</td>
<td>320</td>
<td>14</td>
<td>317</td>
<td>3.4%</td>
<td>0.99 [0.48, 2.04]</td>
</tr>
<tr>
<td>Hajjar 2010</td>
<td>15</td>
<td>249</td>
<td>13</td>
<td>253</td>
<td>3.4%</td>
<td>1.17 [0.57, 2.41]</td>
</tr>
<tr>
<td>Palmieri 2017</td>
<td>16</td>
<td>168</td>
<td>15</td>
<td>177</td>
<td>3.8%</td>
<td>1.12 [0.57, 2.20]</td>
</tr>
<tr>
<td>Gregersen 2015</td>
<td>21</td>
<td>144</td>
<td>12</td>
<td>140</td>
<td>3.9%</td>
<td>1.70 [0.87, 3.32]</td>
</tr>
<tr>
<td>Walsh 2015</td>
<td>12</td>
<td>51</td>
<td>16</td>
<td>49</td>
<td>4.2%</td>
<td>0.72 [0.38, 1.36]</td>
</tr>
<tr>
<td>Jairath 2015</td>
<td>14</td>
<td>257</td>
<td>25</td>
<td>382</td>
<td>4.2%</td>
<td>0.83 [0.44, 1.57]</td>
</tr>
<tr>
<td>Murphy 2015</td>
<td>26</td>
<td>1000</td>
<td>19</td>
<td>1003</td>
<td>4.7%</td>
<td>1.37 [0.76, 2.46]</td>
</tr>
<tr>
<td>Villanueva 2013</td>
<td>19</td>
<td>416</td>
<td>34</td>
<td>417</td>
<td>5.3%</td>
<td>0.56 [0.32, 0.97]</td>
</tr>
<tr>
<td>Carson 2011</td>
<td>43</td>
<td>1009</td>
<td>52</td>
<td>1007</td>
<td>7.9%</td>
<td>0.83 [0.56, 1.22]</td>
</tr>
<tr>
<td>Mazier 2017</td>
<td>74</td>
<td>2427</td>
<td>87</td>
<td>2429</td>
<td>10.2%</td>
<td>0.85 [0.63, 1.15]</td>
</tr>
<tr>
<td>Hébert 1999</td>
<td>78</td>
<td>418</td>
<td>98</td>
<td>420</td>
<td>11.4%</td>
<td>0.80 [0.61, 1.04]</td>
</tr>
<tr>
<td>Bergamin 2017</td>
<td>84</td>
<td>151</td>
<td>67</td>
<td>149</td>
<td>12.6%</td>
<td>1.24 [0.99, 1.55]</td>
</tr>
<tr>
<td>Holst 2014</td>
<td>168</td>
<td>502</td>
<td>175</td>
<td>496</td>
<td>14.4%</td>
<td>0.95 [0.80, 1.13]</td>
</tr>
</tbody>
</table>

Total (95% CI) 7792 7889 100.0% 1.00 [0.86, 1.16]

Total events 641 660

Heterogeneity: Tau² = 0.03, Chi² = 34.44, df = 23 (P = 0.06); I² = 33%

Test for overall effect: Z = 0.02 (P = 0.99)
• Transfusion not indicated until hemoglobin
  – 70 g/L for hemodynamically stable hospitalized patients
  – 80 g/L for orthopedic surgery, cardiac surgery or with preexisting cardiovascular disease

• Recommendations do not apply to acute coronary syndrome, severe thrombocytopenia (heme onc), and chronic transfusion dependent anemia

Carson et al. JAMA 2016;316:2025-35
# Inpatients – Acute Leukemia

**Feasibility Trial**  
Excluded: ACS, known active blood loss with hemodynamic instability

89 pts with acute leukemia

![2:1 ratio](attachment:image)

<table>
<thead>
<tr>
<th></th>
<th>Low Hb &lt; 70 g/L</th>
<th>High Hb &lt; 80 g/L</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Hb pre (g/L)</td>
<td>68</td>
<td>77</td>
<td></td>
</tr>
<tr>
<td>Mean Hb post (g/L)</td>
<td>77</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>RBC units, median (IQR)</td>
<td>8 (6-11)</td>
<td>10 (8-12)</td>
<td>P=0.01</td>
</tr>
<tr>
<td>Fatigue (NCI score out of 10)</td>
<td>4.8</td>
<td>4.5</td>
<td>P=NS</td>
</tr>
<tr>
<td>Bleeding</td>
<td>32%</td>
<td>37%</td>
<td>P=NS</td>
</tr>
</tbody>
</table>

