

**RIC Allogeneic transplant vs.  
Myeloablative allogeneic  
transplant for Elderly (>55yr)  
High Risk AML**

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- A 55 years old man with adverse karyotype AML (monosomy 7) and no comorbidities has an HLA identical sibling. The patient has inquired if you would opt for full intensity or RIC allografting?

# Rationale of conditioning

- Treat the underlying disease
- “Clear the way”
- Prevent rejection (immunosuppression of the host)
- Prevent/modify GvHD  
(immunosuppression of the Graft)

# Myeloablation

- Busulfan 16mg/kg PO or 12,8mg/kg IV
- Whole body irradiation 11-14 Gy
- Combined with either above,  
Cyclophosphamide 120-200mg/kg

# What is Reduced Intensity Conditioning?

- Anything less than full myeloablation
- Any attempt to reduce toxicity of chemotherapy or radiation
- Any immune manipulation or modulation
- Incorporation or “piggy-backing” of disease specific therapies and conditioning

# Reduction of toxicity

- Reducing dose of busulfan or radiation
- Alternate immunosuppression:- e.g. changing cyclophosphamide to fludarabine
- Use of alternate myeloablative drugs:- e.g. intermediate dose melphalan
- Pharmacologic dosing:- maintaining steady state plasma levels of busulfan

# Immune manipulation or modulation

- Acute-GvHD increases TRM
- Direct T-cell antagonists such as anti-thymocyte globulin, alemtuzumab, daclizumab in addition to cortico-steroids, methotrexate and cyclosporine/tacrolimus/mycophenolate mofetil
- Given in-vivo prior to or during the transplant vs. into the graft (in-the-bag)
- Have less effect on chronic-GvHD
- Chronic GvHD reduces incidence of relapse

