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AIBT
Associazione Italiana
di Immunogenetica
e Biologia dei Trapianti

**MODELLO DI APPROCCIO IMMUNOLOGICO AL
TRAPIANTO COMBINATO O SIMULTANEO FEGATO-RENE
NEL PAZIENTE FORTEMENTE IMMUNIZZATO:
2 CASI CLINICI**



Napoli, 10-12 Ottobre 2024

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TRAPIANTO COMBINATO o SIMULTANEO FEGATO-RENE

Case Reports > Lancet. 1984 May 12;1(8385):1077-8. doi: 10.1016/s0140-6736(84)91486-7.

Combined liver and kidney transplantation

R Margreiter, R Kramar, C Huber, E Steiner, D Niederwieser, G Judmaier, W Vogel

PMID: 6144007 DOI: 10.1016/s0140-6736(84)91486-7

Primo trapianto simultaneo
fegato-rene (SLKT)

Ottimo outcome a breve e lungo termine

World Journal of Urology (2024) 42:489
<https://doi.org/10.1007/s00345-024-05174-z>

REVIEW



Simultaneous liver-kidney transplantation: future perspective

Thomas Prudhomme^{1,2} · Benoit Mesnard^{2,3} · Julien Branchereau^{2,3} · Mathieu Roumiguié¹ · Charlotte Maulat⁴ · Fabrice Muscari⁴ · Nassim Kamar⁵ · Michel Soulié¹ · Xavier Gamé¹ · Federico Sallusto¹ · Marc Olivier Timsit⁶ · Sarah Drouin⁷

Dati UNOS su SLKT:

- migliore outcome rispetto al Tx di solo fegato (LT)
- Minore incidenza rigetto acuto e maggiore sopravvivenza dell'organorispetto al Tx di solo rene (KT)

EFFETTO IMMUNOLOGICO PROTETTIVO DEL FEGATO SU RENE NEL TRAPIANTO COMBINATO: CLEARANCE ANTICORPI

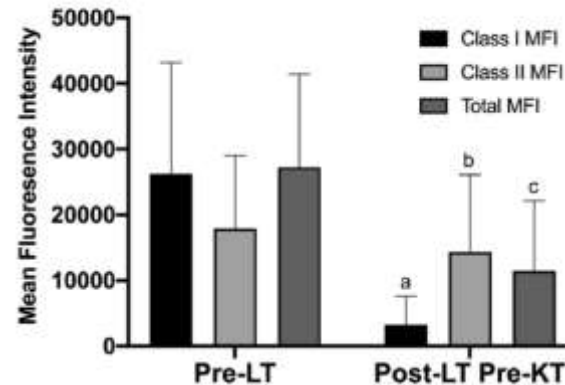
ASPETTI CONTROVERSI

- HLA I vs HLA II
- TITOLO DSA
- DSA vs NON DSA

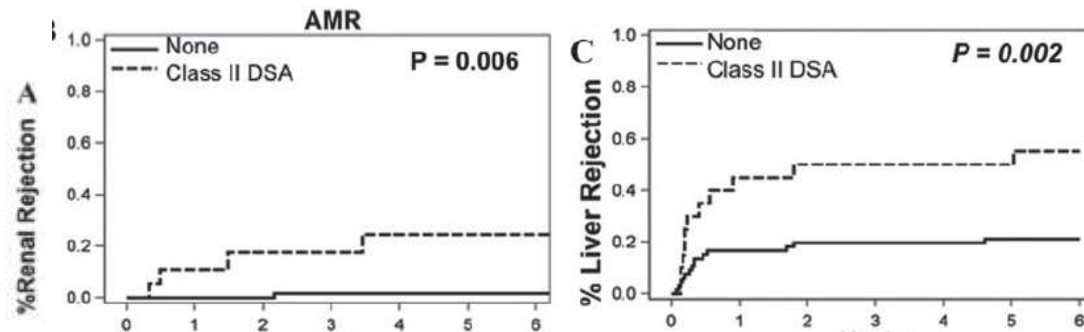
- XM POSITIVO: RISCHIO?

