Minutes from the Tissue Typers Meeting, September 20,2021, Uppsala, Virtually on Teams

1. Mats Bengtsson welcomed everyone to this year's Tissue typers meeting. A short round of presentations of the participants were done and it was concluded that there were participants from all member laboratories.

2. Mats Bengtsson was elected as chairman of the meeting and Carina Knutson Uppsala as secretary.

3. The circulated agenda was approved

4. Helle Bruunsgaard was elected to present the suggestions on behalf of the Tissue Typers group at the upcoming NKG meeting planned for Copenhagen November 11th 2021

5. Jouni Lauronen was elected to report from the Tissue Typers meeting at the Council of representatives meeting planned for Iceland August 31, 2022

6. Ilse Duus Weinreich the presented updates from the Scandiatransplant office and news in YASWA. One of the requests from several laboratories has been to implement double entry of ABO to decrease the error rate. This feature was introduced in November 2020, but so far no one have used it. It was discussed if a similar feature should be available also for HLA but it was decided to wait until the ABO function is used as intended.
   Ilse continued to report on that the Fusion to YASWA software has been updated and also that discussion has started with Immucor to establish a similar transfer from Matchit.
   The evaluation view for STAMP has also been modified and it is now easier to review new entries for the STAMP committee. Every time new information is added an e-mail will be sent both to committee members and those responsible for the patient. All comments and questions during the review process are stored in the system. A new QC check has also been implemented that compare reported HLA antibodies with the recipients own HLA type.
   There is ongoing work to make YASWA more of a working tool for coordinators during the donation process and a pancreatic Islets registry will be implemented and we can look forward to improved reports from the system.

7. Unfortunately, Pernille Koefoed-Nielsen could not present an update of the work on the follow up publication on STAMP but Ilse gave us a summary update. At last years meeting it was decided that the focus of the article should be. 1) Transplantability score as an acceptance criterion 2) 10 years graft survival 3) ABO identity vs compatibility 4) the introduction of matching for 9 loci.
   Ilse showed that the number of STAMP entries increased from 2017 when TS was introduced from a rather steady 20/year to at present almost 100 new entries/year. And this is also paralleled by an increase in the number of transplants. The most significant data is however that the 10 years graft survival for the STAMP patients are the same as any other transplant within Scandiatransplant.

Before the changing the exchange criteria from ABO identical to compatible, simulations were made that estimated that 8% mainly 0 donors would go to compatible recipients and real-world data shows 9%.
The introduction of matching also for HLA DPB1 was introduced in Jan 2019 followed by HLA DRB3/4/5, DQA1 and DPA1 in April 2020. Since April 2020 a remarkably 84% of new patients included had antibodies against the newly introduced loci. Before the change those "hard to transplant" patients were not eligible for the STAMP program
A draft manuscript is in preparation

8. Ilse then continued with a general overview of the STAMP program. Since its introduction in March 2009, 590 patients have been entered and the success rate for transplantation is 44%. The current mean waiting time on STAMP until tx is 280 days with huge variability according to transplantability score.
During 2020 there were 11 cases where a donor search resulted in more than one STAMP prio 1 exchange and currently there are no common agreement on how to prioritize. Mats gave one example with a donor with three different matching patients. The input data is ABO, time on the WL and TS score. In the case presented it was not the patient with the lowest TS that was transplanted. Mats continued with that time on WL is from first entry and that the immunization, time on STAMP is different. A check on current active STAMP patients also show that it is not uncommon that the active waiting time is less than 50%. TS could be used as the defining factor or a combinations such as WT/TS that gives priority both to waiting time and high PRA. After discussion it was decided that TS should be the selection criteria and in case same TS priority should be given to ABO identical and if that is also the same, exchange in the same country. This suggestion will be presented at the NKG meeting.
Ilse and Mats then gave a recapitulation on how the TS is calculated and some items related to ABO compatibility. Today a TS≤2 is the acceptance criteria for the STAMP program and that is calculated on ABO identity, but once accepted it will be matched on compatibility: Data from 240 patients showed that for some patients, AB and B patients there is a huge increase, In one case up to 7.05 that converts to three kidney offers per month. It was then discussed if the STAMP inclusion and matching criteria should be the same or if one should keep the current acceptance criteria but add an upper limit on compatible TS. It was concluded to suggest that there must be two acceptance criteria that must be fulfilled. 1: TS ≤2 based on AB0 identical (current criteria) 2. TS<3 based on AB0 compatibility (new criteria). This suggestion will be presented at the NKG meeting.

Mats then continued with a brief introduction of Ideferix that has recently been approved by EMEA. It is indicated for desensitization of highly immunized patients with a positive XM against a deceased donor. The use should be reserved for patients unlikely to be transplanted under available kidney allocation systems including prioritization programs. Mats gave a short description of previous protocols and also some patient examples. Mats ended with those patients on STAMP would be the ideal candidates, especially those with a TS=0. He however pointed out that the most highly immunized patients might be the one with a more vigorous rebound that might be difficult to control and AMR is expected. A more conservative approach

with de- listing of antigens with a high frequency but moderate high levels of MFI would be a good starting point. It would increase the possibility for those patients that they could remain on the WL with selected antigens removed. The group agreed on this approach and it will be presented to NKG.

9. Ilse then gave an update on the STEP program. Until now there have been seven runs and one re-run. There has been an average of 23 pairs included in each ran and on average 14 pairs came out as a match in each run. In total there been 40 chains. Out of those 15 chains have let to 35 transplantations but 22 chains have been broken. There are three remaining chains that are waiting for tx. The reasons for the broken chains are in 14 cases immunological. At present Denmark, Sweden, Finland have participated, Norway and Iceland is ready to participate but still have some work to do. Estonia is not ready at present. There are ongoing discussions on prioritizations rules and a European cooperation have made simulation tools available.
   Mats then described the 11 cases that were broken of immunological reasons and that a little less than half was related to the non-bead issue. Mats has checked the pairs in a recent run and almost all cases had issues with non-bead issues. YASWA compares if there is reactivity against a bead that carries the same allele as the potential donor. The standard OLI SAB kit only contains a bead with C*07:02 but if the donor is C*07:01- the algorithm will miss this. The problem was discussed and there was a general consensus that there should be a possible to manually block a whole antigen group.

10. Juha Perasaari then gave a comprehensive overview on background patterns seen in Labscreen. There are several typical patterns that can be recognized such as reactivity against Cw1+12+15. One important aspect is the lot-to-lot variations- in one lot you can recognize typical patterns but in the next lot a different pattern can be seen. One example was the DR4+DR16 pattern seen in previous lot that is now rarely seen. Juha pointed out that many of those patterns are not seen when testing with Immucor but that kit also has some issues (DQ2). Both vendors also seem to have issues with Cw7. The real problem is when true antibodies are mixed with background reactivity that makes it hard to recognize. Juha ended with the recommendation to carefully follow patterns and always to look for reactivity against own antigens

11. Mats then shortly presented data on a variant of the OLI SAB test. By tweaking the test, it can be run in 25 minutes instead of 85 min with excellent correlation between the two tests. To run the test in such a short time can be helpful in situations with complex reactivity in recipients or unexpected cross match reactivity.

12. The final presentation was from David Berglund, Uppsala that presented fascinating data of the CD2 monoclonal Siplizumab that will be used in several clinical trials.

13. Mats ended the meeting with thanking the participants and especially Ilse for all her hard work at Scandiatransplant. Next years meeting will be held in Copenhagen