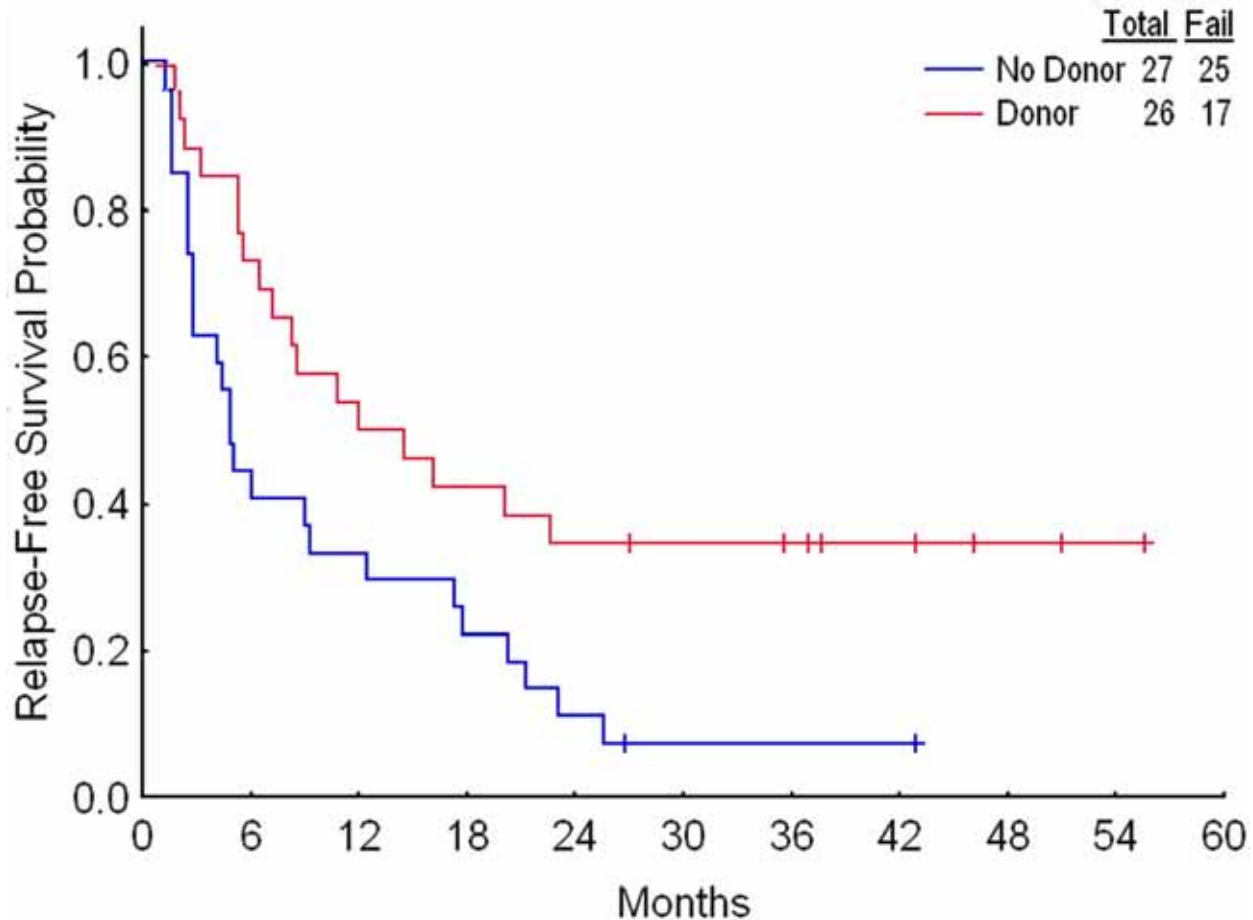
# Piggy-backing

- Disease specific agents such as Gemtuzumab Ozogamicin, imatinib and farnesyl transferase inhibitors
- Have less toxicity than conventional cytotoxics
- Allow better disease control, buying time for GvL effect
- Eradicate minimal residual disease

# Why RIC?

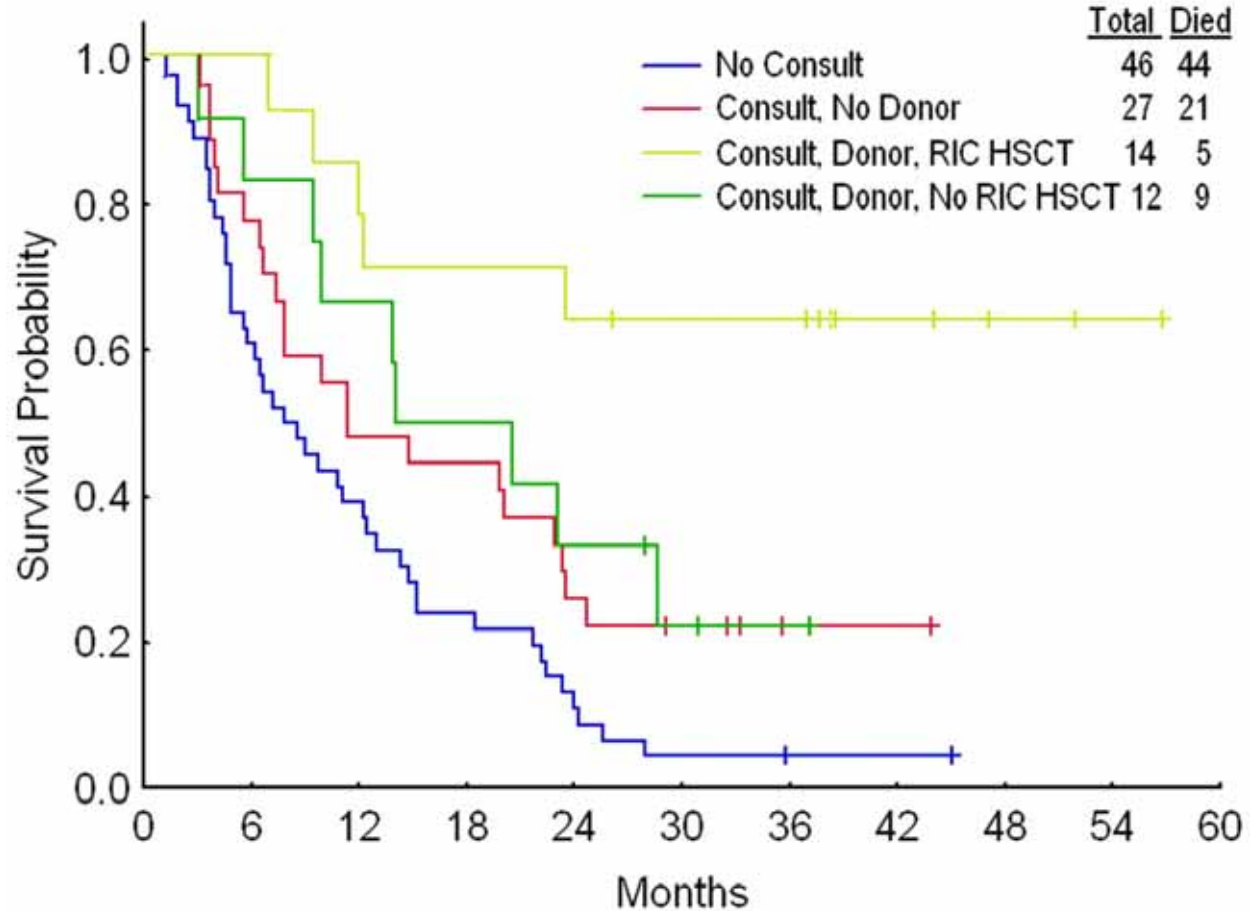
- Efficacy of allogeneic haemopoietic stem cell transplant in the eradication of malignant disease
- Provide access to HST for patients with co-morbidities or advanced age who have an increased TRM from conventional myeloablation
- Disease demographics:- increased incidence of AML/MDS in older patients and worse prognosis disease in these patients
- In some diseases GvL effect is important and especially if MRD
- Allows the use of alternative donor/stem cell sources e.g. MUD's & UCB

