Cuurent Role of Stem Cell Transplantation for CML

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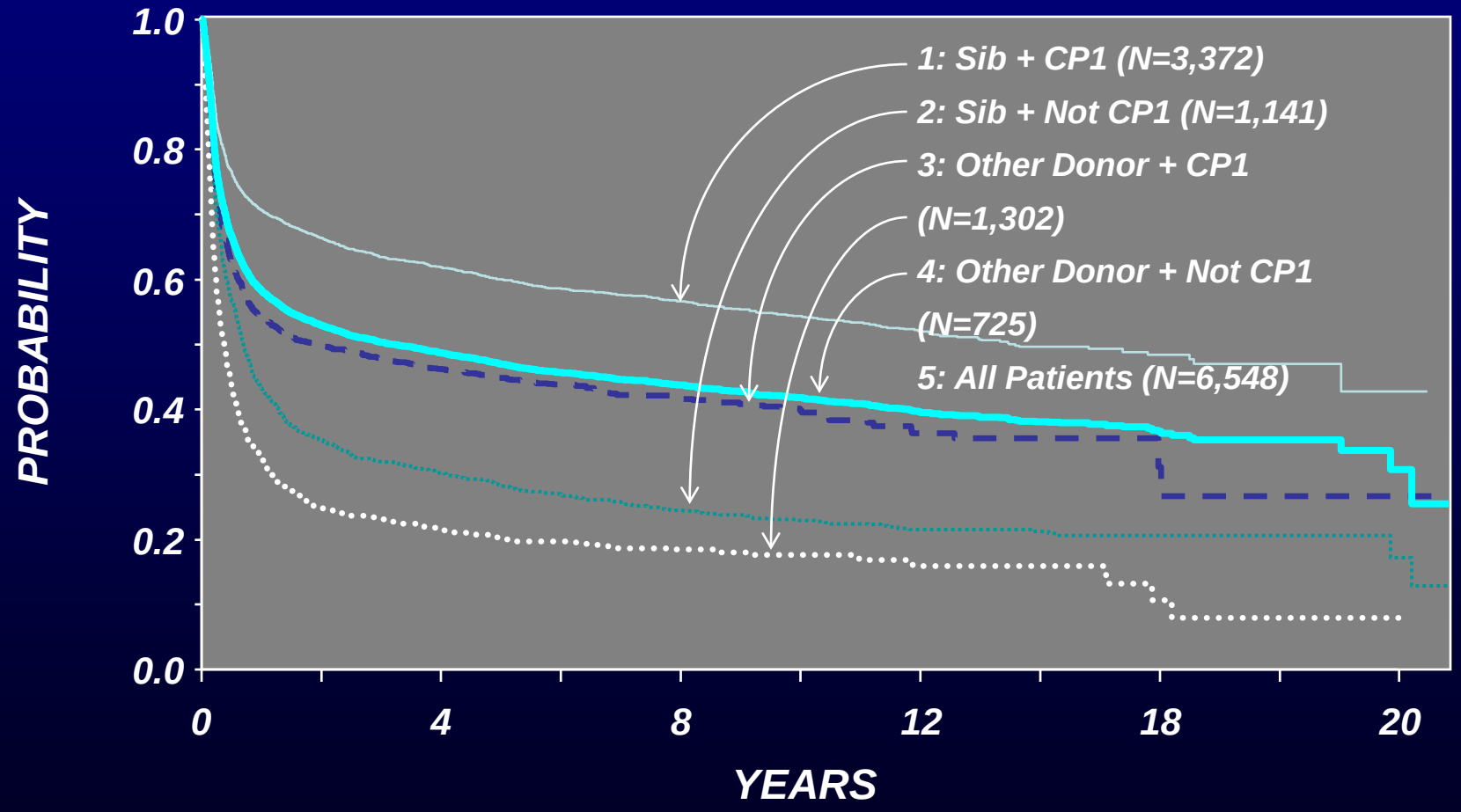
CML- Prototype Disease for Targeted Curative Therapy

