Leiden University Medical Center

Eurotransplant Reference Laboratory

# Extramural Meeting 2023

## Patient Based Cases 2022

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# Patient case 2022-01: Recipient information

The **female recipient aged** 44,with **blood group A pos**, was admitted to the waitlist 6 years before this organ offer. She has two children.

**Recipient HLA type:** A2, A3, B5, B52, B12, B44, Bw4, Cw7, Cw12, DR7, DR53, DQ2

**HLA type first child**: A3, A19, A33, B12, B44, B27, Bw4, Cw7, Cw12, DR4, DR7, DR53, DQ2, DQ3, DQ8
**HLA type second child**: A2, A19, A33, B5, B52, B27, Bw4, Cw12, DR4, DR7, DR53, DQ2, DQ3, DQ8

**Antibody information:**
CDC: negative (in all tested sera since the recipient was waitlisted)
LMX is consistently positive for both HLA Class I and Class II during the time the recipient was waitlisted.

# Patient case 2022-01 : Donor information

**Donor:** Female aged 58, DBD

**Donor blood group:** A pos

**Donor HLA type:** A2, A10, A34, B21, B49, B53, Bw4, Cw2, Cw4, DR3, DR17, DR6, DR13, DR52, DQ1, DQ6, DQ2

**CDC crossmatch results unseparated spleen cells: negative** (decisive crossmatch)

| Unseparated | | T cells | | B cells | | Final results | |
|---|---|---|---|---|---|---|---|
| (-) DTT | (+) DTT | (-) DTT | (+) DTT | (-) DTT | (+) DTT | (-) DTT | (+) DTT |
| Neg | Neg | | | | | Neg | Neg |

# Patient case 2022-01: Histocompatibility

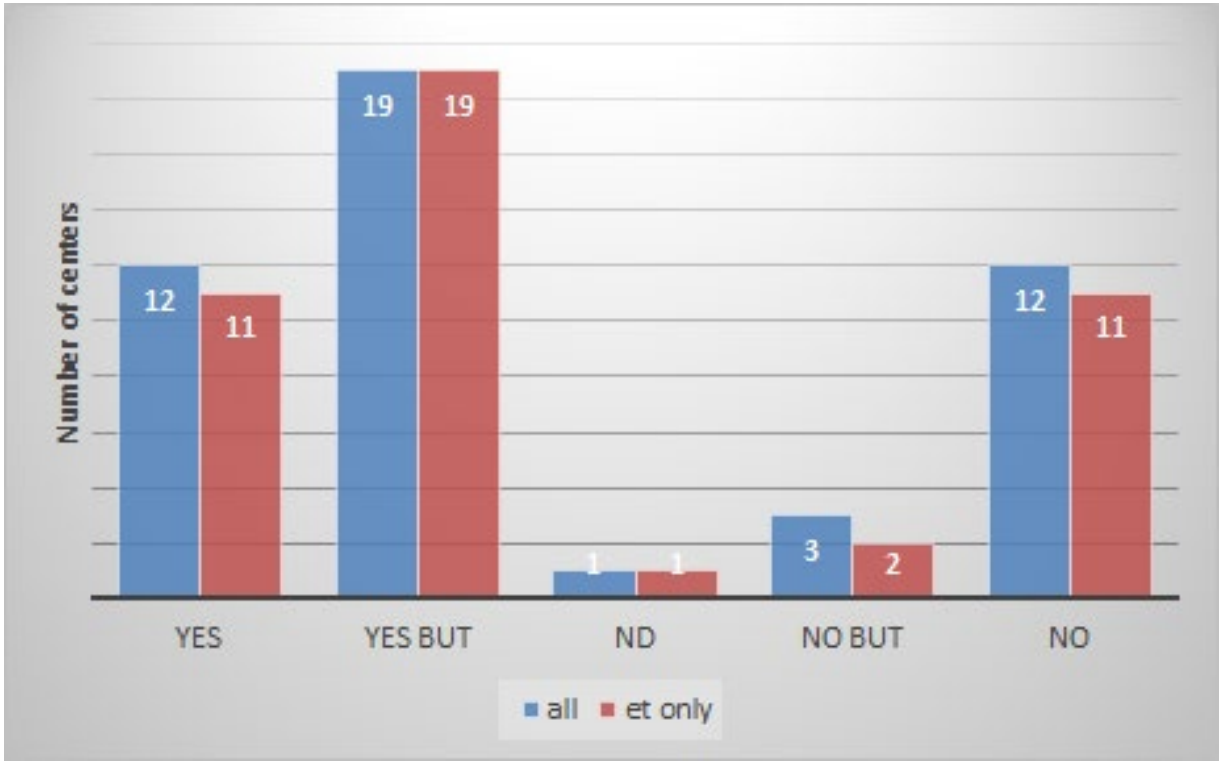
**Patient**: A2, A3, B5, B52, B12, B44, Bw4, Cw7, Cw12, DR7, DR53, DQ2
**First child**: A3, A19, A33, B12, B44, B27, Bw4, Cw7, Cw12, DR4, DR7, DR53, DQ2, DQ3, DQ8
**Second child**: A2, A19, A33, B5, B52, B27, Bw4, Cw12, DR4, DR7, DR53, DQ2, DQ3, DQ8