DeZern AE et al. Transfusion 2016;56:1760-7
Transfusion in Stem cell transplant

300 pts with heme malignancy requiring SCT

Low
Hb < 70 g/L

High
Hb < 90 g/L

Multicentre, non-inferiority RCT at 4 Canadian Centres. Transfused 2 units at a time.*

<table>
<thead>
<tr>
<th></th>
<th>Low Hb &lt; 70 g/L</th>
<th>High Hb &lt; 90 g/L</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Hb pre (g/L)</td>
<td>70.9</td>
<td>84.6</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>RBC units, median (IQR)</td>
<td>2.7 (SD 4.8)</td>
<td>5.0 (6.1)</td>
<td>P=0.0004</td>
</tr>
<tr>
<td>FACT-BMT Baseline</td>
<td>108</td>
<td>103</td>
<td>Difference non-inferior</td>
</tr>
<tr>
<td>FACT-BMT Day 100</td>
<td>113</td>
<td>108</td>
<td></td>
</tr>
</tbody>
</table>

No difference in secondary outcomes including TRM, hospital LOS, ICU admission, hospital re-admission

What is different about outpatients?

- MDS pts are often older with comorbidities
- Prescribers and patients may have differing views on important transfusion related outcomes or impact on QoL
- Patients may want less disruption to daily life and fewer hospital visits

Wood EM, McQuilten ZK. Hematology 2020:167.
What can we use to guide transfusion in outpatients with MDS?
Consensus Surveys of MDs

Hematology patients - US

<table>
<thead>
<tr>
<th>TABLE 2. Most common reported Hb level thresholds for RBC transfusions in hospitalized and ambulatory patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Threshold</td>
</tr>
<tr>
<td>7 g/dL</td>
</tr>
<tr>
<td>7.5 g/dL</td>
</tr>
<tr>
<td>8 g/dL</td>
</tr>
<tr>
<td>Only if bleeding or symptomatic</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>8.5 g/dL</td>
</tr>
<tr>
<td>9 g/dL</td>
</tr>
<tr>
<td>No specific threshold</td>
</tr>
<tr>
<td>Hematocrit instead of Hb</td>
</tr>
</tbody>
</table>

*Data are reported as number (%).

MDS patients – Australia & NZ

- Commonest thresholds
  - Asymptomatic 50 y.o. < 70 g/L
  - Symptomatic 50 y.o. < 80 g/L
  - Patient with prior MI < 90 g/L
  - 80 y.o. pt < 80 g/L

- Commonest post transfusion Hb target 90-100 g/L

Pine et al. Transfusion 2017;57:289-95
Mo et al. Internal Medicine Journal 2017; 47:695-8
Consensus Minimum Hb

- Modified Delphi method of 13 expert MDS clinicians
  - 100% consensus that given no end organ effects of anemia, patients with MDS can safely forgo transfusion with hemoglobin 75 g/L or higher
What should the goals of RBC and platelet transfusion be in MDS?

<table>
<thead>
<tr>
<th>Transfusion type</th>
<th>Goal of transfusion</th>
<th>Measured by</th>
<th>Desired outcomes</th>
</tr>
</thead>
</table>
| Red cell transfusion   | • Improve acute and chronic symptoms of anemia (fatigue, dyspnea, chest pain, palpitations, effects on cognitive function)  
                        | • Minimize major complications of (severe) anemia                                | • Hemoglobin and hematocrit  
                        | • Improve functional outcomes                                                | • Control of symptoms  
                        |                                                                      | • Functional measures using standardized tool (e.g., fatigue score, walk distance, grip strength) or self-report  
                        |                                                                      | • Better functional status in activities of daily living  
                        |                                                                      | • Increased ability to participate in work or social and community interests  
                        |                                                                      | • Improved health-related QoL                                                |
| Platelet transfusion   | • Improve symptoms of thrombocytopenia (patient experience of skin bruising and other bleeding)  
                        | • Minimize major complications of (severe) thrombocytopenia  
                        | • Improve functional outcomes                                                |
RETRO Study

- Effect of transfusion on outpatient functional status
- 208 pts with benign or malignant hematology/ oncology diagnosis
- Predictors of response
  - Hb ≥ 80 g/L x 1 week post
  - No recent cancer therapy within 4 weeks
  - No hospitalization during study period

Lezin et al. Transfusion 2019;59:1934-43
Ask the Patients...