- VALUTAZIONE DOPO RIFERFUSIONE FEGATO

- TRAPIANTO SIMULTANEO vs RENE DOPO FEGATO



Goggins, Surgery 2021



O'Leary, AJT 2013



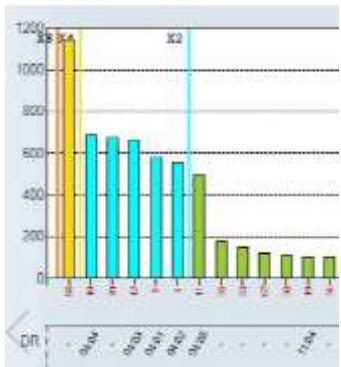
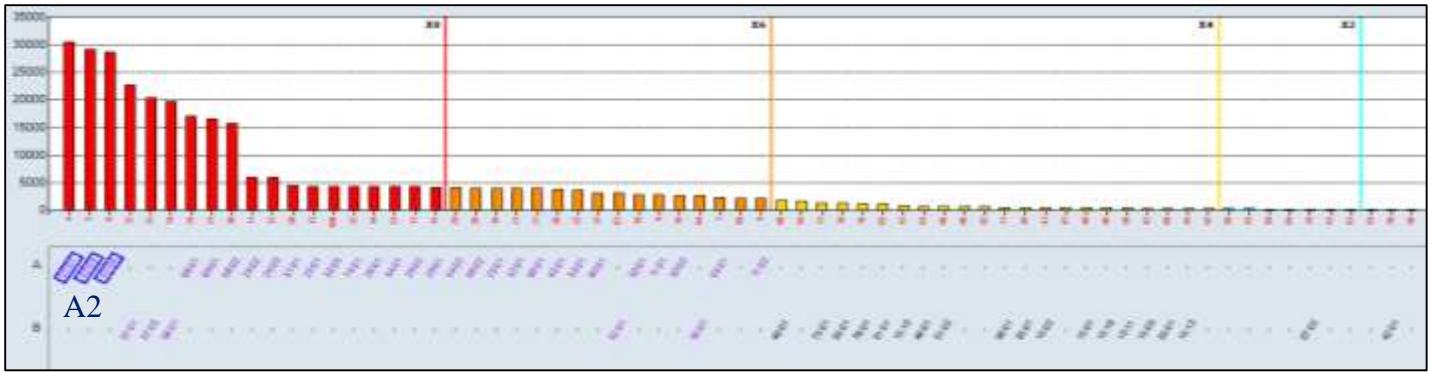
Combined liver-kidney transplantation: University of Bologna experience, S. Orsola experience