**Donor:** A2, A10, A34, B21, B49, B53, Bw4, Cw2, Cw4, DR3, DR17, DR6, DR13, DR52, DQ1, DQ6, DQ2

**Unacceptable antigens**: B7 B13 B27 B40 B47 B48 B81 DR4 DQ8 DQ9

Green: match
Blue: mismatch without proven antibodies
Black: mismatch with specificity CDC proven
Orange: mismatch with specificity Luminex proven

# Patient case 2022-01: Is this a suitable organ offer?



# Patient case 2022-01: Discussion (Pro)

- The donor doesn’t share HLA molecules with the children
- No CDC antibodies, negative CDC crossmatch (unseparated spleen cells)
- The antibodies found with Luminex SA cannot be explained with known immunizing events
- The recipient is young and is waitlisted 6 years

# Patient case 2022-01: Discussion (Con)

- HLA-compatibility is (too) low
- The patient is broadly immunized (Luminex SA only); these non-complement fixing antibodies indicate a risk

# Patient case 2022-01: Suggested extra actions

- Additional crossmatch on separated B cells (and T cells)
- Apply intensified immunosuppression protocol
- Additional treatment like plasmapheresis

# Patient case 2022-01: Outcome

Follow up:

Good graft function. So far, no rejection episode occurred

(almost two year after transplantation)

# Patient case 2022-02

The female recipient, aged 66 years, blood group O pos, waitlisted almost 3 years before this organ offer

**Recipient HLA type:** A19, A33, A19, A74, B12, B45, B35, Bw6, Cw4, Cw16, DR2, DR15, DR6, DR13, DR51, DR52, DQ1, DQ6, DQ3, DQ9

**Immunizing events:**

**HLA type 1st child:** A19, A74, A28, A68, B12, B45, B17, B58, Bw4, Bw6, Cw6, Cw16, DR5, DR12, DR6, DR13, DR52, DQ1, DQ5, DQ3, DQ9

**HLA type 2nd child:** A19, A29, A19, A74, B12, B45, B40, B60, Bw6, Cw3, Cw10, Cw16, DR3, DR17, DR6, DR13, DR52, DQ2, DQ3, DQ9

**Antibody information:**

- CDC: in all tested sera positive for B60, B61, Cw2
- LMX is consistently positive for HLA Class I and consistently negative for Class II
- Autologous crossmatch: consistently positive

# Patient case 2022-02; Donor information

**Donor age:** 55
**Donor gender:** Male
**Donor blood group:** O pos

**Donor HLA type:** A2, A19, A33, B12, B44, B17, B58, Bw4, Cw3, Cw10, Cw7, DR5, DR11, DR6, DR13, DR52, DQ1, DQ6, DQ3, DQ8

