Case studies: Applying 2012 HLA matching guidelines for HCT selection

Dennis Confer, MD
Chief Medical Officer, NMDP
October 17, 2012

Learning Objectives

At the conclusion of the program, the participants should be able to:

- Select pre- and post-transplant HLA and non-HLA factors that impact hematopoietic cell transplantation (HCT) transplant outcomes for patients.
- Apply new matching criteria guidelines and research to identify optimal donors or cord blood units for patients in need of HCT.
- Review/evaluate the impact of matching criteria search limitations that may eliminate identification of viable donor and cord blood unit selections and delay transplant.

Financial Disclosure

The following in control of content had no relevant financial relationships to disclose.

• Dennis Confer, MD	Presenter
• Darlene Haven	Planning Committee
• Ellyce Hayes, RD	Planning Committee
• Mary Horowitz, MD	Planning Committee
• Craig Malmberg, CHS	Planning Committee
• Michelle Setterholm, CHS	Planning Committee
• Stephen Spellman, MS	Planning Committee

Outline

- 2 case studies
  - 1: Best adult donor match = 9/10
  - 2: Cord blood unit (CBU) may be best transplant option

- Within each case
  - Polling questions: practice applying the guidelines!
  - Data highlights

- Q & A, time allowing

Recent Update to Matching Guidelines

2012 120: 259-265
Prepublished online May 17, 2012;
doi:10.1182/blood-2012-03-379032

A perspective on the selection of unrelated donors and cord blood units for transplantation

Stephen R. Spellman, Mary Eapen, Brent R. Logan, Carlheinz Mueller, Pablo Rubinstein, Michelle I. Setterholm, Ann E. Woolfrey, Mary M. Horowitz, Dennis L. Confer and Carolyn K. Hurley

Spellman SR, et al. *Blood* (2012); 120:259-265

Factors that Affect Transplant Outcomes

Pre-transplant

- HLA matching
- Patient CMV seropositivity
- Performance score
- Disease
- Disease status
- Graft cell dose

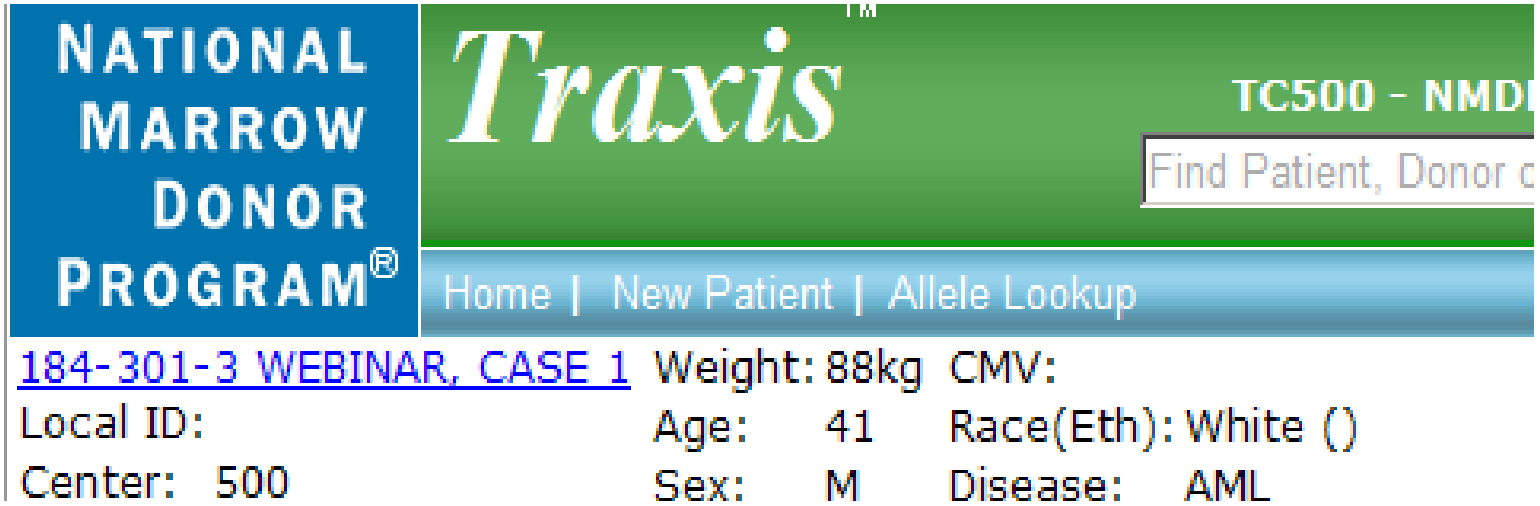
Post-transplant

- Infections
- aGVHD and cGVHD
- Organ toxicity
- Recurrent/2nd malignant neoplasms

Notes on Case Presentation

- NMDP's Traxis® system with HapLogic℠ algorithm
- Screen shots only
  - Mock patients
  - HLA from actual cases
- Traxis navigation and HapLogic III questions/training
  - https://network.bethematchclinical.org/Transplant-Centers/Search-and-Testing/Search-Tools/Traxis

Case 1



- Patient in complete 1st remission
  - Early disease stage

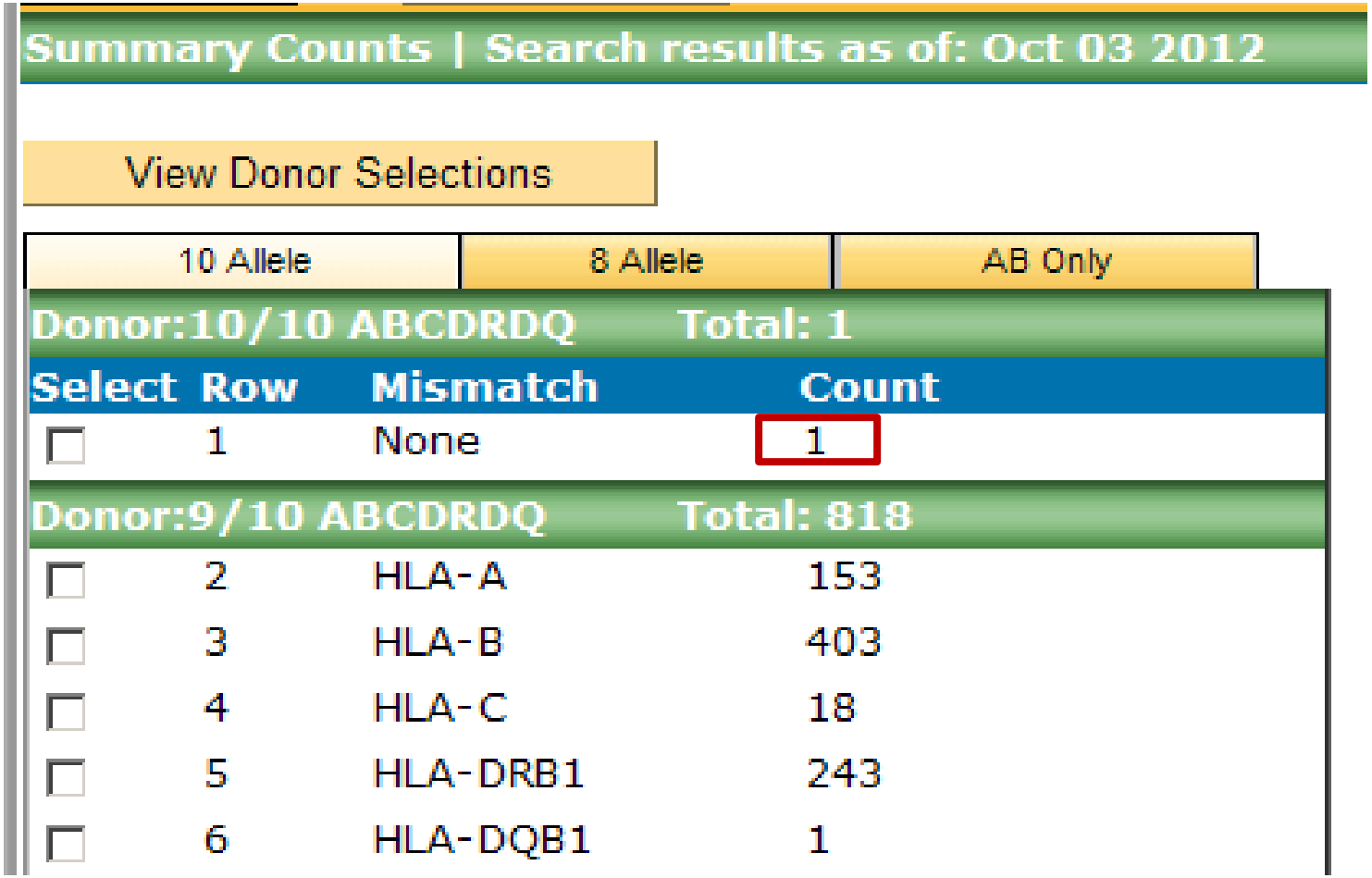
Case 1 Patient Typing

Status	Phenotype	A	B	C	DRB1	DQB1	DRB3	DRB4	DRB5
PRLM	Phenotype 1	03:01	07:ANVB	07:WCP	08:01	06:02	03:01		01:01
		11:01	56:01	02:02	15:01	04:02			

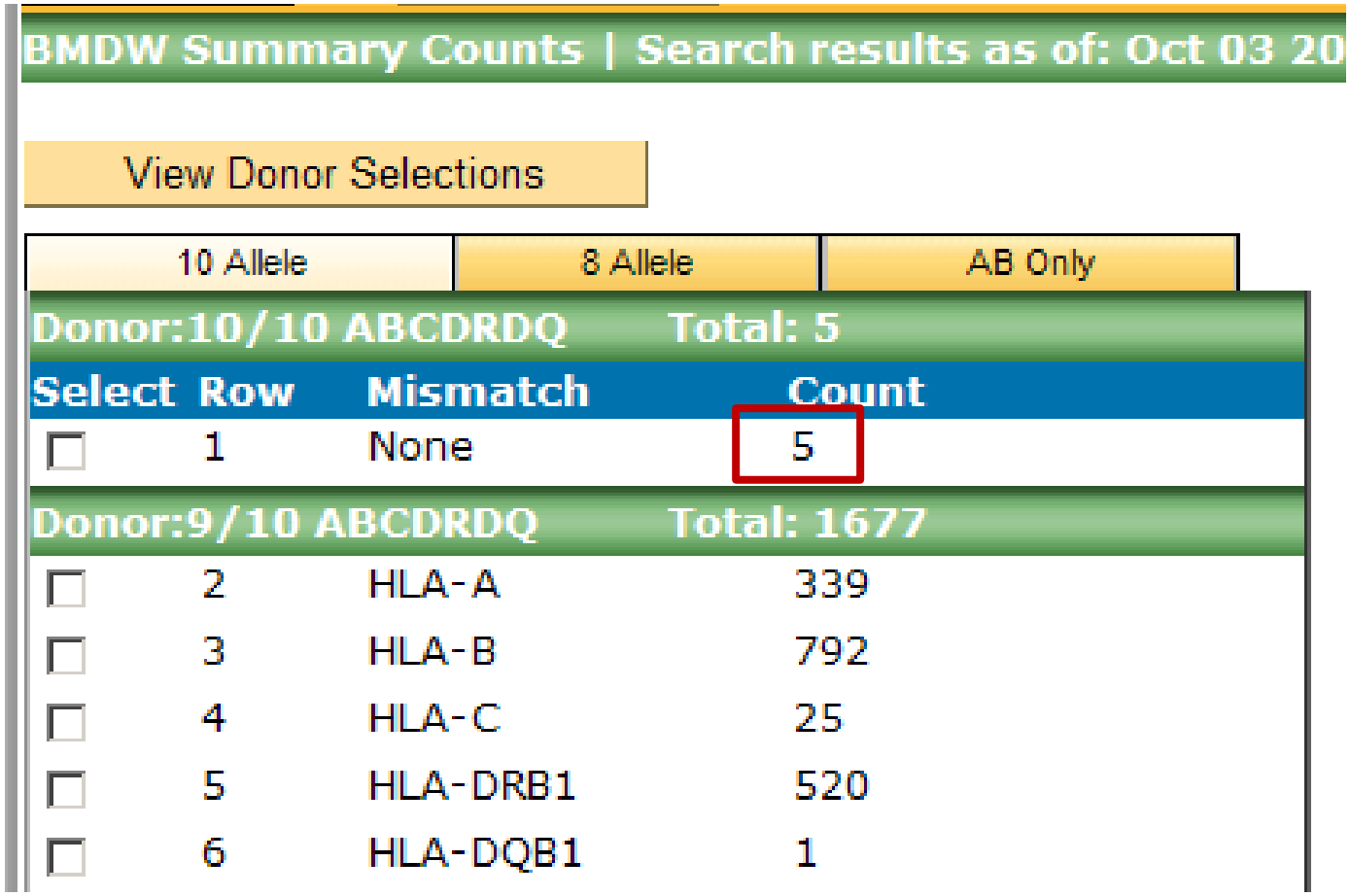
07:ANVB = 07:02/07:61; C*07:WCP = 07:02/07:50

- HLA search strategist comments
  - B*56:01-C*02:02 is an uncommon association; B*56:01 more commonly associates with C*01:02
  - **C mismatch is likely in all B matched donors**

