Leiden University Medical Center

Eurotransplant Reference Laboratory

Pilot on inclusion of a case report in the external proficiency testing program

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ET EXTRA MURAL MEETING 2016

Eurotransplant

Background

- At the extramural meeting 2015 in Mannheim, the ETRL proposed to include patient-based cases in the ETRL EPT scheme

- The main goal of such scheme is to discuss the results and policies in the different centres to reach maximum consistency within ET affiliated centres

- Two schemes were proposed:
  - A paper-based scheme in which all histocompatibility data is provided
  - A sample-based scheme in which selected cells and sera from regular EPT shipments are used

Pilot on paper-based EPT

- In June 2015 a pilot paper-based EPT was sent to the centers that participate in the ETRL EPT scheme
- This first exercise concerned a virtual donor-recipient combination
- Participation rate:

	Total within EPT	Participated	Participation rate
ET	48	39	81%
Non-ET	23	9	39%

The patient case: recipient information

Recipient age at time of Tx:	59 years
Recipient gender:	female
Recipient blood group:	A
Recipient HLA type :	A1 A10 A34 B15 B75 B37 Bw4 Bw6 DR2 DR15 Cw4 Cw6 DQ1 DQ6 DR51
Immunizing events:	previous transplant
HLA-type of previous Tx:	A2 A19 A32 B15 B62 B35 Bw6 DR4 DR5 **DR11** Cw3 Cw10 Cw4 DQ3 DQ7 DQ8 DR53
CDC antibody specificities:	A2 A28 DR4 DR5 DQ8
Luminex antibodies:	A2 A9 A28 B17 DR3 DR4 DR5 DR6 DR7 DR9 DR10 DR52 DR53 DQ3

The patient case: donor information

Donor type: Deceased

Donor blood group: A

Donor HLA type: A1 A10 A26 B8 B15 B75 Bw6 DR2 DR15 DR3 DR17 Cw7 DQ1 DQ6 DQ2 DR51 DR52

CDC crossmatch results:

Unseparated		T cells		B cells	
(-) DTT	(+) DTT	(-) DTT	(+) DTT	(-) DTT	(+) DTT
Pos	Neg	-	-	Pos	Neg

Flow cross match results: Negative

Luminex data

Specificity	A2*	A9	A28*	B17	DR4*	DR5*	DR6
Median of MFI	24180	12874	19492	14239	17155	10283	9725

Specificity	DR7	DR9	DR10	DR17	DR18	DR52	DR53	DQ3*
Median of MFI	11687	12530	6841	**9971**	8515	**3173**	17592	8883

*Also found by CDC

Histocompatibility

Patient:

A1 A10 A34 B15 B75 B37 Bw4 Bw6 DR2 DR15 Cw4 Cw6 DQ1 DQ6 DR51

CDC Abs: A2 A28 DR4 DR5 DQ8

Luminex Abs: A2 A9 A28 B17 DR3 DR4 DR5 DR6 DR7 DR9 DR10 DR52 DR53 DQ3

Donor:

A1 A10 A26 B8 B15 B75 Bw6 DR2 DR15 DR3 DR17 Cw7 DQ1 DQ6 DQ2 DR51 DR52

Green: match

Blue: mismatch without proven antibodies

Black: mismatch with specificity CDC proven

Orange: mismatch with specificity Luminex proven

Overview

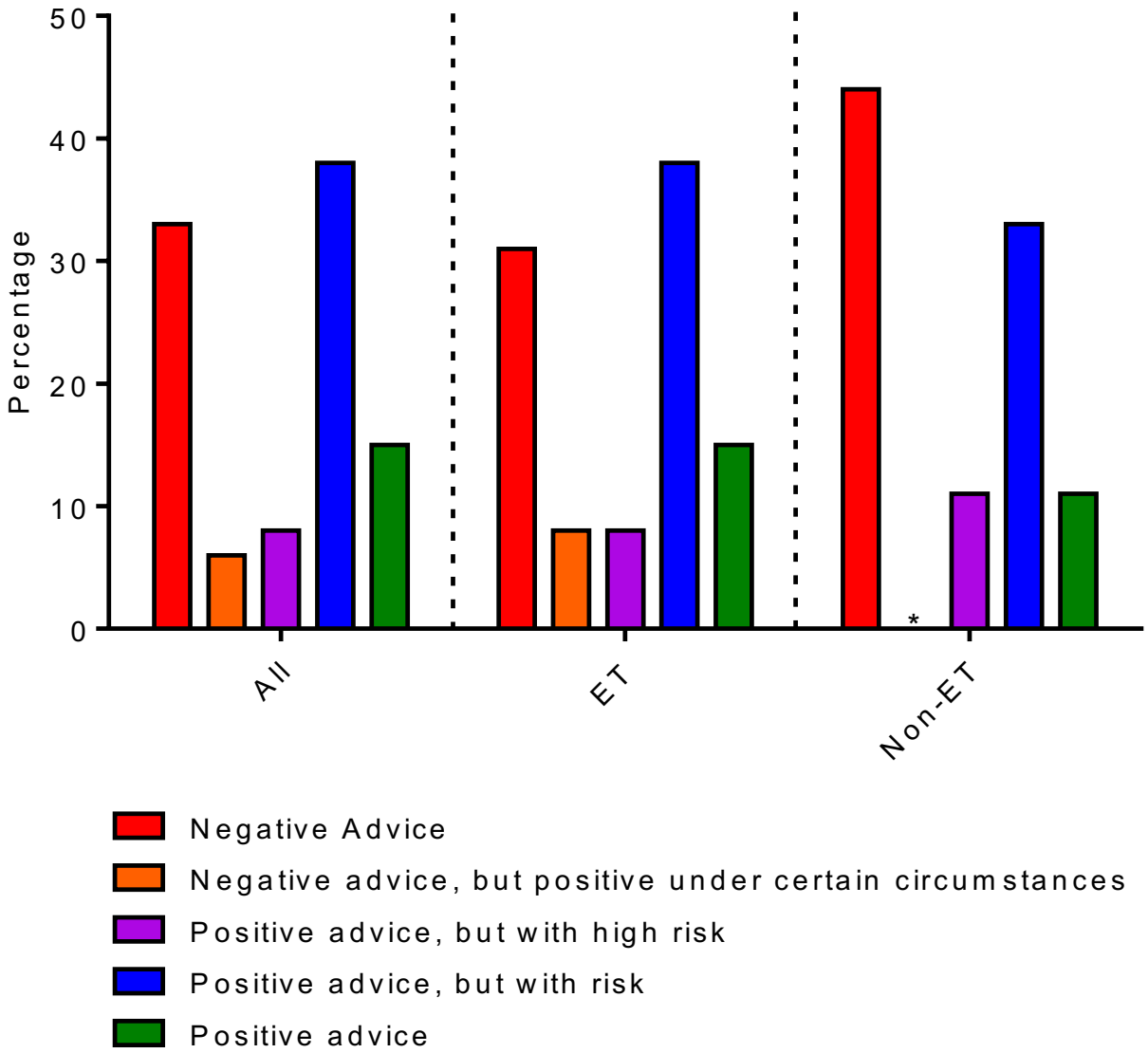
- Mismatch: 0/1/1
- CDC crossmatch: (-) DTT: positive, (+) DTT: negative
- Flow crossmatch: negative
- No auto-crossmatch performed

- No CDC-proven donor-reactive Abs
- Luminex-proven donor-reactive Abs: - DR17 (no repeat mismatch)
  - DR52 (repeat mismatch?)
  - DRB1*03:01 bead **MFI 9971**
  - DRB3*01:01 **MFI 3173**, DRB3*02:02 **MFI 6401**, DRB3*03:01 **MFI 2819**

Some information was lacking

- Need for extra information:
  - Patient's autoantibody status
  - Immunizing events
  - Flow XM cell source
  - Complete antibody profile with serum dates
  - Diagnosis, reason for graft loss, nephrectomy 1st transplant

Results


50
40
30
20
10
0
Percentage
*
All
ET
Non-ET
Negative Advice
Negative advice, but positive under certain circumstances
Positive advice, but with high risk
Positive advice, but with risk
Positive advice

Discussion

- What to do in case of crossmatch results:

  Positive (-) DTT

  Negative (+) DTT

  No autologous crossmatch performed

- How to deal with antibodies detected by Luminex only in case of a negative CDC crossmatch?

  No repeat mismatch

  Repeat mismatch

Pilot on sample-based EPT

- September 2015: A case based on the regular EPT cross match exercise material
- Divided into 2 regions: donor centers and recipient centers
- From the regular EPT serum and cell samples a virtual patient case was made
- 3 serum samples (patients) needed to be crossmatched with 1 cell sample (donor). Tissue type and serum antibody data could also be used for analysis
- Compatibility between serum samples (patients) and cell sample (donor) needed to be determined

Pilot on sample-based EPT

- Participation rate:

	Total within EPT	Participated	Participation rate
Donor centers	31	25	81%
Recipient centers	31	17	55%

Results

- Donor centers:

	Crossmatch	Crossmatch DTT	Advice (n=25)
'Patient' serum J	Pos	Pos	No: 25
'Patient' serum K	Neg	Neg	Yes: 21 / No: 4
'Patient' serum L	Neg	Neg	Yes: 15 / No: 10

- Recipient centers:

	Crossmatch	Crossmatch DTT	Advice (n=17)
'Patient' serum J	Pos	Pos	Yes: 1 / No: 16
'Patient' serum K	Pos	Pos	No: 17
'Patient' serum L	Neg	Neg	Yes: 13 / No: 4

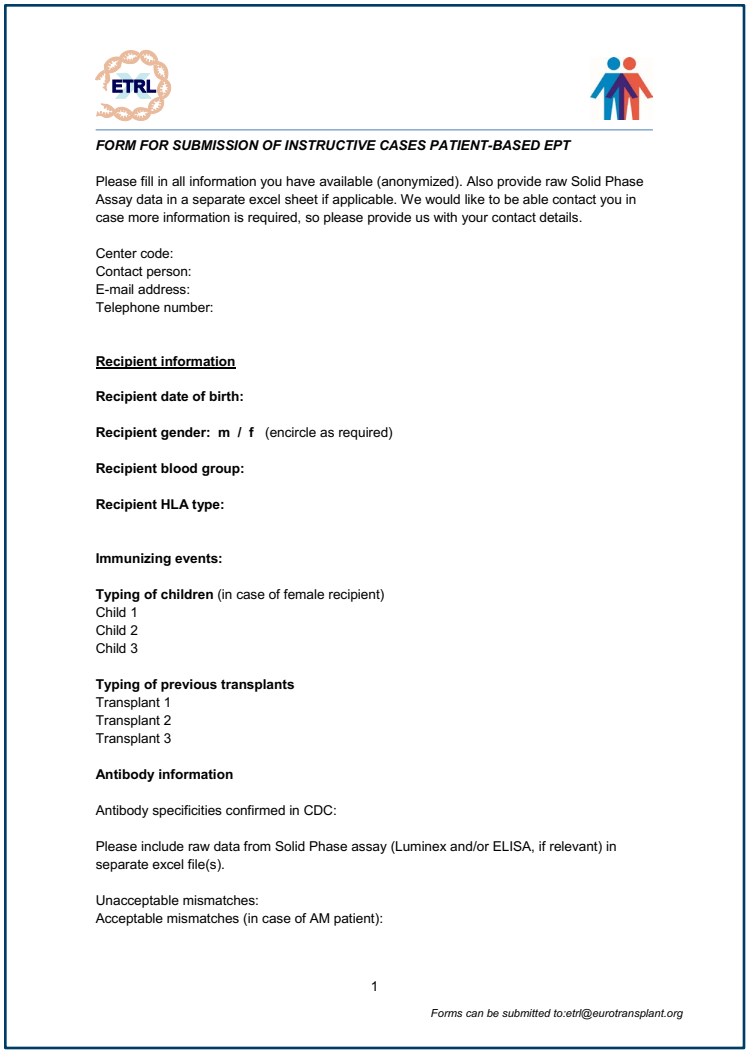
- Differences in advice when crossmatch is negative mainly due to DSA only detectable in Luminex or local match criteria

Comments received from participants

- Main issue is that the sample based exercise is purely based on the regular EPT material
- Lack of background data, such as number of prior transplants, pregnancies, AB0 type, age of recipient

Please send in your anonymized patient cases

- http://etrl.eurotransplant.org/cms/index.php?page=Forms



FORM FOR SUBMISSION OF INSTRUCTIVE CASES PATIENT-BASED EPT

Please fill in all information you have available (anonymized). Also provide raw Solid Phase Assay data in a separate excel sheet if applicable. We would like to be able contact you in case more information is required, so please provide us with your contact details.

Center code:
Contact person:
E-mail address:
Telephone number:

Recipient information

Recipient date of birth:

Recipient gender: m / f (encircle as required)

Recipient blood group:

Recipient HLA type:

Immunizing events:

Typing of children (in case of female recipient)
Child 1
Child 2
Child 3

Typing of previous transplants
Transplant 1
Transplant 2
Transplant 3

Antibody information

Antibody specificities confirmed in CDC:

Please include raw data from Solid Phase assay (Luminex and/or ELISA, if relevant) in separate excel file(s).

Unacceptable mismatches:
Acceptable mismatches (in case of AM patient):

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Forms can be submitted to:etrl@eurotransplant.org

Leiden University Medical Center

Eurotransplant Reference Laboratory
etrl.eurotransplant.org

Many thanks to the centres that have participated and provided feedback!

The ETRL team:

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