**CDC crossmatch results on blood:** Unseparated Cells without DTT: Positive, with DTT: Negative

# Patient case 2022-02

Unacceptable Antigens as defined by the laboratory:

| | A66 | B7 | B13 | B27 | B40* | B47 | B48 | B73 | B81 | Cw2* |
|---|---|---|---|---|---|---|---|---|---|---|
| MFI Value** | 16768 | 20946 | 18180 | 19652 | 20254 | 15187 | 20220 | 20271 | 21629 | 11535 |

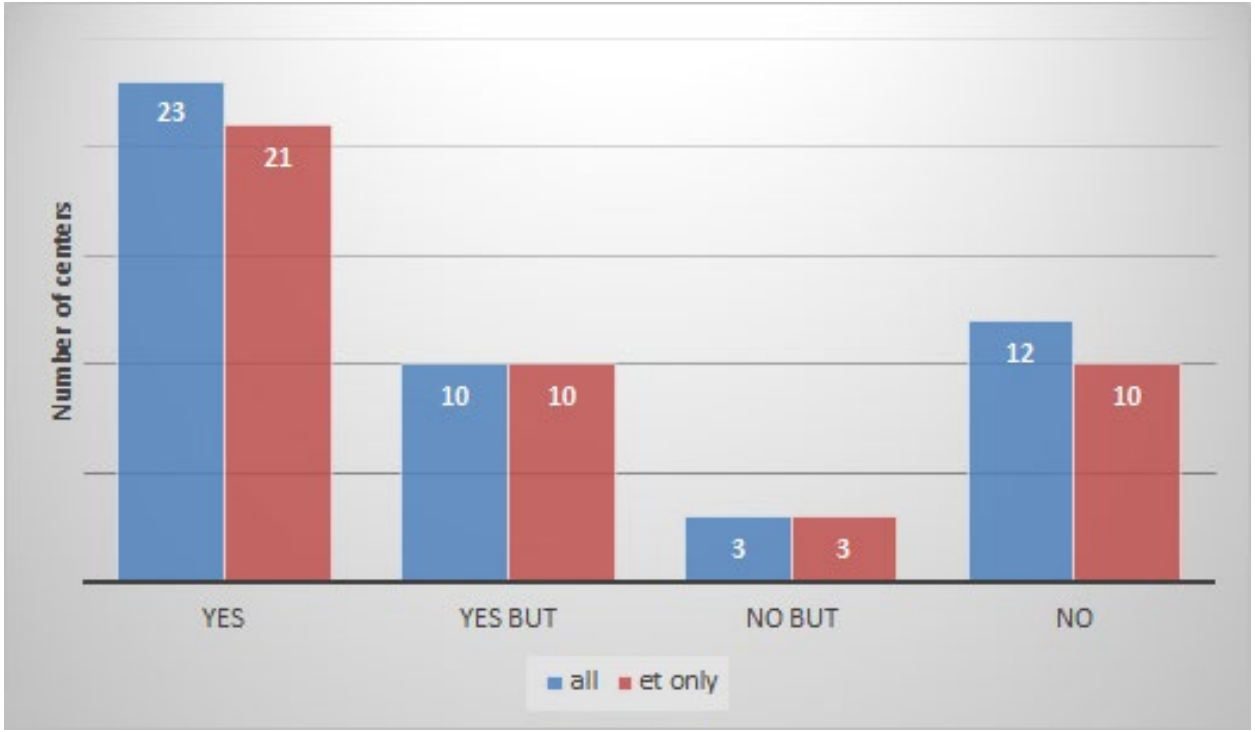
*CDC positive, **Normal values (One Lambda)

**Recipient HLA type:**

A19, A33, A19, A74, B12, B45, B35, Bw6, Cw4, Cw16, DR2, DR15, DR6, DR13, DR51, DR52, DQ1, DQ6, DQ3, DQ9

Green: match
Blue: mismatch without proven antibodies
Black: mismatch with specificity CDC proven
Orange: mismatch with specificity Luminex proven

