

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



25 year AM

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

G.F.J. Hendriks, P. de Lange, J. D'Amaro, G.M.Th. Schreuder, F.H.J. Claas, G.G. Persijn & J.J. van Rood.

Eurotransplant experience with highly immunized patients. 1985

B.A. Bradley, S.M. Gore, E. Albert, F.H.J. Claas, G.G. Persijn, R. Fauchet, M. Jeannet, L. Lamm (and others).

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.

F.H.J. Claas, Y. Gijbels, J.J. van der Velden-de Munck, L.P. de Waal, J. D'Amaro, G.F.J. Hendriks, G.G. Persijn & J.J. van Rood.
Transpl. Proc. v. XX, no. 5: 947-948, 1988.

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**

**HLA phenotype
used for allocation**

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 etc.

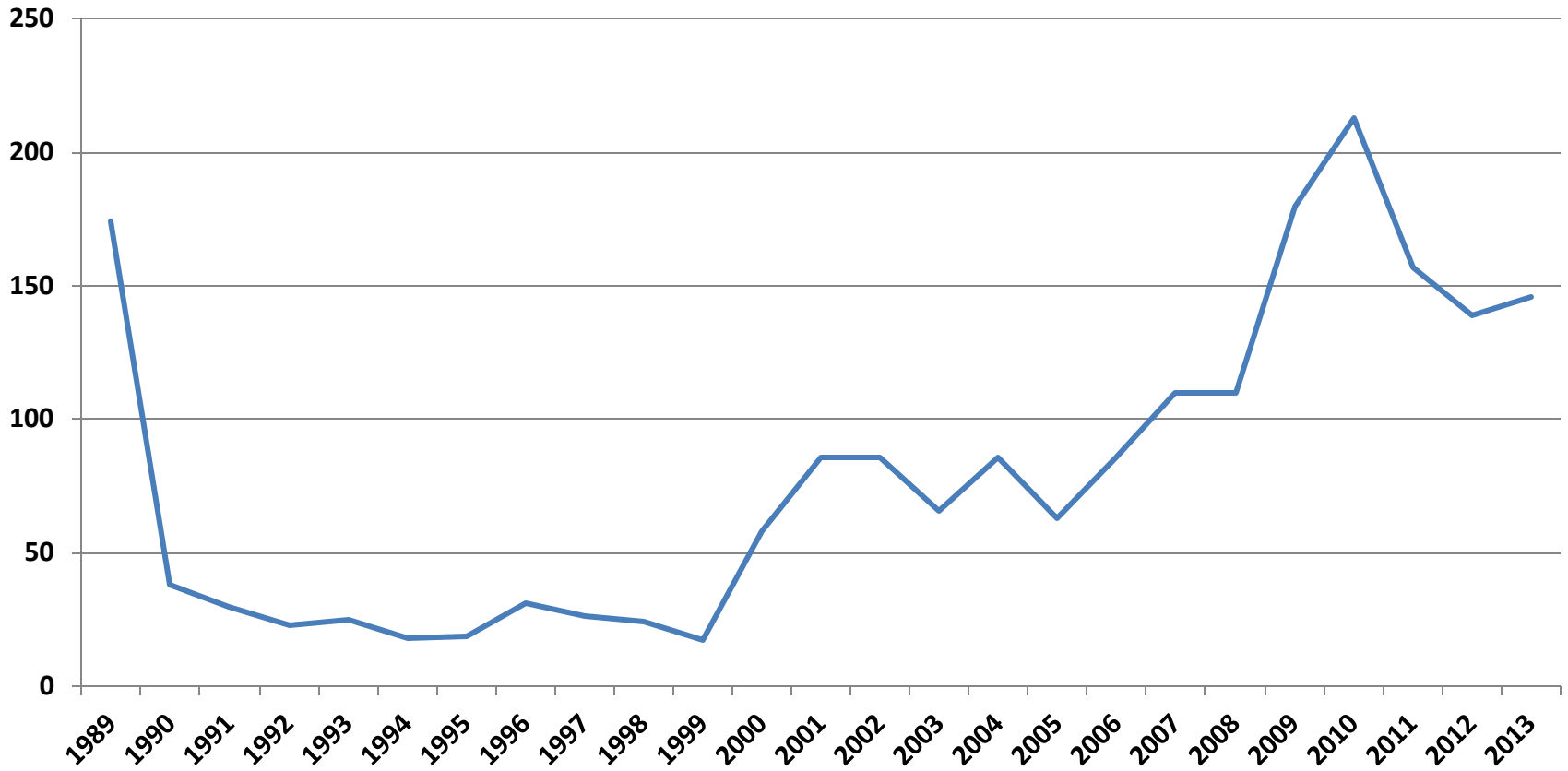
If such a donor becomes available, mandatory shipment of the kidney to the recipient center