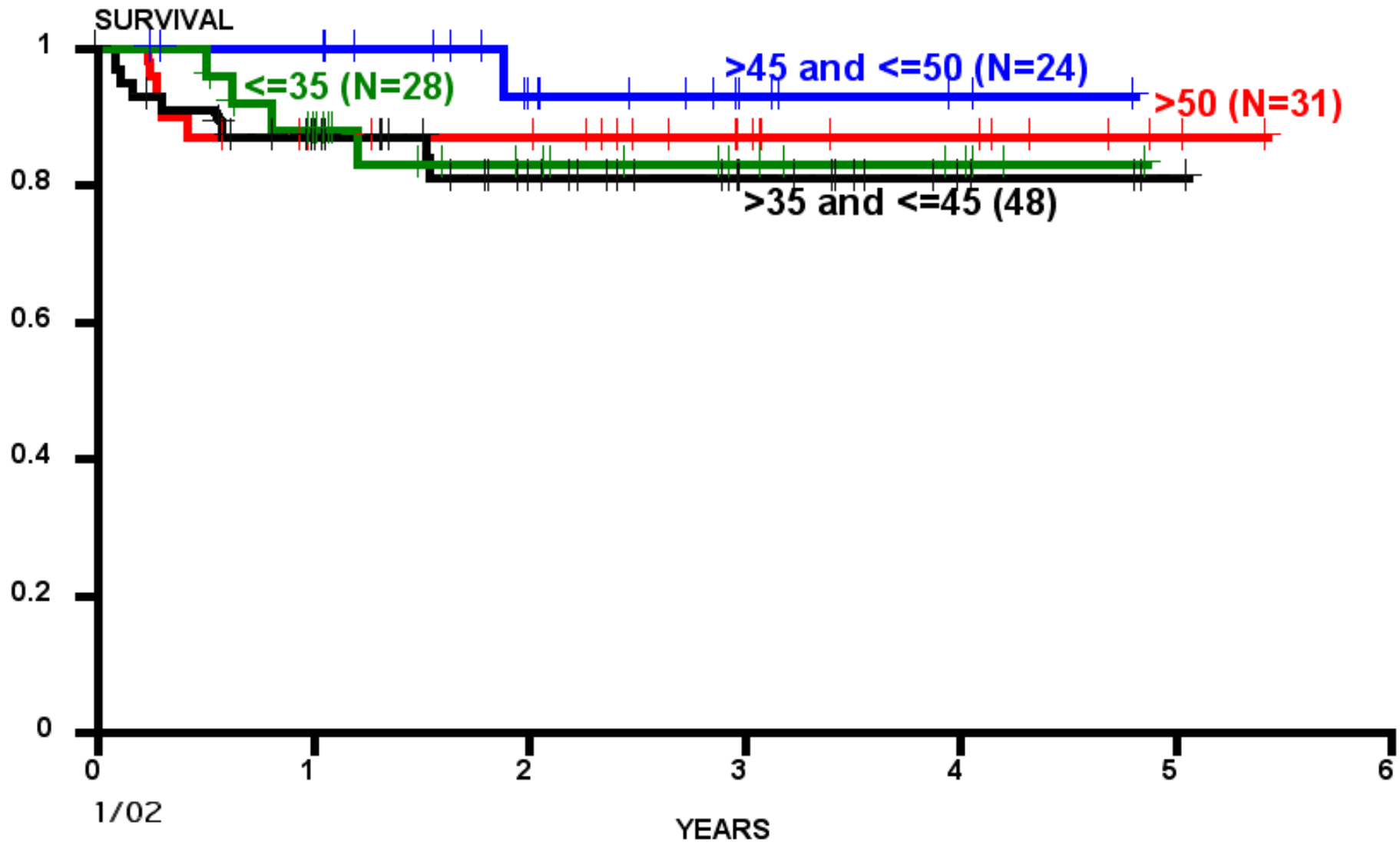
- Allogeneic transplantation potentially curative
- Graft-vs-leukemia effect
- Donor lymphocyte infusions can cure patients with recurrent disease

