Guidelines SFGM-TC

Quality controls on cord blood unit contiguous segments: Recommendation of the SFGM-TC

Contrôle de qualité des USP via segments attachés : recommandations de la SFGM-TC

J. De Vos a, B. Birebent b, C. Faucher c, O. Giet d, Y. Hicheri e, C. Lemarie f, E. Baudoux d, F. Boulanger g, F. Garnier h, J. Larghero i, F. Pouthier j, J.-B. Thibert k, I. Yakoub-Agha l,*

a Unité de thérapie cellulaire, CHU de Montpellier, 80, avenue Fliche, 34295 Montpellier cedex 5, France
b UFT, EFS Île-de-France, 5, rue Gustave-Eiffel, 94017 Créteil cedex, France
c Direction médicale et scientifique, agence de la biomédecine, 1, avenue du Stade-de-France, 93212 Saint-Denis, France
d Laboratoire de thérapie cellulaire et génique, CHU de Liège, tour 2 niveau-4E, 4000 Liège, Belgique
e Département d'hématologie clinique, CHRJ de Montpellier, 80, avenue Augustin-Fliche, 34295 Montpellier cedex 5, France
f Département de thérapie cellulaire, institut Poilly-Calmettes, 232, boulevard Sainte-Marguerite, BP 156, 13273 Marseille cedex 09, France
g EFS Nord de France, 21, rue Camille-Gaévin, BP 2018, 59012 Lille cedex, France
h Registre France greffe de moelle, agence de la biomédecine, 1, avenue du Stade-de-France, 93212 Saint-Denis, France
i Unité de thérapie cellulaire et de clinique transfusionnelle, hôpital Saint-Louis, 1, avenue Claude-Vellefaux, 75475 Paris cedex 10, France
j EFS BFC, activité ingénierie cellulaire et tissulaire, 1, boulevard A-Fleming, 25020 Besançon cedex, France
k Service de thérapie cellulaire, EFS Bretagne, rue Pierre-Jean Gineste, BP 91614, 35016 Rennes cedex, France
l Maladies du sang, CHUJ de Lille, rue Michel-Polonovski, 59037 Lille cedex, France

A R T I C L E   I N F O

Article history:
Received 27 April 2014
Accepted 14 May 2014
Available online 1 July 2014

Keywords:
Attached segment
BU release
Specifications
Cord blood transplantation

Mois clés :
Segment attaché
Spécifications
Greffes de sang de cordon

A B S T R A C T

In the attempt to harmonize clinical practices between different French transplantation centers, the French Society of Bone Marrow Transplantation and Cell Therapies (SFGM-TC) set up its fourth annual series of workshops which brought together practitioners from all of its member centers. These workshops took place in September 2013 in Lille. Literature and intra-laboratories studies suggest that attached segment is representative of cord blood unit (CBU). Nevertheless, some discrepancies have been observed when analyzing large data registries. To address these issues, we have listed recommendations to increase the standardization of segment processing and quality control (QC), information on units of measurement and specifications and action to be taken in case of out of specifications QC results on segment.

© 2014 Elsevier Masson SAS. All rights reserved.

R É S U M É

Dans une démarche qui vise à uniformiser les procédures d'allogreffe de cellules souches hématopoïétiques (CSH), la Société française de greffe de moelle et de thérapie cellulaire (SFGM-TC) a organisé les quatrièmes ateliers d'harmonisation des pratiques en septembre 2013 à Lille. Cet atelier a été consacré au segment attaché des unités de sang placentaire dans le but d'établir des recommandations quant à la standardisation du traitement de ce segment et les mesures à prendre en cas de rupture de ce segment.

© 2014 Elsevier Masson SAS. Tous droits réservés.

1. Questions

- Is the distal segment representative of thawed bag?
- How to prepare segments?
- How to thaw segments?
- What minimal quality control (QC) should be performed?
- Information to communicate to the transplant center?
- Measures taken in case of insufficient total nucleated cell viability?

