Donor Selection and Release Criteria for Cellular Therapy Products

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NATIONAL MARROW DONOR PROGRAM®

BE THE MATCH®

Learning Objectives

- How to select the best HSC donor for a particular patient to achieve the best *clinical outcome* of tranplantation
- How to select the best HSC donor for a particular patient for *optimal donor, product and patient safety*
- Describe the impact of donor selection by transplant physicians on future donor recruitment
- Understand the medical evaluation process for HSC donors to *ensure donor safety*
- Discuss *release criteria* for cellular therapy products once they have been collected

Differences Between HSC and Blood Donors

	Blood	HSC
Annual # of Events	More than 20,000,000 in the US alone	30,000 alloHSCT/yr worldwide
Donor → Patient	1:1, 1:2, 1:3 whole blood	Usually 1:1
Donor Testing	Day of Collection, strict release criteria	Up to 30 days prior to donation, flexible release criteria, DOC not available for release
Donor Assessment	HHQ, limited physical assessment	HHQ, complete H&P, labs, EKG, CXR and extended testing possible
Matching	ABO/Rh +/- RBC Ag	**HLA**, ABO, KIR Only/best match

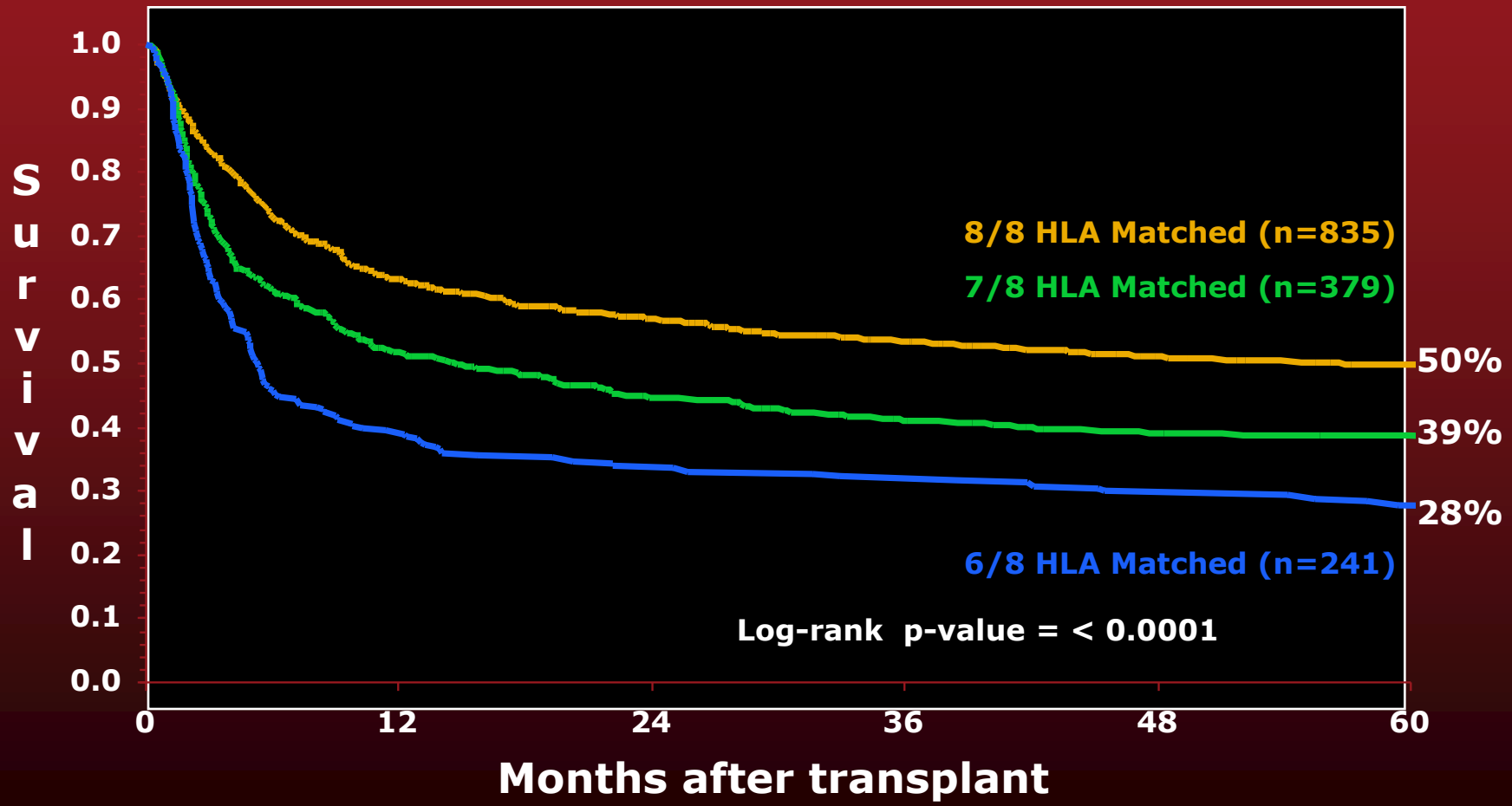
High-resolution donor-recipient HLA matching contributes to the success of unrelated donor marrow transplantation