PROBABILITY OF OVERALL SURVIVAL



CML CP Targetted BU+CY+SC

The influence of age at transplant



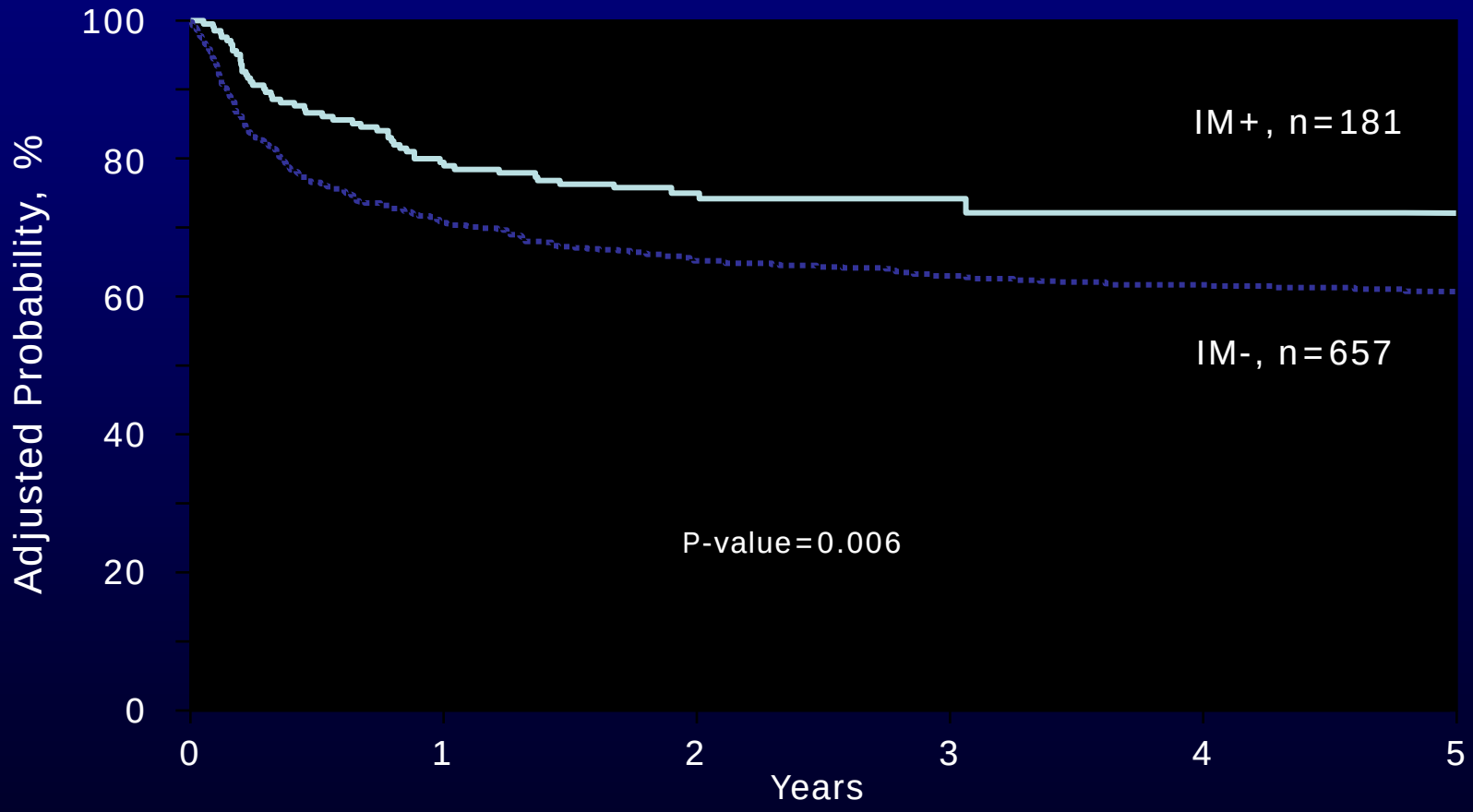
BCR-ABL Mutations

- Approximately half of patients with progression have mutations
- Second line tyrosine kinase inhibitors effective (except in T315I), but with short term f/u

  dasatanib

  nilotenib
- T315I associated with resistance to all tyrosine kinase inhibitors- but this is rare in chronic phase CML
  - Stem Cell Transplant effective in patients T315I and other mutations