- 1: Faenza A, Fuga G, Nardo B, Varotti G, Faenza S, Stefoni S, D'Arcangelo GL, Mosconi G, Feliciangeli G, Pinna AD. **Combined liver-kidney transplantation: the experience of the University of Bologna and the case of preoperative positive cross-match.** Transplant Proc. 2006 May;38(4):1118-21. doi: 10.1016/j.transproceed.2006.03.048. PMID: 16757282.
- 2: Di Laudo M, Ravaioli M, La Manna G, Comai G, Cescon M, Del Gaudio M, Zanfi C, Cucchetti A, Ercolani G, Pinna AD. **Combined liver-dual kidney transplant: Role in expanded donors.** Liver Transpl. 2017 Jan;23(1):28-34. doi: 10.1002/lt.24472. Epub 2016 Nov 28. PMID: 27113672.
- 3: Del Gaudio M, Ravaioli M, Ercolani G, Cescon M, Amaduzzi A, Neri F, Pellegrini S, Feliciangeli G, Lamanna G, Morelli C, D'Arcangelo GL, Comai G, Cucchi M, Stefoni S, Pinna AD. **Induction therapy with alemtuzumab (campath) in combined liver-kidney transplantation: University of Bologna experience.** Transplant Proc. 2013 Jun;45(5):1969-70. doi: 10.1016/j.transproceed.2013.02.108. PMID: 23769085.
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- 5: Bertelli R, Nardo B, Cavallari G, Ercolani G, Lauro A, Neri F, Tsvian M, Grazi GL, Mikus PM, Pilato E, Mikus E, Arpesella G, Pinna AD, Stefoni S, Fuga G, Faenza A. **Kidney transplantation combined with other organs in Bologna: an update.** Transplant Proc. 2008 Jul-Aug;40(6):1867-8. doi: 10.1016/j.transproceed.2008.05.024. PMID: 18675073.
- 6: Nardo B, Beltempo P, Montalti R, Bertelli R, Cavallari G, Ercolani G, Lauro A, Grazi G, Mikus PM, Pilato E, Mikus E, Arpesella G, Pinna A, Stefoni S, Cavallari A, Faenza A. **Kidney transplantation combined with other organs: experience of Bologna s. Orsola hospital.** Transplant Proc. 2005 Jul-Aug;37(6):2469-71. doi: 10.1016/j.transproceed.2005.06.008. PMID: 16182712.
- 7: Cavallari G, Nardo B, Montalti R, Beltempo P, Bertelli R, Puviani L, Faenza A, Cavallari A. **Combined liver-kidney transplantation: experience at Bologna's transplant center.** Transplant Proc. 2004 Apr;36(3):541-2. doi: 10.1016/j.transproceed.2004.02.026. PMID: 15110586.
- 8: Mosconi G, Scolari MP, Feliciangeli G, D'Addio F, D'Arcangelo GL, Cappuccilli ML, Comai G, Conte D, La Manna G, Borgnino LC, Falaschini A, Stefoni S. **Nephrological indications in combined liver-kidney transplantation.** Transplant Proc. 2006 May;38(4):1086-8. doi: 10.1016/j.transproceed.2006.03.011. PMID: 16757272.
- 9: Mosconi G, Scolari MP, Feliciangeli G, Zanetti A, Zanelli P, Buscaroli A, Piccari M, Faenza S, Ercolani G, Faenza A, Pinna AD, Stefoni S. **Combined liver-kidney transplantation with preformed anti-HLA antibodies: a case report.** Transplant Proc. 2006 May;38(4):1125-6. doi: 10.1016/j.transproceed.2006.03.045. PMID: 16757284.

CASO 1: DSA I CLASSE

- F, 46 Anni, 2 GRAVIDANZE
- Severa malattia Policistica epatica e renale complicata END-STAGE kidney disease
- Sintomatica massa sterica addominale con calcificazione pareti cistiche, ascite ed ernia ombelicale
- NOV 23: IN LISTA TRAPIANTO COMBINATO URGENTE FEGATO-RENE