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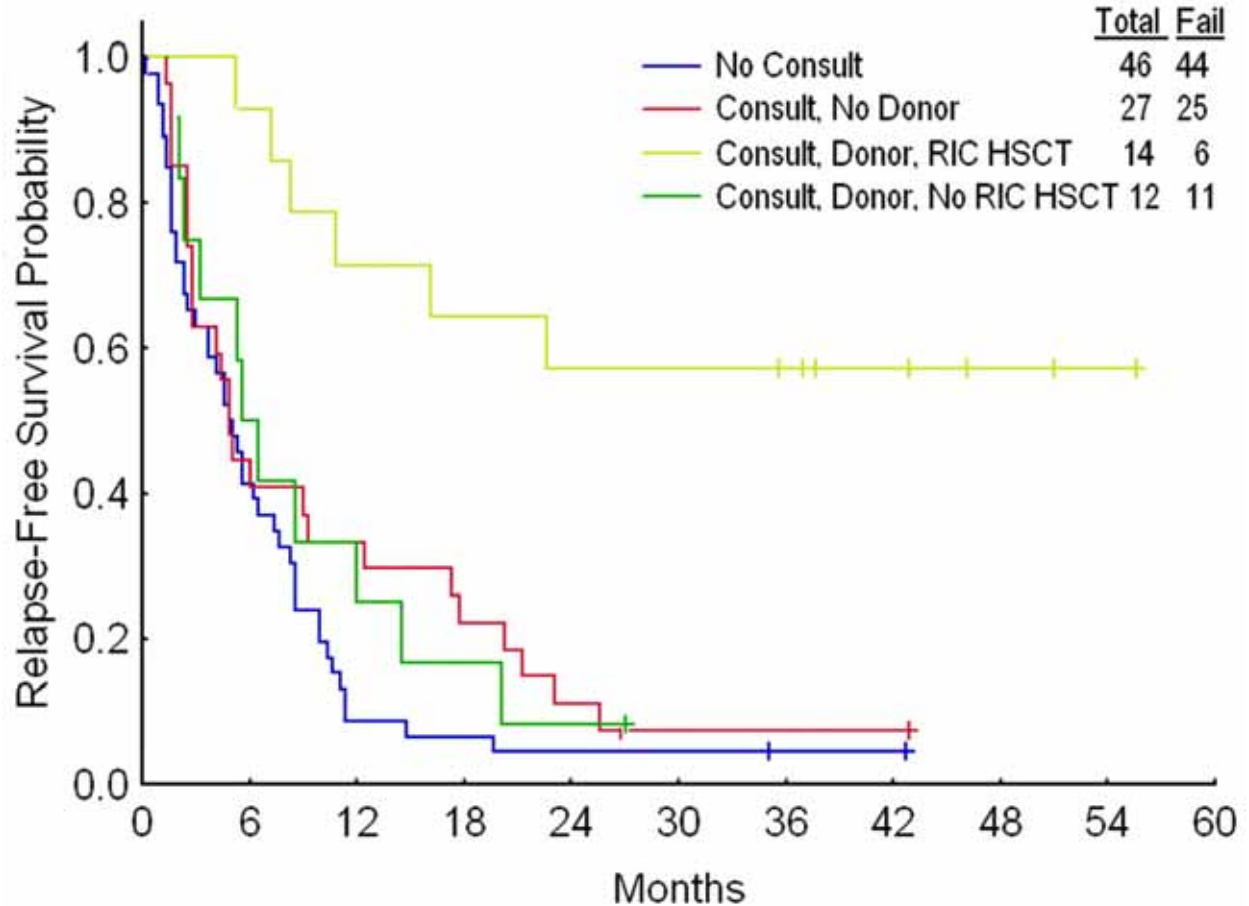
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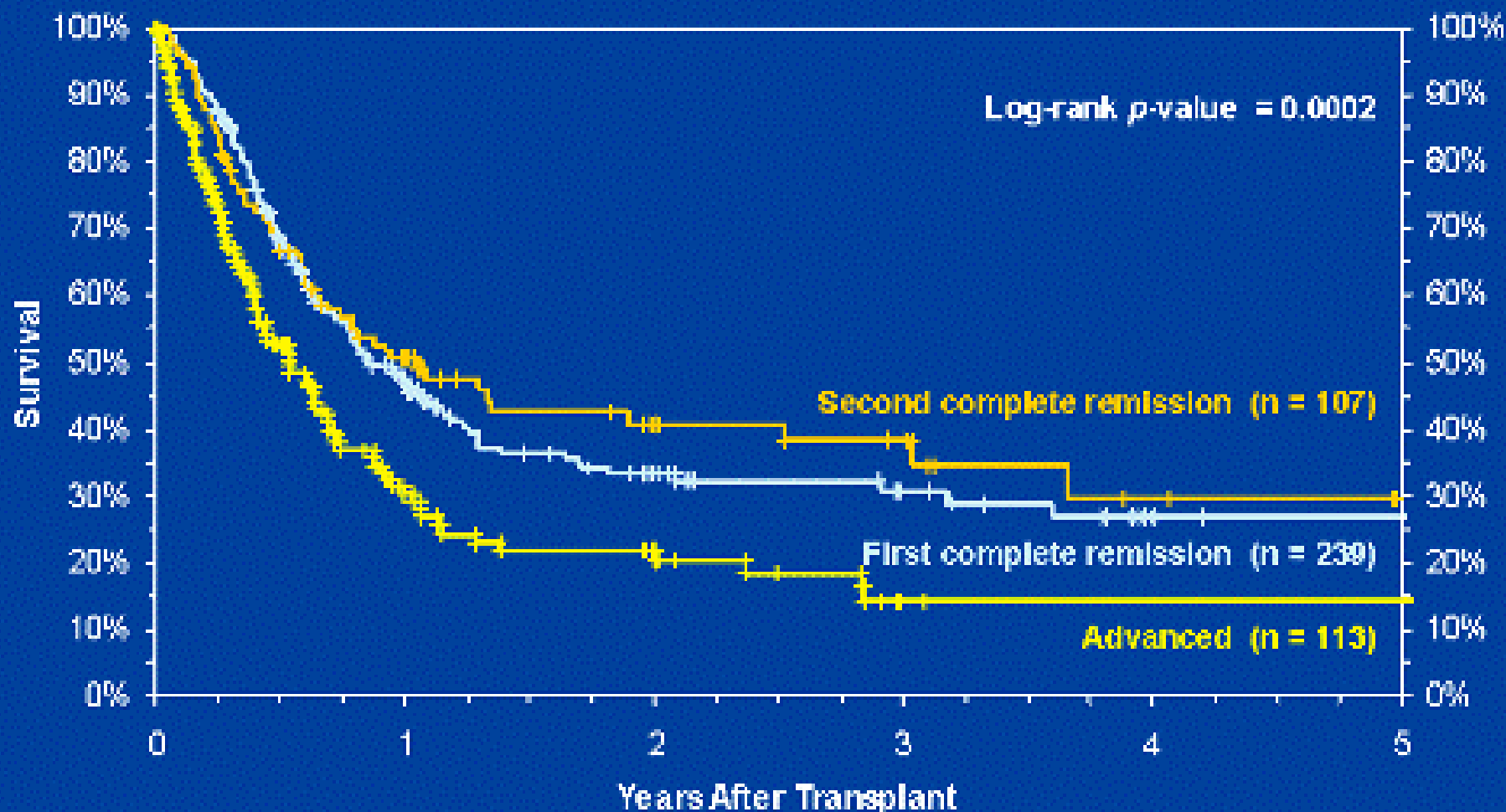
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# Why not RIC