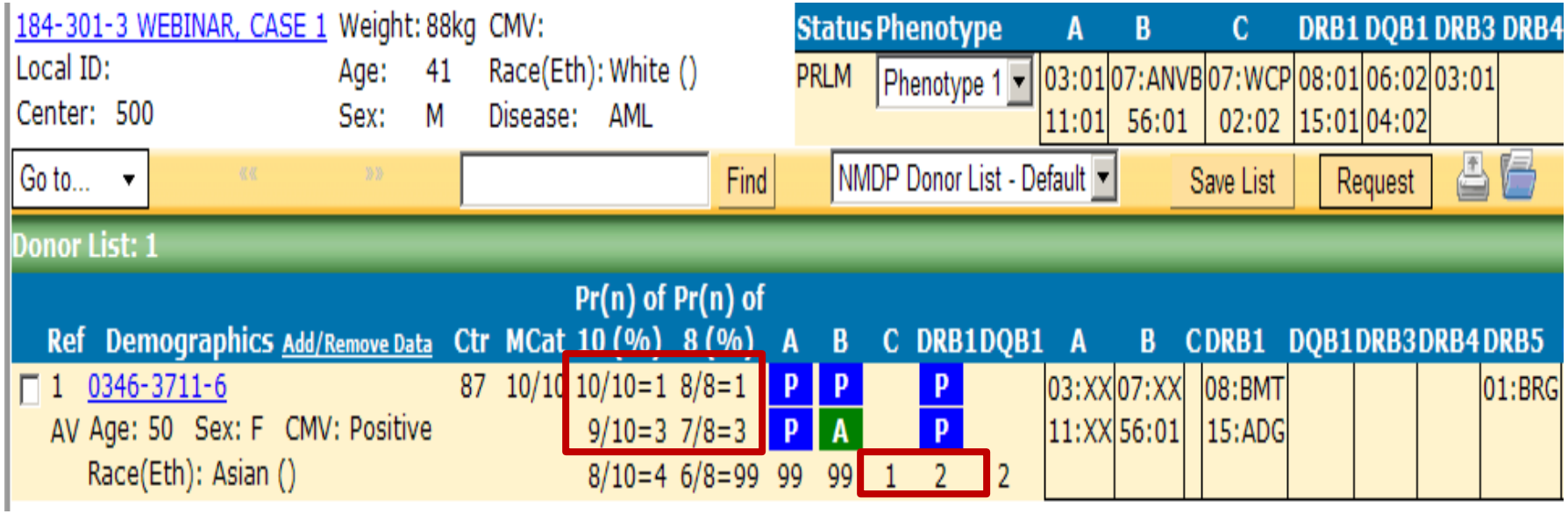
NMDP Donor Overview



BMDW Donor Overview



NMDP Potential 10/10 Donor



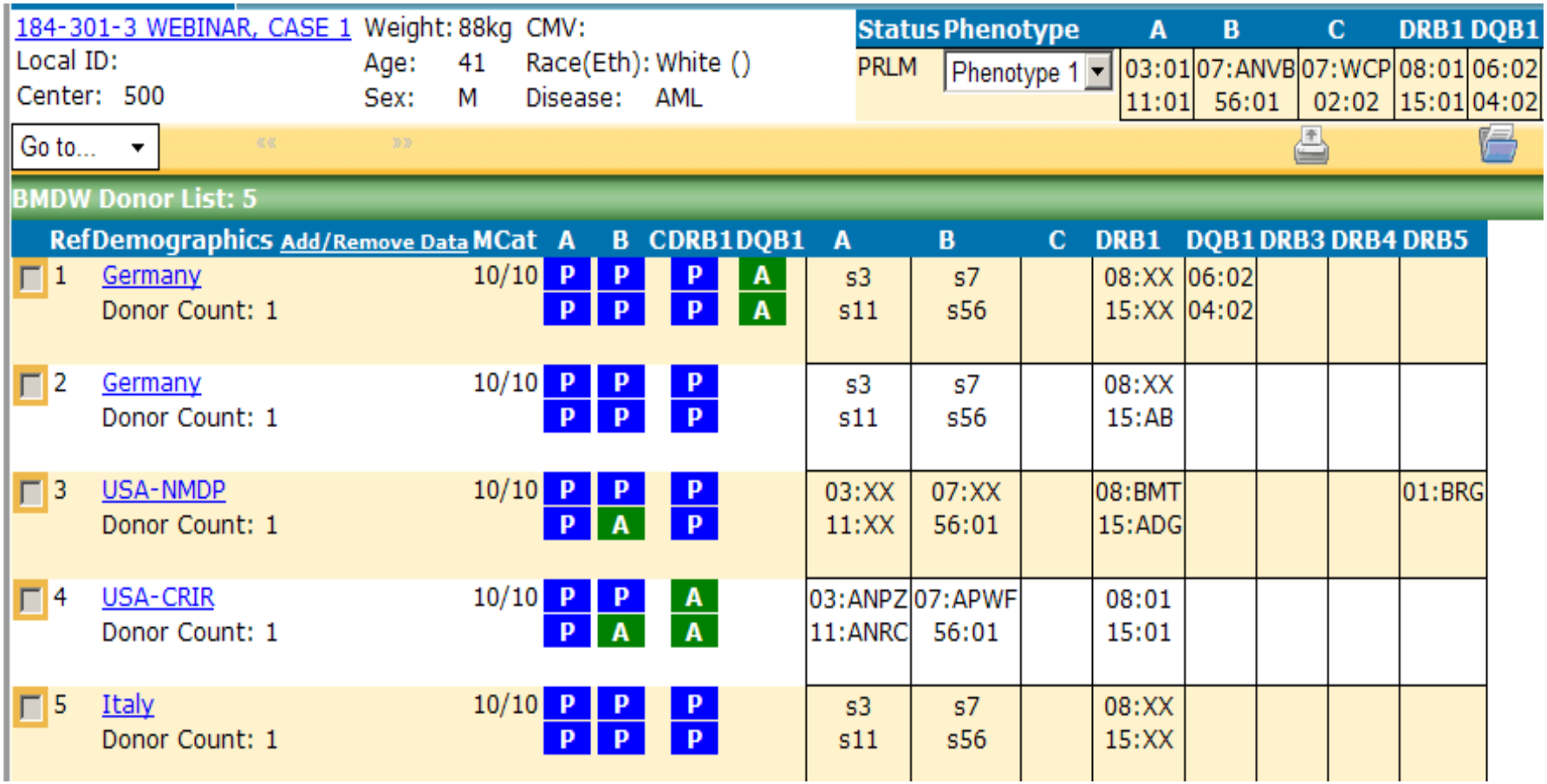
DRB1*08:BMT = 08:01/08:03/08:06/08:10/08:16/08:17

DRB1*15:ADG = 15:01/15:02/15:03/15:04/15:05/15:06/16:01/16:03/16:04/16:05/16:07

DRB5*01:BRG = 01:01/01:04/01:05/01:07/01:09

- Could screen DRB1 and C, mismatches likely

BMDW Potential 10/10 Donors



184-301-3 WEBINAR, CASE 1 Weight: 88kg CMV:
Local ID: Age: 41 Race(Eth): White ()
Center: 500 Sex: M Disease: AML

Status	Phenotype	A	B	C	DRB1	DQB1
PRLM	Phenotype 1	03:01 11:01	07:ANVB 56:01	07:WCP 02:02	08:01 15:01	06:02 04:02

Go to...

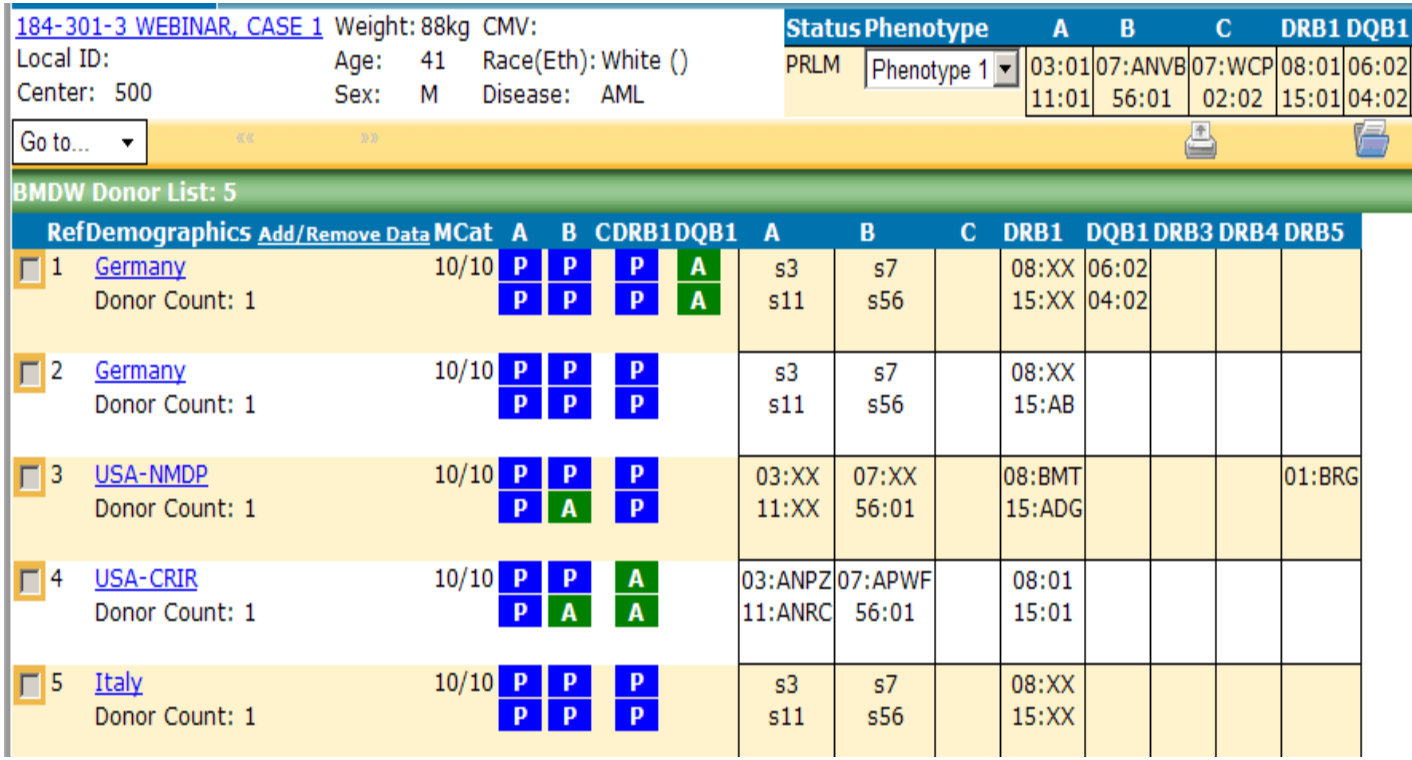
BMDW Donor List: 5

Ref	Demographics (Add/Remove Data)	MCat	A	B	C	DRB1	DQB1	A	B	C	DRB1	DQB1	DRB3	DRB4	DRB5
1	Germany Donor Count: 1	10/10	P P	P P	P P	A A		s3 s11	s7 s56		08:XX 15:XX	06:02 04:02			
2	Germany Donor Count: 1	10/10	P P	P P	P P			s3 s11	s7 s56		08:XX 15:AB				
3	USA-NMDP Donor Count: 1	10/10	P P	P A	P P			03:XX 11:XX	07:XX 56:01		08:BMT 15:ADG				01:BRG
4	USA-CRIR Donor Count: 1	10/10	P P	P A	A A			03:ANPZ 11:ANRC	07:APWF 56:01		08:01 15:01				
5	Italy Donor Count: 1	10/10	P P	P P	P P			s3 s11	s7 s56		08:XX 15:XX				

Poll: Question 1

Though unlikely to match, would you consider spending *this patient's* time and available resources to screen potential 10/10 donors at C and/or DRB1?

- a.) Yes
- b.) No
- c.) Maybe

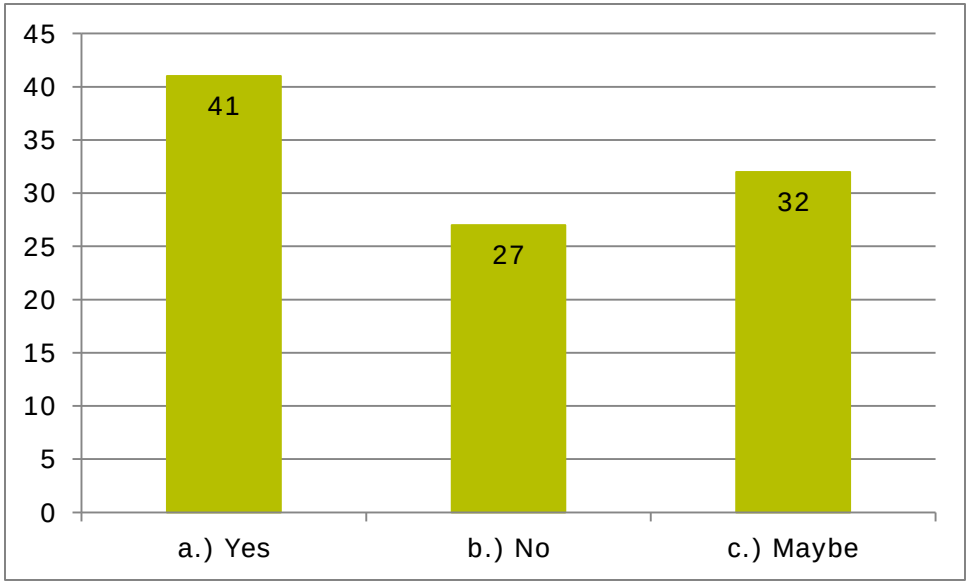


Poll: Question 1 (RESULTS)

Though unlikely to match, would you consider spending *this patient's* time and available resources to screen potential 10/10 donors at C and/or DRB1?

- a.) Yes
- b.) No
- c.) Maybe

Correct Answer – b.) No



Lee Study

blood

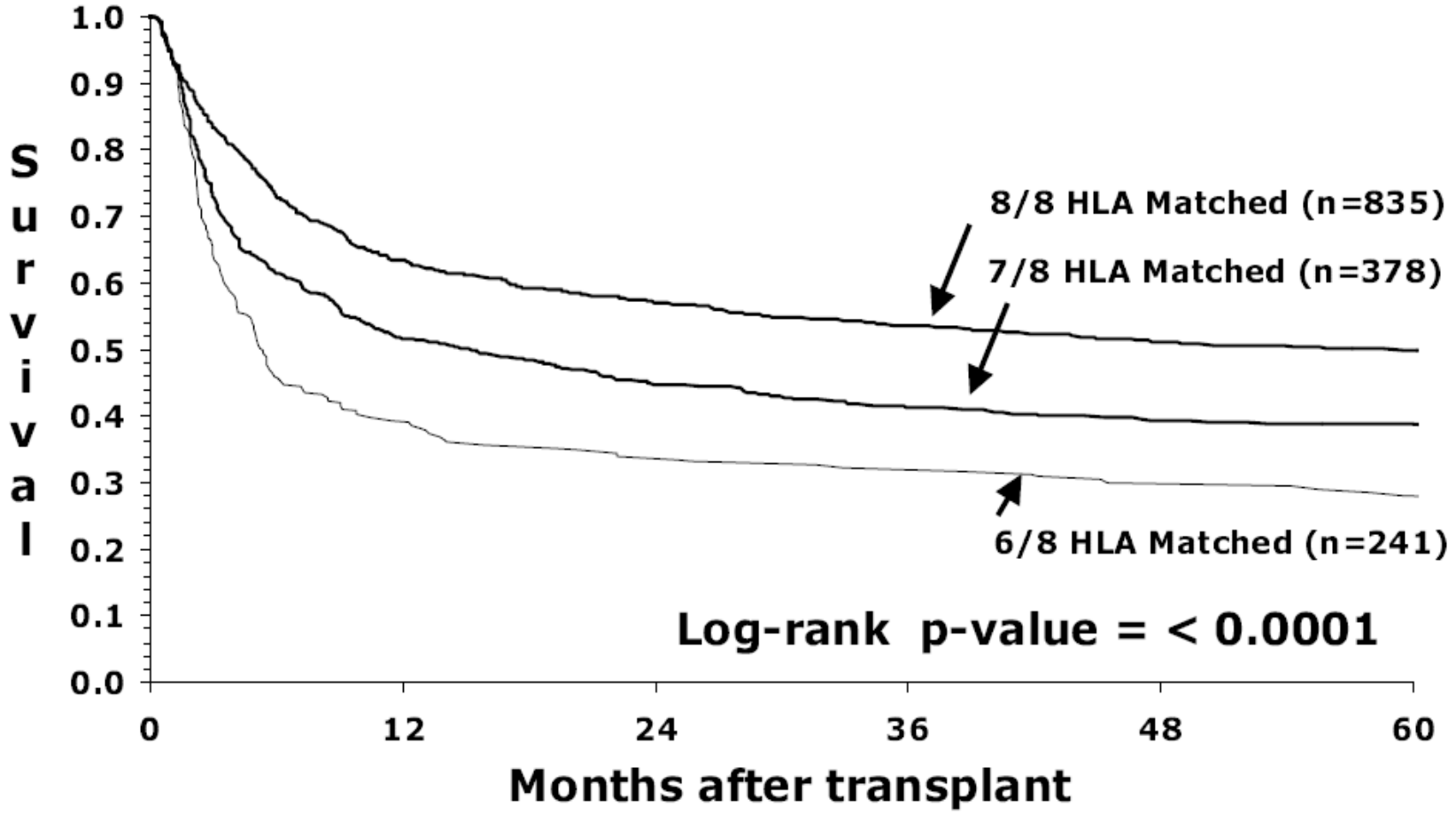
2007 110: 4576-4583
Prepublished online September 4, 2007;
doi:10.1182/blood-2007-06-097386