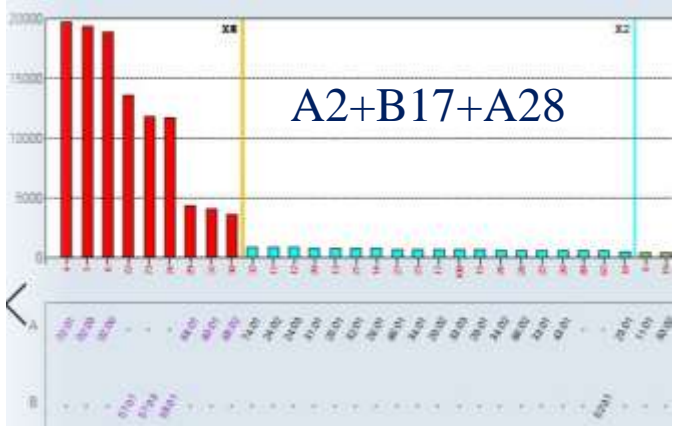


HLA-I cPRA 99.6%

HLA-II NEG

Allele	Ab Verified
A*02:06	62GE, 62GK, 107W, 127K, 144TKH, 145KHA, 150AAH, 253Q
A*02:03	62GE, 62GK, 107W, 127K, 144TKH, 149TAH, 253Q
A*02:01	62GE, 62GK, 107W, 127K, 144TKH, 145KHA, 150AAH, 253Q
A*68:01	127K, 144TKH, 145KHA, 150AAH, 253Q
A*68:02	127K, 144TKH, 145KHA, 150AAH, 253Q
A*69:01	107W, 127K, 144TKH, 145KHA, 150AAH, 253Q
B*57:01	62GE, 62GRN
B*57:03	62GE, 62GRN
B*58:01	62GE, 62GRN
A*33:03	253Q
A*74:01	253Q
A*25:01	76ESI, 145RT, 149TAH, 163RW, 253Q
A*29:01	62LQ, 253Q
A*29:02	62LQ, 253Q
A*26:01	145RT, 149TAH, 163RW, 253Q
A*34:02	145RT, 149TAH, 253Q
A*31:01	56R, 253Q
A*32:01	76ESI, 253Q
A*66:01	145RT, 149TAH, 163RW, 253Q
A*24:02	62EE, 65GK, 127K, 150AAH
A*66:02	145RT, 149TAH, 253Q
A*33:01	253Q
A*24:03	62EE, 65GK, 127K, 150AAH
A*34:01	145RT, 149TAH, 253Q
A*43:01	62LQ, 145RT, 149TAH, 163RW, 253Q
A*11:01	150AAH, 151AHA, 163RW
A*30:02	56R, 76EG
A*23:01	62EE, 65GK, 127K
A*30:01	56R
A*03:01	150AAH, 161D
B*52:01	
C*07:02	193PL, 253Q, 267QE
A*11:02	150AAH, 151AHA, 163RW
C*17:01	253Q, 267QE
A*80:01	62EE
B*49:01	

DIL1:16



EPITOPE ANALYSIS:

A2 IMMUNODOMINANT

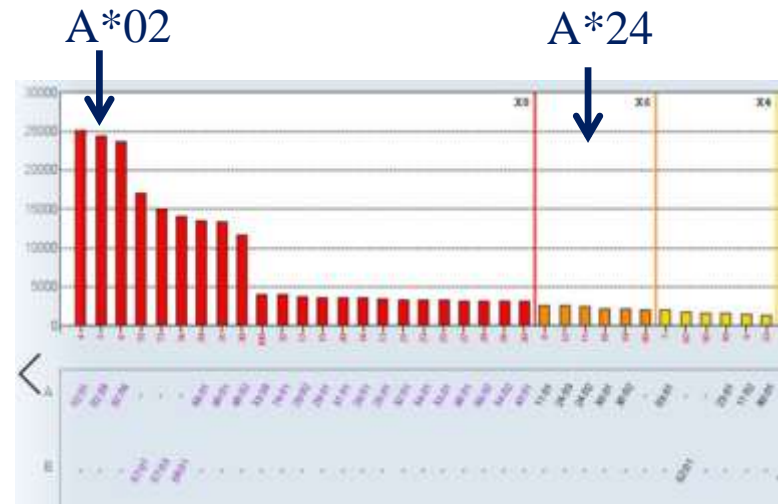
HIGH AND LOW CROSS-REACTIVE ALLELES

DONATORE

- DBD, F, 50 ANNI
- HLA: **A*02,*24**; B*44,*51; C*05,*07

- DSA:

- A*02 MFI >25.000
- A*24 MFI >2500

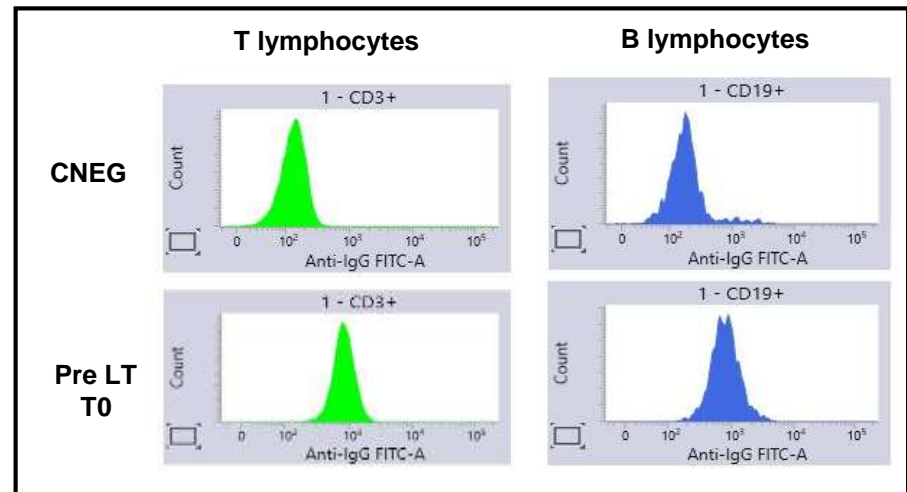


- FC-XM

- MCS-T 730
- MCS-B 553

- CDC-XM

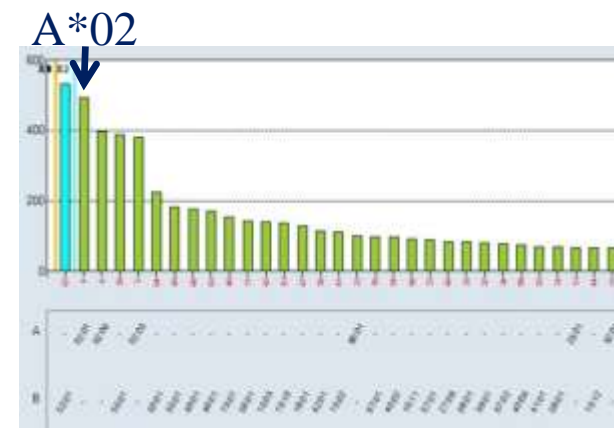
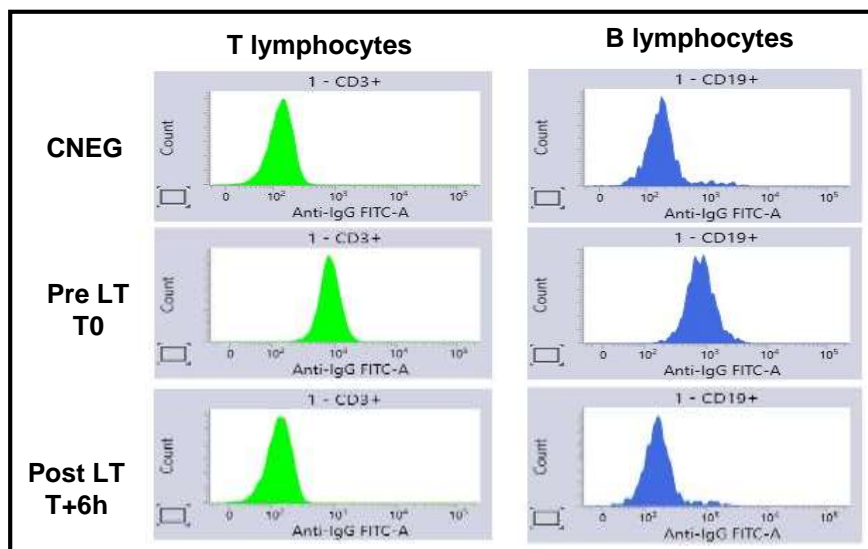
- T NIH 8
- B NIH 8