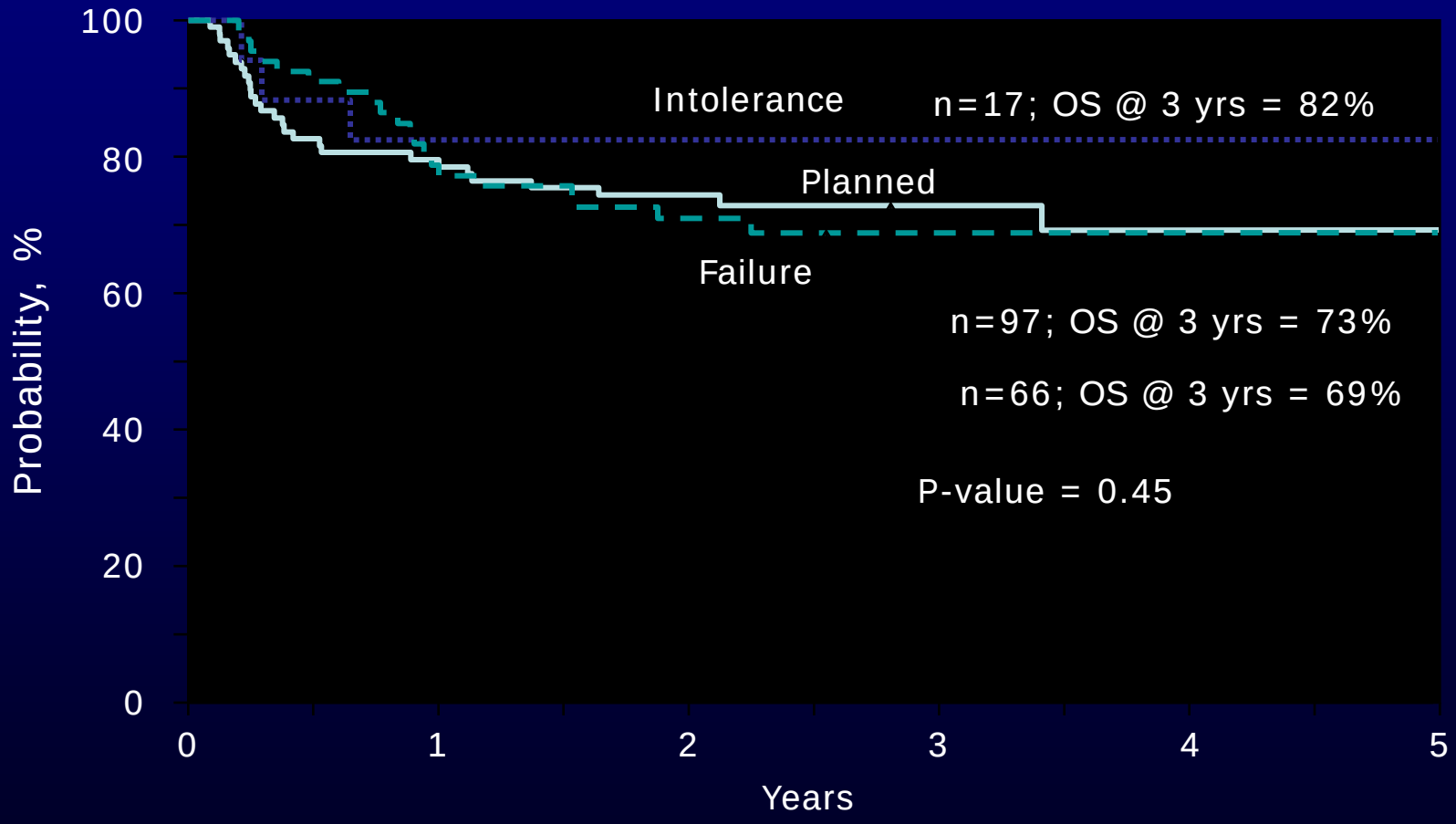
Survival
by prior imatinib treatment for Chronic Phase CML



Stratified Cox regression Model with adjustment for covariates
(HLA match, graft type, time from Dx to Tx)

