Leiden University Medical Center

Eurotransplant Reference Laboratory

Patient HLA typing on split antigen level

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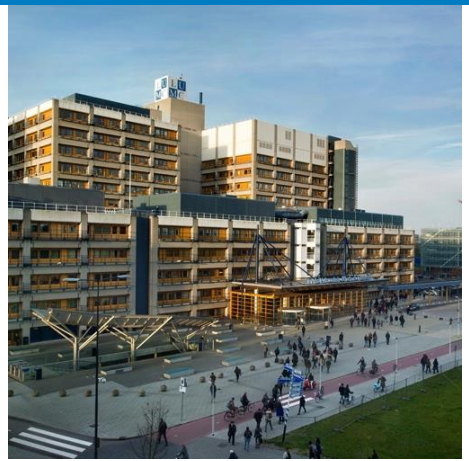

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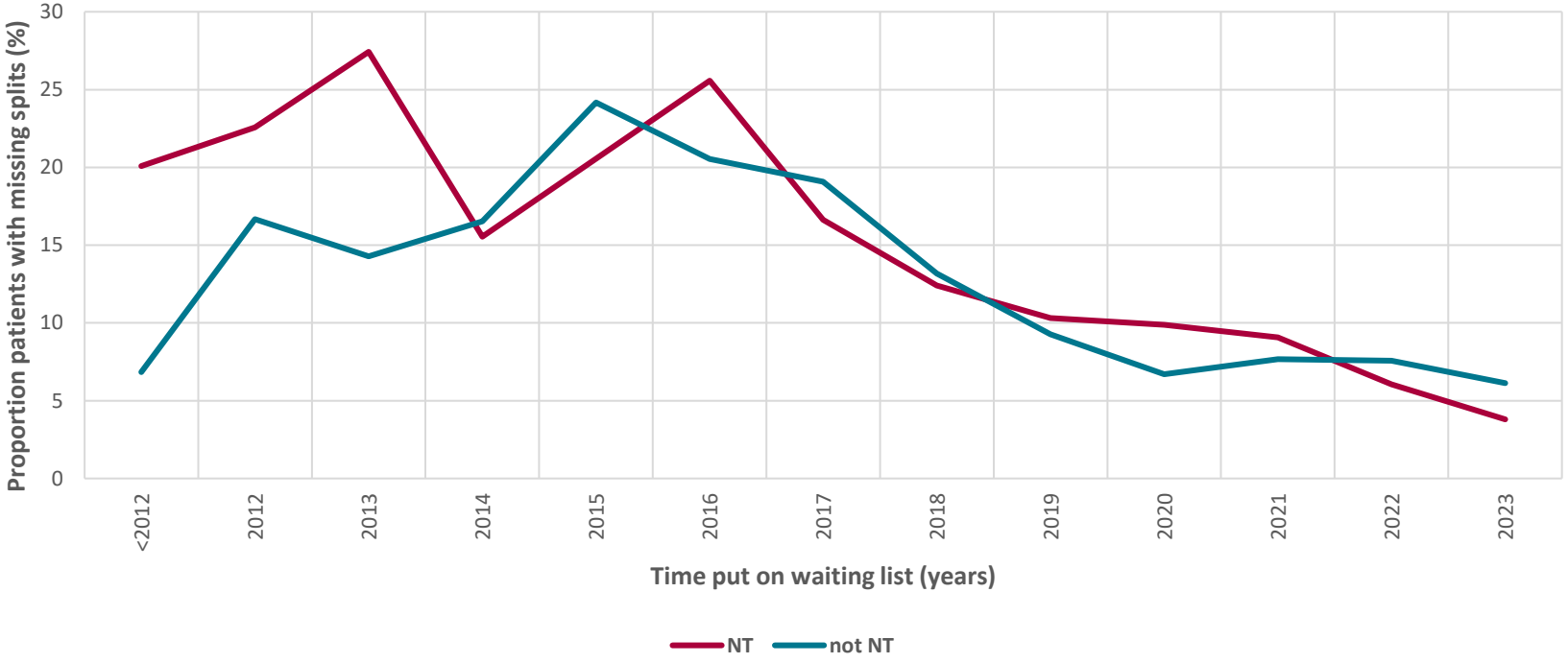
Unsplittable broads