BLOOD (2007) 110: 4576-83

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

CIBMTR
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

Probability of Overall Survival by HLA Matching for Early Disease Stage



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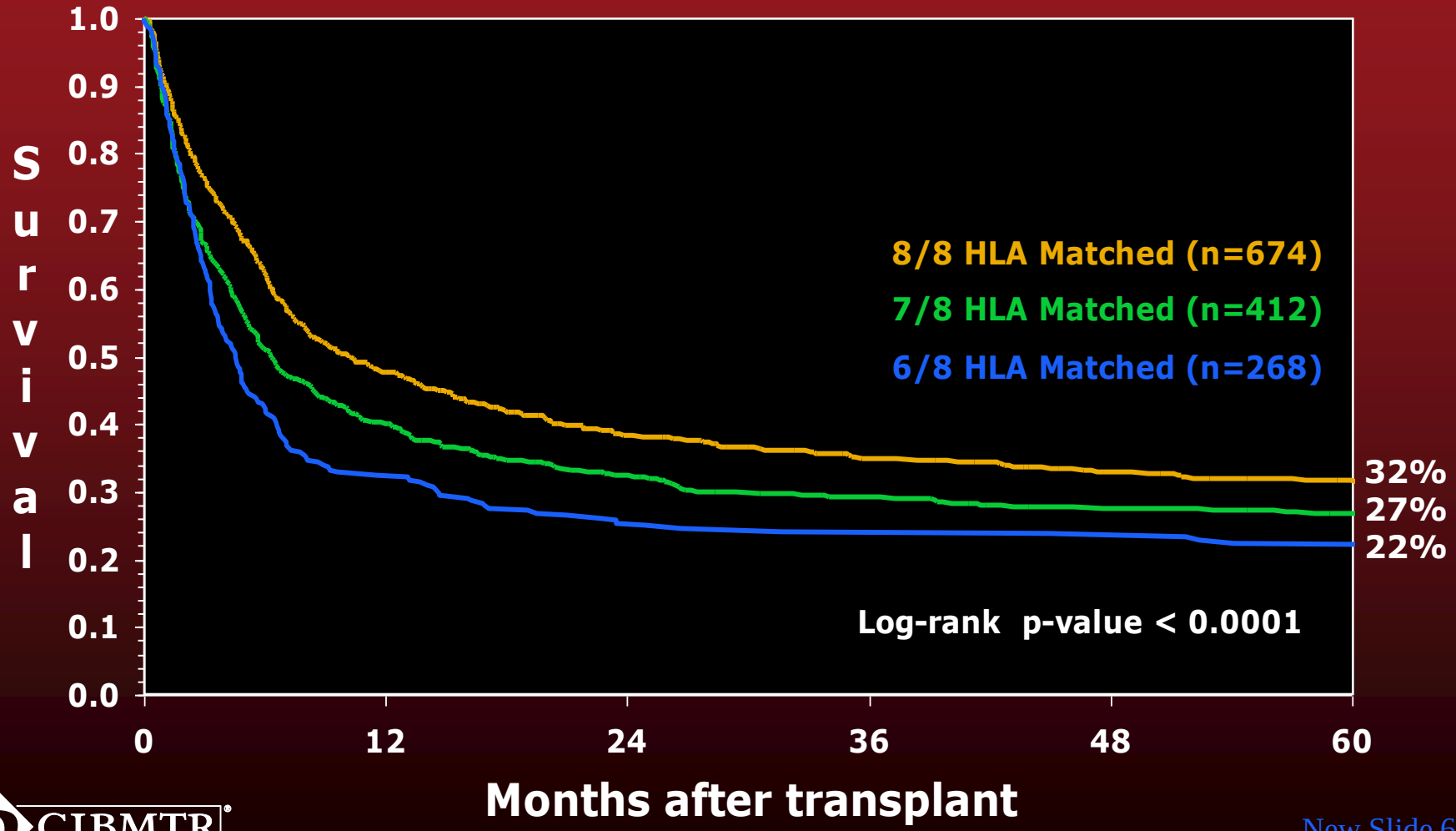
New Slide 5