High-resolution donor-recipient HLA matching contributes to the success of unrelated donor marrow transplantation

Stephanie J. Lee, John Klein, Michael Haagenson, Lee Ann Baxter-Lowe, Dennis L. Confer, Mary Eapen, Marcelo Fernandez-Vina, Neal Flomenberg, Mary Horowitz, Carolyn K. Hurley, Harriet Noreen, Machteld Oudshoorn, Effie Petersdorf, Michelle Setterholm, Stephen Spellman, Daniel Weisdorf, Thomas M. Williams and Claudio Anasetti

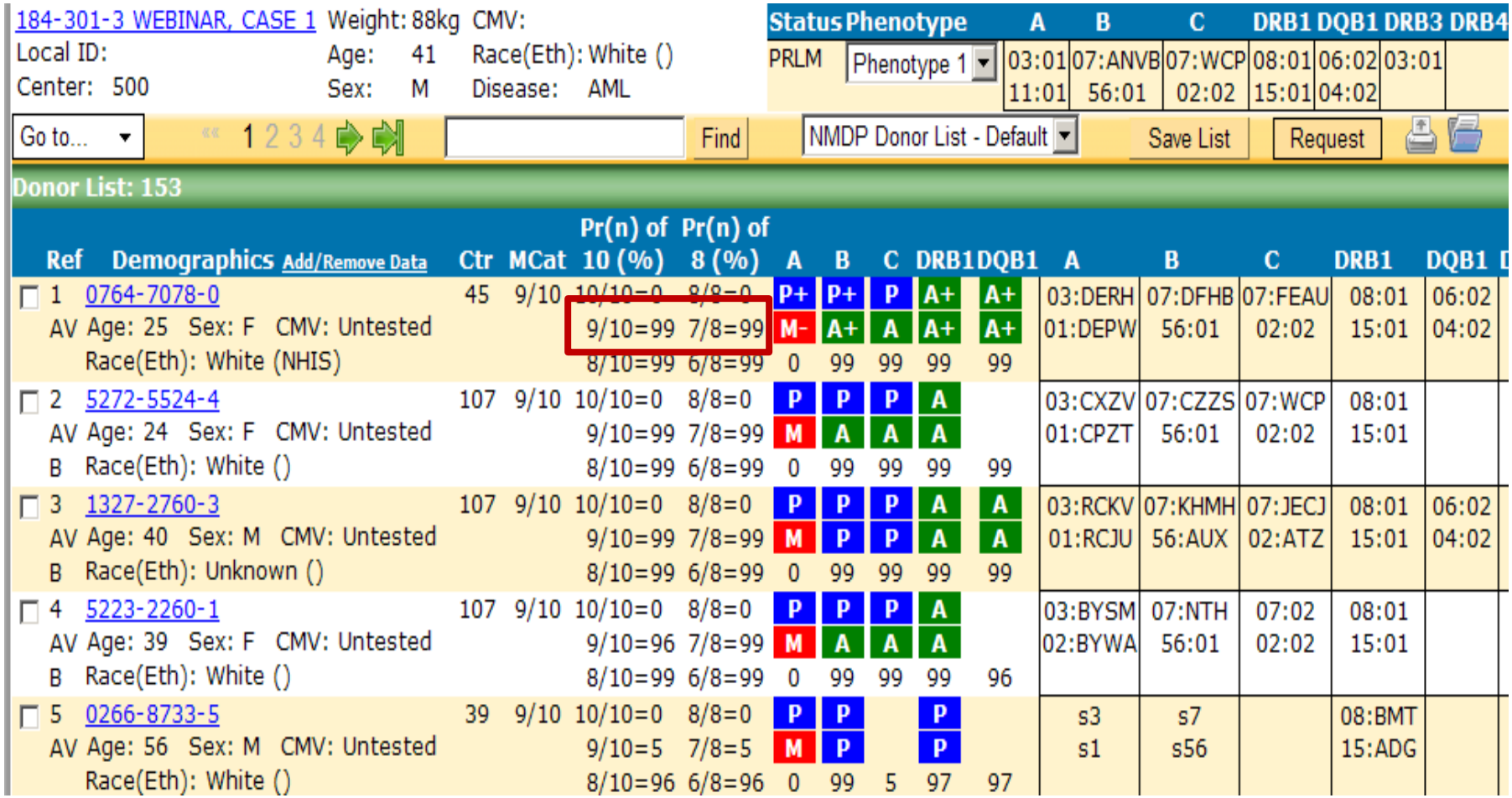
Lee S, et al. *Blood* (2007); 110:4576-83

Early stage disease



Lee SJ, et al. *Blood (*2007); 110:4576-4583

Likely 9/10 A Mismatches



184-301-3 WEBINAR, CASE 1 Weight: 88kg CMV:
Local ID: Age: 41 Race(Eth): White ()
Center: 500 Sex: M Disease: AML

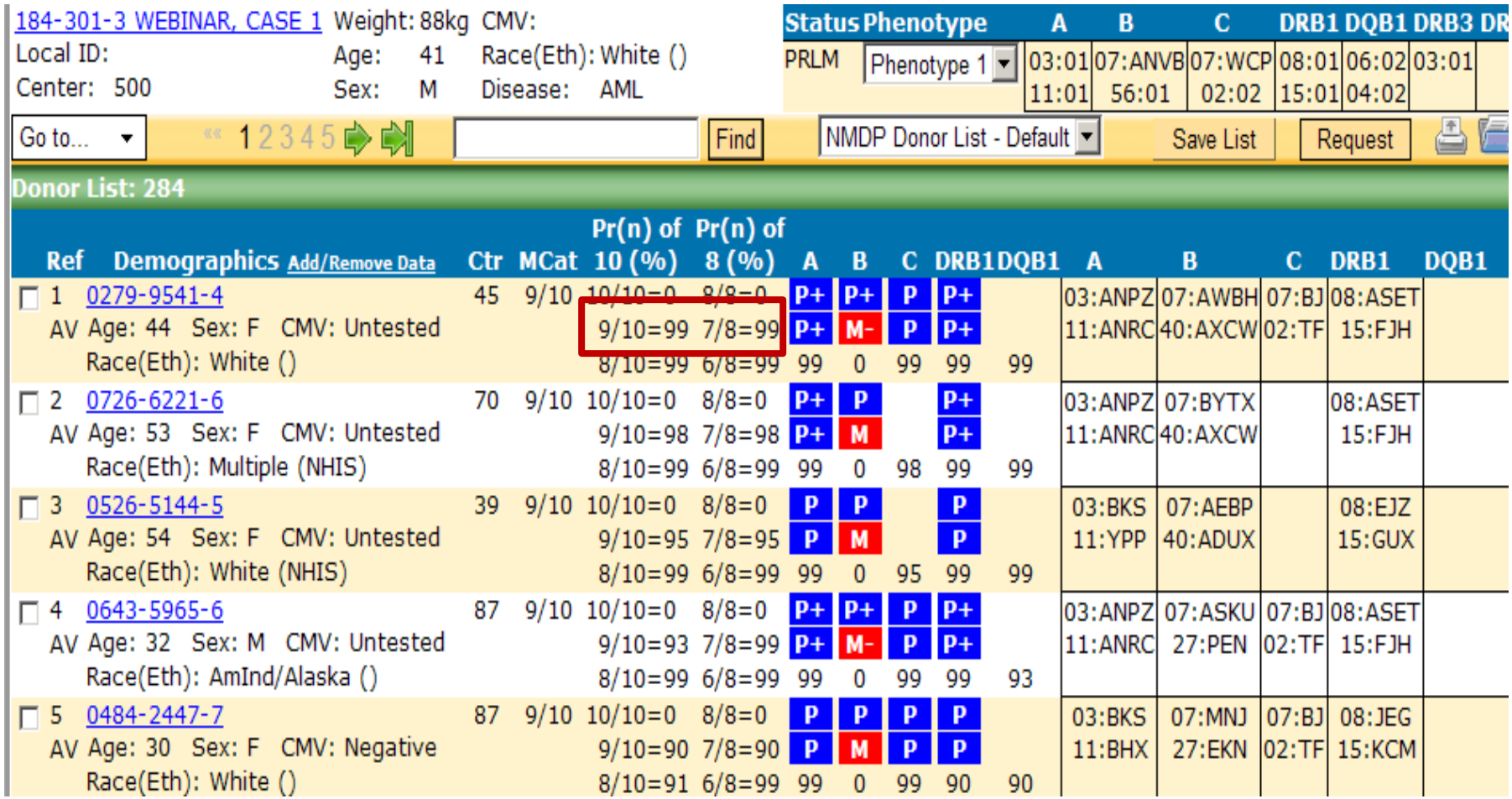
Status	Phenotype	A	B	C	DRB1	DQB1	DRB3	DRB4
PRLM	Phenotype 1	03:01	07:ANVB	07:WCP	08:01	06:02	03:01	
		11:01	56:01	02:02	15:01	04:02		

Go to... « 1 2 3 4 Find NMDP Donor List - Default Save List Request

Donor List: 153

Ref	Demographics Add/Remove Data	Ctr	MCat	Pr(n) of 10 (%)	Pr(n) of 8 (%)	A	B	C	DRB1	DQB1	A	B	C	DRB1	DQB1
1	0764-7078-0	45	9/10	10/10=0	8/8=0	P+	P+	P	A+	A+	03:DERH	07:DFHB	07:FEAU	08:01	06:02
AV	Age: 25 Sex: F CMV: Untested			9/10=99	7/8=99	M-	A+	A	A+	A+	01:DEPW	56:01	02:02	15:01	04:02
	Race(Eth): White (NHIS)			8/10=99	6/8=99	0	99	99	99	99					
2	5272-5524-4	107	9/10	10/10=0	8/8=0	P	P	P	A		03:CXZV	07:CZZS	07:WCP	08:01	
AV	Age: 24 Sex: F CMV: Untested			9/10=99	7/8=99	M	A	A	A		01:CPZT	56:01	02:02	15:01	
B	Race(Eth): White ()			8/10=99	6/8=99	0	99	99	99	99					
3	1327-2760-3	107	9/10	10/10=0	8/8=0	P	P	P	A	A	03:RCKV	07:KHMH	07:JECJ	08:01	06:02
AV	Age: 40 Sex: M CMV: Untested			9/10=99	7/8=99	M	P	P	A	A	01:RCJU	56:AUX	02:ATZ	15:01	04:02
B	Race(Eth): Unknown ()			8/10=99	6/8=99	0	99	99	99	99					
4	5223-2260-1	107	9/10	10/10=0	8/8=0	P	P	P	A		03:BYSM	07:NTH	07:02	08:01	
AV	Age: 39 Sex: F CMV: Untested			9/10=96	7/8=99	M	A	A	A		02:BYWA	56:01	02:02	15:01	
B	Race(Eth): White ()			8/10=99	6/8=99	0	99	99	99	96					
5	0266-8733-5	39	9/10	10/10=0	8/8=0	P	P		P		s3	s7		08:BMT	
AV	Age: 56 Sex: M CMV: Untested			9/10=5	7/8=5	M	P		P		s1	s56		15:ADG	
	Race(Eth): White ()			8/10=96	6/8=96	0	99	5	97	97					

Likely 9/10 B Mismatches



184-301-3 WEBINAR, CASE 1 Weight: 88kg CMV:
Local ID: Age: 41 Race(Eth): White ()
Center: 500 Sex: M Disease: AML

Status	Phenotype	A	B	C	DRB1	DQB1	DRB3	DR
PRLM	Phenotype 1	03:01	07:ANVB	07:WCP	08:01	06:02	03:01	
		11:01	56:01	02:02	15:01	04:02		

Go to... « 1 2 3 4 5 Find NMDP Donor List - Default Save List Request

Donor List: 284

Ref	Demographics Add/Remove Data	Ctr	MCat	Pr(n) of 10 (%)	Pr(n) of 8 (%)	A	B	C	DRB1	DQB1	A	B	C	DRB1	DQB1
1	0279-9541-4	45	9/10	10/10=0	8/8=0	P+	P+	P	P+		03:ANPZ	07:AWBH	07:BJ	08:ASET	
AV	Age: 44 Sex: F CMV: Untested			9/10=99	7/8=99	P+	M-	P	P+		11:ANRC	40:AXCW	02:TF	15:FJH	
	Race(Eth): White ()			8/10=99	6/8=99	99	0	99	99	99					
2	0726-6221-6	70	9/10	10/10=0	8/8=0	P+	P		P+		03:ANPZ	07:BYTX		08:ASET	
AV	Age: 53 Sex: F CMV: Untested			9/10=98	7/8=98	P+	M		P+		11:ANRC	40:AXCW		15:FJH	
	Race(Eth): Multiple (NHIS)			8/10=99	6/8=99	99	0	98	99	99					
3	0526-5144-5	39	9/10	10/10=0	8/8=0	P	P		P		03:BKS	07:AEBP		08:EJZ	
AV	Age: 54 Sex: F CMV: Untested			9/10=95	7/8=95	P	M		P		11:YPP	40:ADUX		15:GUX	
	Race(Eth): White (NHIS)			8/10=99	6/8=99	99	0	95	99	99					
4	0643-5965-6	87	9/10	10/10=0	8/8=0	P+	P+	P	P+		03:ANPZ	07:ASKU	07:BJ	08:ASET	
AV	Age: 32 Sex: M CMV: Untested			9/10=93	7/8=99	P+	M-	P	P+		11:ANRC	27:PEN	02:TF	15:FJH	
	Race(Eth): AmInd/Alaska ()			8/10=99	6/8=99	99	0	99	99	93					
5	0484-2447-7	87	9/10	10/10=0	8/8=0	P	P	P	P		03:BKS	07:MNJ	07:BJ	08:JEG	
AV	Age: 30 Sex: F CMV: Negative			9/10=90	7/8=90	P	M	P	P		11:BHX	27:EKN	02:TF	15:KCM	
	Race(Eth): White ()			8/10=91	6/8=99	99	0	99	90	90					