Lee et al CIBMTR

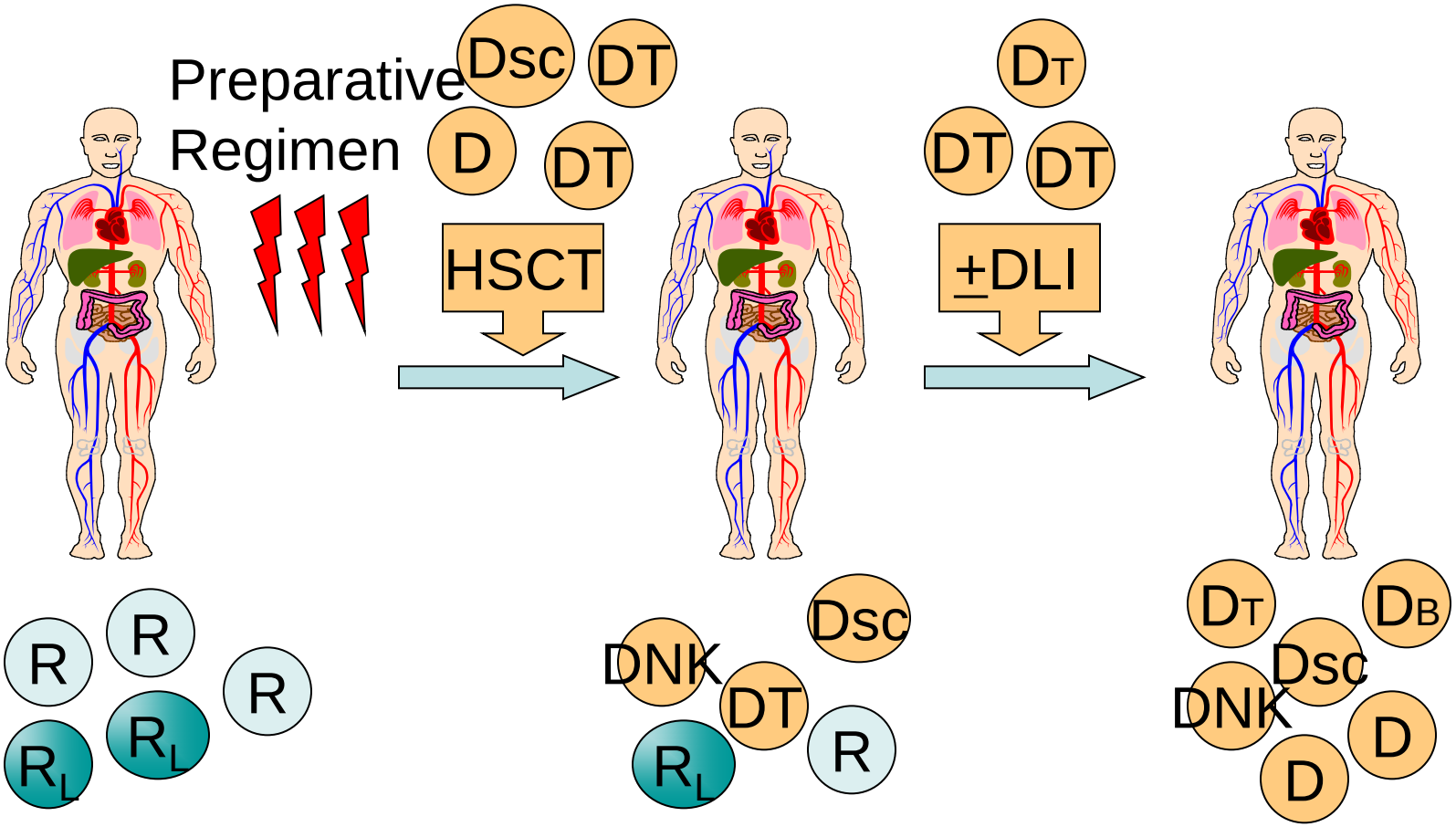
Probability of Overall Survival by 3 Reasons to Proceed to Transplantation for CP1 CML Prior Treated with Imatinib Mesylate