Probability of Overall Survival by HLA Matching for Intermediate Disease Stage



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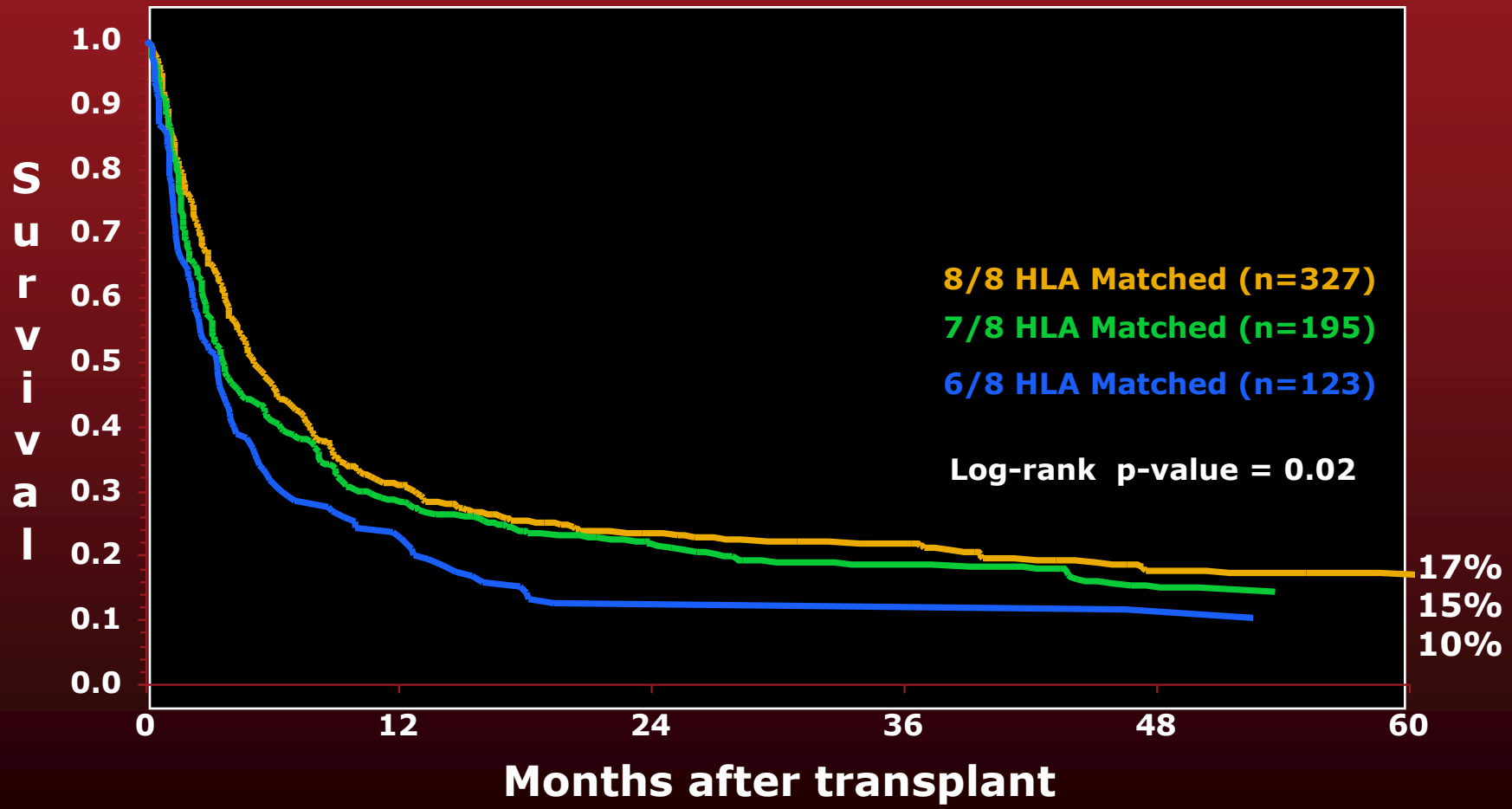
New Slide 6

