



Dear colleagues,

In this edition of the newsletter we report on the extra mural meeting that was held in Groningen in March this year. Besides the regular agenda points of this meeting, important discussions took place on the plans of a revision of the Acceptable Mismatch (AM) program and the pathway to the introduction of virtual crossmatching within Eurotransplant. Furthermore, Marian Witvliet, who is retiring this year, showed her experience with the AM program.

Extramural meeting 2019

Many of you attended the Extra Mural Meeting held in Groningen, the Netherlands on the 8th of March. The meeting covered the following subjects: EPT results, the positive crossmatch inventory, patient based cases 2018, news from the TTAC, the road towards virtual crossmatching within Eurotransplant and more. In this newsletter more information will be given on some of these topics. A full summary and all presentations can be found on the [ETRL website](http://etrnl.org).



AM program 2.0

The Eurotransplant Acceptable Mismatch Program has been running for almost 30 years, resulting in more than 1600 transplants to highly sensitized patients with excellent outcomes. While the program is very successful, the field of histocompatibility and transplantation has progressed substantially during the last 30 years. During this time, many minor adaptations and additions to the AM program have been made, but the time has come to make some substantial changes to the AM program.

Therefore an integrated proposal to the ETKAC was discussed in the meeting of the TTAC, the day before the extra mural meeting, and was presented during the extra mural meeting. The proposal to the ETKAC includes the following:

- Change from PRA>85% to chance of receiving an organ via ETKAS of <2% as inclusion criterion.
- Change of Minimal Matching Criterion from two HLA-DR, or one HLA-DR and one HLA-B (split level) to one HLA-DR broad level.
- Waiting time before eligibility for AM is currently 2 years for all patients. Proposal is to change this towards mean waiting time of the country (separate for pediatric patients). For patients with a chance < 0.01% the waiting time criterion will be omitted.
- Determining unacceptable HLA antigens will be the responsibility of the recipient center, ETRL will check and monitor vPRA levels of patients for sudden changes around the time of AM eligibility.
- Change blood group compatible rule from ABO compatible to ABO ET compatible.

ABO compatible	
Donor	Recipient
O	O, A, B, AB
A	A, AB
B	B, AB
AB	AB

ABO ET compatible	
Donor	Recipient
O	O, B
A	A, AB
B	B
AB	AB

Please bear in mind that this is a first proposal which will be discussed in the relevant advisory committees and is therefore subject to change. For the time being, the AM rules remain as described in chapter 10 of the Eurotransplant manual.

Towards virtual crossmatching with Eurotransplant

The physical donor center crossmatch has several pitfalls and limitations, such as the need for a mandatory serum exchange program, the absence of immunological history data at the donor center, false positive crossmatches due to irrelevant antibodies, low sensitivity for HLA class II and longer cold ischemia times.

Therefore, Eurotransplant should start to implement the virtual crossmatch.

With the virtual crossmatch, the recipient center characterizes HLA antibodies in the transplant candidate in advance and decides on clinically relevant antibody specificities, which are registered as being 'unacceptable antigens' for this particular patient. Organs carrying unacceptable antigens are not allocated to the specific patient.

Several requirements need to be met to facilitate a safe transition to the virtual crossmatch:

- Alternative parameter of being sensitized: virtual PRA instead of % PRA in antibody screening
- Proper definition of unacceptable antigens
- More extensive HLA typing i.e. HLA-A, -B, -C, -DR, -DQA, -DQB, -DPA, -DPB. The TTAC will come up with a proposal for the required alleles to be reported to Eurotransplant.

Analysis by the ETRL shows that at the moment these requirements are not yet met, and therefore the ETRL has proposed a timeline for the gradual implementation of the virtual crossmatch within Eurotransplant:

1. Inventory of positive donor center crossmatches by ETRL: Q3 of 2018 and onwards
2. Introduction of vPRA as the sole way to indicate whether a patient is immunized: Q1-2 of 2019
3. Possibility to submit extended HLA typing of donor and recipient to Eurotransplant: Q2-3 of 2019
 - Monitor HLA typing progress within Eurotransplant
 - Gather data for vPRA based on all loci (retrospective data gathering may be required)
4. Minimize the number of positive donor-center crossmatches due to inadequate unacceptable antigen definition
5. Mandatory HLA typing for HLA-A, -B, -C, -DR, -DQA, -DQB, -DPA, -DPB of donors: Q2 of 2021
6. Test phase in which both virtual and physical crossmatches are performed simultaneously: Q3-4 of 2021
7. Introduction of virtual crossmatch in Eurotransplant: Q1 of 2022

The proposed timelines are indications as the implementation of some of these depend on activities and capacity of the IT department of Eurotransplant.

Goodbye to Marian Witvliet

After a career of more than 40 years in histocompatibility, Marian Witvliet will retire the 31st of May this



year. During her career, Marian has worked as technician, lab head, and of course, as AM Program officer. She has had a major role in the success of the AM program, and we are very thankful to Marian. In the last months, she has passed the work on to Marissa van der Linden-van Oevelen who will be the main AM Program officer from June onwards.

During the last extra mural Meeting Marian presented data from the AM program through the years and talked about her work for the AM program. Frans Claas took the opportunity to thank her for her efforts and commitment over the years.

What to do when receiving unlabeled samples

Sporadically, laboratories will receive samples that are not properly labeled, or not labeled at all. In case such sample is received, please file a complaint at the Eurotransplant office through email. You can send your reaction to complaints@eurotransplant.org. Within two weeks the complainant is informed how the complaint will be handled. Eurotransplant aims for a reaction within four weeks.