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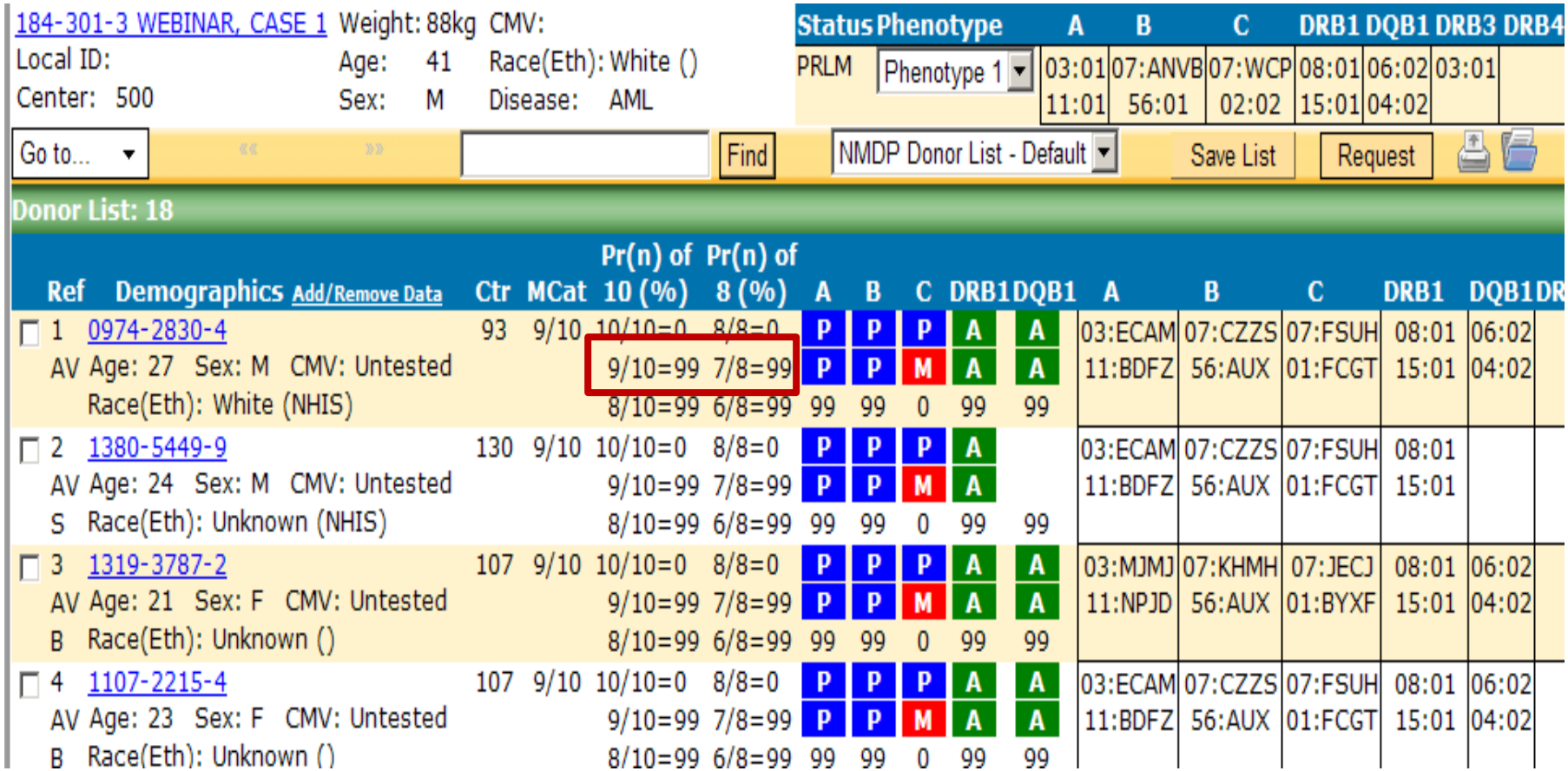
Likely 9/10 C Mismatches



184-301-3 WEBINAR, CASE 1 Weight: 88kg CMV:
Local ID: Age: 41 Race(Eth): White ()
Center: 500 Sex: M Disease: AML

Status	Phenotype	A	B	C	DRB1	DQB1	DRB3	DRB4
PRLM	Phenotype 1	03:01	07:ANVB	07:WCP	08:01	06:02	03:01	
		11:01	56:01	02:02	15:01	04:02		

Go to... | Find | NMDP Donor List - Default | Save List | Request

Donor List: 18

Ref	Demographics Add/Remove Data	Ctr	MCat	Pr(n) of 10 (%)	Pr(n) of 8 (%)	A	B	C	DRB1	DQB1	A	B	C	DRB1	DQB1	DR
1	0974-2830-4	93	9/10	10/10=0	8/8=0	P	P	P	A	A	03:ECAM	07:CZZS	07:FSUH	08:01	06:02	
AV	Age: 27 Sex: M CMV: Untested			9/10=99	7/8=99	P	P	M	A	A	11:BDFZ	56:AUX	01:FCGT	15:01	04:02	
	Race(Eth): White (NHIS)			8/10=99	6/8=99	99	99	0	99	99						
2	1380-5449-9	130	9/10	10/10=0	8/8=0	P	P	P	A		03:ECAM	07:CZZS	07:FSUH	08:01		
AV	Age: 24 Sex: M CMV: Untested			9/10=99	7/8=99	P	P	M	A		11:BDFZ	56:AUX	01:FCGT	15:01		
S	Race(Eth): Unknown (NHIS)			8/10=99	6/8=99	99	99	0	99	99						
3	1319-3787-2	107	9/10	10/10=0	8/8=0	P	P	P	A	A	03:MJMJ	07:KHMH	07:JECJ	08:01	06:02	
AV	Age: 21 Sex: F CMV: Untested			9/10=99	7/8=99	P	P	M	A	A	11:NPJD	56:AUX	01:BYXF	15:01	04:02	
B	Race(Eth): Unknown ()			8/10=99	6/8=99	99	99	0	99	99						
4	1107-2215-4	107	9/10	10/10=0	8/8=0	P	P	P	A	A	03:ECAM	07:CZZS	07:FSUH	08:01	06:02	
AV	Age: 23 Sex: F CMV: Untested			9/10=99	7/8=99	P	P	M	A	A	11:BDFZ	56:AUX	01:FCGT	15:01	04:02	
B	Race(Eth): Unknown ()			8/10=99	6/8=99	99	99	0	99	99						

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Poll: Question 2

Which mismatch would you choose for PBSC donation?

- a.) A antigen mismatch

Demographics Add/Remove Data	Ctr	MCat	Pr(n) of 10 (%)	Pr(n) of 8 (%)	A	B	C	DRB1	DQB1	A	B	C	DRB1	DQB1
0764-7078-0	45	9/10	10/10=0	8/8=0	P+	P+	P	A+	A+	03:DERH	07:DFHB	07:FEAU	08:01	06:02
Age: 25 Sex: F CMV: Untested			9/10=99	7/8=99	M-	A+	A	A+	A+	01:DEPW	56:01	02:02	15:01	04:02
Race(Eth): White (NHIS)			8/10=99	6/8=99	0	99	99	99	99					

- b.) C antigen mismatch

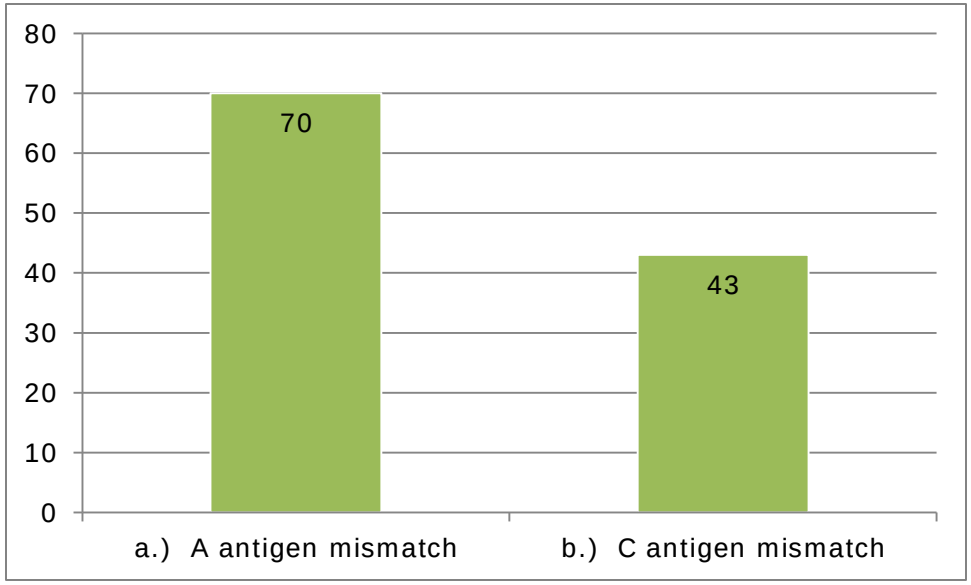
0974-2830-4	93	9/10	10/10=0	8/8=0	P	P	P	A	A	03:ECAM	07:CZZS	07:FSUH	08:01	06:02
Age: 27 Sex: M CMV: Untested			9/10=99	7/8=99	P	P	M	A	A	11:BDFZ	56:AUX	01:FCGT	15:01	04:02
Race(Eth): White (NHIS)			8/10=99	6/8=99	99	99	0	99	99					

Poll: Question 2 (RESULTS)

Which mismatch would you choose for PBSC donation?

- a.) A antigen mismatch
- b.) C antigen mismatch

Correct Answer – a.) A antigen mismatch



ASBMT
American Society for Blood and Marrow Transplantation

HLA-C Antigen Mismatch Is Associated with Worse Outcome in Unrelated Donor Peripheral Blood Stem Cell Transplantation

Ann Woolfrey,[1] John P. Klein,[2] Michael Haagenson,[3] Stephen Spellman,[4] Effie Petersdorf,[1] Machteld Oudshoorn,[5] James Gajewski,[6] Gregory A. Hale,[7] John Horan,[8] Minoo Battiwalla,[9] Susana R. Marino,[10] Michelle Setterholm,[4] Olle Ringden,[11] Carolyn Hurley,[12] Neal Flomenberg,[13] Claudio Anasetti,[14] Marcelo Fernandez-Vina,[15] Stephanie J. Lee[1]

Woolfrey A, et al. *Biol Blood Marrow Transplant (*2011);17:885-892

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Locus-Specific Analysis — Mortality

	N	RR	95% CI	p value
8/8 match	1243	1.00		
A allele MM	51	1.16	0.80-1.67	0.43
A antigen MM	85	1.17	0.88-1.55	0.29
B allele MM	57	1.29	0.92-1.28	0.14
B antigen MM	16	1.01	0.50-2.04	0.97
C allele MM	61	0.82	0.57-1.19	0.30
C antigen MM	***187***	***1.41***	***1.16-1.70***	***0.0005***
DRB1 MM	39	1.30	0.87-1.94	0.20
C allele vs. antigen		***0.58***	***0.39-0.88***	***0.009***

C antigen mismatch increases risk for mortality, DFS, TRM & GVHD III-IV

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Can’t avoid C antigen mismatch?

- Further Lee and Woolfrey data analysis

- ***No* significant advantage to using marrow over PBSC** as graft source with **isolated C antigen mismatch**

Poll: Question 3

Which mismatch would you choose for marrow donation?

- a.) A antigen mismatch

Demographics Add/Remove Data	Ctr	MCat	Pr(n) of 10 (%)	Pr(n) of 8 (%)	A	B	C	DRB1	DQB1	A	B	C	DRB1	DQB1
0764-7078-0	45	9/10	10/10=0	8/8=0	P+	P+	P	A+	A+	03:DERH	07:DFHB	07:FEAU	08:01	06:02
Age: 25 Sex: F CMV: Untested			9/10=99	7/8=99	M-	A+	A	A+	A+	01:DEPW	56:01	02:02	15:01	04:02
Race(Eth): White (NHIS)			8/10=99	6/8=99	0	99	99	99	99					

- b.) C antigen mismatch

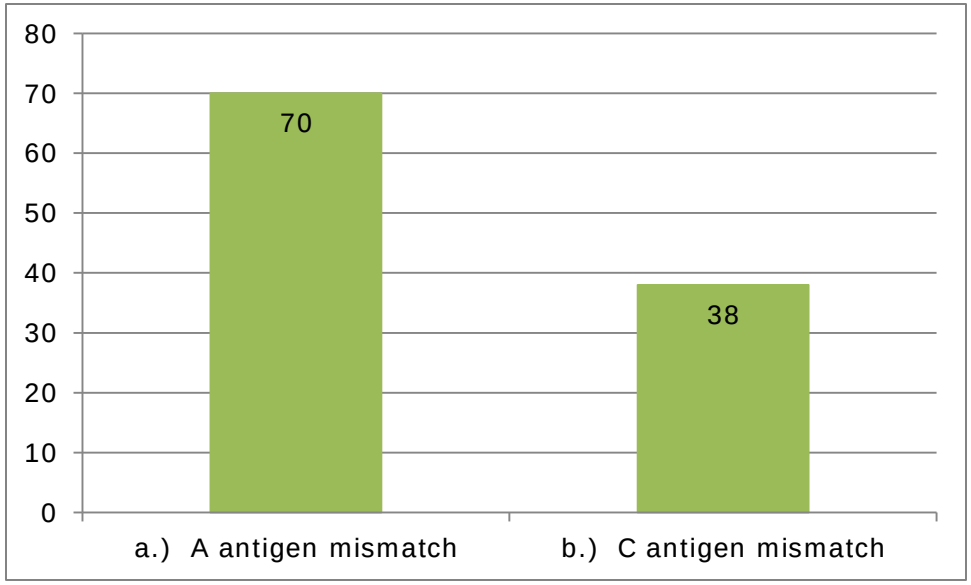
0974-2830-4	93	9/10	10/10=0	8/8=0	P	P	P	A	A	03:ECAM	07:CZZS	07:FSUH	08:01	06:02
Age: 27 Sex: M CMV: Untested			9/10=99	7/8=99	P	P	M	A	A	11:BDFZ	56:AUX	01:FCGT	15:01	04:02
Race(Eth): White (NHIS)			8/10=99	6/8=99	99	99	0	99	99					

Poll: Question 3 (RESULTS)

Which mismatch would you choose for marrow donation?