- Web-based survey in the US, Canada and UK: 475 TD-RBC MDS pts

  - Median Hb threshold 80g/L
    - 40% pts preferred higher Hb;
    - 15% lower Hb

  - Fatigue, SOB most common symptoms and had most negative impact

  - While majority felt better, 20% felt worse post transfusion for 1-2 days and 7% no change

31% experienced undue financial hardship due to transfusion dependence

Starkman, Buckstein et al. ASH Abstract 2018; Blood 2018;132(Suppl1):3092
REDDS-1 Study

- Pilot: RBC transfusion thresholds and QOL in MDS in UK/Aus/NZ

38 pts TD-MDS
6 week run-in period to Hb 100g/L

Restrictive
Maintain Hb 85-100 g/L
1 unit if Hb < 80 g/L
2 units if 80-85 g/L

Liberal
Maintain Hb 110-120 g/L
1 unit if Hb < 105 g/L
2 units if 105-110 g/L

Transfusion dependent: ≥ 1 RBC per month in past 8 weeks

Pilot study deemed feasible with ≥ 70% compliance in both arms (86% vs 99% )

Stanworth et al. BJH 2020;189:279-290
REDDS-1 Pilot Study

Pre-tx Hb 80 vs. 97 g/L

Total # of units 82 vs. 192

Stanworth et al. BJH 2020;189:279-290
## REDDS-1 Pilot Study - QoL

<table>
<thead>
<tr>
<th>Measure</th>
<th>Restrictive (n=20)</th>
<th>Liberal (n=18)</th>
<th>Overall (n=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EQ-5D-5L: Descriptive part (Higher=better)</td>
<td>0.76 (0.51-0.81)</td>
<td>0.83 (0.69-0.86)</td>
<td>0.78 (0.68-0.86)</td>
</tr>
<tr>
<td>EORTC: Physical functioning (Higher=better)</td>
<td>61 (50-86)</td>
<td>69 (48-94)</td>
<td>68 (50-86)</td>
</tr>
<tr>
<td>EORTC: Global health scores (Higher=better)</td>
<td>63 (60-75)</td>
<td>70 (53-87)</td>
<td>68 (56-76)</td>
</tr>
<tr>
<td>EORTC: Fatigue (Lower=better)</td>
<td>38 (33-54)</td>
<td>34 (14-66)</td>
<td>37 (21-63)</td>
</tr>
<tr>
<td>EORTC: Dyspnoea (Lower=better)</td>
<td>42 (31-64)</td>
<td>25 (1-77)</td>
<td>40 (12-67)</td>
</tr>
</tbody>
</table>
ENHANCE-RBC Study

- Pilot: RBC transfusion thresholds and QoL in MDS in Toronto/Hamilton

30 pts TD-MDS
No run-in period

Transfusion dependent: ≥ 1 RBC per month in past 8 weeks

Restrictive
Maintain Hb 85-100 g/L
1 unit if Hb < 80 g/L
2 units if 80-85 g/L

Liberal
Maintain Hb 110-120 g/L
1 unit if Hb < 105 g/L
2 units if 105-110 g/L

Buckstein et al. Blood 2020;136(Supplement):3-4
**Pre-txn Hb 101 vs. 90 g/L**

**Table 1.**

<table>
<thead>
<tr>
<th></th>
<th>Liberal Arm, n=15 (IQR)</th>
<th>Restrictive Arm, n=13 (IQR)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td># CBC</td>
<td>16 (14-20)</td>
<td>12 (10-14)</td>
<td>0.01</td>
</tr>
<tr>
<td># CBC after 4 week run-in</td>
<td>8 (7-12)</td>
<td>7 (5-8)</td>
<td>0.04</td>
</tr>
<tr>
<td># transfusion visits</td>
<td>8 (7-9)</td>
<td>5 (4-7)</td>
<td>0.001</td>
</tr>
<tr>
<td># RBC units overall</td>
<td>12 (12-16)</td>
<td>9 (8-12)</td>
<td>0.02</td>
</tr>
<tr>
<td># RBC units after 4 week run in</td>
<td>7 (6-9)</td>
<td>6 (4-8)</td>
<td>0.07</td>
</tr>
<tr>
<td>Days between transfusions</td>
<td>9 (8-15)</td>
<td>15 (11-22)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean change in ferritin ug/L</td>
<td>803</td>
<td>155</td>
<td>0.003</td>
</tr>
<tr>
<td>New allo-antibody</td>
<td>1</td>
<td>0</td>
<td>0.3</td>
</tr>
<tr>
<td>Febrile non hemolytic reaction</td>
<td>1</td>
<td>0</td>
<td>0.3</td>
</tr>
</tbody>
</table>