Unsplittable broads are antigens that use to be difficult to distinguish on the split level with HLA typing methods and therefore were considered on **broad level** instead of split level

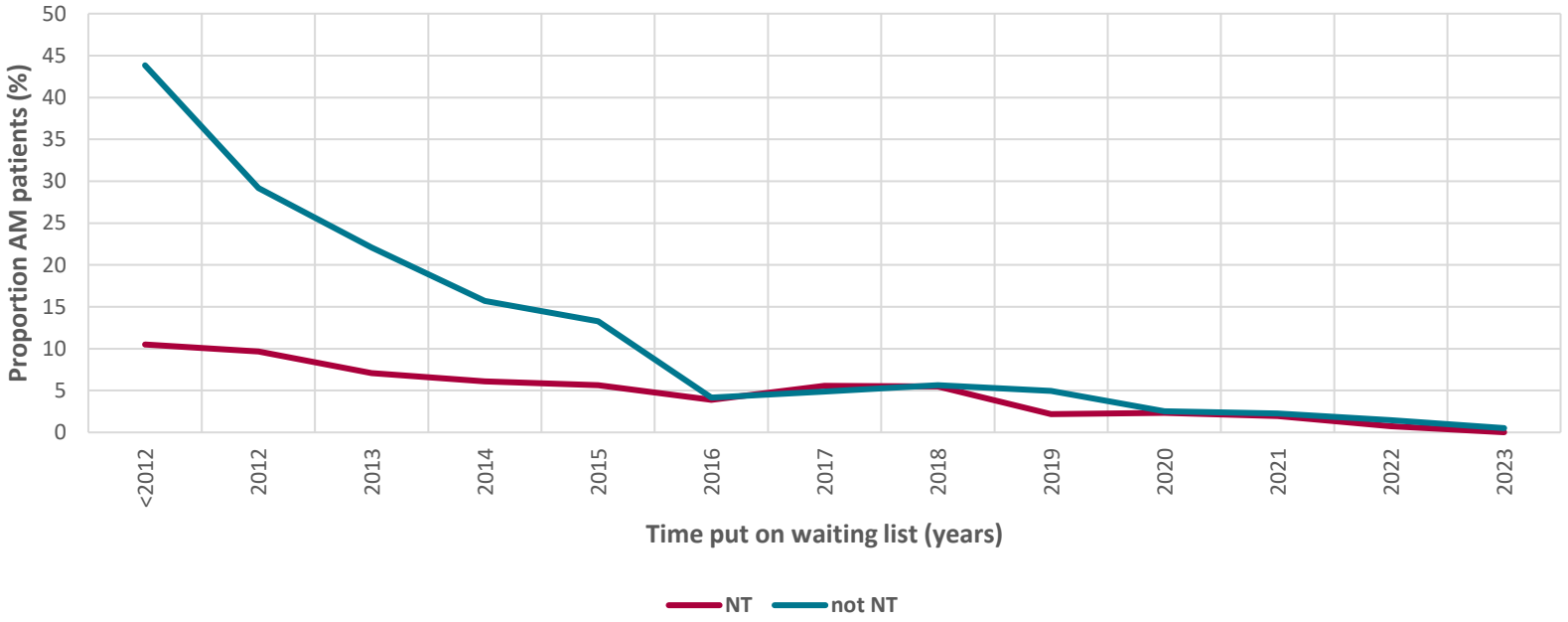
Cw3	B14	DR3
Cw9	B64	DR17
Cw10	B65	DR18

Number of patients with missing HLA typing on split level decreases



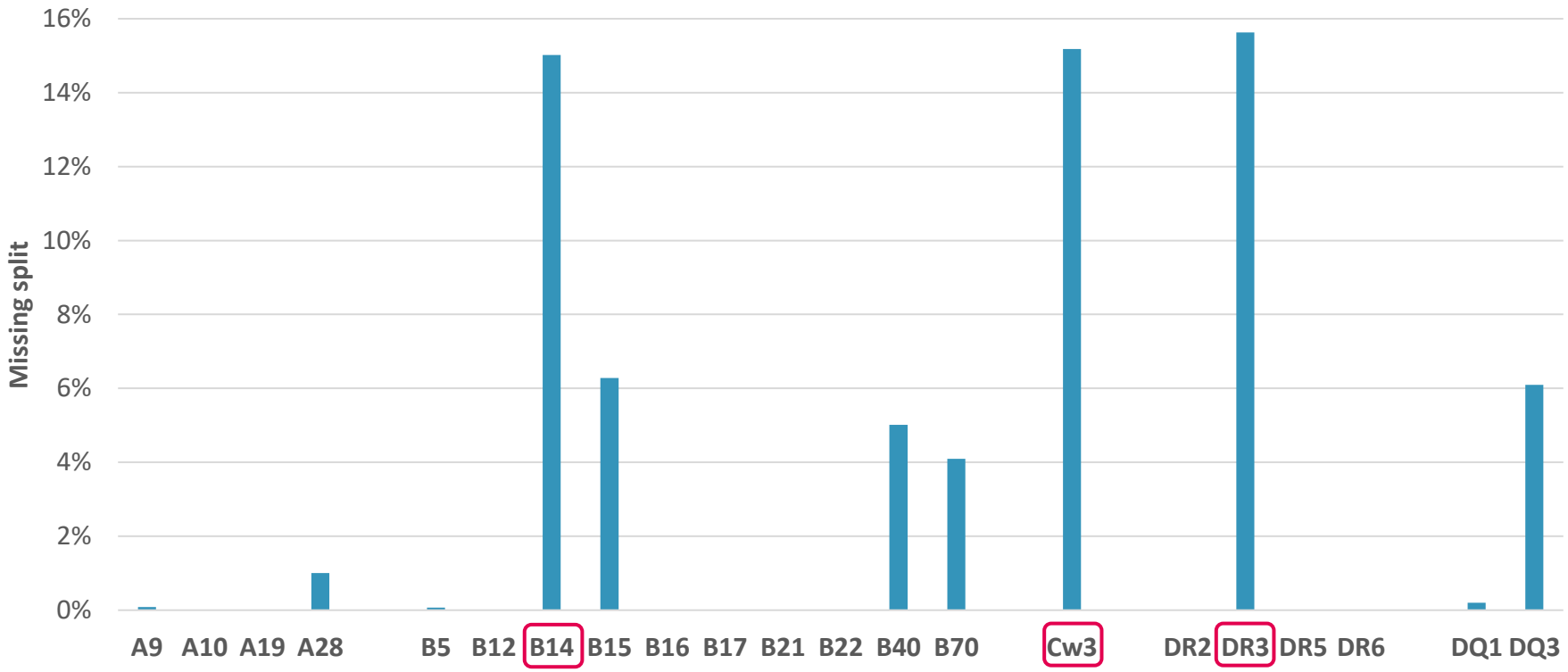
ETKAS waiting list as of 18-01-2024

HLA typing of AM patients on waiting list are completely at split level



AM ETKAS waiting list as of 18-01-2024

Split antigens are mainly missing for HLA-B14, HLA-Cw3, and HLA-DR3



ETKAS waiting list as of 18-01-2024

Patient HLA typing completely on split antigen level

- Donor HLA typing analysis indicated that it is possible to distinct the split of a broad antigen
- HLA-DR match is performed on split level, except for HLA-DR3
- Exception rules for unsplittable broads are currently incorporated in matching algorithm
- Unacceptable antigens are listed on more detailed level

- **We kindly request all centers to review their patients' HLA typing for completeness in terms of antigen split level, especially for HLA class II. If necessary, please add any missing split antigens.**

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Feasibility of retrospective recipient center crossmatches

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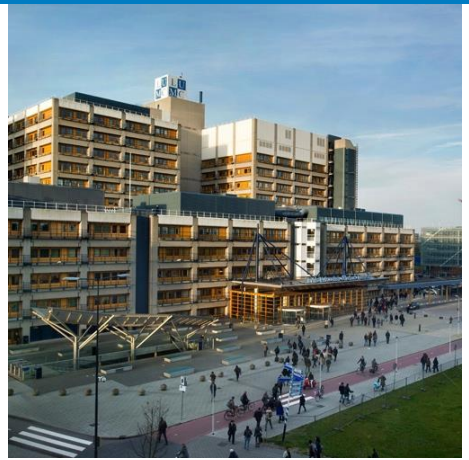

