Report on the extramural tissue typers meeting, Cologne, Germany, February 23, 2018

The extra mural meeting was opened by Vanessa Ditt (local organizer) and Sebastiaan Heidt (ETRL).

The first topic on the agenda was an update of the EPT results from 2017, presented by Yvonne Zoet (ETRL). For HLA typing, a discrepancy rate of 1.4% was observed. Bw4 was still assigned in combination with the A-locus in 5 occasions, though it was decided in 2016 that Bw4 only should be assigned in combination with the B-locus. This is due to the fact that Bw4/Bw6 assignment can be useful in assigning HLA-B antigens. For cross-matching, discrepancy rates of 3.6% and 3.1% for respective donor centers and recipient centers were observed.
To complete the overview, data from screening detection and screening identification scheme were also shown. For screening detection, a discrepancy rate of 0.5% for HLA class I antibodies, and 1.9% for HLA class II antibodies was observed. For screening identification, CDC and SPA Single Antigen techniques were assessed. In CDC, 14 consensus specificities were found and in SPA SA 422 consensus specificities were found (373 HLA class I and 49 HLA class II). In general, the discrepancy rates for the 2017 EPT were comparable to previous years.

The next speaker was Sebastiaan Heidt (ETRL), who discussed the three patient-based cases that were send to all EPT participants in 2017. Prior to the extramural meeting, a summary of the results was sent to the participants. This summary can also be found on the ETRL website. This year, one of the patient cases was on the interpretation of crossmatch results at the donor center. The two other cases involved patients with complicated immunological profiles. A lively discussion followed on crossmatch practices in donor centers, how to deal with allele-specific antibodies, as well as DQA-specific antibodies.

The meeting continued with Frans Claas (ETRL), who showed the issues discussed during the TTAC meeting on the 22nd of March 2017. He discussed the following issues:

- Relevance of the B-cell cross match in the donor center. It is known from literature that only 30% of the positivity in B cell cross matches is caused by the presence of HLA antibodies. Therefore, B cell crossmatches performed at the donor center should not be taken into account for the final crossmatch result. In case B-cell cross matches are performed in the donor center and the result is positive, the recipient center can be informed.
- Toward virtual cross matching. First the following requirements must be fulfilled:
    - A PRA >5% must always be accompanied by unacceptable antigens. The ETRL has analysed waitlist data and found many patients with a PRA >5% without any unacceptables. This goes hand in hand with the number of positive crossmatches at the donor centers.
    - Donor typing must be extended and include HLA-DRB3,4,5, -DQA, -DPB and -DPA. The TTAC has made a recommendation that this extended typing should become mandatory.
- The term vPRA has been a matter discussion for some time. Since no panel reactivity is determined for this value, but rather a calculation of the percentage of donors in the ET donor population for which the crossmatch will most likely be positive, the term vPRA will be replaced by ET-CRF, which stands for the Eurotransplant calculated Reaction Frequency.

- Minimal match criteria (for AM patients, minimal match is two HLA-DR antigens or one HLA-DR and one HLA-B antigen). For patients with a chance below 0.1% of receiving a kidney offer within the AM program, the minimal match criteria are abandoned. In the last two years, a total of 417 offers were declined based on not fulfilling the minimal match criteria. The ETRL has analysed 10-year graft survival for patients transplanted with or without the minimal match criteria, and found that graft survival is comparable. Based on these data, the TTAC has prepared a policy change to skip the minimal match criteria for all AM patients, with analysis of the effect after two years.

Next a discussion was held about the value of determining unacceptable by Screening CDC and Luminex Single Antigen, in the context of AM patients. For inclusion in the AM program, antibodies detected by CDC are leading, with antibodies detected by Luminex only taken into consideration when these can be attributed to an immunizing event. For some patients this can result in a decline to enter the AM program. One of the subjects discussed was how to include HLA epitope analysis into this process.

The final speaker of the day was Dr. Wolfgang Arns from Cologne who showed his view on HLA Antibodies in transplantation. In summary:

- HLA antibodies, especially DSAs, are important before and after transplantation
- Preformed DSAs are relevant for allocation and risk stratification
- Desensitization is an option in selected cases, however the AM program is more convincing
- The formation of de novo DSAs after transplantation is strongly correlated to antibody mediated rejection (ABMR)
- The therapeutical options to treat ABMR are still limited

Herewith the Extra mural meeting was ended. Next year's extra mural meeting will be hosted by the Tissue Typing laboratory in Groningen, the Netherlands.

In case you are interested, all presentations are published on the ETRL website.