Scandiatransplant Tissue typers meeting, Uppsala Feb 6th 2012-Minutes

1. Welcome and presentation of participants

Mats B welcomed all to the meeting, especially the guest from Tartu, Estonia, Liina Vassil. This year 26 participants attended the meeting, unfortunately no representatives from Copenhagen could attend the meeting.

2. Election of meeting chairman and secretary

Mats B was elected chairmen of the meeting; Torsten E was elected secretary

3. Election of two persons to adjust the minutes

Frank P and Bjarne M was elected to adjust the minutes

4. Confirmation of the agenda

The agenda was adopted without any alterations

5. EU-53/2010 Directive. Implementation procedures ongoing until August 27

The chairman of Scandiatransplant, Krister Höckerstedt gave a lecture about the EU directive EU53/2010 of the European Parliament and of the Council of 7 July 2010 of standards of quality and safety of human organs intended for transplantation. This directive sets out a common framework on quality and safety standards for organs of human origin intended for transplantation. It also aims to protect donors and to optimize exchanges between Member states and third countries. The directive covers only those organs to be transplanted and not the use of organs for research purposes. The directive should be implemented in the member states by August 2012. The directive applies to:

a. Donation
b. Procurement
c. Testing
d. Characterisation
e. Transport

KH reported from a recent meeting with the health authorities in the Nordic countries in Reykjavik September 2011. Many of the objectives in the directive such as establishment of national authorities and authorisation of activities are not a problem in the Nordic countries with the existing structure. Scandiatransplant has also together with Eurotransplant worked closed together with EU in those questions. There will be a need for a new law for this directive in Sweden, Denmark and Norway. Finland already has a new law since autumn 2010. In Iceland it will be implemented in the existing law. There has also been a lot activity and discussions about other items such as the Efretos (European Framework for the evaluation of organ transplants) a project that ended in May 17 2011. The main goal was to create a common registry of registries for organ donations and transplantations in Europe. Sctp has not been in favour of this. At present Finland and Norway have national transplant registries. In Sweden every transplant centre has it own registry. At present transplant data is collected into several different registries. Finland, Norway

and some centres in Sweden are sending data to the CTS registry in Heidelberg for kidney tx. At present the SCtp system includes all organs, kidneys, livers, pancreas, hearts and lungs. Quarterly reports on transplantation activity and waiting list statistics are published on the Sctp homepage. What is needed is a definition of a common minimum data set for each organ. The authorities in the Scandinavian countries seem to be in favour of this solution. From the Directive all data in Annex A is mandatory. This includes

Type of donor

- Blood group
- Gender
- Cause of death, date
- Weight and height
- Past/present history of IV drug abuse
- Malignant neoplasia
- Viral test
- Evaluation of the donated organs
- NB. Nothing about Immunology!!

All the data in annex B is not mandatory
KH ended the presentation with that it is possible that Sctp will have to implement changes in how it works because of the Directive, at present it is however unclear how and how much.

6. STAMP, current status and follow up

Mats B pointed out that the STAMP discussions started at the Tissue typers meeting 10 years ago in Uppsala. It has been a long road until it was finally launched in April 2009. Torbjörn L then presented the latest data from STAMP. In November 2011 53 patients are listed). All centres now have patients listed, Malmö/Lund has their first entry accepted just a few days before this meeting. So far 19 kidneys have been exchanged through STAMP plus two more organs exchanged by prio 1 in the exchange rules. 15 transplants have also been performed with local organs, 4 with STAMP and 11 non-STAMP. There has been in total 8 shipments with a positive x-match at the receiving centre. Many of those were from the first period before HLA-DQ typing of the recipients was reported. Lately it seems that some positive cross matches have been caused by antibodies against HLA-DP.
Of the total 23 transplants in STAMP there have been two graft loses. One because of probable surgical complications and one with AMR at day 5. There have been three rejections reported (2 AMR+1ACR) in 18 month. TL concluded that the program so far has been successful with the possibility to have HI patients transplanted within a relative short time period with good transplantation outcome overall.

7. Quality aspects on HLA data in the Sctp database-

Torbjörn L then continued with some reflections on the quality of HLA data entered into Sctp database. Not all centres seem to be aware that DNA data always overrules serological data when entered during "search". If an organ donor is typed as B60,62 but then also DNA data is entered as B*40,15, this overrules the serological data. For STAMP patients with antibodies directed against HLA antigens, and with acceptable mismatches defined by split antigens this will render those donors useless from a

matching point of view. Torbjörn L also reminded us of the Quality assurance aspects of the Sctp database. It is very easy for the centres to check their data on a regular basis, for instance Bw4/6 missing.