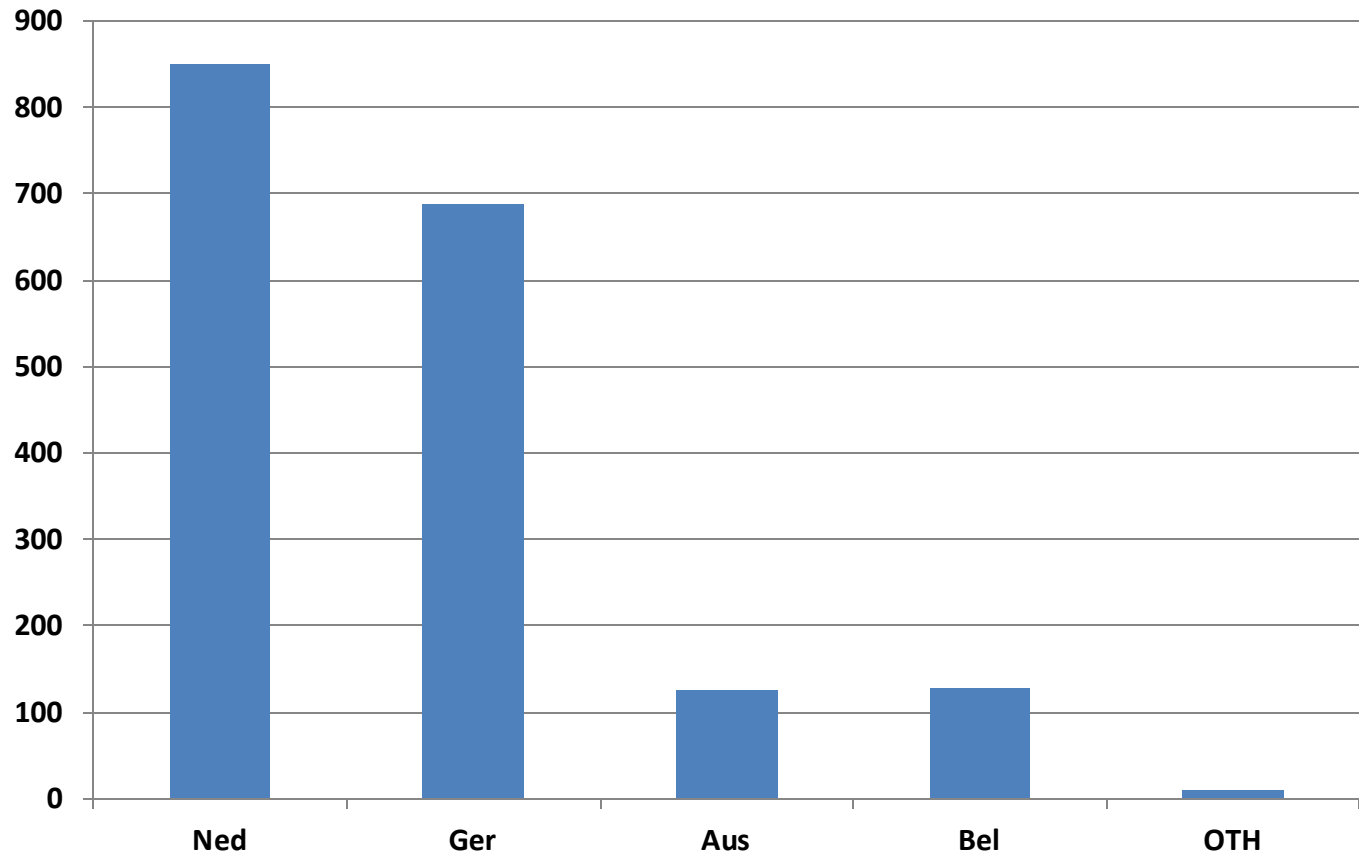
Period 1989-2013

New on AM waitinglist n= 2011





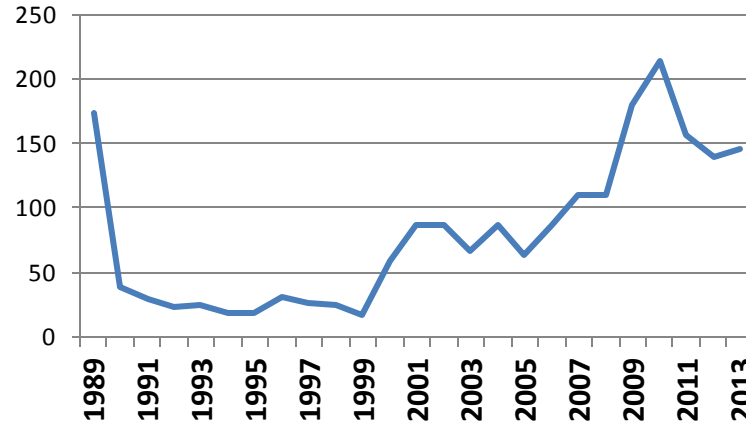
AM patients per country



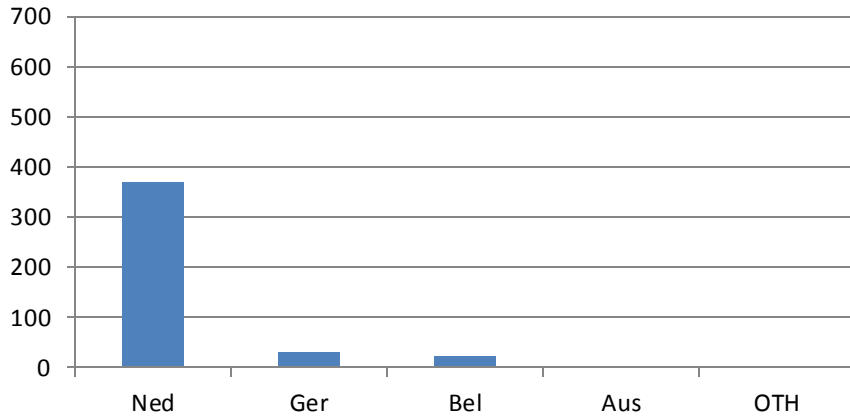