- a.) A antigen mismatch
- b.) C antigen mismatch

Correct Answer – b.) C antigen mismatch



Specific Single Locus Mismatches

Considering 8/8 as "fully matched"

	Survival		TRM		Acute GVHD	
	RR	p	RR	p	RR	p
8/8	1.00		1.00		1.00	
A MM	1.36	<0.0001	1.47	<0.0001	1.57	<0.0001
B MM	1.16	0.20	1.32	0.03	1.63	0.001
C MM	1.19	0.006	1.32	0.0002	1.43	<0.0001
DR MM	1.48	0.0005	1.56	0.0007	1.27	0.16

Survival: Mismatch at A or DRB1 vs. B or C, RR 1.18 (1.10-1.38), p=0.04

Lee S, et al. *Blood* (2007); 110:4576-83

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Poll: Question 4

You've identified an optimal 9/10 donor and a backup donor. What antibody specificities would you consider?

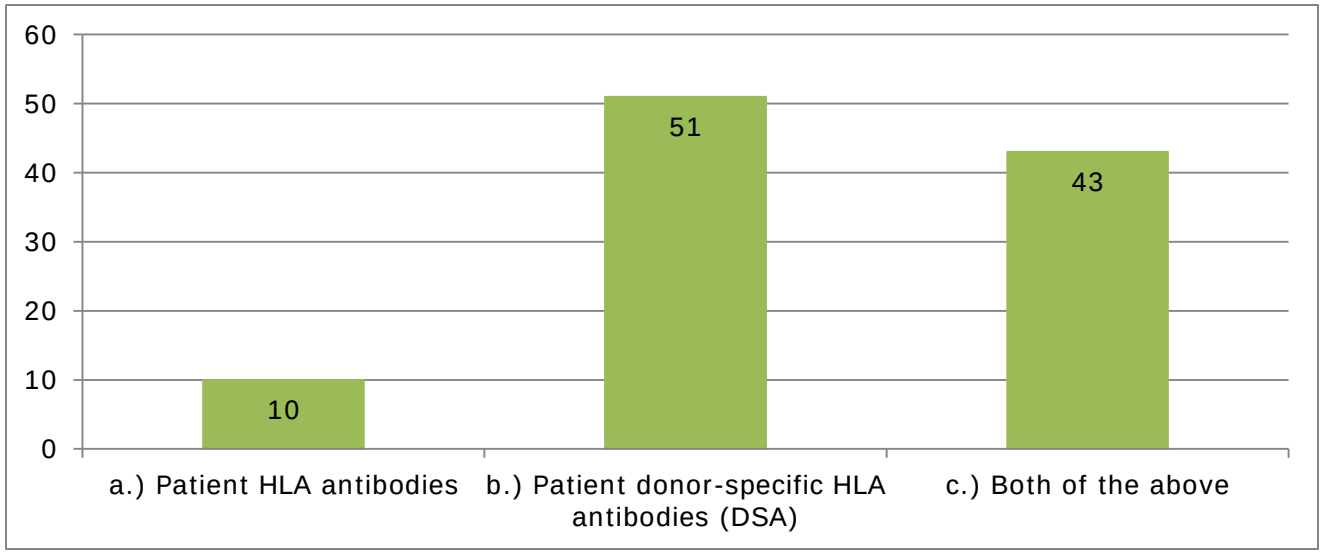
- a.) Patient HLA antibodies
- b.) Patient donor-specific HLA antibodies (DSA)
- c.) Both of the above

Poll: Question 4 (RESULTS)

You've identified an optimal 9/10 donor and a backup donor. What antibody specificities would you consider?

- a.) Patient HLA antibodies
- b.) Patient donor-specific HLA antibodies (DSA)
- c.) Both of the above

Correct Answer – b.) Patient donor-specific HLA antibodies (DSA)



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blood

2010 115: 2704-2708
Prepublished online January 20, 2010;
doi:10.1182/blood-2009-09-244525

The detection of donor-directed, HLA-specific alloantibodies in recipients of unrelated hematopoietic cell transplantation is predictive of graft failure

Stephen Spellman, Robert Bray, Sandra Rosen-Bronson, Michael Haagenson, John Klein, Susan Flesch, Cynthia Vierra-Green and Claudio Anasetti

Spellman S, et al. *Blood* (2010);115:2704-2708

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Study Conclusions

- Approximately 35% of patients receiving unrelated stem cell transplants possess HLA antibodies
- The presence of donor-specific HLA antibodies associates with graft failure
- HLA antibody evaluations should be part of the routine workup for unrelated stem cell transplantation

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Poll: Question 5

You've identified 3-5 optimal 9/10 donors

- Tests show no evidence of patient DSA

Would you consider typing patients/donors at DPB1?

- a.) Yes
- b.) No
- c.) Maybe

Poll: Question 5

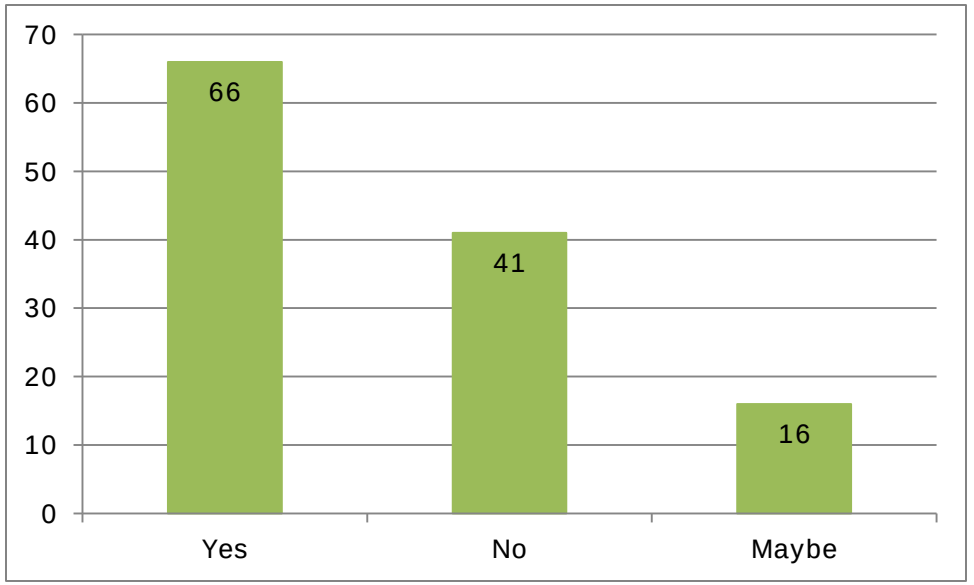
You've identified 3-5 optimal 9/10 donors

- Tests show no evidence of patient DSA

Would you consider typing patients/donors at DPB1?

- a.) Yes
- b.) No
- c.) Maybe

Correct Answer – c.) Maybe



Newer DPB1 Data

Effect of T-cell-epitope matching at HLA-DPB1 in recipients of unrelated-donor haemopoietic-cell transplantation: a retrospective study

Katharina Fleischhauer, Bronwen E Shaw*, Theodore Gooley, Mari Malkki, Peter Bardy, Jean-Denis Bignon, Valérie Dubois, Mary M Horowitz, J Alejandro Madrigal, Yasuo Morishima, Machteld Oudshoorn, Olle Ringden, Stephen Spellman, Andrea Velardi, Elisabetta Zino, Effie W Petersdorf, on behalf of the International Histocompatibility Working Group in Hematopoietic Cell Transplantation*

Fleischhauer K, et al. *Lancet Oncol (*2012); 13:366-374

DPB1 Permissive Mismatches May Benefit 9 of 10 Matched Transplant

	HLA 10/10 match, non-permissive DPB1 mismatch (n=1654)	HLA 9/10 match, permissive DPB1 mismatch (n=1595)		HLA 9/10 match, DPB1 match (n=500)	
		HR or OR	p value	HR or OR	p value
Overall mortality	1 (ref)	1·04 (0·94–1·14)	0·39	1·02 (0·89–1·18)	0·70
Non-relapse mortality	1 (ref)	1·01 (0·90–1·13)	0·81	1·00 (0·84–1·19)	0·98
Relapse*	1 (ref)	1·12 (0·96–1·31)	0·14	1·16 (0·92–1·45)	0·19
Grade 3–4 aGvHD	1 (ref)	1·00 (0·84–1·19)	0·97	0·93 (0·72–1·21)	0·62

Fleischhauer K, et al. *Lancet Oncol (*2012); 13:366-374

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DPB1 Non-Permissive Mismatches May be Detrimental to 9 of 10 Matched Transplant

	HLA 10/10 match, non-permissive DPB1 mismatch (n=1654)	HLA 9/10 match, non-permissive DPB1 mismatch (n=1001)	
		HR or OR	p value
Overall mortality	1 (ref)	1·13 (1·02–1·26)	0·01
Non-relapse mortality	1 (ref)	1·19 (1·05–1·35)	0·006
Relapse*	1 (ref)	1·04 (0·87–1·24)	0·64
Grade 3–4 aGvHD	1 (ref)	1·36 (1·13–1·65)	0·001

Fleischhauer K, et al. *Lancet Oncol (*2012); 13:366-374

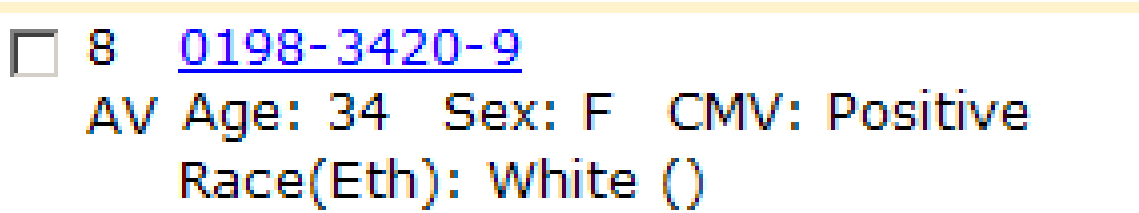
Is a DPB1 Mismatch Permissive?

- European Bioinformatics Institute (EBI) website
  - DPB1 T-Cell Epitope Algorithm
  - http://www.ebi.ac.uk/imgt/hla/dpb.html

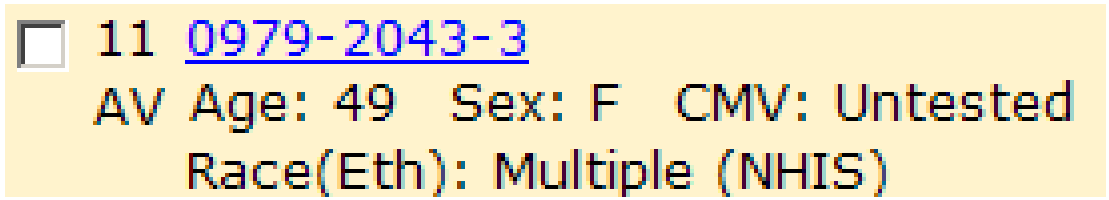
Poll: Question 6

Assume this 41 y/o M patient is CMV positive. If each donor is equally matched, which would you choose?

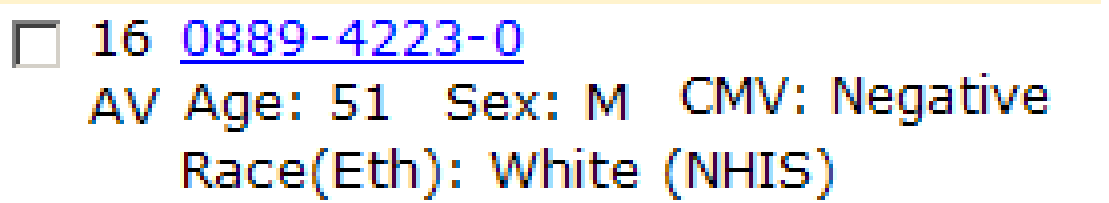
- a.)



- b.)



- c.)

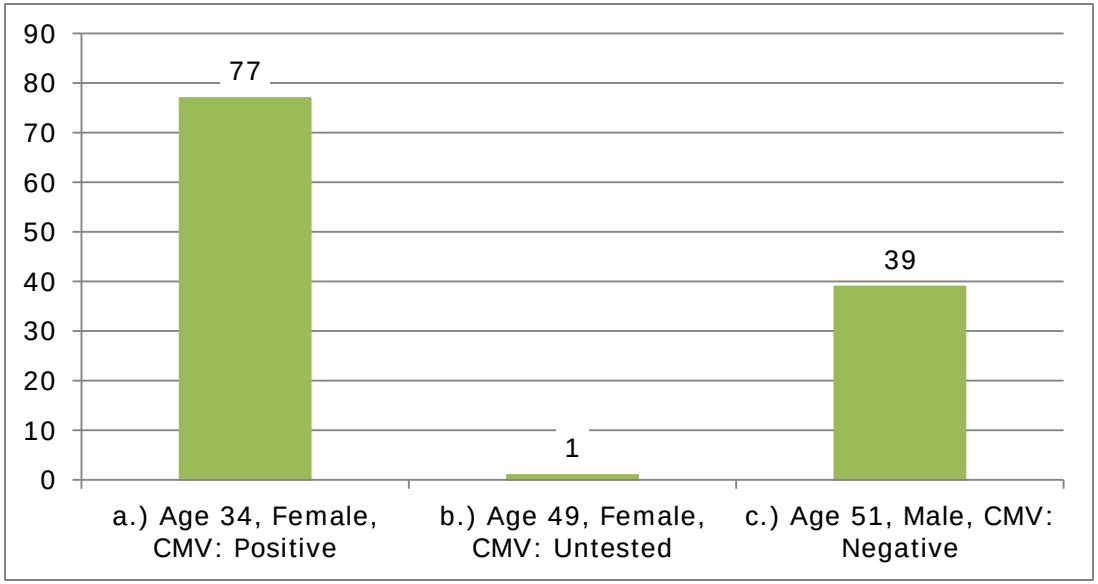


Poll: Question 6 (RESULTS)

Assume this 41 y/o M patient is CMV positive. If each donor is equally matched, which would you choose?