- RENE IN PERFUSIONE MECCANICA

- RIVALUTAZIONE IMMUNOLOGICA: +6h DA RIPERFUSIONE FEGATO

+6h: RIVALUTAZIONE IMMUNOLOGICA



	CDC-XM		FC-XM	
	Pre LT, T0	Post LT, T+6h	Pre LT, T0	Post LT, T+6h
T lymphocytes	Positive (score 8)	Negative (score 1)	Positive (MCS 686)	Negative (MCS -6)
B lymphocytes	Positive (score 8)	Negative (score 1)	Positive (MCS 647)	Negative (MCS -12)

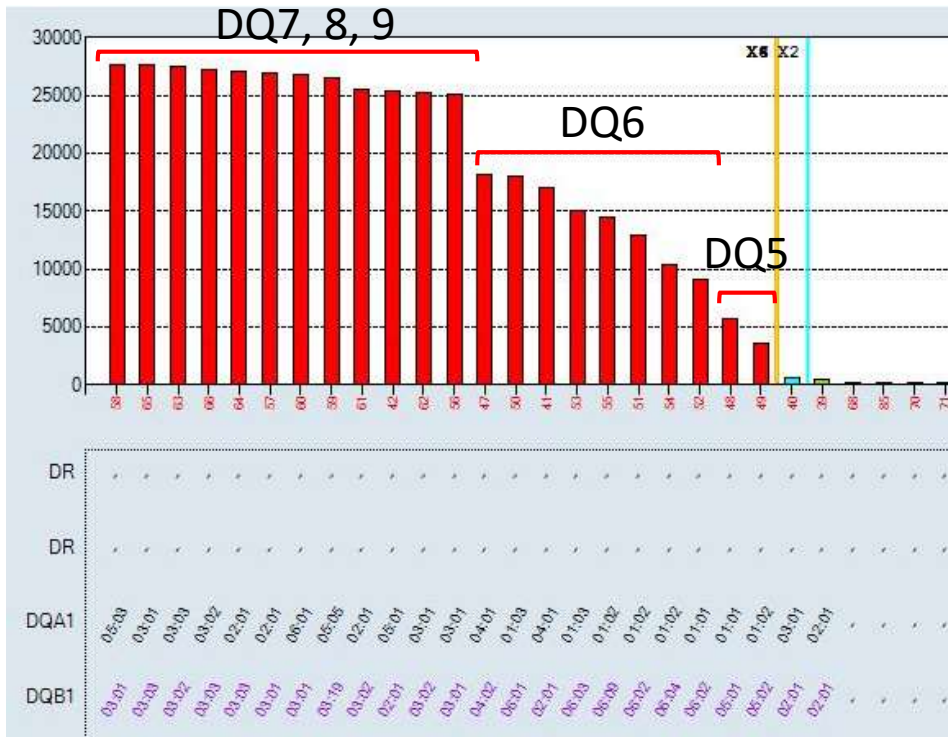
Luminex DSA Class I	
Pre LT, T0	Post LT, T+6h
A*02:01: MFI>25000	A*02:01: Negative (MFI<500)
A*24:02: MFI>2500	A*24:02: Negative (MFI<500)

TRAPIANTO SIMULTANEO FEGATO-RENE
FOLLOW-UP +4G, +9M: NO DSA, NO RIGETTO

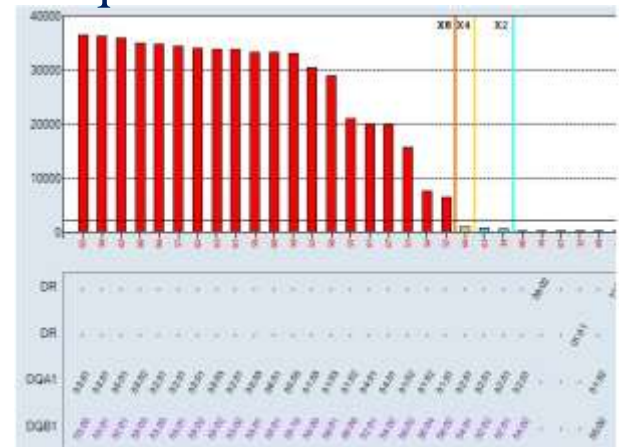
CASO 2: DSA II CLASSE

- F, 21 Anni, TX SIMULTANEO NEL 2008
- PERDITA FEGATO-RENE PER NON COMPLIANCE
- GIU 24: IN LISTA TRAPIANTO URGENTE FEGATO-RENE