Participation AM by the time

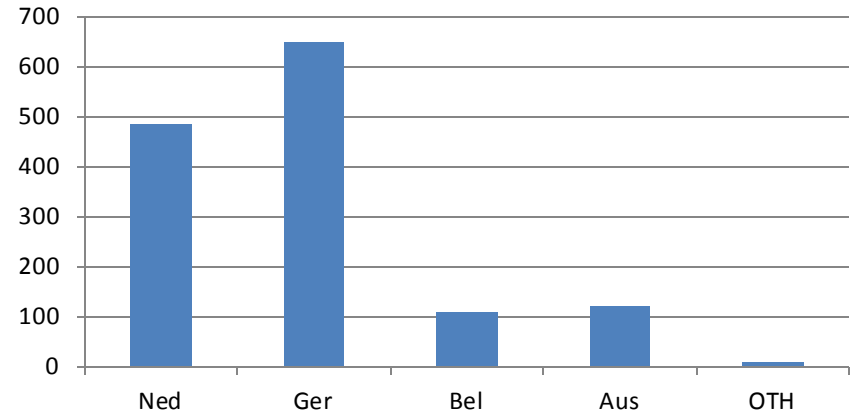
New on AM waitinglist



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

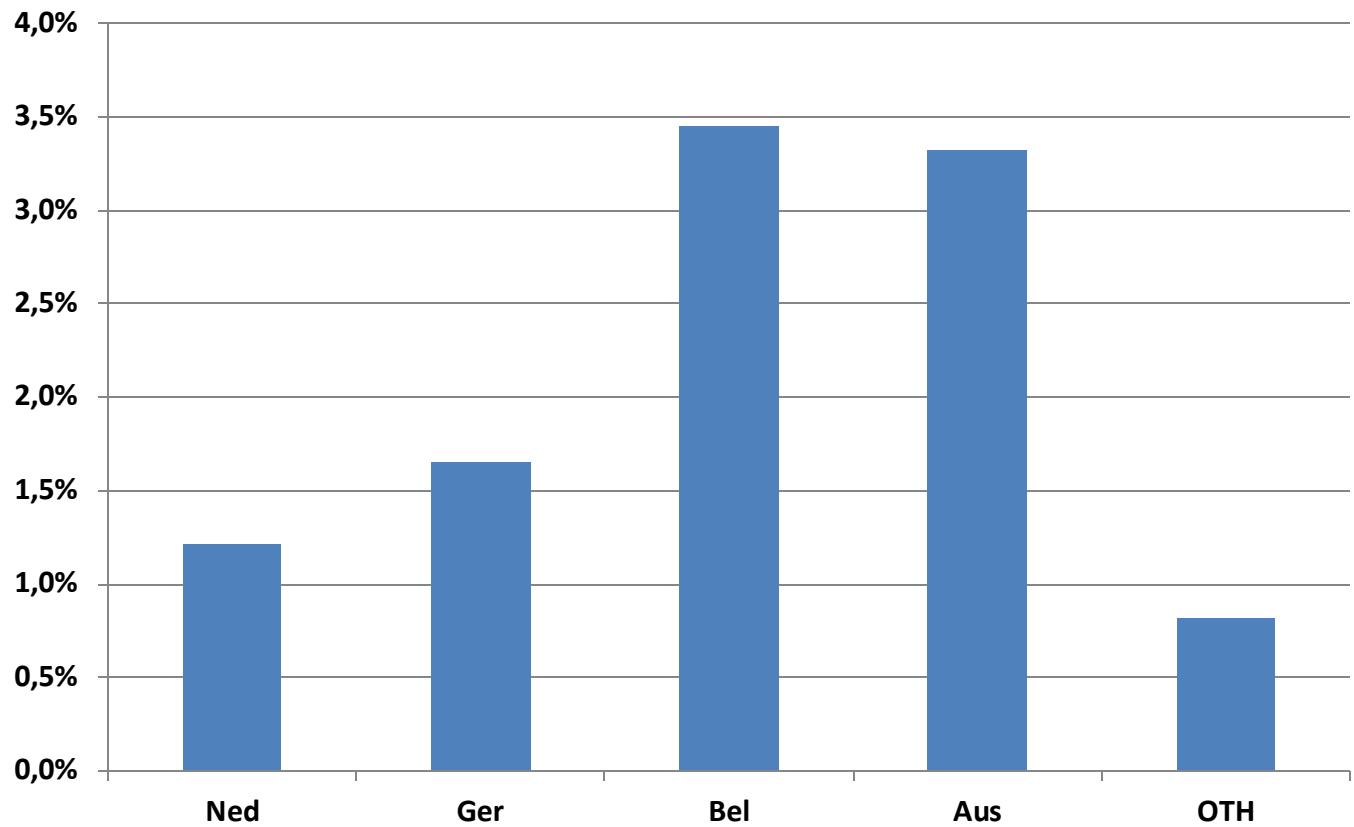
Many publications about AM i.e.