**Figure 1.** Mean Hb (SD) at weeks 1-12 in patients from 2 treatment arms

**Figure 2.** Mean (EQ-5D) visual analog score over 12 weeks from 2 treatment arms

**QOL**
What can we use to make the transfusion experience safer and better for the patient?
Iron Overload

- Ineffective iron metabolism due to ineffective erythropoiesis
- Secondary to transfusion
- Screen: Ferritin > 1000 mcg/L and > 15-20 RBC units
- Iron overload associated with reduced survival
- TELESTO RCT trial of iron chelation: median EFS 3.9 y vs 3 y with placebo (HR 0.64; 95%CI 0.42-0.96)

Volpe et al. Ther Adv Hematol 2021;12:1-10
Table 1: Adverse transfusion reactions observed in transfused patients with aplastic anaemia or myelodysplastic syndrome from 1 January 2010 to 30 June 2016 in the Auvergne-Rhône-Alpes region.

<table>
<thead>
<tr>
<th>Type of adverse transfusion reaction</th>
<th>Myelodysplastic syndrome (193)</th>
<th>Auvergne-Rhône-Alpes (7174)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Febrile non-haemolytic transfusion reaction</td>
<td>56 (29.0)</td>
<td>1767 (24.6)</td>
</tr>
<tr>
<td>Post-transfusion red blood cell alloimmunization</td>
<td>43 (22.3)</td>
<td>2346 (32.7)</td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>33 (17.1)</td>
<td>978 (13.6)</td>
</tr>
<tr>
<td>Suspected transfusion-transmitted bacterial infection</td>
<td>16 (8.3)</td>
<td>693 (9.7)</td>
</tr>
<tr>
<td>Transfusion-associated circulation overload</td>
<td>8 (4.1)</td>
<td>237 (3.3)</td>
</tr>
</tbody>
</table>

aNumber of adverse transfusion reactions.
bPercentage.
Alloimmunization & MDS

- Rates of alloimmunization: 11% - 57% (smaller studies report higher rates)
  - 75% antibodies in Rh, Kell blood group systems
  - Associated with ↑ RBC units (70% by 20 units)
  - ↓ with disease modifying therapies
  - ↑ transfusion intensity post alloimmunization

- Rates of autoantibodies: 4-10% (40-45% DAT+)
  - More common in alloimmunized pts

Lin Y et al. Vox Sanguinis 2017;112:79-86
Chhetri et al. Haematologica; 2019;104:e453
Alloimmunization & MDS

- Consequences
  - Delayed hemolytic transfusion reactions
  - Autoantibodies: pathological \(\rightarrow\) autoimmune hemolysis
  - Delayed serologic transfusion reactions
  - Challenge to resolve in Transfusion Lab
  - Longer time to prepare RBC units for transfusion

Prevention

- MDS Registry: Compared pts receiving transfusion at site with prophylactic antigen matching for RhCEK vs not

<table>
<thead>
<tr>
<th>Alloimmunization</th>
<th>Rh/K matching site</th>
<th>No matching site</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clin significant alloAbs</td>
<td>11%</td>
<td>23%</td>
<td>0.06</td>
</tr>
<tr>
<td>Rh/K alloantibodies</td>
<td>7%</td>
<td>22%</td>
<td>0.008</td>
</tr>
</tbody>
</table>

- No pt receiving Rh/K matched developed Rh/K alloantibody (0 vs. 18%)

- Alloimmunization still occurs: plt transfusion, non Rh/K alloabs

Lin Y et al. Vox Sanguinis 2017;112:79-86
Case Study

- 72 M with myelodysplastic syndrome (MDS) and severe anemia, not responding to treatment
- The hematologist asks.....
  - Are there transfusion guidelines for outpatients?
  - Any blood bank testing or measures that I need to order to help my patient?
Case Study - Summary

• No current guidelines for MDS outpts
• Reasonable: Hb 70-80 g/L and adjust considering comorbidities, QOL
• Consider prophylactic Rh/K matching for transfusion dependent pts
• Explore ways to simplify the process: same day crossmatch, home G&S
• Explore ways to capture QOL and what is important to patients
What about chronic platelet transfusion in MDS outpatients?
What about MDS outpatients?