- Some diseases need the chemotherapy or radiation dose (myeloablative dose)
- Active or progressive disease
- Refractory disease

# Acute Myelogenous Leukemia

Survival of Older Adult (Age  $\geq 55$  Years) Marrow and PBSC Recipients with Non-Myeloablative Preparative Regimens, by Disease Stage 1998–2006

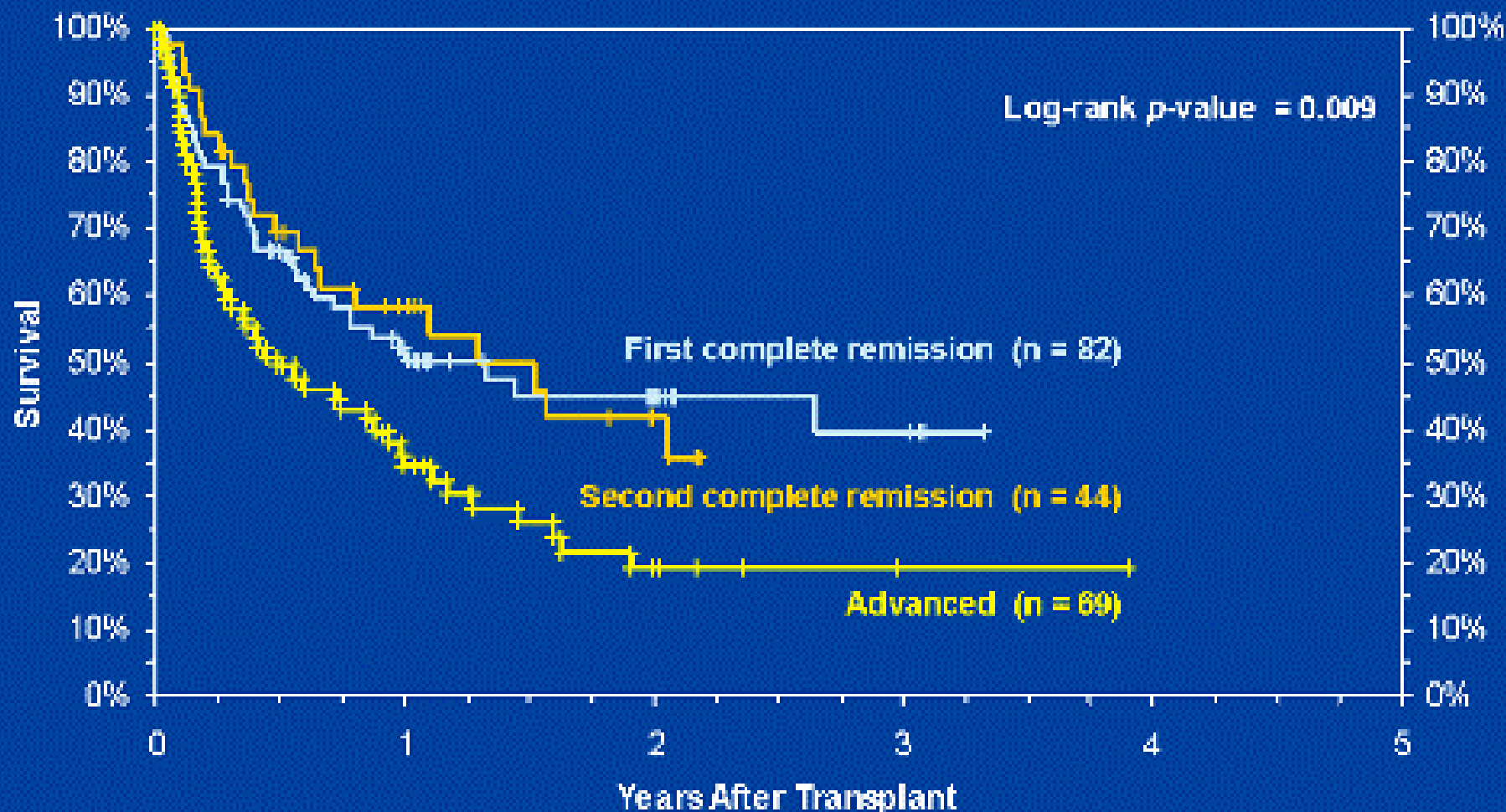


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# Acute Myelogenous Leukemia

