JACIE accreditation: demonstrating high quality of clinical and laboratory practice in stem cell transplantation centres

I. Van Riet

Joint Accreditation Committee of ISCT and EBMT (JACIE) is an international non-profit organisation aiming to implement across Europe a standardised accreditation system for haematopoietic stem cell transplantation centres that organise and execute their clinical and laboratory activities according to high quality standards. Since 2008, three Belgian transplantation programmes and one stand-alone facility have received a JACIE accreditation, two other programmes are actively within the accreditation process and several other centres are preparing their application. During the past years, the Belgian Hematological Society took several initiatives to support the national centres for implementation of the JACIE quality standards. Through this accreditation system, the quality level of stem cell transplantation centres becomes objectively measurable, allowing centres to demonstrate that they achieved in Europe the high level of 'excellence'.

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Introduction

Haematopoietic stem cell transplantation became a standard treatment modality for patients with malignant blood diseases such as leukaemia, lymphoma or multiple myeloma or patients with non-malignant diseases such as aplastic anaemia and thalassaemia. Based on the origin of the stem cells, two forms of transplantation can be distinguished. In the case of allogeneic transplantation, the stem cells are derived from a donor with a (partial) compatible HLA type. This donor can be family-related with the patient (sibling, HLA-identical or haplo-identical) or not related. In the latter case, the donor is selected in national and international donor registries. If no compatible donor is found or the patient is for other reasons not eligible for an allogeneic transplantation, autologous stem cells can be used. For both forms of transplantation, haematopoietic stem cells can be collected from bone marrow or peripheral blood (after mobilisation). For allogeneic transplantation also cord blood can be a source of haematopoietic stem cells. This type of treatment modality necessitates a close collaboration between different functional units within the same centre and/or between units of different centres. These functional units include a clinical transplantation unit, a stem cell collection unit and a stem cell processing laboratory.

Author: I. Van Riet, Division Clinical Hematology - Hematopoietic stem cell bank, UZ Brussel, Belgium.

Please send all correspondence to: Prof. Dr. Sc. I. Van Riet, national JACIE representative, Division Clinical Hematology - Hematopoietic stem cell bank, Laarbeeklaan 101, 1090 Brussel, tel: 0032 02 477 67 11, email: ivan.vanriet@uzbrussel.be

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Within Europe, all clinical activities related to stem cell transplantation are recorded by the European Group for Blood and Marrow Transplantation (EBMT). In 2007, 25,563 stem cell transplantations (SCT's) were reported by 613 European centres in 43 different countries. The same year, 715 SCT's were performed in 19 Belgian centres.[1,2]

The requirement to demonstrate the quality of practice has currently become one of the main priorities for health care professionals in general. National authorities, funding foundations, health care organisations and medical industry increase pressure on clinical centres to demonstrate that clinical and laboratory practices are compliant with high quality standards of care. This required level of excellence can be demonstrated by means of accreditation.

What is JACIE?

JACIE was founded in 1998 by the EBMT and International Society for Cellular Therapy (ISCT), two leading organisations in the field of transplantation of haematopoietic stem cells. A JACIE accreditation certifies that a stem cell transplantation centre conducts its activities according to specific 'standards of excellence', being the JACIE standards. In particular, the centre has to prove that it has an effective quality system and must ensure that all procedures and policies, implemented according to the quality standards, are continuously followed by the team members. There must be clear evidence for optimal communication between the various functional units of the stem cell transplantation centre, being the collection facility, where the stem cells are collected, the laboratory where the stem cells are processed, stored and distributed and finally the clinical unit where the stem cell grafts are infused. The quality system must also ensure that (severe) adverse events and mistakes are immediately detected, recorded and corrected to prevent as much as possible their re-occurrence. An efficient quality system also implies that the team members receive adequate training and retraining, that there is a regular competency evaluation and that all the tasks and responsibilities of staff members are clearly defined and documented.

