Do liberal thresholds for red cell transfusion result in improved quality of life for patients undergoing intensive chemotherapy for acute myeloid leukemia? A randomized crossover feasibility study

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Supplementary information

Supplementary Figure 1: CONSORT diagram

Assessed for eligibility (n=128)

Not eligible (n=44)
- Patients unable in the opinion of the attending clinician to tolerate restrictive red cell transfusion thresholds (n=5)
- Patients with Acute Promyelocytic Leukaemia (APML) (n=3)
- Patients who have been diagnosed with myelodysplasia prior to diagnosis of AML (n=2)
- Psycho/social reasons (n=13)
- Patient’s inability to provide informed consent (n=1)
- Other (n=19)
- Unknown (n=1)

Eligible (n=84)

Not randomized (n=41)
- Patient declined to consent (n=25)
- Psycho/social reasons (n=4)
- Patient’s inability to provide informed consent (i.e. due to language barrier) (n=1)
- Other (n=11)

Randomized (n=43)

Allocated to restrictive then liberal (n=21)
- Completed cycle one (restrictive) (n=17)
- Completed cycle two (liberal) (n=14)
- Did not complete both cycles (n=7)
  - Withdrawal of consent (n=2)
  - Moved to supportive care only, prior to completion of Cycle 2 (n=1)
  - There has been a change in the participant’s conditions that justifies the discontinuation of treatment in the opinion of the clinician (n=1)
  - Other (n=3)*

Lost to follow-up (no three-month follow up) (n=2)
- Replaced (n=3)

Analysed (n=21)

Allocated to liberal then restrictive (n=22)
- Completed cycle one (liberal) (n=20)
- Completed cycle two (restrictive) (n=15)
- Did not complete both cycles (n=7)
  - Withdrawal of consent (n=1)
  - Died (n=1)
  - Moved to supportive care only, prior to completion of Cycle 2 (n=1)
  - Participant proceeded straight to allogenic stem cell transplantation after Cycle 1 (n=1)
  - Other (n=3)*

Lost to follow-up (no three-month follow up) (n=1)
- Withdrawal of consent at the end of cycle 2 (n=1)
- Replaced (n=3)

Analysed (n=22)

* Intermittent withdrawal of consent (2 in ‘Restrictive then Liberal’ and 1 in ‘Liberal then Restrictive’)
**Supplementary Figure 2:** Quality of life score by time period and policy

<table>
<thead>
<tr>
<th></th>
<th><strong>Mean</strong> QOL score</th>
<th><strong>Mean</strong> QOL score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Higher score is better)</td>
<td>(Lower score is better)</td>
</tr>
<tr>
<td><strong>Descriptive</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Physical function</strong></td>
<td><img src="image1" alt="Graph" /></td>
<td><img src="image2" alt="Graph" /></td>
</tr>
<tr>
<td><strong>Global</strong></td>
<td><img src="image3" alt="Graph" /></td>
<td><img src="image4" alt="Graph" /></td>
</tr>
<tr>
<td><strong>Fatigue</strong></td>
<td><img src="image5" alt="Graph" /></td>
<td><img src="image6" alt="Graph" /></td>
</tr>
<tr>
<td><strong>Dyspnoea score</strong></td>
<td><img src="image7" alt="Graph" /></td>
<td><img src="image8" alt="Graph" /></td>
</tr>
<tr>
<td><strong>Chemotherapy Cycle 1</strong></td>
<td><img src="image9" alt="Graph" /></td>
<td><img src="image10" alt="Graph" /></td>
</tr>
<tr>
<td><strong>Chemotherapy Cycle 2</strong></td>
<td><img src="image11" alt="Graph" /></td>
<td><img src="image12" alt="Graph" /></td>
</tr>
<tr>
<td><strong>Both Chemotherapy Cycles</strong></td>
<td><img src="image13" alt="Graph" /></td>
<td><img src="image14" alt="Graph" /></td>
</tr>
</tbody>
</table>

**Policy**
- **Restrictive**
- **Liberal**

*R = number of respondents on restrictive thresholds*

*L = number of respondents on liberal thresholds*

*For row three where ‘Both Chemotherapy Cycles’ is presented, Standard Deviation (SD) is also presented.*
**Supplementary Table 1: Discontinuation of trial treatment**

<table>
<thead>
<tr>
<th>Centre number</th>
<th>Arm</th>
<th>Stage of withdrawal</th>
<th>Reason given</th>
<th>Further information</th>
<th>Withdrew consent for data collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>L/R</td>
<td>After Cycle 1 (did not proceed to cycle 2)</td>
<td>Participant given poor prognosis Felt they were allocated to restrictive arm</td>
<td>Participant was allocated to liberal strategy for cycle 1</td>
<td>Yes</td>
</tr>
<tr>
<td>1</td>
<td>R/L</td>
<td>Cycle 1 Day 16</td>
<td>Participant had too much to think about</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>R/L</td>
<td>After Cycle 1 (did not proceed to cycle 2)</td>
<td>Participant felt they were allocated to restrictive threshold and that was too low</td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>L/R</td>
<td>Cycle 2 Day 30 (Last day)</td>
<td>Participant felt they were allocated to restrictive threshold and that they were excessively tired due to that</td>
<td></td>
<td>No</td>
</tr>
</tbody>
</table>

Additionally, the following participants agreed to restart the trial on the subsequent cycle

<table>
<thead>
<tr>
<th>Centre number</th>
<th>Arm</th>
<th>Stage of withdrawal</th>
<th>Reason given</th>
<th>Further information</th>
<th>Withdrew consent for data collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>R/L</td>
<td>Cycle 1 Day 20</td>
<td>Participant felt very unwell</td>
<td>Participant re-consented to continue for Cycle 2.</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>R/L</td>
<td>Cycle 1 Day 7</td>
<td>Hemoglobin dropped to 50 g/L and Participant felt this would not have happened off trial Participant did not feel 90 g/L was appropriate for second cycle either Participant did not feel QoL was robust</td>
<td>Participant withdrew consent after Cycle 1 but re-consented to cycle 2.</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>L/R</td>
<td>Between Cycle 1 &amp; Cycle 2</td>
<td>Participant did not feel they could tolerate lower threshold for cycle 2</td>
<td>Participant withdrew consent after first chemotherapy cycle as felt unwell. Later re-consented to continue with second chemotherapy cycle.</td>
<td>No</td>
</tr>
</tbody>
</table>

L= Liberal cycle; R= Restrictive cycle