Survival of Older Adult (Age  $\geq 55$  Years) Marrow and PBSC Recipients with Myeloablative Preparative Regimens, by Disease Stage 1998–2006

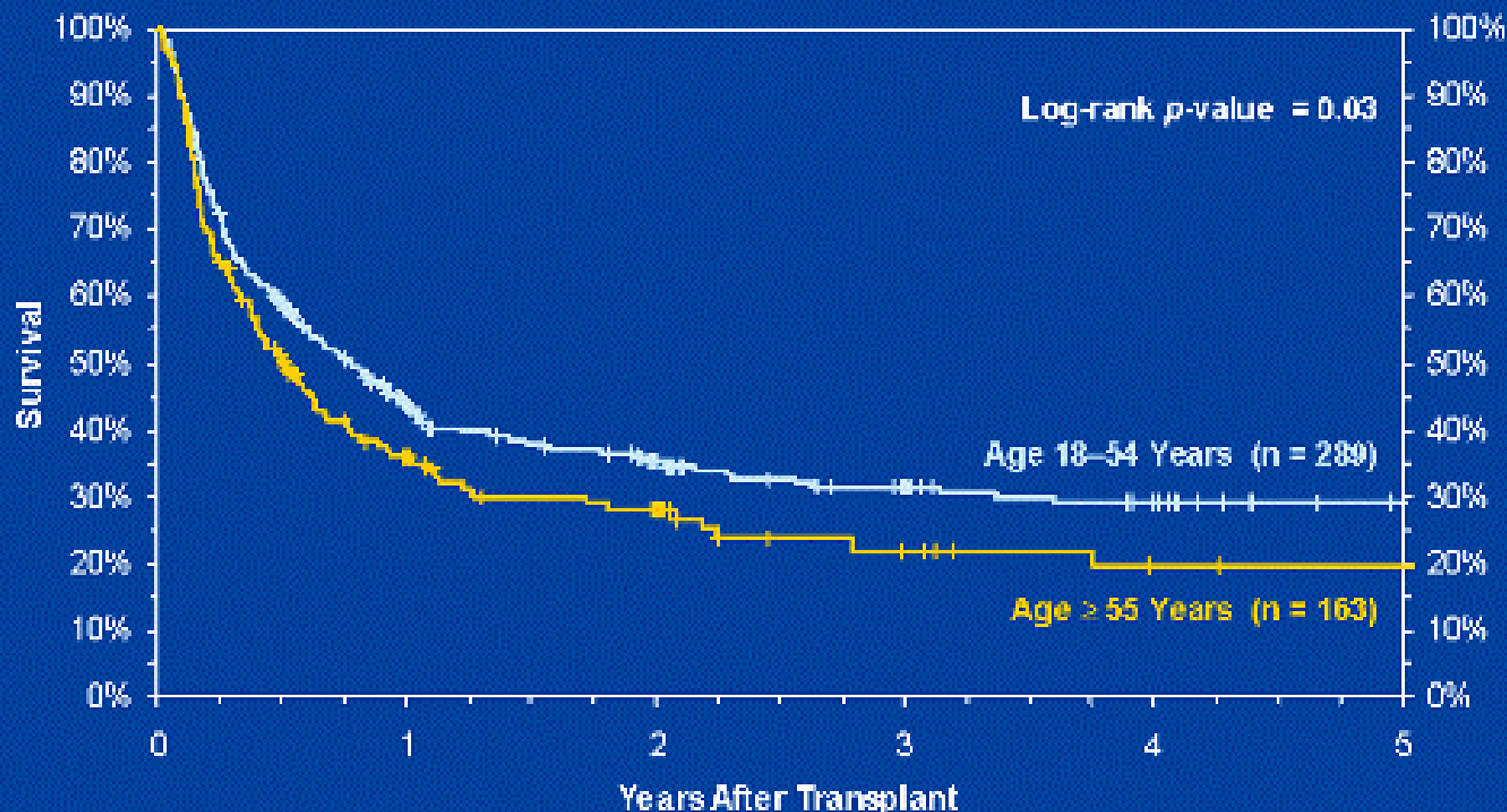


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# Myelodysplastic Syndromes

Survival of Adult (Age  $\geq 18$  Years) Marrow and PBSC Recipients with All Preparative Regimens, by Age at Transplant 1998–2006