DIL 1:16



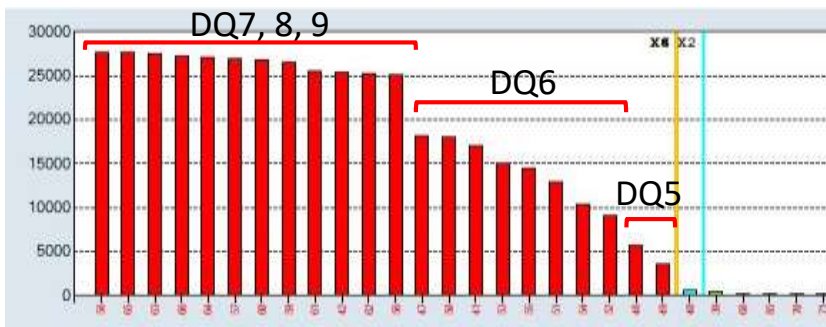
C1q



PRA-I NEG

PRA-II 96%

DSA r-MM: DQ7, DQA1*05, DQA1*04



DQ7, DQ8, DQ9,
DQA1*04, DQA1*05
PROIBITI

Allele	Sero	Raw	Baseline	Ratio	Rxn	Ab Verified
DQB1*03:03	DQ9	27749	27633	629.98	POS	55PP
DQB1*03:02	DQ8	27601	27525	836.12	POS	55PP
DQB1*03:03	DQ9	27268	27246	1529.43	POS	55PP
DQB1*03:03	DQ9	27136	27062	837.6	POS	55PP
DQB1*03:02	DQ8	25617	25587	1272.21	POS	55PP
DQB1*03:02	DQ8	25282	25203	743.98	POS	55PP
DQA1*01:03	DQ6	17996	17968	920.52	POS	52SK
DQA1*01:03	DQ6	15085	15023	515.58	POS	52SK
DQA1*01:02	DQ6	14490	14445	594.58	POS	52SK
DQA1*01:02	DQ6	12916	12885	627.44	POS	52SK
DQA1*01:02	DQ6	10478	10387	282.66	POS	52SK
DQA1*01:01	DQ6	9256	9181	283.65	POS	52SK
DQA1*01:01	DQ5	5695	5678	377.26	POS	52SK
DQA1*01:02	DQ5	3557	3540	226.27	POS	52SK
DQB1*06:09	DQ6	14490	14445	594.58	POS	52PQ, 87Y, q57V
DQB1*06:04	DQ6	10478	10387	282.66	POS	52PQ, 87Y, q57V
DQB1*05:01	DQ5	5695	5678	377.26	POS	52PQ, 87Y, 116L
DQB1*05:02	DQ5	3557	3540	226.27	POS	52PQ, 87Y, 116I
DQB1*06:01	DQ6	17996	17968	920.52	POS	52PQ, 87F
DQB1*06:03	DQ6	15085	15023	515.58	POS	52PQ, 87F
DQB1*06:02	DQ6	12916	12885	627.44	POS	52PQ, 87F
DQB1*06:02	DQ6	9256	9181	283.65	POS	52PQ, 87F
DQB1*03:01	DQ7	27691	27650	1193.64	POS	45EV, 55PP
DQB1*03:01	DQ7	27022	26965	978.69	POS	45EV, 55PP
DQB1*03:01	DQ7	26835	26819	2737.14	POS	45EV, 55PP
DQB1*03:19	DQ7	26543	26500	1114.94	POS	45EV, 55PP
DQB1*03:01	DQ7	25179	25093	703.46	POS	45EV, 55PP
DQA1*05:03	DQ7	27691	27650	1193.64	POS	40GR, 75S
DQA1*05:05	DQ7	26543	26500	1114.94	POS	40GR, 75S
DQA1*05:01	DQ2	25399	25336	867.8	POS	40GR, 75S
DQA1*06:01	DQ7	26835	26819	2737.14	POS	40GR
DQA1*04:01	DQ4	18212	18177	842.65	POS	40GR
DQA1*04:01	DQ2	17153	17106	693.41	POS	40GR