Probability of Overall Survival by HLA Matching for Advanced Disease Stage



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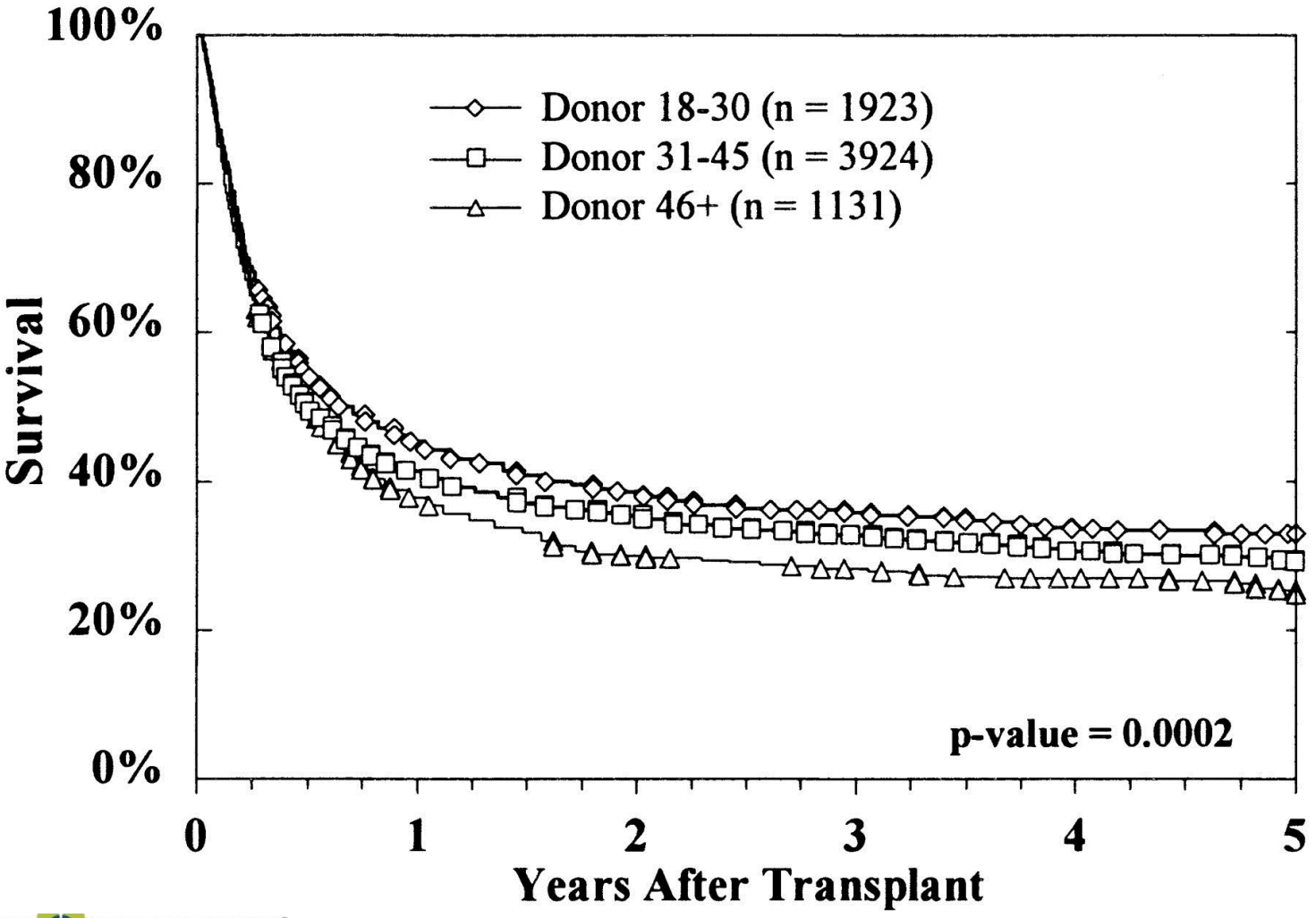
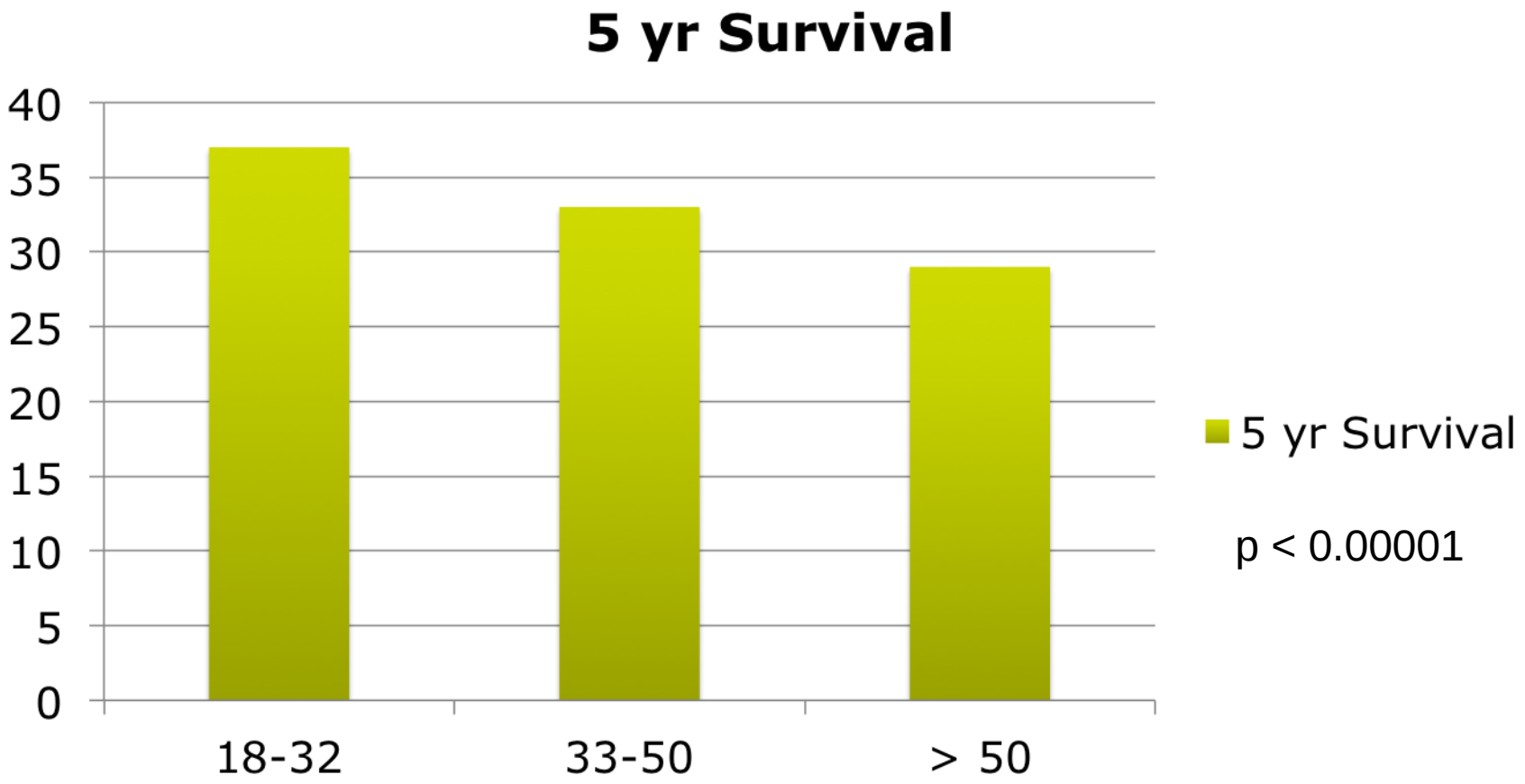
New Slide 7