- Hyperimmunized patients do not need to wait for an HLA identical donor. Tissue Antigens 1989.
- Permissible mismatches, acceptable mismatches and tolerance: New trends in decision making. Clinical Transplants 1993.
- Acceptable HLA mismatches for highly immunized patients. Immunogenetics 1999.



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

Waitinglist January 2014





Summary first part

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



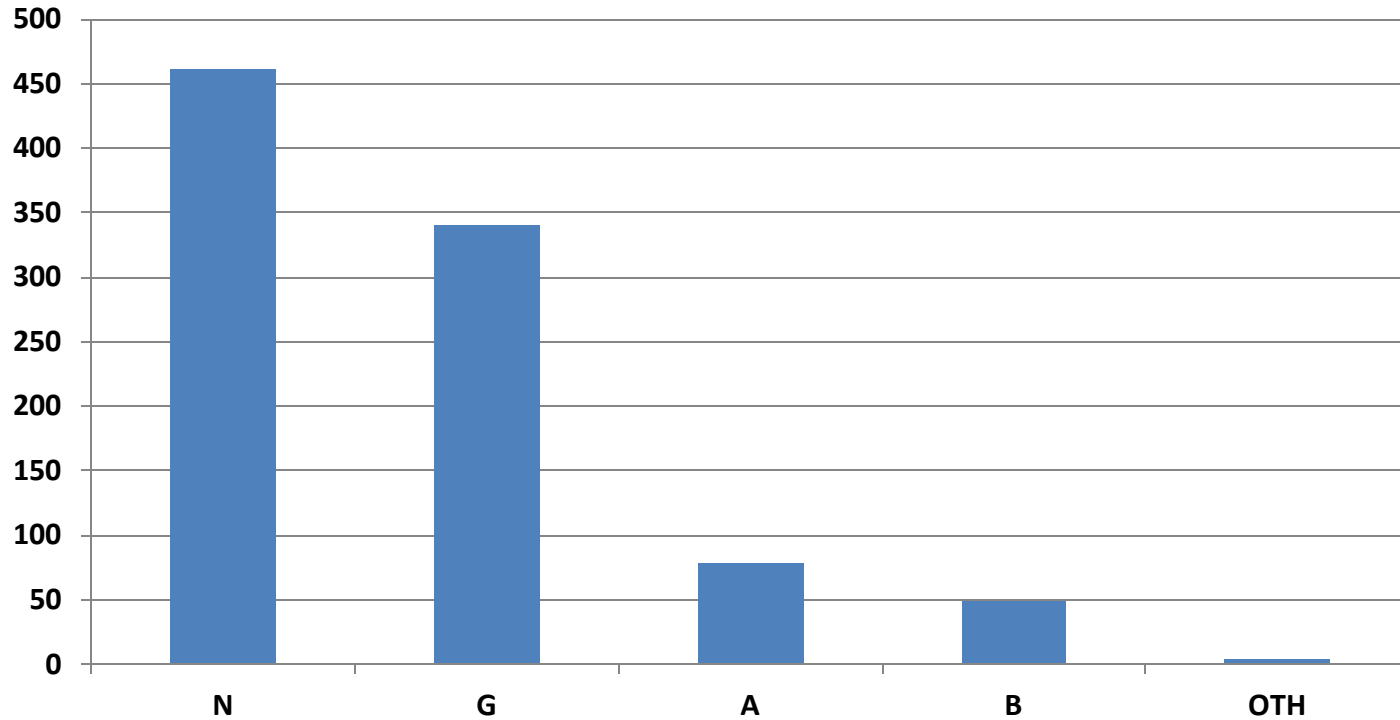
25 YEAR AM

- Transplant results



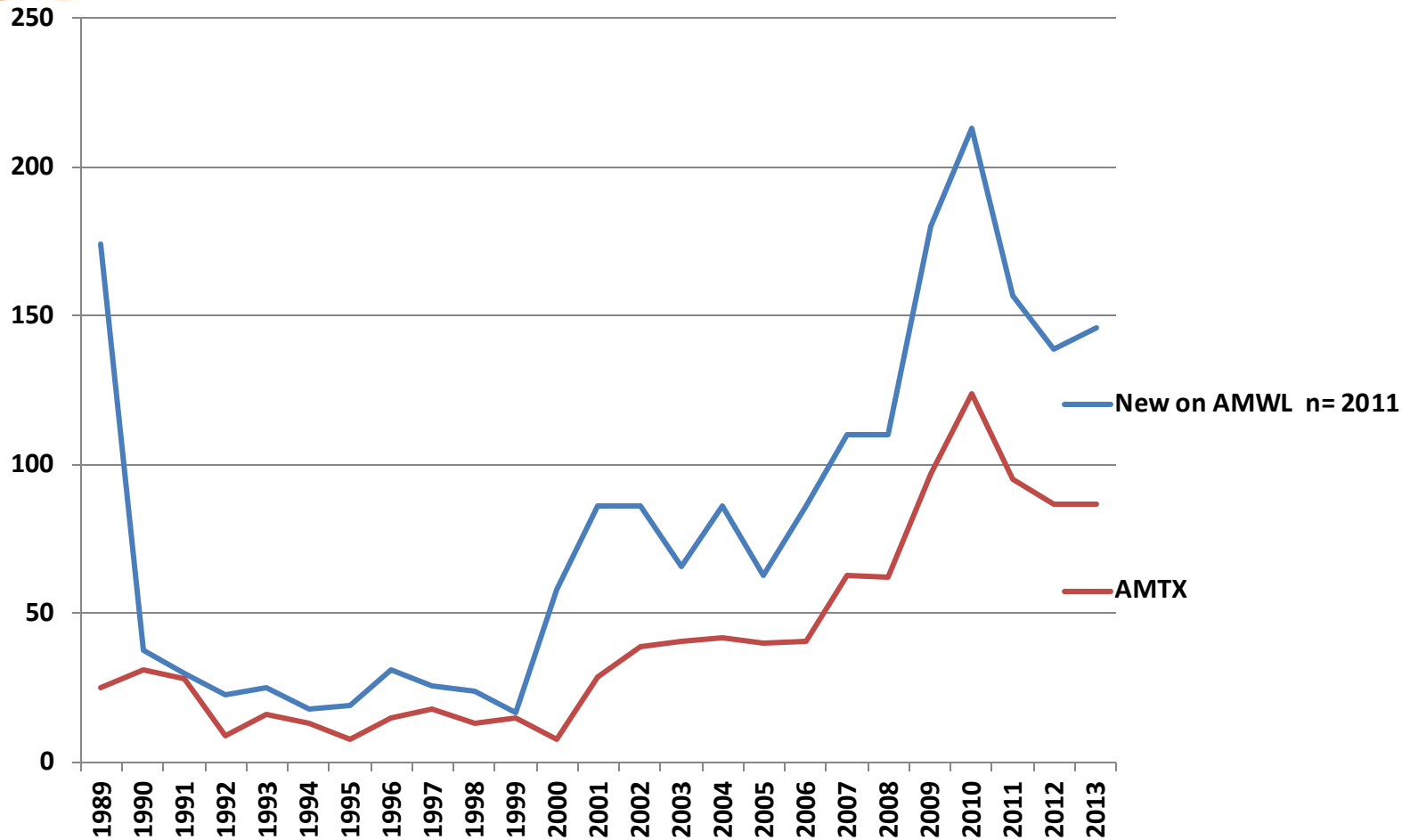
Number of transplants via the AM program n=938