- a.) Age 34, Female, CMV: Positive
- b.) Age 49, Female, CMV: Untested
- c.) Age 51, Male, CMV: Negative

Correct Answer – a.) Age 34, Female, CMV: Positive



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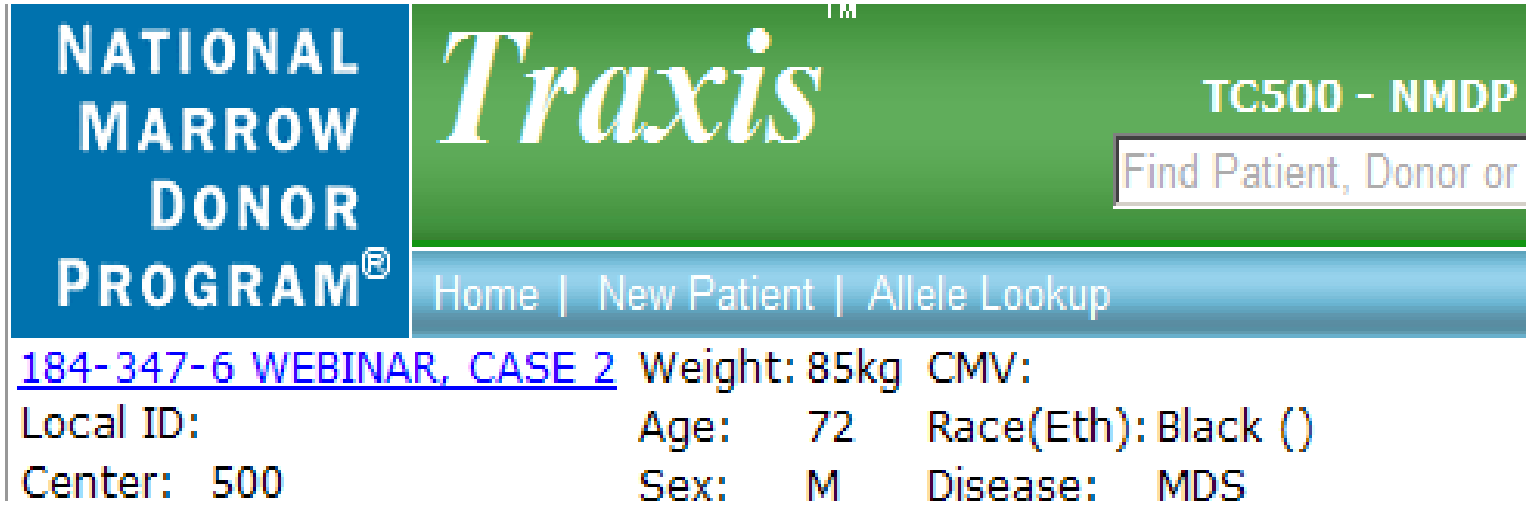
Case 2



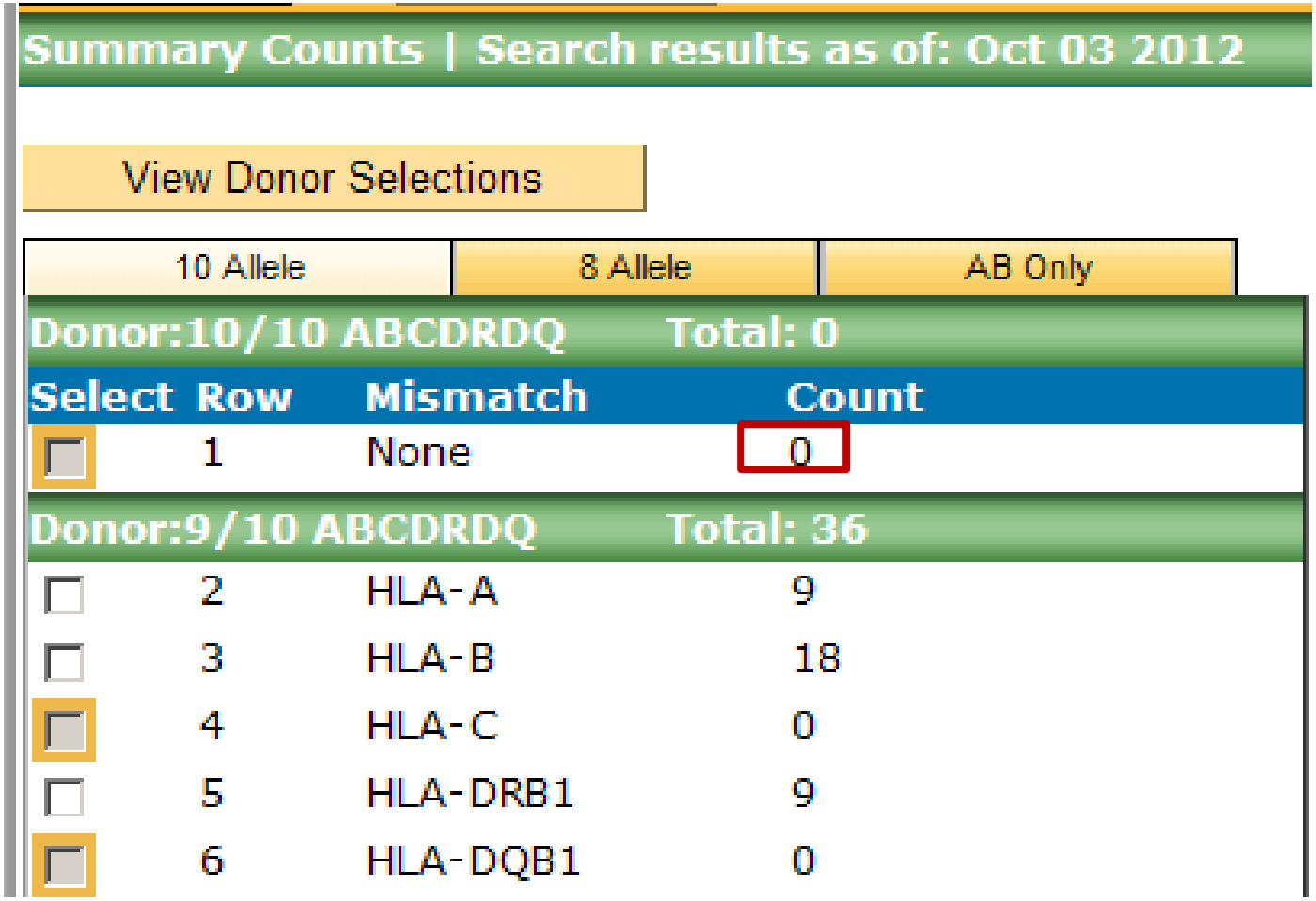
- MDS, not otherwise classified
  - Advanced phase disease

Case 2 Patient Typing

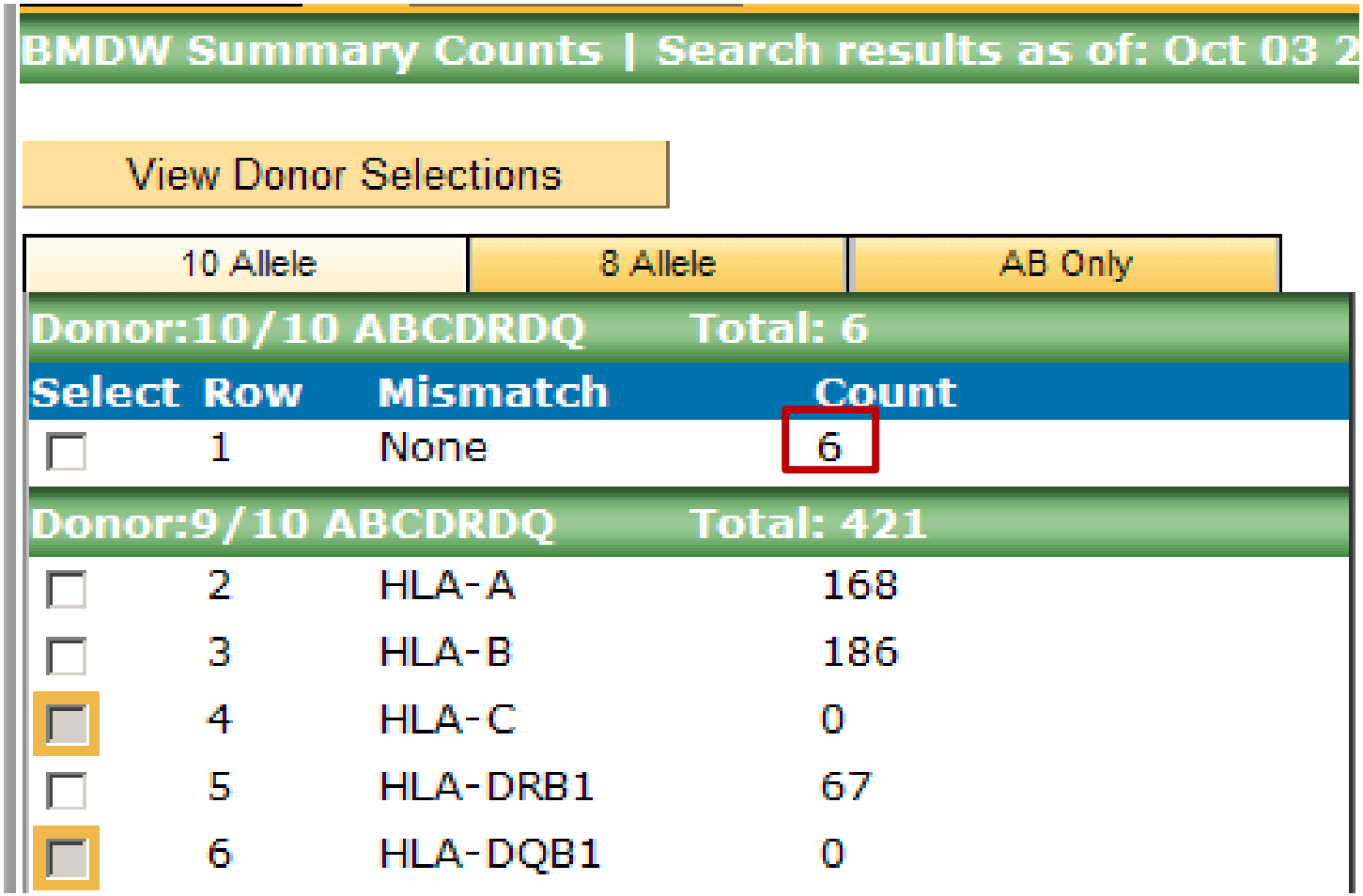
Status	Phenotype	A	B	C	DRB1	DQB1	DRB3	DRB4	DRB5
PRLM	Phenotype 1	01:02	15:03	02:10	07:01	02:02	02:02	01:XX	
		68:02	58:01	03:02	13:04	03:19			

- HLA search strategist comments
  - Other A*01, A*68, B*15, and DRB1*13 alleles may be common in donor haplotypes
  - B*58:01 commonly associates with either C*03:02 or C*07:01
  - DQB1*03:01 and DQB1*03:19 are Antigen Recognition Site (ARS) identical alleles

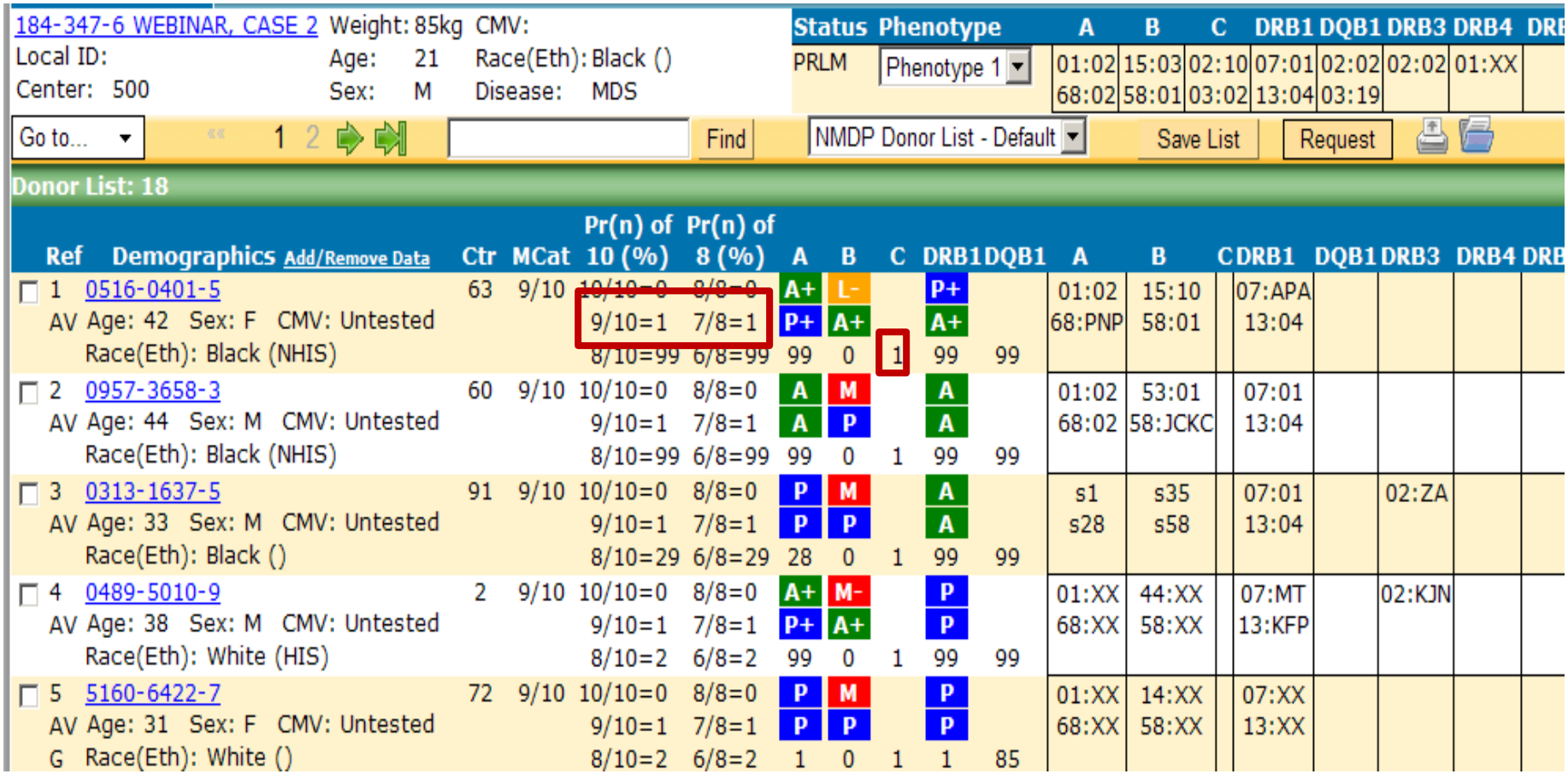
NMDP Donor Overview



BMDW Donor Overview



Potential 7/8 B Mismatches Unlikely



184-347-6 WEBINAR, CASE 2 Weight: 85kg CMV:
Local ID: Age: 21 Race(Eth): Black ()
Center: 500 Sex: M Disease: MDS

Status	Phenotype	A	B	C	DRB1	DQB1	DRB3	DRB4	DRB
PRLM	Phenotype 1	01:02	15:03	02:10	07:01	02:02	02:02	01:XX	
		68:02	58:01	03:02	13:04	03:19			