- Thrombocytopenia = adverse prognostic factor in MDS
- Death from bleeding in MDS ~ 9-13%

- MDS registry in Australia
  - 50% required at least 1 plt transfusion
  - 9% required HLA matched platelets for platelet refractoriness

Bowen et al. Editorial. Transfusion 2020;60:2164-7
Cheok et al. Transfusion 2020;60:2192-8
Guidance on Platelet Transfusion for Patients With Hypoproliferative Thrombocytopenia

See Editorial, pages 1–2

Susan Nahirniak a,*, Sherrill J. Slichter b, Susano Tanael c, Paolo Rebull a d, Katerina Pavenski e, Ralph Vassallo f, Mark Fung g, Rene Duquesnoy h, Chee-Loong Saw i, Simon Stanworth j, Alan Tinmouth k, Heather Hume l, Arjuna Ponnapalam m, Catherine Moltzan n, Brian Berry o, Nadine Shehata p, for the International Collaboration for Transfusion Medicine Guidelines (ICTMG)

Annals of Internal Medicine

Clinical Guideline

Platelet Transfusion: A Clinical Practice Guideline From the AABB

Richard M. Kaufman, MD; Benjamin D'volbic, MD, PhD; Terry Gernsheimer, MD; Steven Kleinman, MD; Alan T. Tinmouth, MD; Kelley E. Capocelli, MD; Mark D. Cipolle, MD, PhD; Claudia S. Cohn, MD, PhD; Mark K. Fung, MD, PhD; Brenda J. Grossman, MD, MPH; Paul D. Mintz, MD; Barbara A. O'Malley, MD; Deborah A. Sesok-Pizzini, MD; Aryeh Shander, MD; Gary E. Stack, MD, PhD; Kathryn E. Webert, MD, MSc; Robert Weinstein, MD; Babu G. Welch, MD; Glenn J. Whitman, MD; Edward C. Wong, MD; and Aaron A.R. Tobian, MD, PhD

• Prophylactic transfusion at < 10 x 10⁹/L

Nahirniak et al. Transfusion Med Reviews 2015;29:3-13
Prophylactic platelet transfusion at < 10 x 10⁹/L
- Patients receiving therapy for hematologic malignancies
- Allogeneic stem cell transplantation

Therapeutic platelet transfusion
- Autologous SCT: similar rates of bleeding with decreased platelet usage when patients transfused at first sign of bleeding rather than prophylactically (experienced centers)
- Chronic stable severe thrombocytopenia (MDS, aplastic anemia) not receiving active treatment

Schiffer et al. JCO 2018;36:283-99
Survey in Netherlands

<table>
<thead>
<tr>
<th>Treatment</th>
<th>MDS</th>
<th>PPT, n = 60</th>
<th>TXA, n = 39</th>
<th>HMA</th>
<th>PPT, n = 68</th>
<th>TXA, n = 44</th>
<th>No treatment</th>
<th>PPT, n = 68</th>
<th>TXA, n = 45</th>
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<tbody>
<tr>
<td>Chemo</td>
<td></td>
<td>97</td>
<td>85</td>
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<td>87</td>
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<tr>
<td>No treatment</td>
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</tbody>
</table>

PPT: Yes, independent of (tendency to) bleeding
Yes, but only if (tendency to) bleeding
No

TXA: Yes
No

Cornelissen et al. Eur J Haematol 2021;106:362-70
MDS & Thrombocytopenia

- MDS Registry: 586 registry pts at a single site
  - 99 pts (17%) had persistent plt < 20 x 10^9/L; median OS 0.9 yrs

- No significant difference in grade 3-4 bleeding ➔ retrospective
  - 71% in group 1 and 4 received no plt transfusions

<table>
<thead>
<tr>
<th>Bleeding</th>
<th>TXA alone N=28</th>
<th>TXA + Proph N=39</th>
<th>Proph alone N=19</th>
<th>No tx N= 13</th>
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<tbody>
<tr>
<td>Any bleeding event</td>
<td>86%</td>
<td>74%</td>
<td>89%</td>
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<tr>
<td>Grade 3</td>
<td>7%</td>
<td>10%</td>
<td>11%</td>
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<tr>
<td>Grade 4</td>
<td>11%</td>
<td>5%</td>
<td>5%</td>
<td>0</td>
</tr>
<tr>
<td>Therapeutic plts</td>
<td>32%</td>
<td>--</td>
<td>--</td>
<td>23%</td>
</tr>
</tbody>
</table>

Vijenthira et al. Leuk Res 2019;76:76-81
Tranexamic Acid in Heme

- RCT: TXA vs. placebo every 8 hrs during chemo / HSCT

Figure 1. Kaplan-Meier plot of the proportion of patients without WHO 2+ bleeding or death within 30 days following activation.

Gernsheimer et al. ASH Abstract 2020
Summary

- MDS patients carry a significant transfusion burden with impact on quality of life, prognosis and resource utilization.
- Evidence for transfusion indications is developing.
  - How can we tell if we are over / undertransfusing pts in the outpatient setting?
- Time to focus on the outpatient setting: optimize outcomes, care and the experience for patients.
Thank you!

- Rena Buckstein
- Christine Cserti-Gazdewich