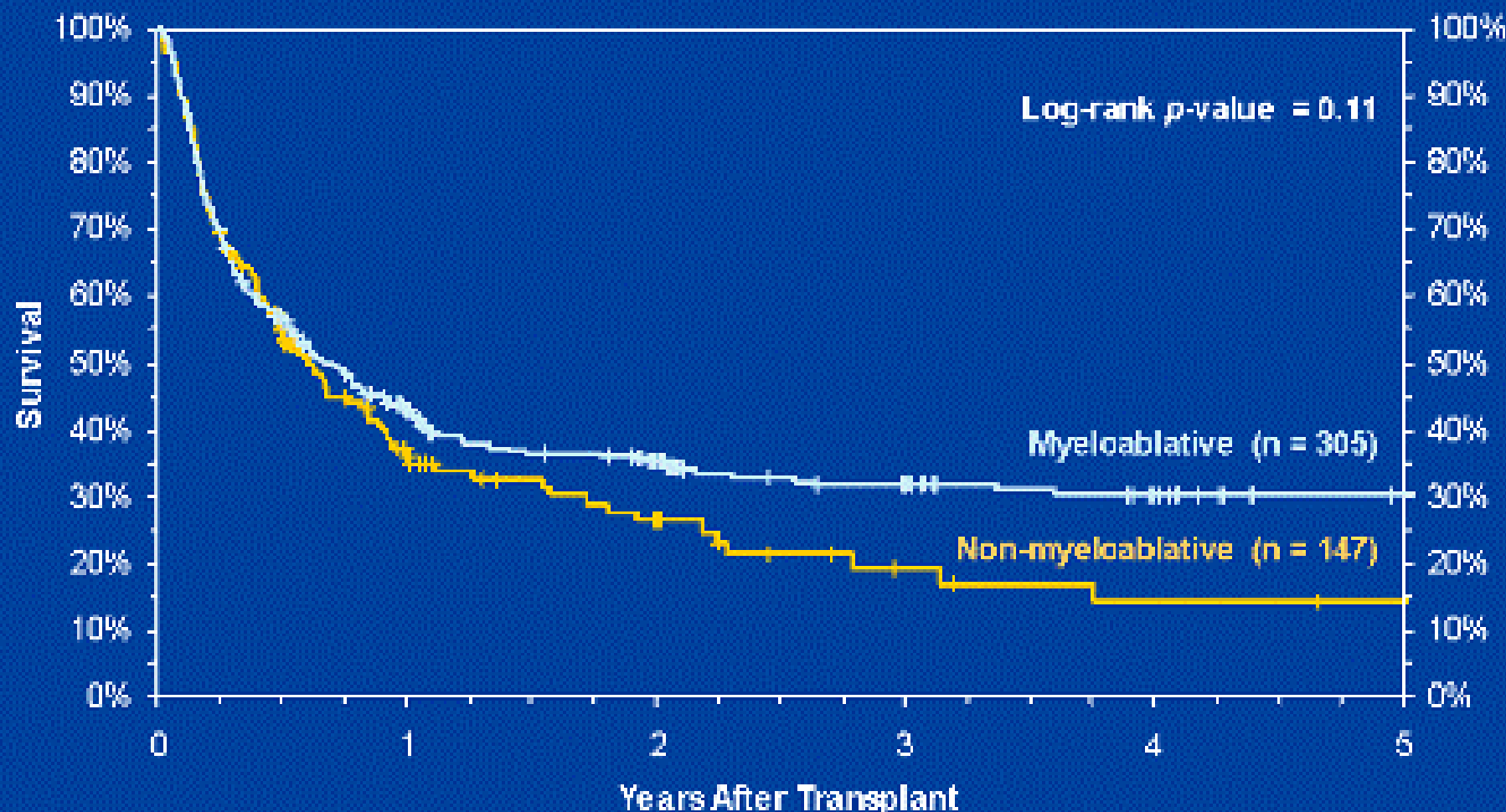


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# Myelodysplastic Syndromes

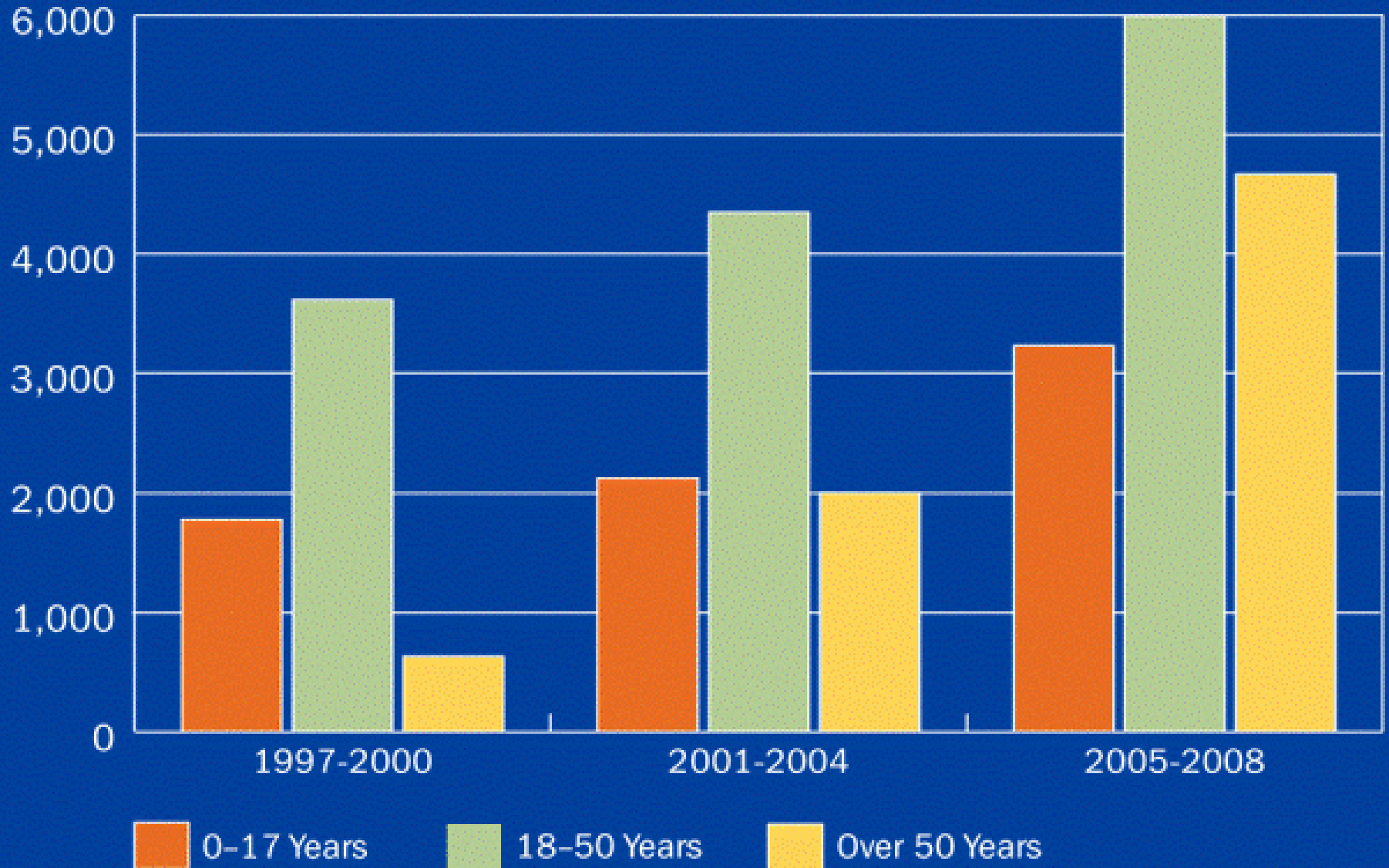
Survival of Adult (Age  $\geq 18$  Years) Marrow and PBSC Recipients with RAEB/RAEB-T by Conditioning Regimen 1998-2006



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# NMDP Transplants by Patient Age and Year



# Case assumptions

- The patient is in CR

# Decision

- This patient without significant co-morbidity but high risk disease can have a RIC allogeneic transplant because:
  - He is in CR
  - Age
- However I would concentrate on modifying the toxicity and on reducing the A-GvHD risk rather than reducing the dose intensity of the ablation
  - i.e. busulfan IV 6,4mg-8,6mg (or plasma level adjusted)
  - Substitution of cyclophosphamide by fludarabine
  - Addition of melphalan
  - T-cell modulation