Go to... « 1 2 Find NMDP Donor List - Default Save List Request

Donor List: 18

Ref	Demographics Add/Remove Data	Ctr	MCat	Pr(n) of 10 (%)	Pr(n) of 8 (%)	A	B	C	DRB1	DQB1	A	B	C	DRB1	DQB1	DRB3	DRB4	DRB
1	0516-0401-5	63	9/10	~~10/10=0~~	~~8/8=0~~	A+	L-		P+		01:02	15:10		07:APA				
AV	Age: 42 Sex: F CMV: Untested			9/10=1	7/8=1	P+	A+		A+		68:PNP	58:01		13:04				
	Race(Eth): Black (NHIS)			8/10=99	6/8=99	99	0	1	99	99								
2	0957-3658-3	60	9/10	10/10=0	8/8=0	A	M		A		01:02	53:01		07:01				
AV	Age: 44 Sex: M CMV: Untested			9/10=1	7/8=1	A	P		A		68:02	58:JCKC		13:04				
	Race(Eth): Black (NHIS)			8/10=99	6/8=99	99	0	1	99	99								
3	0313-1637-5	91	9/10	10/10=0	8/8=0	P	M		A		s1	s35		07:01		02:ZA		
AV	Age: 33 Sex: M CMV: Untested			9/10=1	7/8=1	P	P		A		s28	s58		13:04				
	Race(Eth): Black ()			8/10=29	6/8=29	28	0	1	99	99								
4	0489-5010-9	2	9/10	10/10=0	8/8=0	A+	M-		P		01:XX	44:XX		07:MT		02:KJN		
AV	Age: 38 Sex: M CMV: Untested			9/10=1	7/8=1	P+	A+		P		68:XX	58:XX		13:KFP				
	Race(Eth): White (HIS)			8/10=2	6/8=2	99	0	1	99	99								
5	5160-6422-7	72	9/10	10/10=0	8/8=0	P	M		P		01:XX	14:XX		07:XX				
AV	Age: 31 Sex: F CMV: Untested			9/10=1	7/8=1	P	P		P		68:XX	58:XX		13:XX				
G	Race(Eth): White ()			8/10=2	6/8=2	1	0	1	1	85								

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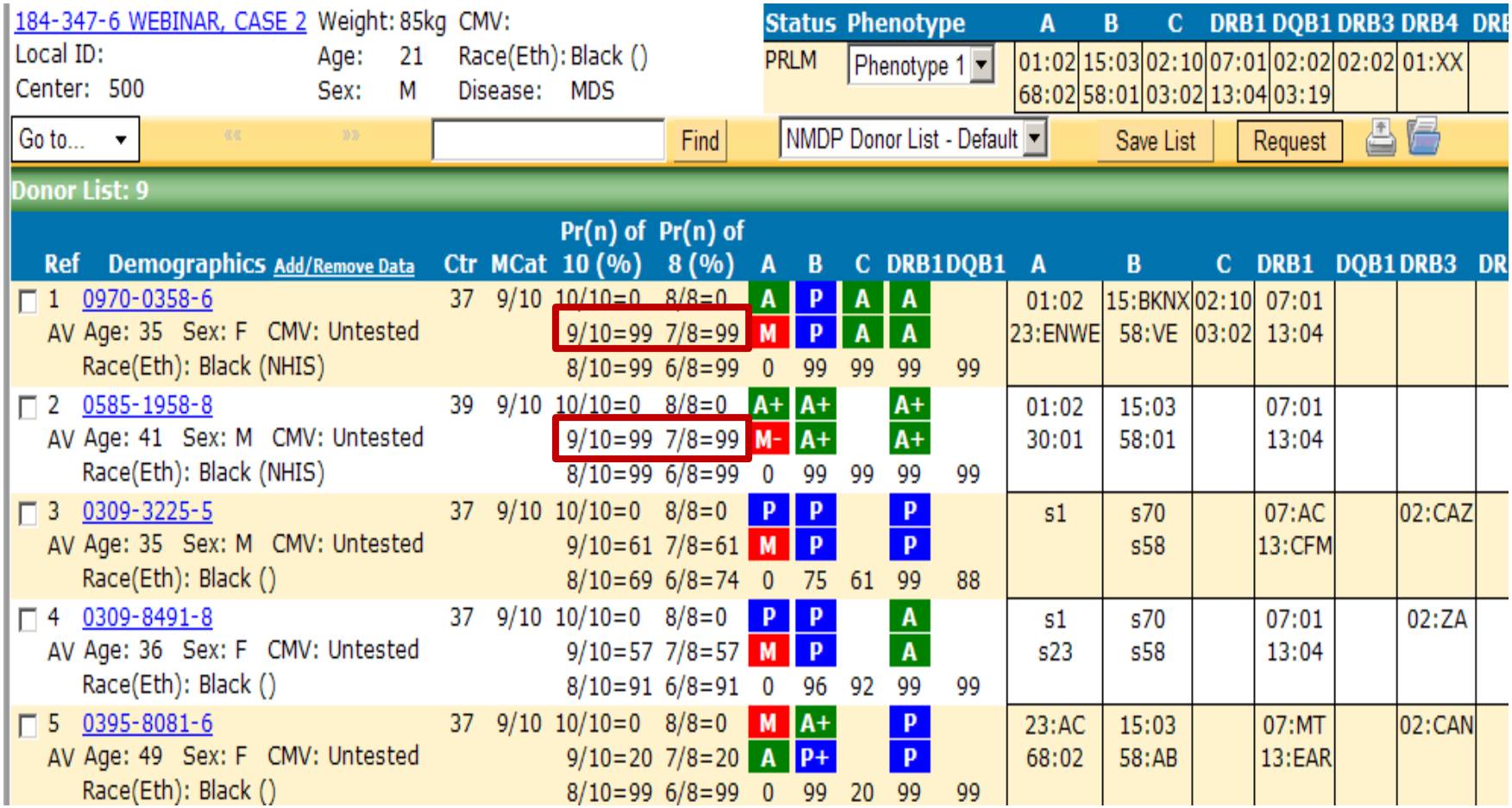
Likely 7/8 A Mismatches



184-347-6 WEBINAR, CASE 2 Weight: 85kg CMV:
Local ID: Age: 21 Race(Eth): Black ()
Center: 500 Sex: M Disease: MDS

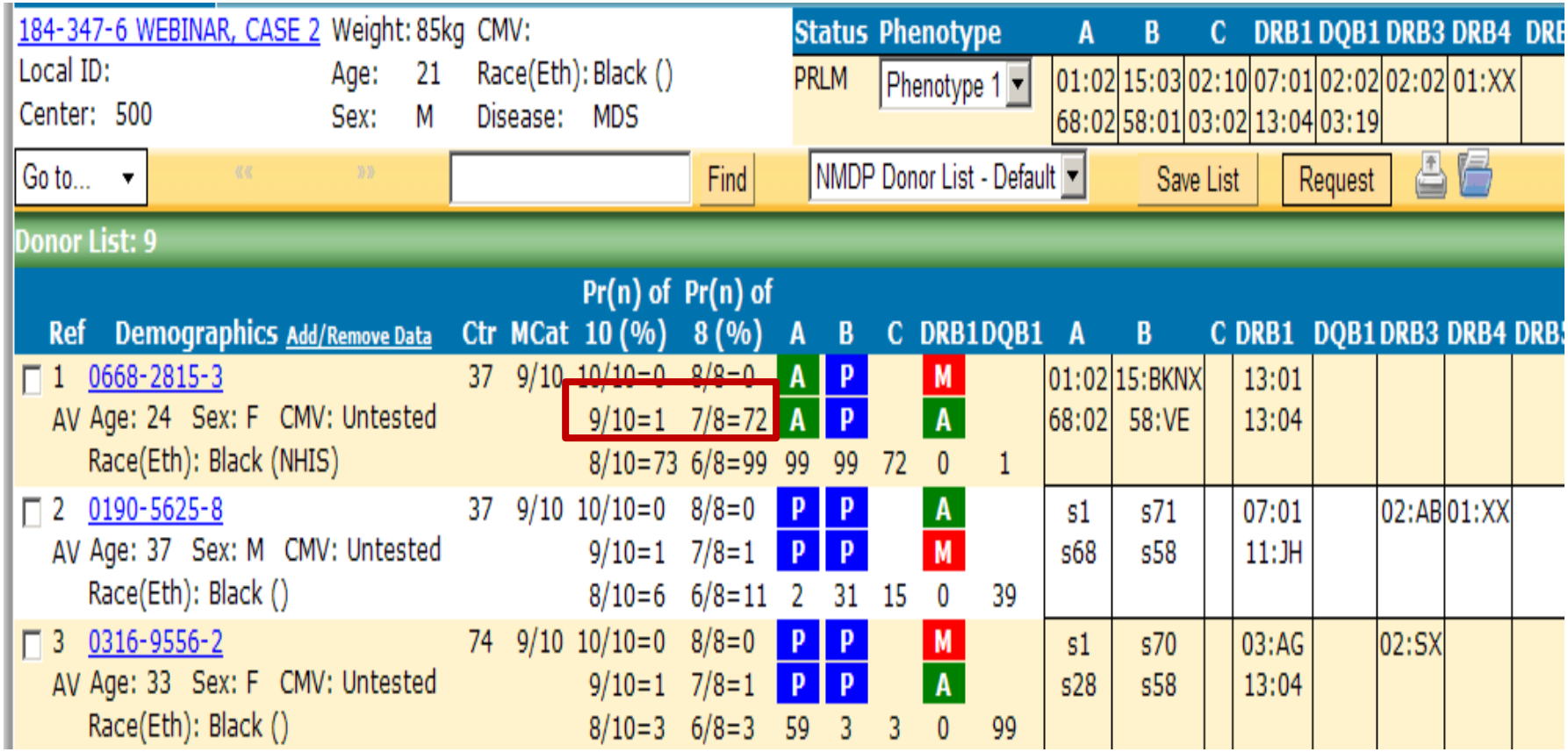
Status	Phenotype	A	B	C	DRB1	DQB1	DRB3	DRB4	DRB
PRLM	Phenotype 1	01:02	15:03	02:10	07:01	02:02	02:02	01:XX	
		68:02	58:01	03:02	13:04	03:19			

Go to... | Find | NMDP Donor List - Default | Save List | Request

Donor List: 9

Ref	Demographics (Add/Remove Data)	Ctr	MCat	Pr(n) of 10 (%)	Pr(n) of 8 (%)	A	B	C	DRB1	DQB1	A	B	C	DRB1	DQB1	DRB3	DR
1	0970-0358-6	37	9/10	10/10=0	8/8=0	A	P	A	A		01:02	15:BKNX	02:10	07:01			
	AV Age: 35 Sex: F CMV: Untested			9/10=99	7/8=99	M	P	A	A		23:ENWE	58:VE	03:02	13:04			
	Race(Eth): Black (NHIS)			8/10=99	6/8=99	0	99	99	99	99							
2	0585-1958-8	39	9/10	10/10=0	8/8=0	A+	A+		A+		01:02	15:03		07:01			
	AV Age: 41 Sex: M CMV: Untested			9/10=99	7/8=99	M-	A+		A+		30:01	58:01		13:04			
	Race(Eth): Black (NHIS)			8/10=99	6/8=99	0	99	99	99	99							
3	0309-3225-5	37	9/10	10/10=0	8/8=0	P	P		P		s1	s70		07:AC		02:CAZ	
	AV Age: 35 Sex: M CMV: Untested			9/10=61	7/8=61	M	P		P			s58		13:CFM			
	Race(Eth): Black ()			8/10=69	6/8=74	0	75	61	99	88							
4	0309-8491-8	37	9/10	10/10=0	8/8=0	P	P		A		s1	s70		07:01		02:ZA	
	AV Age: 36 Sex: F CMV: Untested			9/10=57	7/8=57	M	P		A		s23	s58		13:04			
	Race(Eth): Black ()			8/10=91	6/8=91	0	96	92	99	99							
5	0395-8081-6	37	9/10	10/10=0	8/8=0	M	A+		P		23:AC	15:03		07:MT		02:CAN	
	AV Age: 49 Sex: F CMV: Untested			9/10=20	7/8=20	A	P+		P		68:02	58:AB		13:EAR			
	Race(Eth): Black ()			8/10=99	6/8=99	0	99	20	99	99							

Possible 7/8 DRB1 Mismatch



184-347-6 WEBINAR, CASE 2 Weight: 85kg CMV:
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Center: 500 Sex: M Disease: MDS

Status	Phenotype	A	B	C	DRB1	DQB1	DRB3	DRB4	DRB
PRLM	Phenotype 1	01:02	15:03	02:10	07:01	02:02	02:02	01:XX	
		68:02	58:01	03:02	13:04	03:19			

Go to... | Find | NMDP Donor List - Default | Save List | Request

Donor List: 9

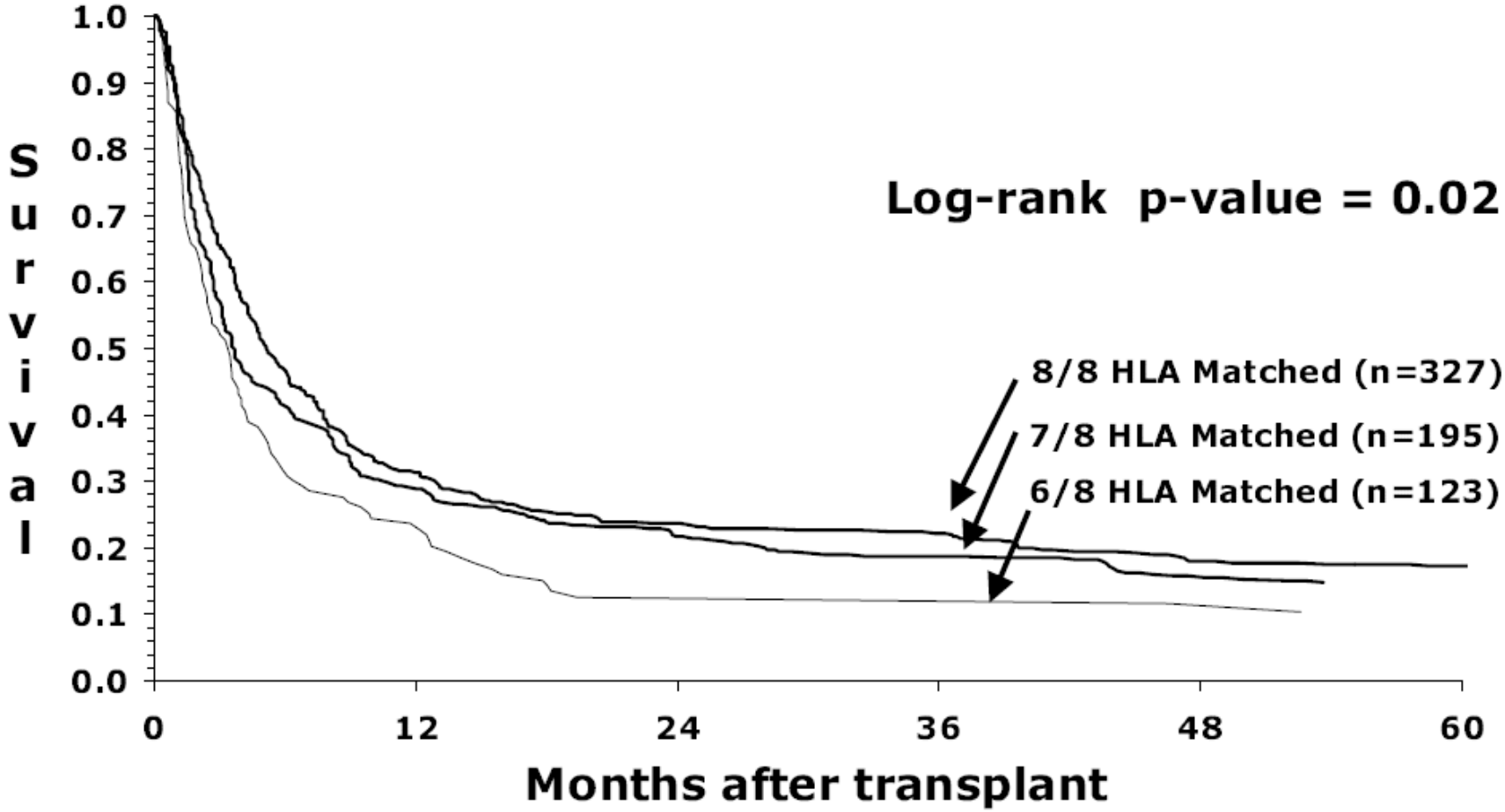
Ref	Demographics Add/Remove Data	Ctr	MCat	Pr(n) of 10 (%)	Pr(n) of 8 (%)	A	B	C	DRB1	DQB1	A	B	C	DRB1	DQB1	DRB3	DRB4	DRB5
1	0668-2815-3	37	9/10	10/10=0	8/8=0	A	P		M		01:02	15:BKNX		13:01				
AV	Age: 24 Sex: F CMV: Untested			9/10=1	7/8=72	A	P		A		68:02	58:VE		13:04				
	Race(Eth): Black (NHIS)			8/10=73	6/8=99	99	99	72	0	1								
2	0190-5625-8	37	9/10	10/10=0	8/8=0	P	P		A		s1	s71		07:01		02:AB	01:XX	
AV	Age: 37 Sex: M CMV: Untested			9/10=1	7/8=1	P	P		M		s68	s58		11:JH				
	Race(Eth): Black ()			8/10=6	6/8=11	2	31	15	0	39								
3	0316-9556-2	74	9/10	10/10=0	8/8=0	P	P		M		s1	s70		03:AG		02:SX		
AV	Age: 33 Sex: F CMV: Untested			9/10=1	7/8=1	P	P		A		s28	s58		13:04				
	Race(Eth): Black ()			8/10=3	6/8=3	59	3	3	0	99								

Can your TC be Flexible?