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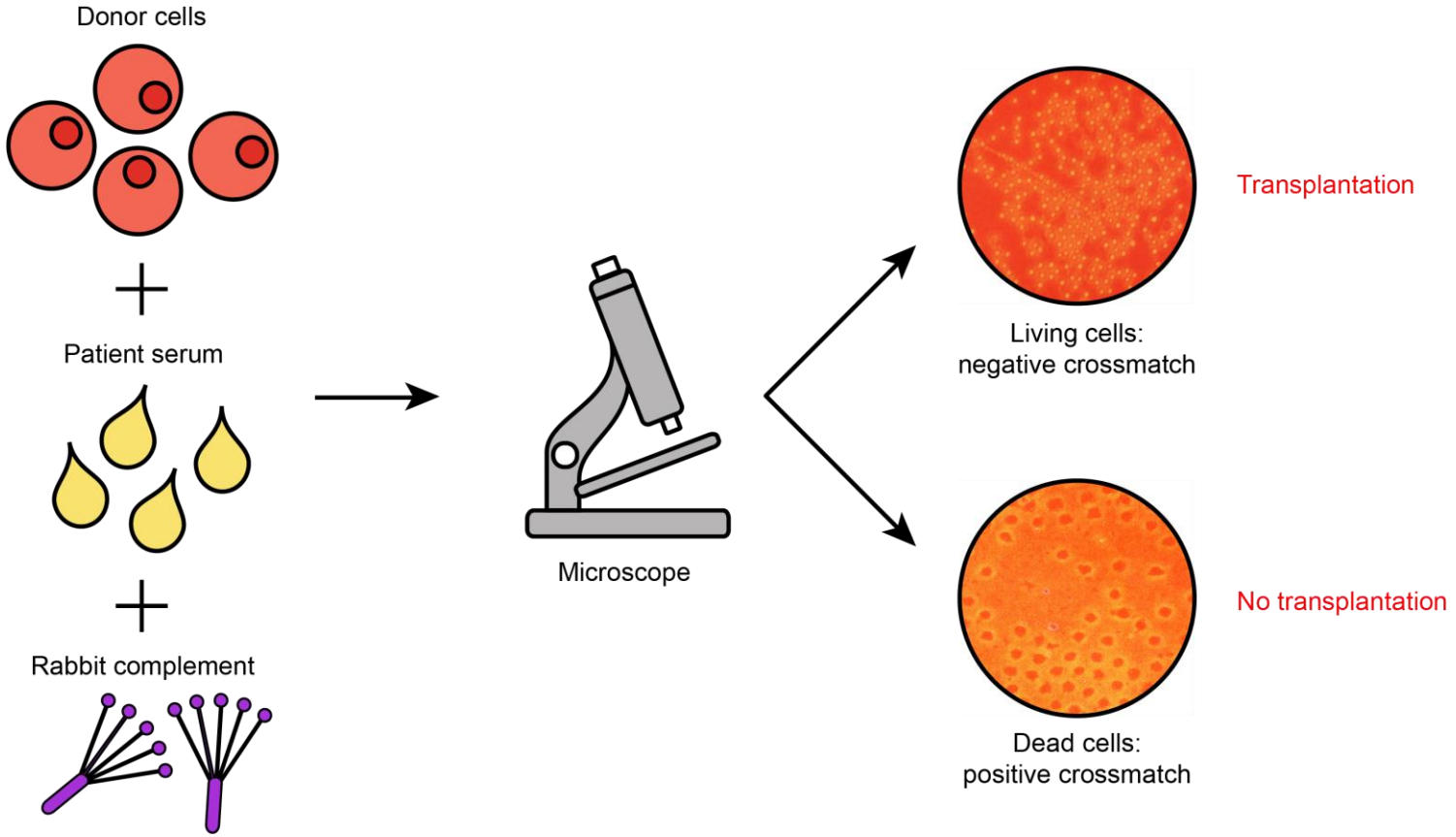
Transplantation can only be performed in case of a negative decisive crossmatch, unless otherwise decided by the local transplant center