# Patient case 2022-02: Is this a suitable organ offer?



# Patient case 2022-02: Discussion

- Repeated mismatches shared  between children and donor: HLA-B17, B58, Bw4, Cw3, Cw10, (having low MFI values in SAB)
- Immunizing events: 2 pregnancies resulting in the following antibodies:
  A66, B7, B13, B27, B40, B60, B47, B48, B73, B81, Cw2 (not present on the donor)
- CDC final crossmatch result is negative; Positive crossmatch without DTT only, is compatibly with the positive autologous crossmatch

# Patient case 2022-02: Remarks and Outcome

- The recipient typing was confirmed by re-typing because of the less frequent DR-DQ association
- The autologous crossmatch was performed both without and without DTT. The result is interpreted as positive when the autologous crossmatch without DTT is positive and with DTT is negative.

The recipient was transplanted with the offered organ 4 years ago without any additional intervention such as desensitization. She had no rejection episodes and the renal function is good.

# Patient case 2022-03: Recipient information

Female recipient aged 38 years, blood group B pos, returned on the waitlist a year ago.
**Recipient HLA type**: A*30:01, A*33:03, B*15:16, B*35:01, C*07:18, C*14:02, DRB1*13:02, DRB1*15:03, DRB3*03:01, DRB5*01:01, DQB1*06:02, DQB1*06:09, DQA1*01:02, DPB1*01:01, DPB1*18:01, DPA1*01:03, DPA1*02:02

The recipient received a living donor kidney from her mother 12 years ago, which failed 1 year ago.
**Donor HLA type**: A*30:01, A*36:01, B*35:01, B*53:01, C*04:01, C*07:18, DRB1*11:01,DRB1*13:02, DRB3*02:02, DRB3*03:01, DQB1*03:01, DQB1*06:09

**Antibody information**:
CDC, Recent serum: A3, A24, A10 (tested with addition of DTT)
Luminex SAB Class I and II: Positive
Autologous crossmatch: Consistently positive

# Patient case 2022-03

Which antigens would you define as unacceptable for this patient in the current ENIS system?

What are the (further) possibilities after the introduction of the virtual crossmatch?

# Patient case 2022-03: Unacceptable antigens Class I

| Class I | CDC | MFI>10000 | MFI>8000 | MFI>5000 | MFI>3000 | pos by software | mothers alleles | Cons % ET |
|---|---|---|---|---|---|---|---|---|
| **A3** | A3 | A3 | A3 | A3 | A3 | A3 | | 100% |
| **A24(9)** | A24(9) | A24(9) | A24(9) | A24(9) | A24(9) | A24(9) | | 100% |
| **A25(10)** | A25(10) | A25(10) | A25(10) | A25(10) | A25(10) | A25(10) | | 100% |
| **A26(10)** | A26(10) | | | A26(10) | A26(10) | A26(10) | | 100% |
| **A66(10)** | A66(10) | A66(10) | A66(10) | A66(10) | A66(10) | A66(10) | | 100% |
| **A34(10)** | A34(10) | A34(10) | A34(10) | A34(10) | A34(10) | A34(10) | | 98% |
| **A36** | | A36 | A36 | A36 | A36 | A36 | A36 | 93% |
| **A1** | | A1 | A1 | A1 | A1 | A1 | | 91% |
| **A2** | | A2 | A2 | A2 | A2 | A2 | | 91% |
| **A11** | | A11 | A11 | A11 | A11 | A11 | | 91% |
| **A68(28)** | | A68(28) | A68(28) | A68(28) | A68(28) | A68(28) | | 91% |
| **A69(28)** | | | A69(28) | A69(28) | A69(28) | A69(28) | | 84% |
| **A80** | | A80 | A80 | A80 | A80 | A80 | | 84% |
| **A74** | | | | A74 | A74 | A74 | | 80% |
| **A32(19)** | | | A32(19) | A32(19) | A32(19) | A32(19) | | 77% |
| **A43** | | | | A43 | A43 | A43 | | 75% |
| **B57(17)** | | | | | B57(17) | B57(17) | | 64% |
| **B37** | | | | | B37 | B37 | | 61% |
| **B58(17)** | | | | | B58(17) | B58(17) | | 61% |
| **Cw4** | | | | | | | Cw4 | 25% |
| **B53** | | | | | | | B53 | 20% |
| **B73** | | | | | | | | 18% |
| **Cw17/A23(9)/A29(19)** | | | | | | | | 2% |