1989 until 19-9-2012



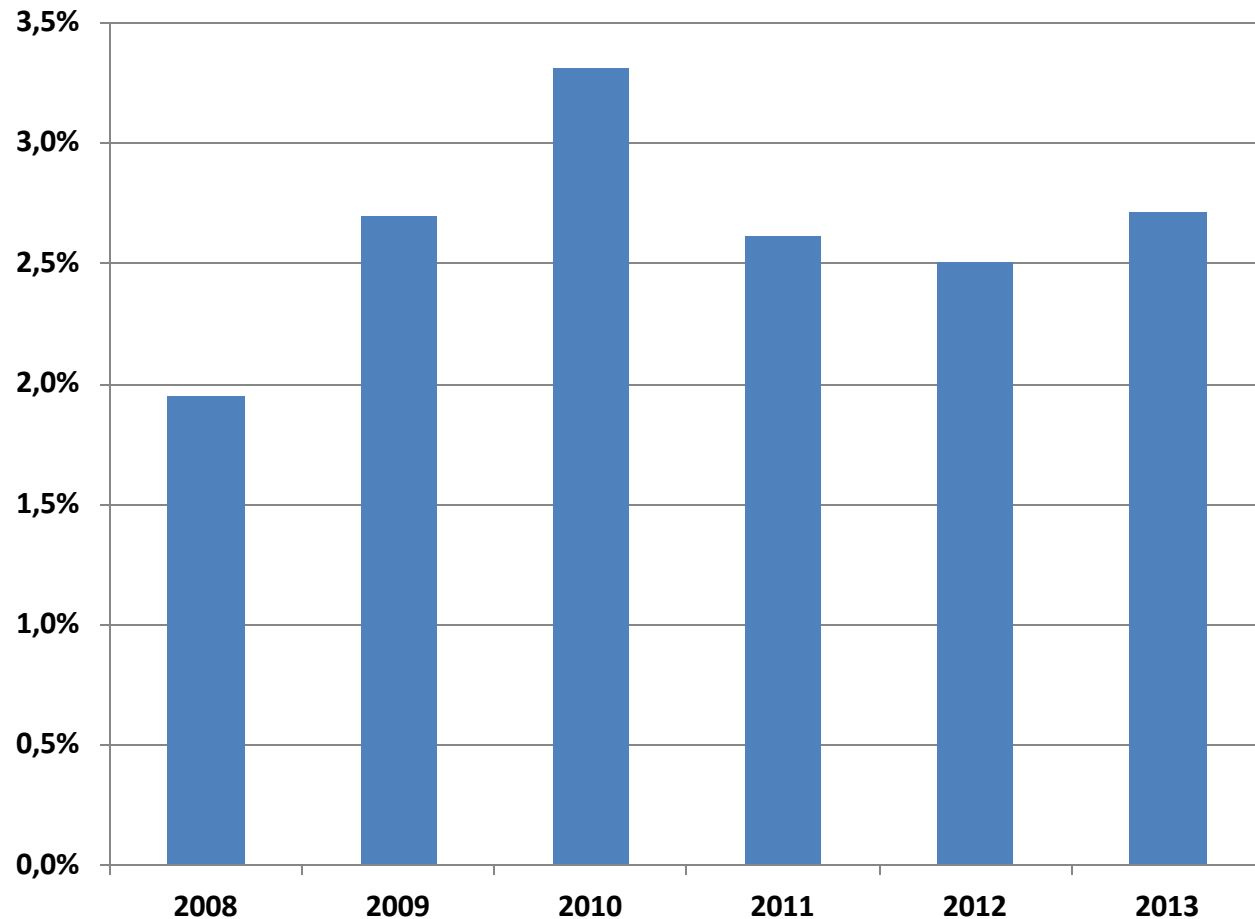


Number of AM patients transplanted versus new AM patients on the waiting list



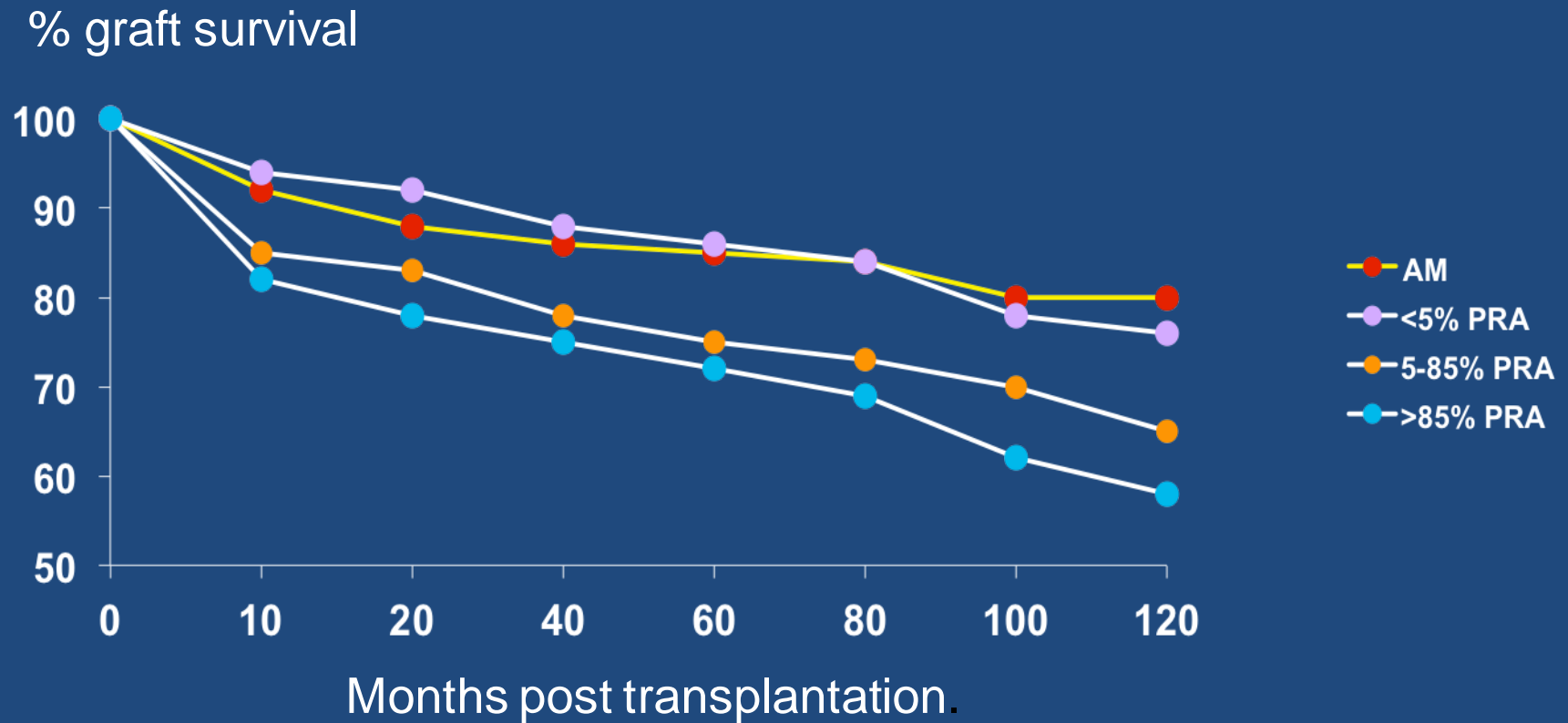


Percentage AM transplants of the total number of deceased transplants/year