The JACIE standards define the specific requirements for the infrastructure of the different functional units. A minimal clinical activity is also required depending on the type of transplantations performed (autologous versus allogeneic, adult patients versus paediatric patients) and in function of the number of stem cell collections (aphaeresis versus bone marrow harvest). Finally, regular internal audits must be organised to determine whether the procedures and policies are compliant with the standards, are correctly interpreted and continuously followed by the team. Once the quality level that permits accreditation is reached, it remains a challenge for the centres to maintain this level. Accreditations are therefore awarded for a (limited) period of four years, with an interim evaluation of the quality system every two years. Then a re-accreditation cycle has to be started.[3-5]

The JACIE standards are based on the standards of the American Foundation for the Accreditation of Cellular Therapy (FACT). They are regularly reviewed depending on new developments in this specific clinical domain and are now available in a fourth version.[5] They cover all stages in the stem cell donor evaluation and selection, collection, processing, storage and clinical transplantation of haematopoietic stem cells from bone marrow and peripheral blood. Recently, the stem cell laboratories have the possibility to apply for accreditation for processing and storage of other therapeutic cell products such as mesenchymal stem cells (which can be used for regenerative medicine or control of graft-versus-host disease in allogeneic haematopoietic stem cell transplantation) and dendritic cells (which can be used for immunotherapy).

Collection, processing and storage of stem cells from cord blood are outside the scope of JACIE-accreditation. At this moment, FACT serves as the only international accreditation body for cord blood banks.

JACIE standards define the 'minimum requirements', but of course, each centre can have its own more stringent standards as defined by national regulations. National regulations always overrule the JACIE standards and JACIE accreditation is only possible if the centre fully complies with the national law.

The inspection of a complete program is conducted by a team of three to four inspectors, one for each functional unit (clinic, collection and laboratory) and an additional inspector (paediatrician) when the

centre also runs a paediatric stem cell transplantation programme. One of these inspectors acts as team leader.

JACIE-inspectors must have sufficient professional experience in the field and are nominated after attending a special training, organised by JACIE, and passing successfully an evaluation test. JACIE favours the exchange of inspectors between different European countries, as far as the inspectors speak the same language as is used in the inspected centre.

When the accreditation application is accepted, JACIE will invite the centre to submit a series of pre-inspection documents (including the quality manual). In advance, the centre has to complete a so-called 'checklist' in which it can be specified which standards have been implemented, which standards have not been implemented (with the specific reasons) and which standards do not apply to the centre. The checklist and other pre-inspection documents are reviewed in advance by the inspection team and then - in consultation with the centre to inspect - a date for a site inspection is agreed.

The inspection takes about one day and a half and includes an assessment of the available infrastructure, thorough inspection of the documents (procedures, meeting reports and internal audits, technical and medical records, validation records, etc.) and interviews with staff members. If possible, clinical or laboratory procedures are attended. During the inspection, the inspection team holds regular internal consultations. Afterwards, the inspection team invites all staff members of the centre to inform them immediately about the main (positive and negative) findings.

After the inspection, the team leader, with the help of the other inspectors, completes an inspection report. This report is then reviewed by the JACIE-accreditation committee. Depending on the findings, this committee can ask the centre to correct deficiencies that have been found.

Within six months time the centre needs to prove that the appropriate corrections were made by providing sufficient evidence in additional or modified documents. Possibly there may be a new on-site inspection required. If all standards are met properly, the centre will receive the accreditation. The duration of the entire process (from application to grant accreditation) varies from 6 to 12 months.

Each of the functional facilities can apply for JACIE accreditation as a stand-alone facility and collaborate with other facilities from other institutes. However a clinical facility is only eligible for JACIE accreditation, if collaboration with JACIE-accredited collection and processing facilities can be demonstrated.

Looking at the experience of 20 European centres, it was found that implementing the standards takes an average of 18 months. The majority of centres (85%) took a full time quality manager in service to support the entire team with the accreditation process. All centres stated that the delivered efforts were justified, given the significant improvement in work organisation, internal communication, monitoring of adverse events and patient satisfaction.[4] In 2004, a Swiss centre published a cost analysis of the implementation of JACIE-standards which showed that 14 months of preparation for accreditation of an autologous stem cell transplantation program (approximately 40 transplantations per year) had cost 150,000 Euros.[6] Very recently, data from a first EBMT megafile analysis showed that the clinical outcome in centres doing allogeneic stem cell transplantations is significantly improved after implementing the JACIE standards.[7]

JACIE in Europe and Belgium

Since 2004, over 210 European centres or stand-alone facilities applied for a JACIE accreditation and so far more than 175 inspections have been completed. At this moment JACIE (re)accreditation has been obtained by 91 centres or stand-alone facilities in 15 European countries with as leaders the United Kingdom, France, the Netherlands and Switzerland. For centres in The Netherlands and Switserland JACIE-accreditation is a requirement to obtain a license as stem cell transplantation centre by the national authorities or to receive reimbursement by the social security, respectively. In France, initiatives were recently taken to link JACIE-accreditation in the future to the national license for allogeneic stem cell transplantation centres (*www.jacie.org*). It is expected that more European countries in the future will include JACIE accreditation in their national legislation.