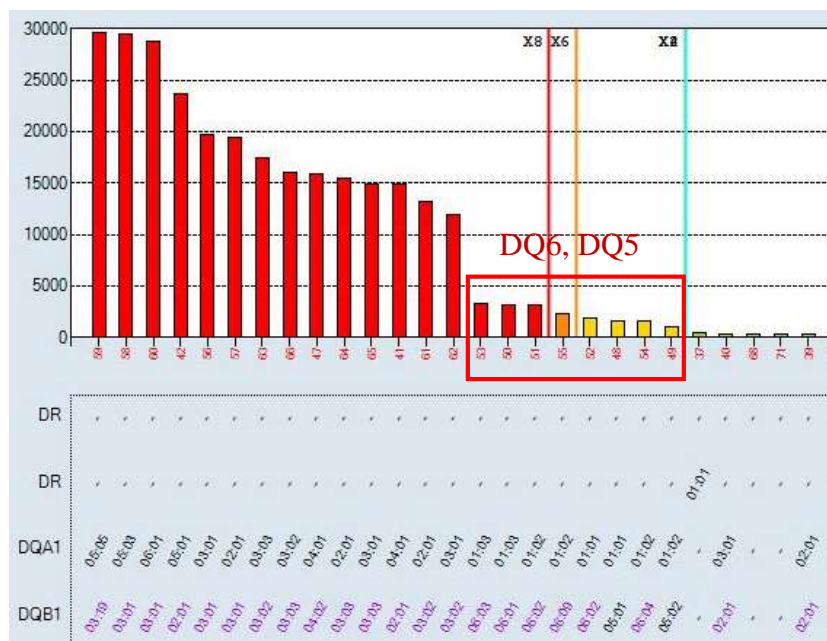
DQ5, DQ6, DQA1*01
RIVALUTARE A +6h

DQ2, DQA1*02
PERMISSIVI

EPITOPE ANALYSIS

- DONOR: DQA1*01, DQA1*03; DQ5, DQ8
 - TRAPIANTO FEGATO (URGENZA CLINICA)
 - NO TRAPIANTO RENE SIMULTANEO (DSA DQ8)

RIVALUTAZIONE +7 G, +21 G DOPO TRAPIANTO FEGATO



- NEGATIVIZZAZIONE DQ5, DQ6
- NO RIDUZIONE DQ7, DQ8, DQ9, DQA1*05

TRAPIANTO RENE DOPO FEGATO (PRIORITARIO)
 DQ2, DQ5, DQ6 PERMISSIVI (PRA 60%)

MODELLO EMILIA-ROMAGNA

DSA HLA CLASSE I

- ALTO MFI / XM+: NO CONTROINDICAZIONE A TX SIMULTANEO FEGATO-RENE
- USO PERFUSIONE MECCANICA E RIVALUTAZIONE IMMUNOLOGICA PER RENE DOPO RIPERFUSIONE FEGATO (+6h)

DSA HLA CLASSE II (DQ)

- ALTO MFI / r-MM / XM+: CONTROINDICAZIONE A TX SIMULTANEO FEGATO-RENE
- MEDIO/BASSO MFI: RIVALUTARE DOPO RIPERFUSIONE FEGATO PER TX RENE SIMULTANEO
- ALTRIMENTI TX RENE DOPO FEGATO (DA ALTRO DONATORE)

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Grazie per l'attenzione

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