Decisive crossmatch must be performed before transplantation for immunized recipients

ET manual 10.4.2 The "transplantation" or "decisive" crossmatch"

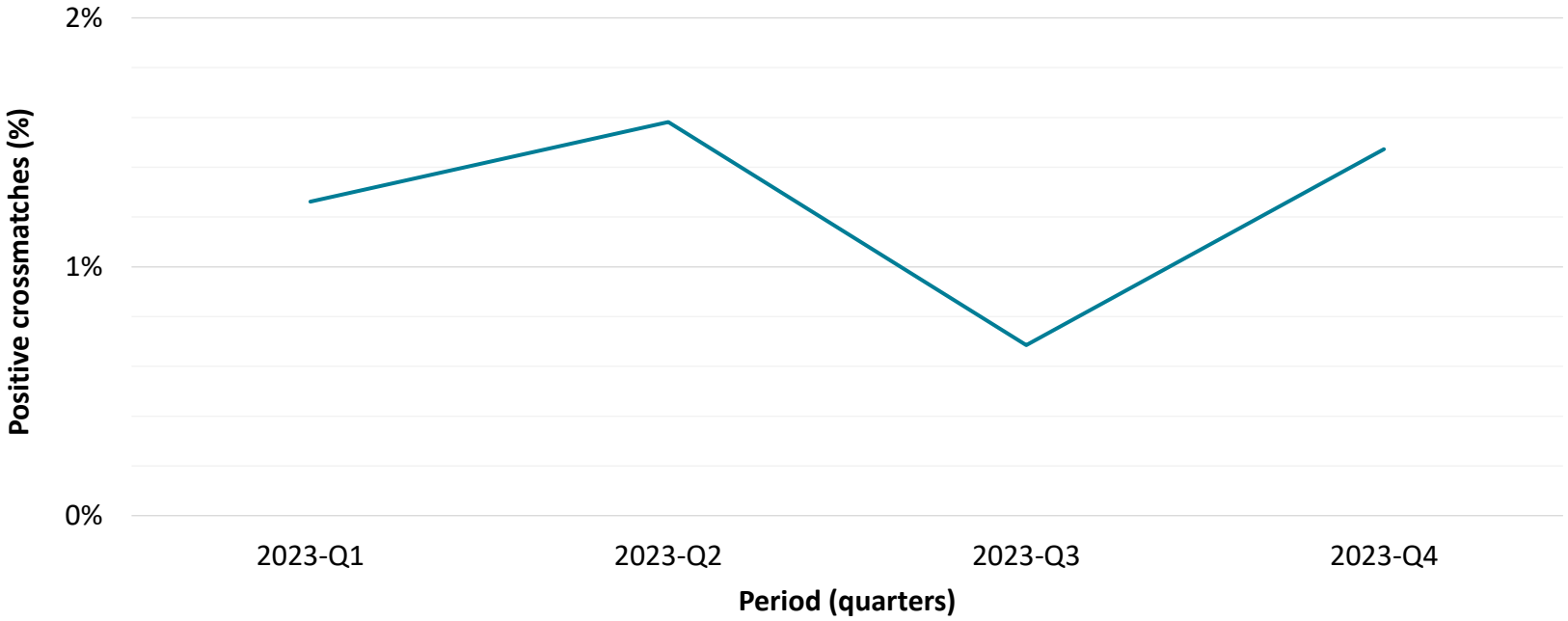
"For kidney and combined kidney/pancreas transplantation of a recipient with a vPRA>0% a decisive crossmatch must be performed before transplantation"

HLA antibody status	Unacceptable antigens defined	vPRA	Decisive crossmatch
No HLA antibodies or only non-complement fixing HLA antibodies	No	0%	Yes (may be retrospective)
	Yes	>0%	Yes
Complement fixing HLA antibodies	Yes	>0%	Yes