8. Improvements and new facilities in the Sctp computer system

Ilse W then showed several of the new features in the database. One of the items the tissue typers asked for last year was the creation of a new category of immunized patients. Patients with <9% PRA will now be called "low immunised" in the system. The new category does not inflict with any search/exchange rule. Ilse then went through many of the improvements in the system. (Described in detail in newsletter from September 2011). Some of the highlights include the possibility to calculate the PRA based on the antibody specificities entered and calculated against a real pool of several thousands of actual donors. At present the calculation is based on HLA-A,B,DR,DQ. Antibodies against HLA-Cw do not contribute to the PRA since the database does not include HLA-Cw data in donor search at present. It is also much more easy to get an overview of previous sensitization history by inactivating antibodies no longer considered relevant. Ilse also informed all centres about the inbuilt quality control for entering new STAMP patients. Each centre can now access the same data log that the STAMP committee use for the evaluation. Hopefully all centres will use this facility prior to submitting their patients to the committee.
The following items will be displayed:

- Waiting time>1 year or child Yes/No
- PRA<3 months Yes/no
- Present immunization status HI Yes/no
- Repeated immunization status HI> 3 months Yes/no
- A,B,DR,DQ splits Yes/no
- Acc mm splits Yes/no
- Id antibodies splits yes/no
- Patient DQ in AM yes/no
- No identified antibodies in AM yes/no

The experience from the STAMP committee is that patients are submitted with errors in all of those items. Very common that patients do not have two different PRA testings within the last 3 months or that patient HLA typing includes broad antigens or that the AM includes broad antigens.

It is now also possible to calculate the transplantibility chance for each patient. It is easy to see what the chance for a particular patient to receive a kidney through Sctp is without STAMP and with STAMP. Again the calculation is against the donor pool, so data is as good as we enter it. Ilse then ended with a brief description of the LAMP program, a tool for local matching for patients not fulfilling the STAMP criteria. At present this is only used by Helsinki and Oslo.

9. Donor search; broad vs. narrow HLA specificities

Ilse W then stressed again to the audience that the search algorithm can never be better than the data we put in it for searches. During 2011 there were 423 searches, among those more than 150 used broad antigens making those donors potentially not useful for the STAMP patients. HLA B15, B40, DR3 and DQ3 are the most common broad antigens that are entered: Some centres have more than 60% of their searches

with broad antigens but even the best centres still have approx. 15% donor searches with broad antigens

10. Report of exchange compliance

Ilse W reported excellent compliance

11. General discussion on improvements in STAMP/exchange obligations

Several issues where discussed. First a quality control in the search menu that warns the user if broad antigens are entered should be implemented in order to increase the quality of search data. It was also discussed if it would be worth the effort to retype those donors with broad antigens in the pool used for PRA calculations etc. It was decided not to do this but instead let new donors with high quality data replace the old donors. The problem will be smaller and smaller over time (hopefully!). From the STAMP committee it was reported that much of the issues with new patients is the problems with antibodies against HLA-C antigens. Since there is no place in a search to enter HLA-C data on donors today and it is not used for matching the STAMP committee spends a lot of time removing B antigens from acceptable mismatch list because of strong linkage. If a patient is reported with antibodies against HLA-Cw7, HLA-B7 and -B8 is not accepted as AM. Other antigens like HLA-B51, -B27 and B44 are more promiscuous so more HLA-C antigens are in linkage. All participants agreed on that prospective HLA-C typings must be included on donors similar to what was decided previously on HLA DQ. Uppsala reported that they have without problems incorporated this in their routine work on all donors the last year. Laboratories should start with HLA-C typing ASAP, and Ilse and Frank will have a look on how to incorporate this in search. A possible solution might be to handle HLA-C similar to current procedures on HLA-DQ. A letter to inform the kidney group and the Sctp board will be formulated and sent by the STAMP committee regarding HLA-C and matching.
It was informed that when removing defined antibodies and adding them as acceptable mismatches the patient must be re-evaluated by the committee. The responsible laboratory is obliged to inform the committee in such cases. Re-evaluation is not needed when adding new antibodies and removing them as acceptable mismatches.

12. Clinical Islet transplantation

Olle K from Uppsala described the Nordic islet transplantation network. At present around 35-40 islet transplants are performed/year. The focus is at present more to transplant patients with unstable diabetes with frequent hypoglycaemias with severe influence of daily activities than to cure diabetes
10-15 patient found dead in bed going back to referral list when started islet alone program. Olle ended with a brief description of a new method for visualization of Islets. The technique relies on the capacity of islets to produce serotonin. This will hopefully be a potent tool for further investigations of islets transplants and diabetes.

13. What is the role of Complement in organ transplantation

Bo N gave an overview of the complement system especially in light of recent

publications with eculizimab and transplantation with humural rejections but also in patients with HUS.

14. Discussion on the format of Sctp TT meeting and next meeting

Mats B presented where the meetings have been last years. He had also had contact with Copenhagen that will host the meeting next year. It will be on Feb 8th 2013. In 2014 it will be in Oslo and in 2015 in Iceland

15. AOB

Malmö/ Lund wanted to discuss if it is necessary to screen patients on the WL/4 year. The participants all thought so, and no change in recommendation

16. Mats B thanked all participant and especially the speakers and closed the meeting at 1600 hrs.