Concerns with AlloSCT

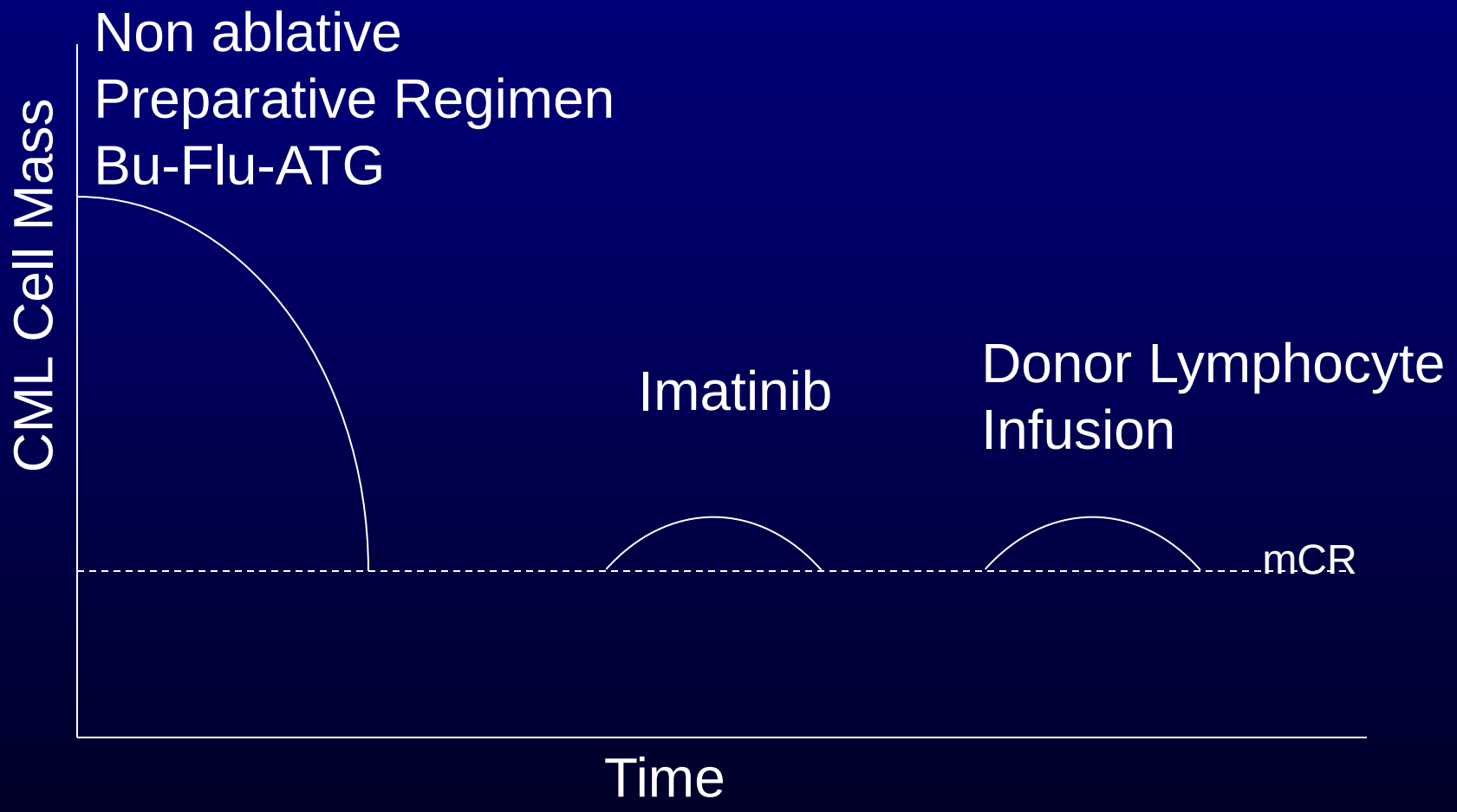
- Toxicity, treatment related mortality
- GVHD