The organisation of JACIE-activities in Belgium is coordinated by the Belgian Hematological Society (BHS). Over the past five years this organisation

has supported various initiatives to inform the national stem cell transplantation centres about the JACIE-quality standards and the accreditation process. Since 2006 two 'JACIE Centre Preparation Courses' and two 'Internal auditor training courses' were sponsored by the BHS and attended by team members of all national centres that report their transplant activities and data to the EBMT. The BHS Board appoints the national representative, as well as candidates for international inspector training whose participation costs are also supported by the BHS. So far, a total of 10 Belgian JACIE-inspectors were trained with support from the BHS. These inspectors are not only available for national inspections, but are also regularly invited to participate in international JACIE-inspections (such as in France, the Netherlands, United Kingdom and Switzerland). In addition, also a BHS Subcommittee 'Accreditation and regulatory affairs' was established, which has a particular focus on JACIE-related topics such as preparation and organisation of national inspections, relationship between JACIE-standards and national legislation, definition of serious adverse events and reactions in transplantation centres, and biovigilance.

So far, five Belgian transplantation programmes actively entered the JACIE accreditation process, of which four have already been inspected and of which three received an accreditation: the Virga Jesse hospital in Hasselt (for a complete autologous stem cell transplantation programme in adult patients), the Saint-Luc hospital (UCL) in Brussels and the combined programme of the Bordet institute, the Saint Pierre hospital and the Reine Fabiola hospital (ULB) in Brussels (for a complete autologous and allogeneic stem cell transplantation programme in both adult and paediatric patients). The Blood Transfusion Service (Red Cross) in Ghent received accreditation as a stand-alone facility for processing and storage of haematopoietic stem cells.

Some centres have decided to apply for JACIE accreditation as part of a combined programme with another centre which makes that there remain in addition to the 3 already accredited programmes about 14 national programmes eligible for JACIE accreditation. As decided by the BHS subcommittee, international inspectors are invited to participate to the national inspections, as far as they are Dutch or French speaking according to the language used in the centre to inspect. So, the inspections that took place so far were conducted by teams that included French or Dutch inspectors.

JACIE and national regulations

In Belgium, stem cell transplantation centres can apply for JACIE accreditation on a voluntary basis. So far, there is no legislation in which JACIE accreditation for transplantation centres is required. As indicated by the law for tissue- and cell banks of 19/12/2008 (largely based on the EU directives 2004/23/EC - 2006/17/EC for cell and tissue banks), transplantation centres must apply to the national authorities for a license as haematopoietic stem cell bank.[8-10] This license covers the collection, the processing, the storage, the import, the distribution and the export of haematopoietic stem cells from bone marrow and peripheral blood. For cord blood banking an additional license is required. The Federal Agency for Medicines and Health Products (FAGG/AFMPS) is responsible for the organisation of inspections that are conducted according to the content of the law mentioned above as well as the related royal decrees and the standards of the Superior Health Council.[10] A stem cell bank can only be formally recognised when it is imbedded in a hospital structure. However, separate facilities or institutes can receive a license as 'intermediate structure' if they provide particular services to recognised stem cell banks. A license is normally valid for 2 years, after which a new inspection takes place. The national regulations as well as the standards of the Superior Health Council show a high level of similarity to the JACIE-standards (for stem cell collection and processing facilities). Obtaining an international JACIE-accreditation will not automatically result in obtaining a national license as a haematopoietic stem cell bank. However, the great similarity between the JACIE standards and national standards, offers JACIE-accredited centres a solid basis to meet the requirements of the national authorities. As the national stem cell bank license does not cover directly the clinical care of the transplantation patient, the only way a Belgian centre can demonstrate high quality of practice in the clinical facility (both in- and outpatient care) is by means of a JACIE accreditation.

Conclusion

Within Europe JACIE represents the leading organisation that stimulates and evaluates high-quality practice in haematopoietic stem cell transplantation programmes. The JACIE accreditation process provides the centres the opportunity to organise quality management in a standardised and controllable way. Successful implementation of the standards offers additional benefits such as better internal work organisation and a more critical self-assessment of clinical and laboratory activities. An important advantage of the accreditation process is the transparency of the inspections and their evaluation. Initiating, developing and maintaining a JACIE-quality system obviously takes a lot of time, and assume the stem cell transplantation centres to additional financial costs (including infrastructure and staff). These efforts seem well justified as the first evidence arises that JACIE accreditation results in a safer and better patient care.

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