# Patient case 2022-03: Unacceptable antigens Class II

| Class II | | MFI>10000 | MFI>8000 | MFI>5000 | MFI>3000 | pos by software | mothers alleles | Cons % ET |
|---|---|---|---|---|---|---|---|---|
| **DQ7(3)** | | DQ7(3) | DQ7(3) | DQ7(3) | DQ7(3) | DQ7(3) | DQ7(3) | 100% |
| **DQ8(3)** | | DQ8(3) | DQ8(3) | DQ8(3) | DQ8(3) | DQ8(3) | | 93% |
| **DQ9(3)** | | DQ9(3) | DQ9(3) | DQ9(3) | DQ9(3) | DQ9(3) | | 93% |
| **DQ4** | | DQ4 | DQ4 | DQ4 | DQ4 | DQ4 | | 89% |
| **DQ2** | | DQ2 | DQ2 | DQ2 | DQ2 | DQ2 | | 89% |
| **DR11(5)** | | | | | | | DR11(5) | 27% |
| **DQ6(1)** | | | | | DQ6(1) | DQ6(1) | | 27% |
| **DR52** | | DR52* | DR52* | DR52* | DR52* | DR52* | DR52* | 18% |
| **DR7** | | | | | | | | 14% |
| **DR9** | | | | | | | | 14% |
| **DR52** | | | | | | | | 7% |
| **DR12(5)** | | | | | | | | 5% |
| **DR14(6)** | | | | | | | | 5% |
| **DR17(3)** | | | | | | | | 2% |
| **DRB3*02:02** | | DRB3*02:02 | DRB3*02:02 | DRB3*02:02 | DRB3*02:02 | DRB3*02:02 | DRB3*02:02 | 82% |
| **DQA1*02:01** | | | | | DQA1*02:01 | DQA1*02:01 | | 41% |

DR52*: the patient self carries a HLA-DR52, the antibody is allele specific and directed against DRB3*02:02

# Patient based case 2022-03: situation until 24th of January 2023

**DRB3*02:02 allele specific antibody and DQA1 antibodies:**

At time of the EPT there was no possibility to enter DRB3*02:02 and DQA1 antibodies in ENIS

What could be done:

- Remove DR52 from the patient's phenotype and add DR52 as unacceptable antigen
- A comment explaining necessity for DRB3 donor typing results should be included in the patient file
- DR11/DR12/DR14/DR17 are set as unacceptable antigen because of linkage with mothers DRB3*02:02; Immunologist on call should be alert in case of an offer of a DR52 donor and use association with DRB1 alleles
- Contact the ETRL to discuss the issue with DRB3*02:02

# Patient based case 2022-03: situation after 24th of January 2023

**DRB3*02:02 allele specific antibody and DQA1 antibodies:**

Enter DRB3*02:02 and DQA1 specificities as unacceptable antigen in ENIS-next (with the exception for patients in the AM program)

# Request: New cases!

Preferably concerning (recipients awaiting) deceased donor kidney transplantations

For example:

- for recipients with an aberrant antibody profile
- with unexpected crossmatch outcomes
- for a recipient waiting longer than average
- with interventions done to facilitate transplantation
- and other…..

Please send a short information to the ETRL: etrl@eurotransplant.org

- All recipient, donor and center data will by anonymized -

**Thanks to the labs who already made cases available!**

Leiden University Medical Center

Eurotransplant Reference Laboratory

# Thank You

## For participating in the patient based cases EPT


**The ETRL team**

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