25th anniversary of the Acceptable Mismatch program

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25 year AM program

- History of the AM program and numbers
- Transplant outcome
- Future plans
In the eighties of the past century it became clear that there was a group of patients who could be hardly transplanted; the highly sensitized patients.

Eurotransplant experience with highly immunized patients. 1985

Council of Europe study of high sensitization in renal transplantation. 1987
Little chance for a donor
25 year AM

Definition of highly sensitized:

At least 85% PRA in two different serum samples caused by HLA allo antibodies or a virtual PRA of at least 85%
25 year AM program

In 1985, Frans Claas received a grant from the Dutch Kidney Foundation to develop a new approach to enhance transplantation of highly sensitized patients in the Netherlands. These patients had often a waiting time of more than 10 years and many of them never received an offer.

Strategy: looking for CDC crossmatch negative blood donors to define antigens against which the patient did not make antibodies.

At first experimental in the Netherlands to show feasibility. No AM registration yet in the ET database.
Selection of acceptable antigens by CDC

- Patient A24 A29 B8 B62 DR1 DR10

- Test donor 1: **A1** A24 B8 B62 DR1 XMNEG

- Test donor 2: A24 **A32** B8 B62 DR10 XM POS

- Test donor 3: A1 **A2** B8 DR1 DR10 XM POS

- **A1** is an acceptable antigen

- **A32** and **A2** are unacceptable antigens
A special strategy to increase the chance of finding cross-match negative kidneys for highly sensitized patients.


The results were very successful and published in 1988. This resulted in the implementation of the Eurotransplant acceptable mismatch program in 1989. The AM of all Dutch patients had already been defined and could be introduced immediately in the AM program.
Principle: any donor with a HLA type which is a combination of the patients’ HLA and AM will have a negative crossmatch.

HLA patient: A24, A31, B27, B51, DR4
AM: A25, A26, B44

Suitable kidney donors:
- A25, A31; B27, B51; DR4
- A26, A31; B27, B51; DR4
- A24, A25; B27, B51; DR4
- A24, A26; B27, B51; DR4
- A24, A31; B44, B51; DR4
- A24, A31; B27, B44; DR4
- A25, A31; B44, B51; DR4
- A26, A31; B44 B51; DR4
- A25, A31; B27, B44; DR4
- A26, A31; B27, B44; DR4
- A24, A25; B44, B51; DR4
- A25, A31; B27, B44; DR4
- A25, A31; B27, B44; DR4

If such a donor becomes available, mandatory shipment of the kidney to the recipient center

HLA phenotype used for allocation
Period 1989-2013

New on AM waitinglist  n= 2011
AM patients per country

- Ned: 850
- Ger: 650
- Aus: 100
- Bel: 100
- OTH: 0
Participation AM by the time

New on AM waitinglist

1989-2000

2000-2013
From 2000 expansion of countries actively participating in the AM program

Patients moved from the HIT (Highly Immunized Tray, developed by Gerhard Opelz) program towards the AM program

Many publications about AM i.e.

Percentage of patients included in the AM program of the national waitinglist per country

Waitinglist January 2014

- Ned: 2.5%
- Ger: 2.0%
- Bel: 3.5%
- Aus: 3.0%
- OTH: 1.5%
The AM program has been available for 25 years

Intended for patients with PRA in CDC above 85%

From 2000, increasing participation by different centers all over ET
25 YEAR AM

- Transplant results
Number of transplants via the AM program n=938

1989 until 19-9-2012
Number of AM patients transplanted versus new AM patients on the waiting list

- New on AMWL n=2011
- AMTX
Percentage AM transplants of the total number of deceased transplants/year
Graft survival of AM patients is similar to that of non-sensitized patients.
AMTX failures

1996 implementation ETKAS match program
2006 DR split matching
What is the result of 25 years of AM

- Already 1000 patients transplanted
- Very good transplant survival, comparable with non-AM transplants
Future plans

There are some problems to be solved:

For some patients the chance to receive a transplant remains very small because of their exotic HLA in relation to the ET donor population.

What to do with antibodies reactive in luminex only?
Different sensitivity of the assays has an enormous impact on the percentage immunized patients on the waiting list.

% sensitized patients

- CDC: 7%
- ELISA: 15%
- Luminex MFI > 1000: 82%

Süsal et al, 2012
Future plans

What to do with DSA luminex? Discussion is needed because so far, antibodies detectable in CDC are still leading for inclusion in the AM program.

Collaboration with other transplant organizations. EUROSTAM project: simulation studies to calculate the chance that patients will be transplanted with a donor derived from other populations with different HLA phenotypes resulting in a limited number of transplants.

Change inclusion criteria from (v)PRA to a very low chance to be transplanted with a compatible donor.
Thank you!!

Eurotransplant
ET labs
Leiden HLA lab and immunologists
ETRL team
Frans Claas