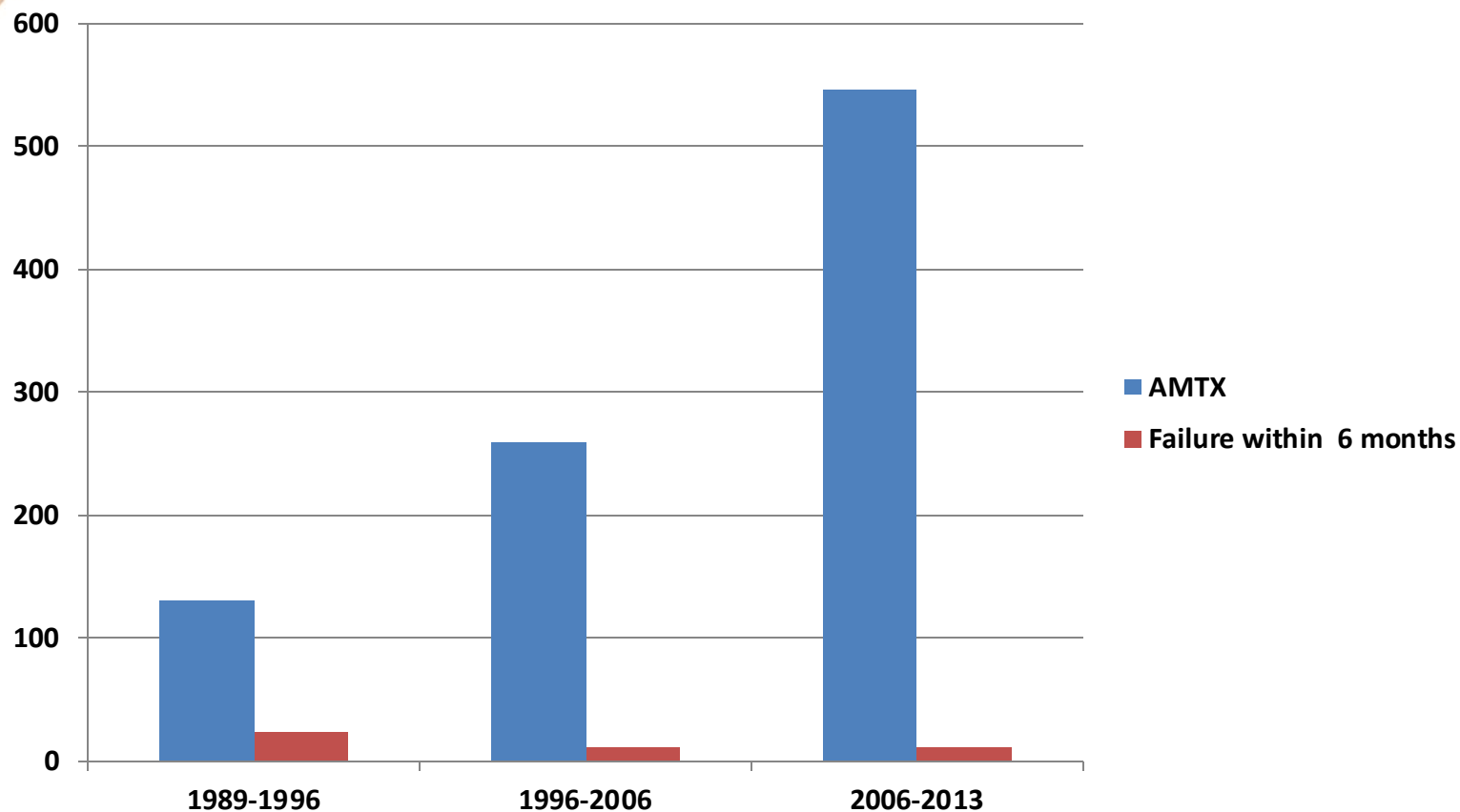


Graft survival of AM patients is similar to that of non-sensitized patients.





AMTX failures



1996 implementation ETKAS match program
2006 DR split matching



Overview second part

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:

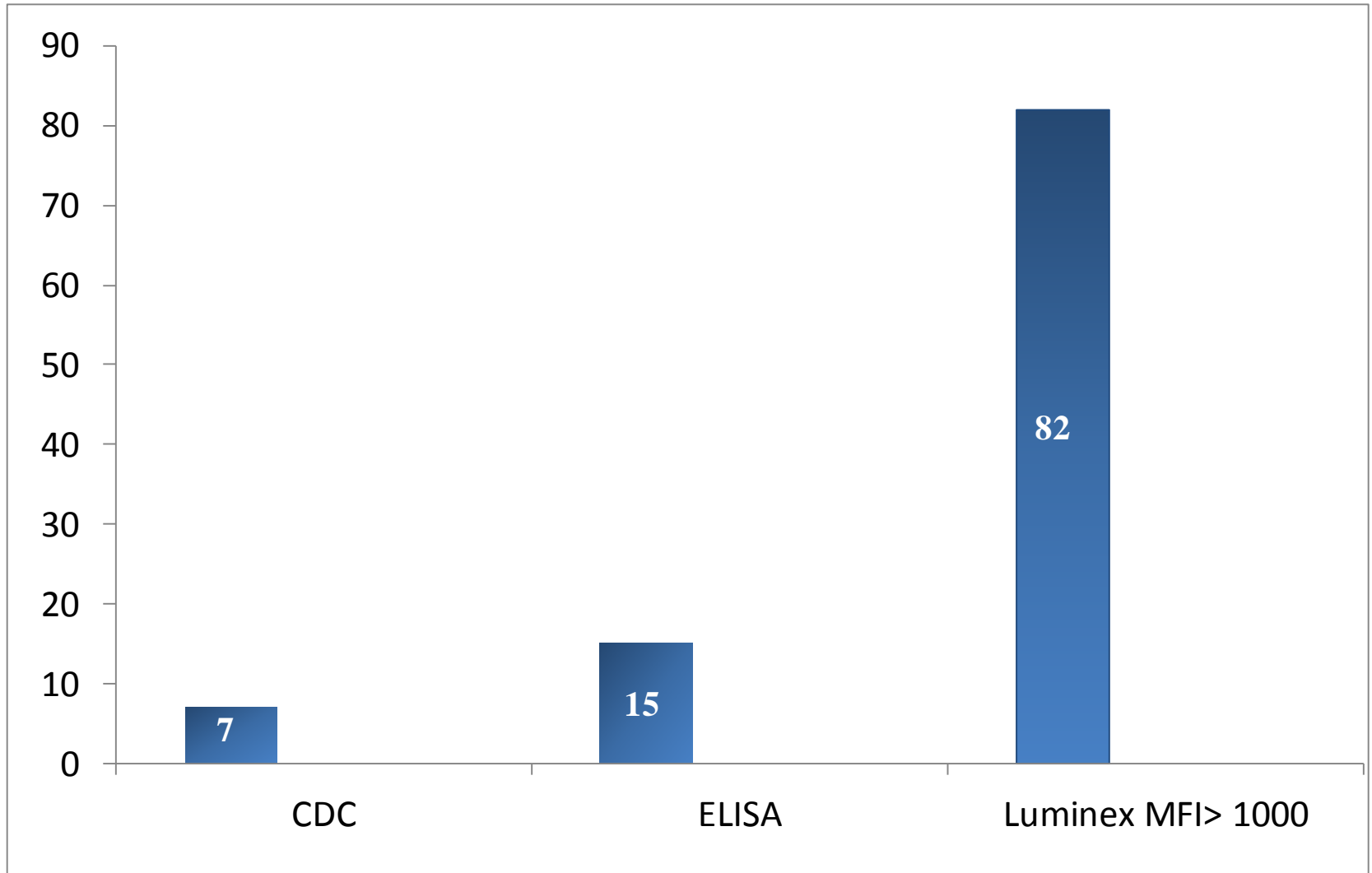
For some patients the chance to receive a transplant remains very small because of their exotic HLA in relation to the ET donor population.

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





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