Table 10.4. Overview of physical crossmatch rules

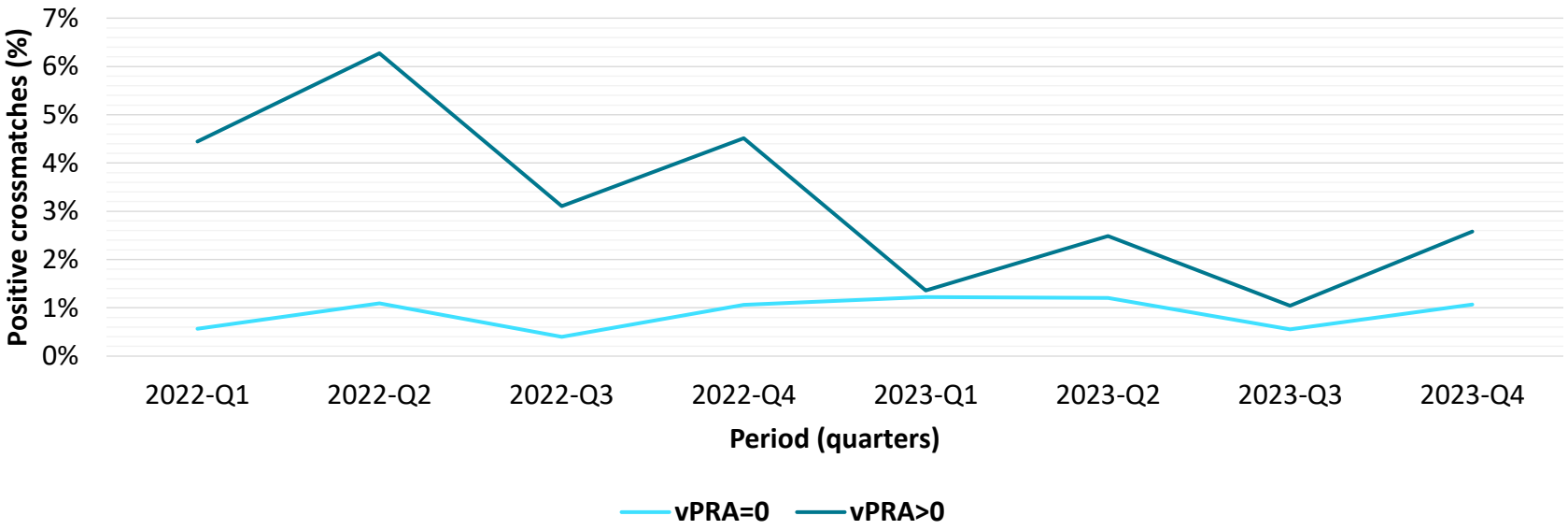
Relative positive recipient center crossmatches in 2023

Out of 5580 crossmatches performed 68 were reported as positive



Kidney & pancreas only

The positive crossmatches for vPRA>0% recipients approaches the same level as the vPRA=0% recipients



Kidney & pancreas only

Most positive crossmatches were reported for back-up recipients with vPRA=0%

	Shadow phase		Post-shadow phase		
	vPRA = 0%	vPRA > 0%	vPRA = 0%	vPRA > 0%	Total
Decisive crossmatches	2	3	3	17	25
Back-up crossmatches	10	2	24	7	43
Total	12	5	27	24	68

Positive transplant crossmatch explanation Germany

Transplant crossmatches in Germany 24.4.2023-12.2.2024:

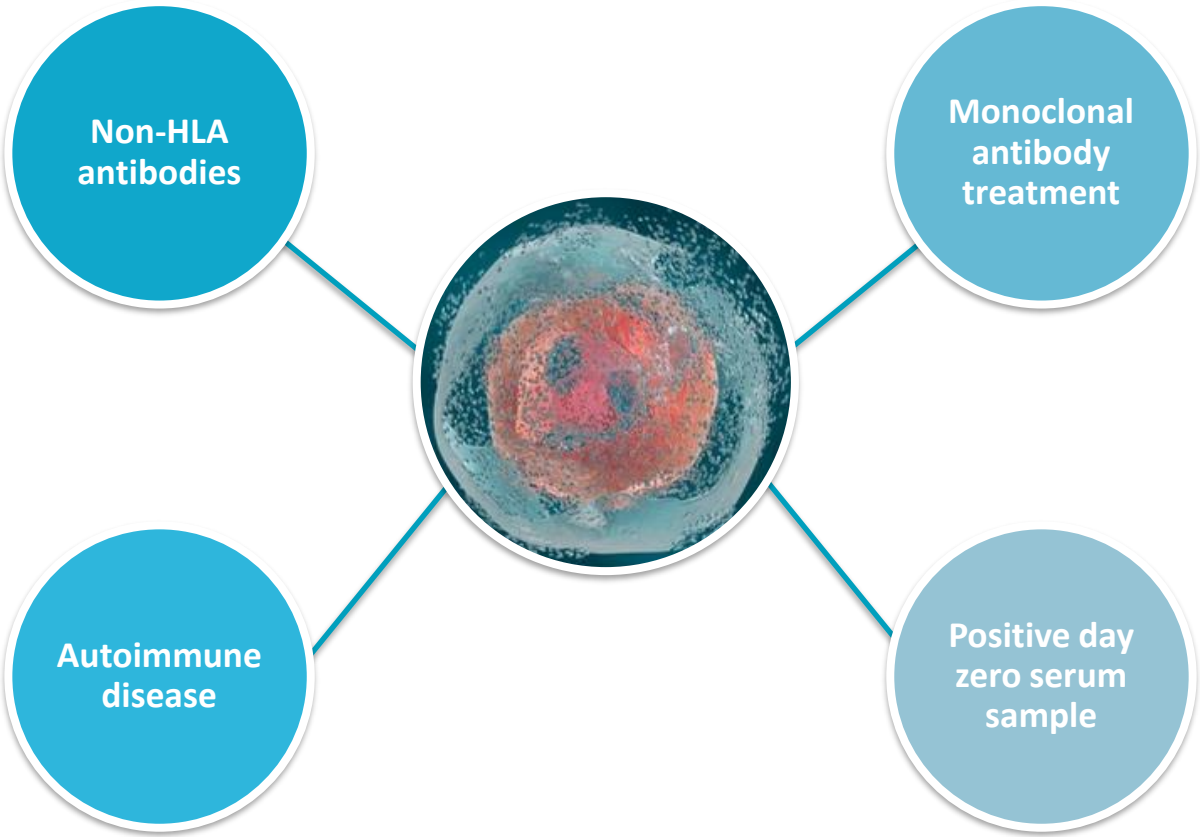
8 positive final results (after exclusion of back-up recipients)

- 1 patient with a positive day-of-transplant serum after recent transfusions
- 1 AM patient with allelespecific unacceptable antigens
- 6 patients without DSA
  - Known autoimmune diseases
  - 4 crossmatches performed only without DTT
  - 2 crossmatches after DTT-treatment positive only for B-cells

➔ Presumably due to non-HLA antibodies.

Data kindly provided by DSO

Explanation of positive decisive crossmatches



EFI standards for omitting prospective crossmatches for immunized patients

- According to EFI standards the prospective crossmatch can be omitted for:
  - Carefully **selected** HLA immunised patients
  - Latest screening performed **within 3 months** of organ offer
  - Latest screening includes **single antigen bead** (SAB) testing
  - SAB testing performed for both **HLA class I and II**
  - Latest screening **without** any potential immunising events in between

Towards retrospective crossmatch for immunized patients

How can we create a situation to omit all prospective crossmatches for all patients including immunised patients?

Towards retrospective crossmatch for immunized patients

- Which patients will be suitable for retrospective crossmatches?
- What are well characterized HLA immunised patients?
  - SAB testing of serum within 3 months of organ offer for both HLA class I and II
  - CDC screening of patient serum must have been performed to confirm absence of cytotoxic HLA antibodies
    - Negative CDC screening will result in negative crossmatch
- Should it be in close consultation with clinicians to exclude the possibility of recent booster and/or immunising event?
- Is a prospective flow crossmatch or rapid SAB assay with day zero sample sufficient?
- Should retrospective crossmatches for immunised patients only be performed for local donor organ offers?

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