Impact of Donor Age on Survival



Kollman 2001

Impact of Donor Age on Survival



Kollman 2013

Impact of Donor Factors on Survival

Donor Age	Hazard Ratio
18-32	1.00
32-50	1.13*
> 50	1.29*

HLA Mismatch	Hazard Ratio
0	1.00
1	1.24*
2	1.62*

ABO Matching	Hazard Ratio
Matched	1.00
Minor Mismatch	1.10*
Major Mismatch	1.23*

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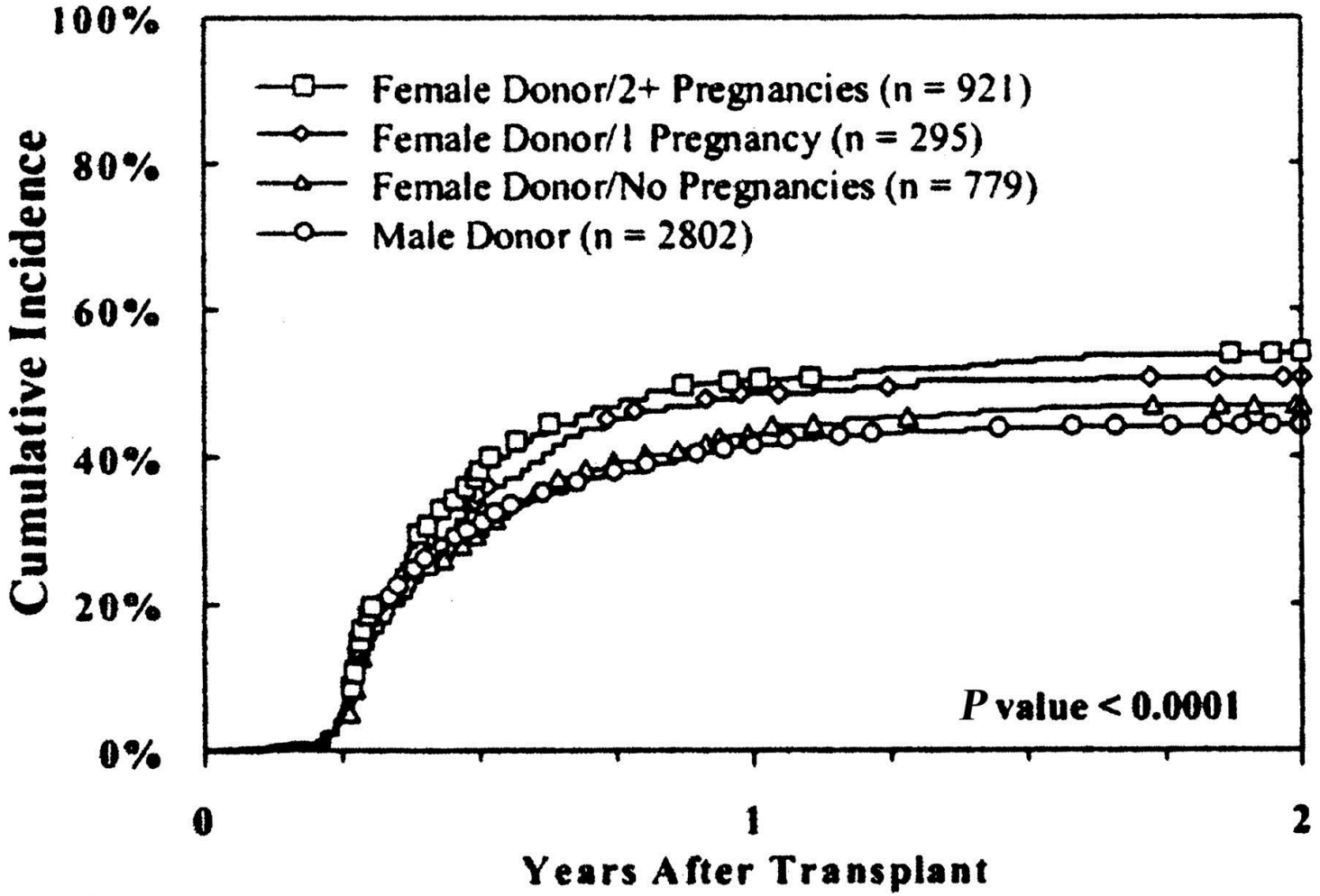
Kollman 2013

Donor Sex and Parity Impact cGVHD



Age/Gender and Donor Selection 2004-2009

Donor Age	Marrow	PBSC	p-value
18 to 30	973 (36)	2380 (35)	0.100
31 to 40	878 (32)	2202 (33)	
41 to 50	684 (25)	1616 (24)	
51 to 61	191 (7)	570 (8)	
Median Age	35	35	0.377

Donor Gender	Marrow	PBSC	p-value
Male	1638 (60)	4170 (62)	0.168
Female	1088 (40)	2598 (38)	

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Pulsipher, *Blood* (2012) epub 10/29/12

Increasingly Focused on Adding Young Adults to the Registry

Effective October 1, 2012:

- Be the Match began concentrating efforts and resources on **adding 18 – 44 year olds** to the registry
- **Registry remains open to age 60**
  - Allowing those 45 – 60 who are interested in joining and willing to pay the ability to join
  - Individuals ages 45 – 60 **must join online**
  - $100 payment required for new members ages 45 – 60 (those already on the registry do not need to pay)

HSC Donor Assessment

Evaluate an individual's suitability to serve as a donor of marrow and/or PBSC

Donor Safety

- Unrelated volunteer
- Risks of donation process

Recipient Safety

- Infectious or genetic disease transmission
- Product quality

Assessment Components and Steps

- **At Recruitment, Preliminary, DR, HR, CT, & WU**
  Donor Health History Screening Questionnaire

- **At CT, Workup, Day of Collection**
  Donor Infectious Disease Testing

- **At Workup**
  History, Physical Examination
  & Testing (CBC, Chemistries, UA, Pregnancy, Sickle screen, CXR, EKG)

Additional NMDP PE Requirements

- Identify conditions that may put donor or recipient at risk such as
  - Sensitivity to filgrastim or E. Coli-derived protein products
  - History of autoimmune conditions
  - History of DVTs
  - History of iritis/episcleritis
  - Thrombocytopenia <150 x 10^6L at baseline
  - Current treatment with Lithium
  - Positive screening test for Hemoglobin S
  - Receiving experimental therapy

  - Anesthesia risks (sleep apnea, asthma)
  - Bone marrow harvest risks (anatomy, h/o back issues)

Evaluation Considerations

Does any information affect

- Donor Safety?
- Product Quality?
- Recipient Safety?