* Corresponding author.
E-mail address: sfgm-tc-iyagazine.fr (I. Yakoub-Agha).

http://dx.doi.org/10.1016/j.pathbio.2014.05.005

0369-8114/© 2014 Elsevier Masson SAS. All rights reserved.
2. State of the art [1–6]

Literature and intra-laboratories studies suggest that attached segment is representative of cord blood unit (CBU). However, some discrepancies have been observed when analyzing large data registries. We analyzed 570 CBU from the French registry (France Greffe de Moelle, FGM) that were recruited for French transplant centers from 2008 to 2012. For 117 CBU, quality control data were available for both the distal segment and thawed bag. All these CBU were infused. Divergence for total nucleated cell (TNC) viability were observed between the thawed distal segment and the thawed bag. A difference between distal segment and bag greater than 10% was noted in 64 cases. Cases where TNC viability was lower in the segment than in the bag were more frequent and of greater magnitude than the opposite way (Table 1).

These results suggest that even though the attached segment can generally be seen as fairly representative of the CBU bag, there are cases where cell viability is discordant between the segment and the bag. The causes of these discordances could be related to random variability in the thawing process, but also to specific difficulties in preparing or thawing the segment. These results also show that, confronted with a low TNC viability in an attached segment, some transplant centers nevertheless decide to use the CBU.

3. Methodology

- Literature review.
- French CB registry review.
- Intra-centers validation data.

4. Abbreviations

CBU Cord Blood Unit
CFU Colony Forming Unit
QC Quality Control
SOP Standard Operating Procedure

5. Recommendations

To address the issues raised above, we have listed recommendations regarding the handling of attached segments and their QC.

- National regulations and FACT standards shall be followed. In particular, number of segments, labeling and required tests has to be closely considered in order to be fully compliant with legislation and standards.
- At the time of recruitment and before CBU release, the transplant physicians should require the expertise of HLA typing laboratory and cell therapy lab that will be in charge of CBU thawing. These teams should jointly review CBU data, including data of the thawed segment.
- Carefully validated SOP should be followed at each step:
  - before freezing. A critical step is the homogenization of DMSO and CBU, including the liquid contained in the tubing. A thorough homogenization by repeatedly (> 3 times) emptying and filling the tubing that will constitute the segment may be adopted;
  - the delay between DMSO addition and CBU cryopreservation is critical in order to avoid cell toxicity;
  - segment removal: executed by trained technical staff member in order to minimize any involuntary warning events;
  - segment thawing:
    - for a short time (< 30 s), in a defined temperature (for instance 37 °C),
    - segment disinfection, for instance with hydro-alcohol 70%,
    - slow dilution of thawed cord blood, with a defined medium volume,
    - accurate measure of the segment volume to infer cell concentration. Such a measure should be carried out after dilution to minimize imprecision.
- In case distal segment is below specifications including HLA discrepancy, after transplant center approval, thawing of proximal segment is acceptable. In such a case, the final decision on the CBU conformity should be based on data obtained from the proximal segment.
- Minimal QC on thawed segment should include:
  - HLA confirmatory typing;
  - TNC viability (%);
  - CD34 viability (%);
  - cloning efficiency: CFU-GM or CFC, expressed as % per CD34 or TNC. Calculation method shall be detailed.

In addition, the following QC can be provided:

- TNC/μl;
- CD34+/μl.

If cell quantities are extrapolated to the whole CBU volume, it shall be clearly specified to the transplant center.
Viabilities and CD34 enumeration should be performed using single platform and follow ISAGHE recommendation.

Table 1

<table>
<thead>
<tr>
<th>Absolute difference in TNC viability (segment versus bag), %</th>
<th>Cell viability segment &gt; bag: number of patients</th>
<th>Cell viability bag &gt; segment: number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–10</td>
<td>22</td>
<td>31</td>
</tr>
<tr>
<td>10–20</td>
<td>2</td>
<td>22</td>
</tr>
<tr>
<td>20–30</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>30–40</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>40–50</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>≥ 50</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Definitions: Fig. 1 depicts proximal and distal segments.
Units shall be defined and should be harmonized among registries.

CB Bank specifications should be precisely defined. If results are below these specifications, the transplant center shall be informed. Exceptional release can be decided after joined discussion.

6. Unanswered questions

- Increase standardization of segment processing (freezing and thawing).
- Proposal of specifications.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References