- Some TC protocols may specify no A or DRB1 mismatches allowed, but HLA experts say these are the likely best matched donors that can be identified for this patient

- Need to be flexible enough on both criteria and graft source to ensure:
  - **The *optimal* HLA match can be selected**

Advanced stage disease



Lee SJ, et al. *Blood.*2007;110(13):4576-4583.10

Lee Advanced Disease Statements

- In most instances, the adverse consequences of using an HLA mismatched donor are less serious than proceeding to HCT with more advanced disease and may still offer better outcomes than other available treatments

- **Expeditious transplantation with the best available donor, even if mismatched, may offer the best chance for survival**

Lee, S.J. et al. *Blood* (2007);110: 4576-4583

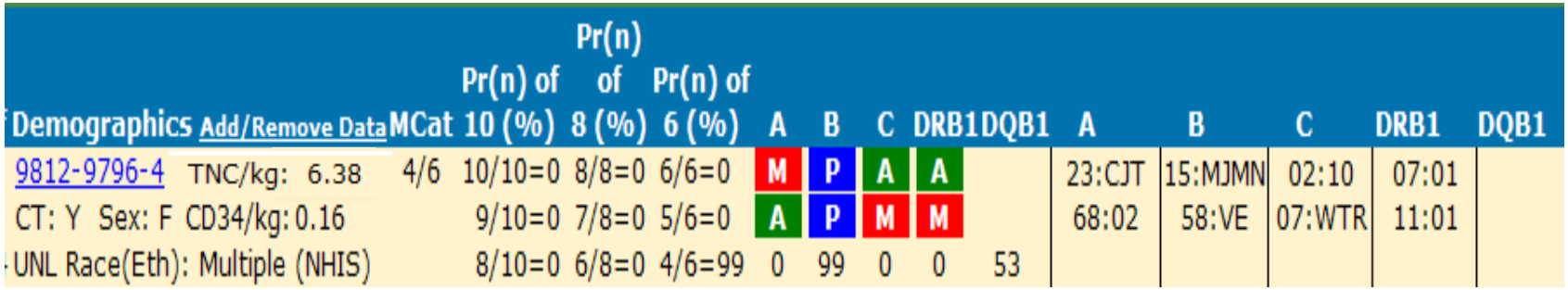
Expedite Transplant for Advanced Disease

- Test patient for HLA antibodies early, to select mismatches with no DSA
- Select donors likely to remain ≥ 7/8 matched after CT
- Can usually move more quickly with CBU

Poll: Question 7

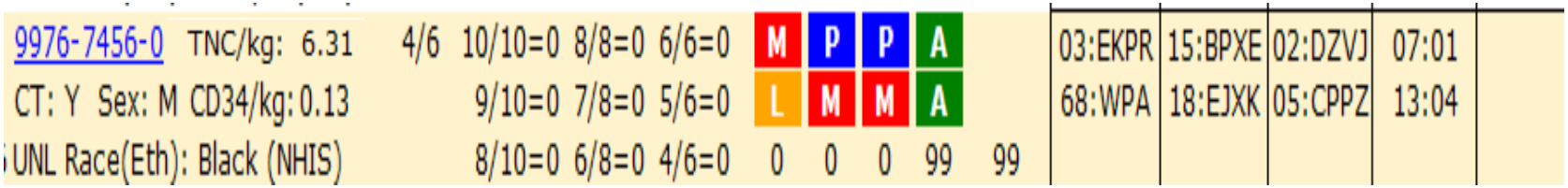
Let's assume units below have nearly identical cell dose. Which 4/6 CBU might be preferable?

- a.) A, C, and DRB1 antigen mismatches



Demographics Add/Remove Data	MCat	Pr(n) of 10 (%)	Pr(n) of 8 (%)	Pr(n) of 6 (%)	A	B	C	DRB1	DQB1	A	B	C	DRB1	DQB1
9812-9796-4 TNC/kg: 6.38	4/6	10/10=0	8/8=0	6/6=0	M	P	A	A		23:CJT	15:MJMN	02:10	07:01	
CT: Y Sex: F CD34/kg: 0.16		9/10=0	7/8=0	5/6=0	A	P	M	M		68:02	58:VE	07:WTR	11:01	
UNL Race(Eth): Multiple (NHIS)		8/10=0	6/8=0	4/6=99	0	99	0	0	53					

- b.) A, B, and C antigen mismatches



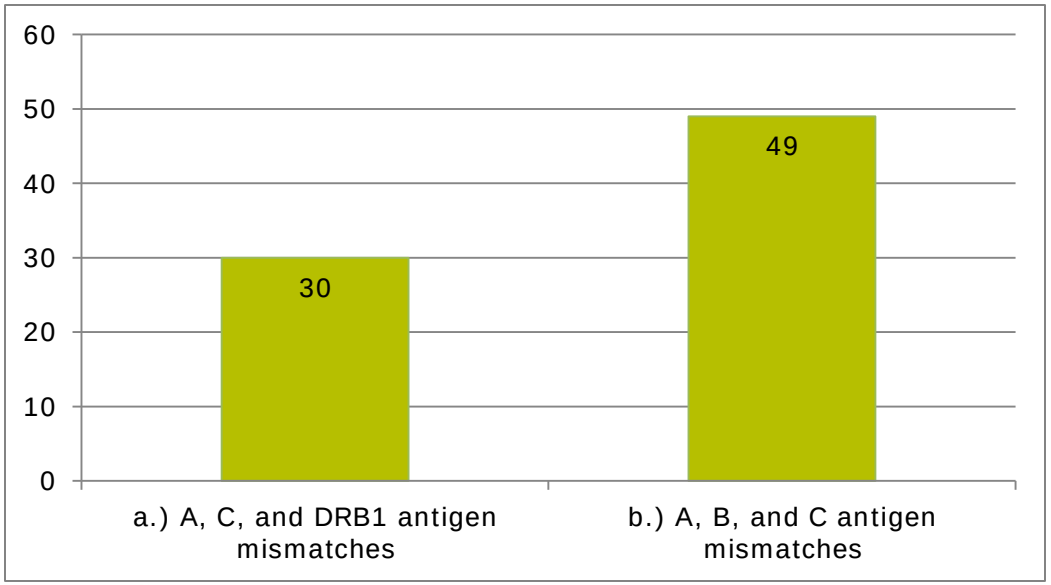
9976-7456-0 TNC/kg: 6.31	4/6	10/10=0	8/8=0	6/6=0	M	P	P	A		03:EKPR	15:BPXE	02:DZVJ	07:01	
CT: Y Sex: M CD34/kg: 0.13		9/10=0	7/8=0	5/6=0	L	M	M	A		68:WPA	18:EJXK	05:CPPZ	13:04	
UNL Race(Eth): Black (NHIS)		8/10=0	6/8=0	4/6=0	0	0	0	99	99					

Poll: Question 7 (RESULTS)

Let's assume units below have nearly identical cell dose. Which 4/6 CBU might be preferable?

- a) A, C, and DRB1 antigen mismatches
- b) A, B, and C antigen mismatches

Correct Answer – b.) A, B, and C antigen mismatches



8/8 Matching in CBU Outcomes

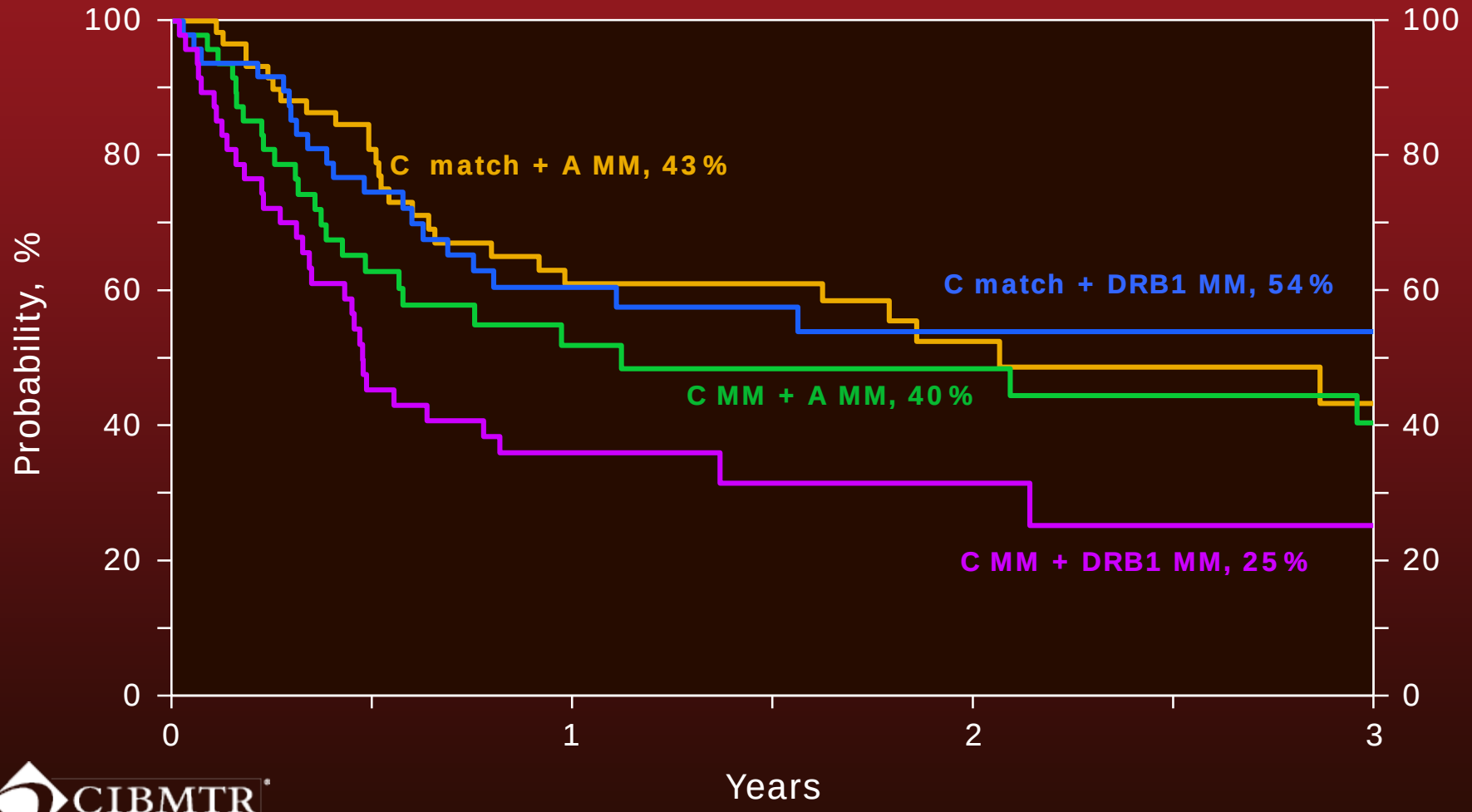
Effect of donor–recipient HLA matching at HLA A, B, C, and DRB1 on outcomes after umbilical-cord blood transplantation for leukaemia and myelodysplastic syndrome: a retrospective analysis

Mary Eapen, John P Klein, Guillermo F Sanz, Stephen Spellman, Annalisa Ruggeri, Claudio Anasetti, Maria Brown, Richard E Champlin, Joan Garcia-Lopez, Gareth Hattersely, Gesine Koegler, Mary J Laughlin, Gerard Michel, Samir K Nabhan, Franklin O Smith, Mary M Horowitz, Eliane Gluckman, Vanderson Rocha, for the Eurocord-European Group for Blood and Marrow Transplantation, Netcord, and the Center for International Blood and Marrow Transplant Research

Eapen M, et al. *Lancet Oncol (*2011); 12:1214-21

Overall Survival

- Mismatch at HLA-C + HLA A or DRB1 -



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Eapen et al. Lancet Oncol 2011

Consider NIMA Matching?

- Non-inherited maternal antigen (NIMA) matches are relatively rare
- Relative frequency of the mismatched antigen(s) will strongly influence the ability to find a NIMA match
- **Searching for NIMA match may delay transplant**
  - *Patient 2 has MDS, advanced stage disease*

LOTS of Info!

- Encourage review of:
  - Matching guidelines paper
  - Studies cited in matching guidelines manuscript
  - Webinar slides

Webinar Slides Online

- Update to Matching Guidelines webinar now available online:

  https://network.bethematchclinical.org/Education/Transplant-Center/HLA-and-Search-Strategy/HLA-Matching-Guidelines/

Acknowledgments

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    - National Heart, Lung and Blood Institute
    - National Institute of Allergy and Infectious Diseases
  - Contract HHSH234200637015C with Health Resources and Services Administration (HRSA/DHHS)

- NMDP is supported by, among others:
  - Two grants, N00014-10-1-0204 and N00014-1-1-0339, from the Office of Naval Research

Q & A

- Please continue to listen to the informative Q & A session
- If you have any questions after listening to this recorded webinar, please contact search-strategies@nmdp.org