Medical Judgment Process

DATA

HHQ
IDMs
H&P
Labs
CXR
EKG
UA

ANALYSIS

Clinical Correlation
Medical Experience

CONCLUSION

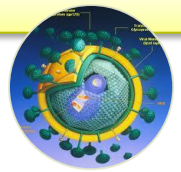
- Accept for both products
- Accept for 1 Product-only
- "Extended" med testing
- Temporary Unavailable
- Medically Defer
- Treat & Wait

Keeping in mind assessment goals:
Safe donation & Safe product

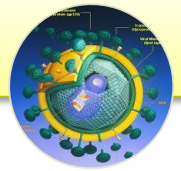
TC Notification Considerations

Is the potential risk significant enough to warrant notifying Transplant Center?

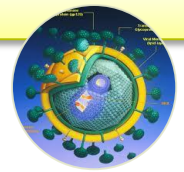
- Is it possibly transmissible?



- Is there a risk the TC MD must weigh against the known risks of transplant?



- Is this providing "too" much info?



Extended Medical Testing Utilization: 2011

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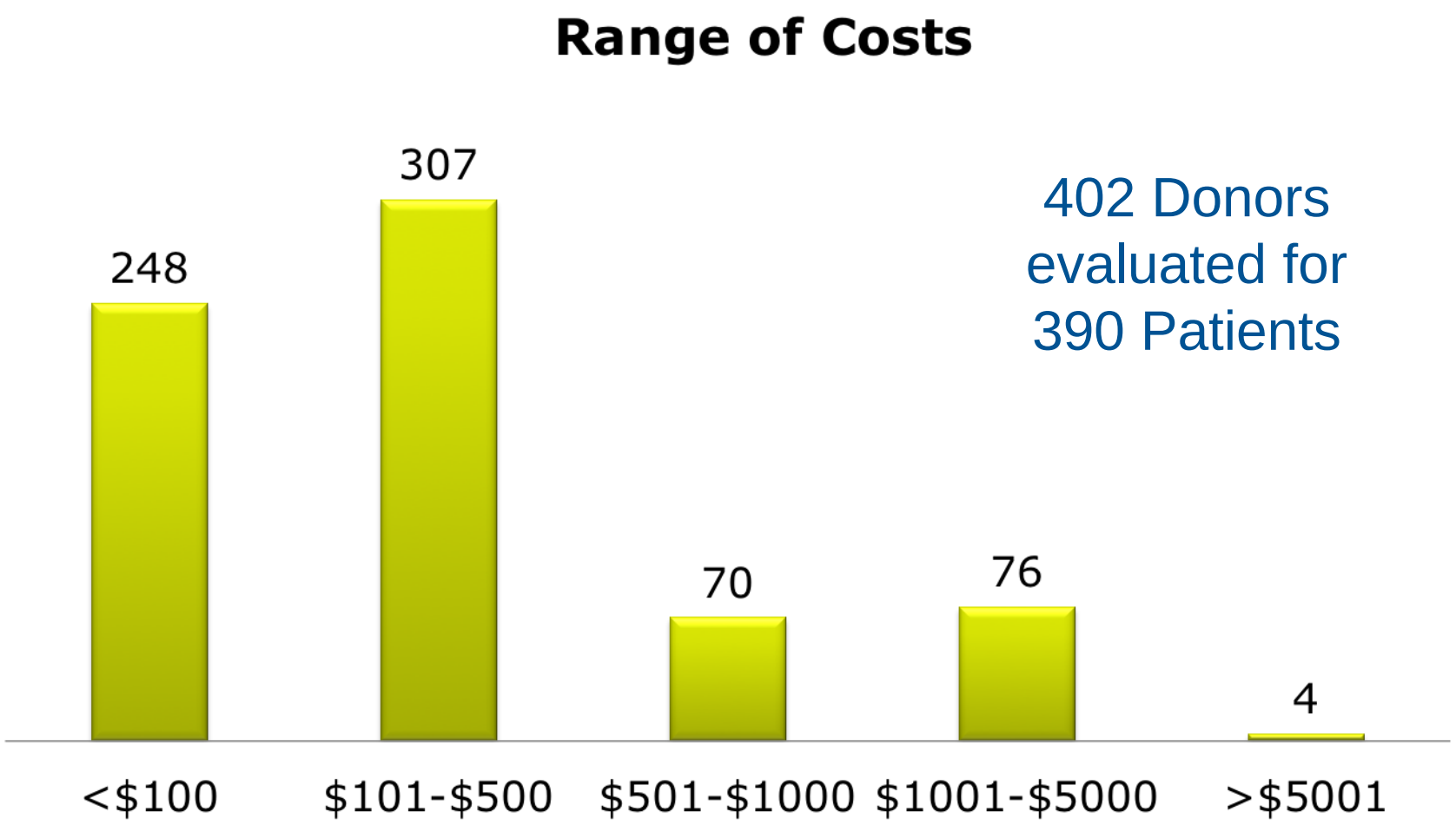