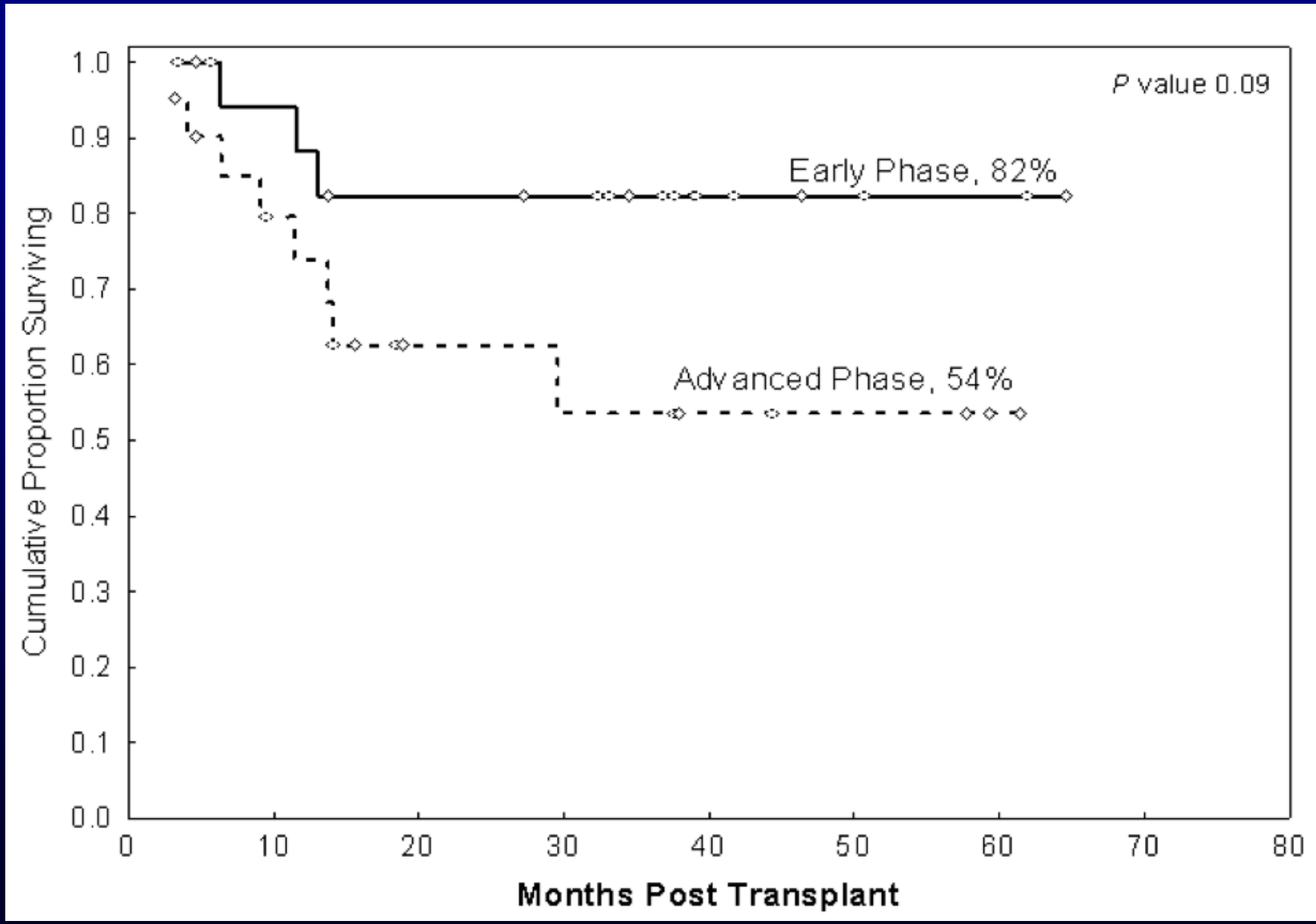
Nonmyeloablative Transplant



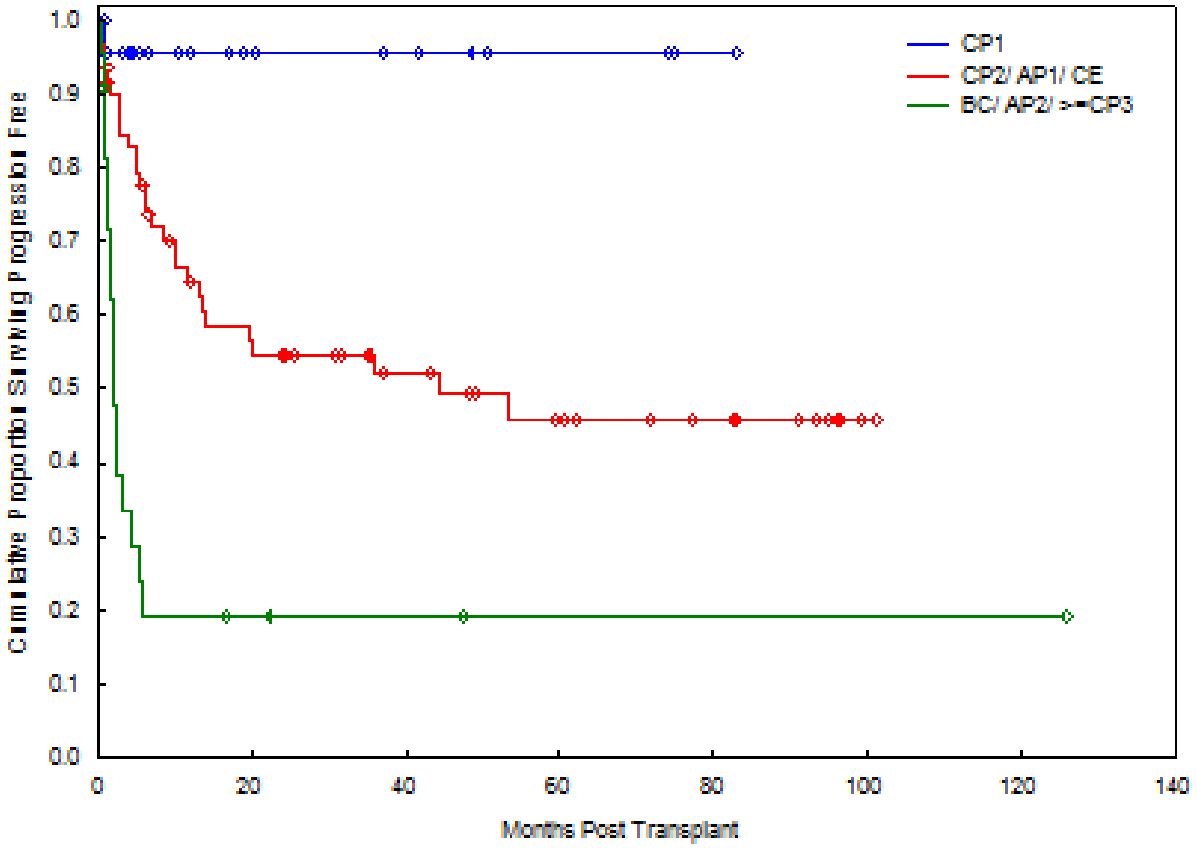
Recipient Donor Mixed Chimera Complete Chimera

Opportunities for Cure in CML

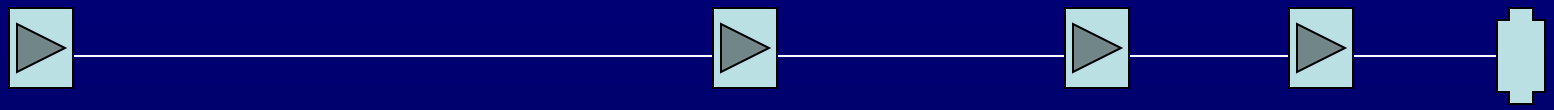



P value 0.09
Early Phase, 82%
Advanced Phase, 54%
Cumulative Proportion Surviving
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
10
20
30
40
50
60
70
80
Months Post Transplant

Progression Free Survival



When to Perform AlloSCT in CML



Diagnosis

Risk of transplant outweighs benefit vs. TKIs

1st Failure

2nd Failure

AP/Blast Crisis

BMT least likely to be successful

Patient-poor PS

Disease- resistant

<u>Considerations:</u>

Patient- age, PS, goal

Disease- Stage, Prognostic factors

Mutations

Donor availability

Efficacy of alternative Rx