402 Donors evaluated for 390 Patients

Issue to Consider with Extended Testing

- Is the donor becoming a patient (counseling, f/u care)?
- Are we testing the donor into suitability (repeat tests)
- What is the risk of the additional test(s), e.g marrow Bx?
- Will the testing influence the donor's decision whether to donate (e.g. monetary incentive if no insurance)?

- What is the impact on the patient – will this delay the transplant?
- Cost – ultimately borne by patients

HSC Product Release Criteria Considerations

Product Safety (SQuIPP)

- Safety
- Quality
- Identity
- Purity
- Potency

Product Efficacy

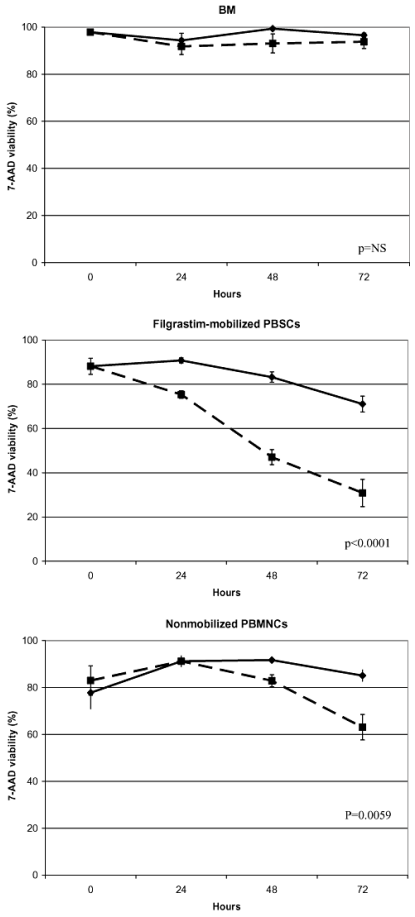
- Dose/Potency: TNC, CD34
- HLA matching

HSC Product Release Criteria: Reality

Release (almost) all products:

- Patient has received their conditioning regimen
- Replacement product from this donor or another, may not available, at least in the short term
- Products need to be released to the courier within hours of collection
- Day of collection IDM results and product testing may not be complete prior to release
- Patients are on broad spectrum antibiotics
- What is the minimum dose for engraftment?
- No rapidly available HLA test for identity/efficacy

Validation of short-term handling and storage conditions for marrow and peripheral blood stem cell products



Transfusion
Volume 51, Issue 1, pages 137-147, 1 JUL 2010 DOI: 10.1111/j.1537-2995.2010.02758.x
http://onlinelibrary.wiley.com/doi/10.1111/j.1537-2995.2010.02758.x/full#f1

Emergency Subsequent Request?

What is the cutoff dose to determine **Emergency Subsequent Donation** versus **Monitor For Engraftment**?

Dose $x10^6$ for PBSC $x10^8$ for Marrow	**Approach**
≥2	Monitor for engraftment x4 wks
1 – <2	Evaluate request
<1	Approve request

Summary

- HLA matching is the major factor affecting clinical outcomes in HSCT, followed by donor age, gender, and ABO matching
- Careful donor evaluation is essential to ensure donor, product and recipient safety; medical evaluation and judgment is required for each donor
- Strict product release criteria are hard to define for HSC products
- Urgent subsequent donations may be requested if the primary donation cell count is low, and are routinely requested for graft failure, relapse, to enhance immune reconstitution and treat certain viral infections (CTLs)