

# The role of stem cell transplantation in CML treatment and blast phase management

*S Saussele*

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# Tasks

- Historical role of transplantation in the pre-imatinib era
- Role of transplantation in the imatinib era
- Management of blast crisis

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# Outcome after SCT pre-imatinib

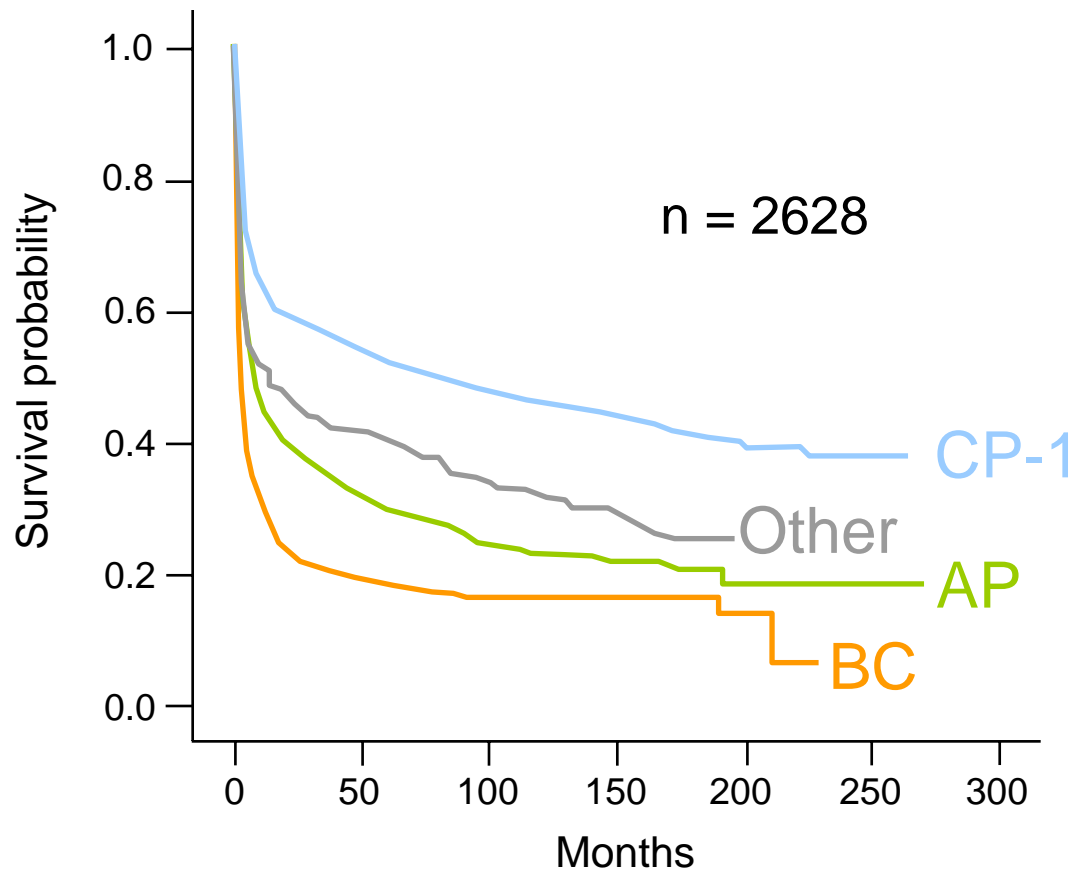
- Allo-SCT in first CP
  - 10-yr OS 60%, 10-yr EFS 50%
  - 10-yr OS 47%, 15-yr EFS 52%
  - 10-yr OS 63%, 15-yr EFS 65% (meta-analysis, n = 316)
- CIBMTR (n = 4513)
  - 18-yr OS 50% (first CP), 37% (others)
  - 18-yr cum. incidence of relapse 25% (CP), 37% (others)
- EBMT (n = 2628)
  - 20-yr OS 34%
    - 41% for first CP, HLA-identical sibling
    - 49% for EBMT risk score 0–1

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# Survival probability (EBMT data, Gratwohl 2006)

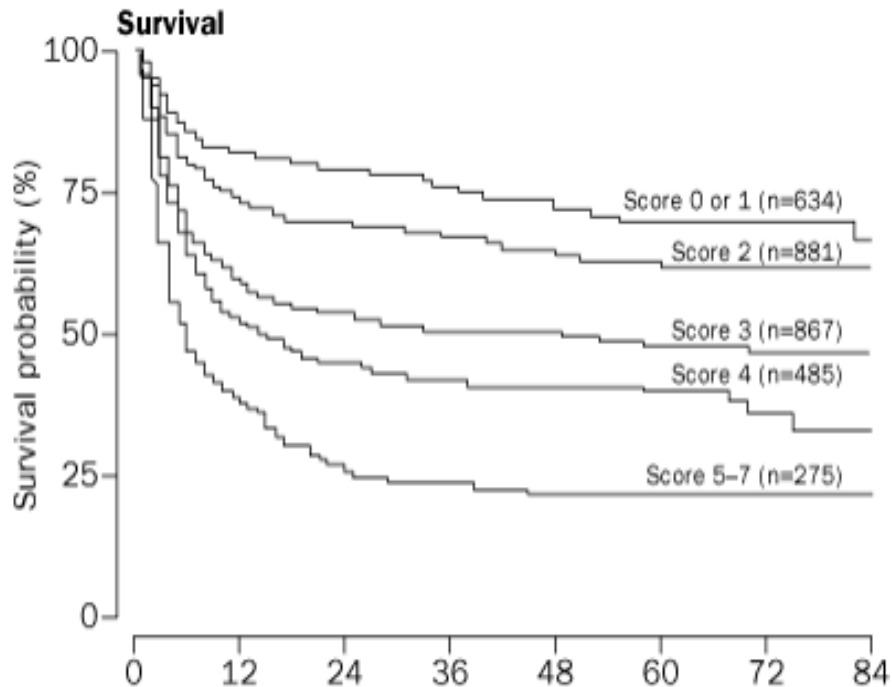


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# EBMT score



Variable	Categories	Score
Donor	HLA-identical sibling	0
	Unrelated donor	1
Stage	First chronic phase	0
	Accelerated phase	1
	Blast crisis	2
Age	< 20 years	0
	20–40 years	1
	> 40 years	2
Sex match	All, except:	0
	Male recipient/female donor	1
Time to transplantation	<12 months	0
	> 12 months	1

Validity of score confirmed by independent studies (Passweg. BJH 2004; DeSouza. Haematologica 2005)

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Gratwohl et al. Lancet 1998



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# CML study III (Hehlmann 2007)

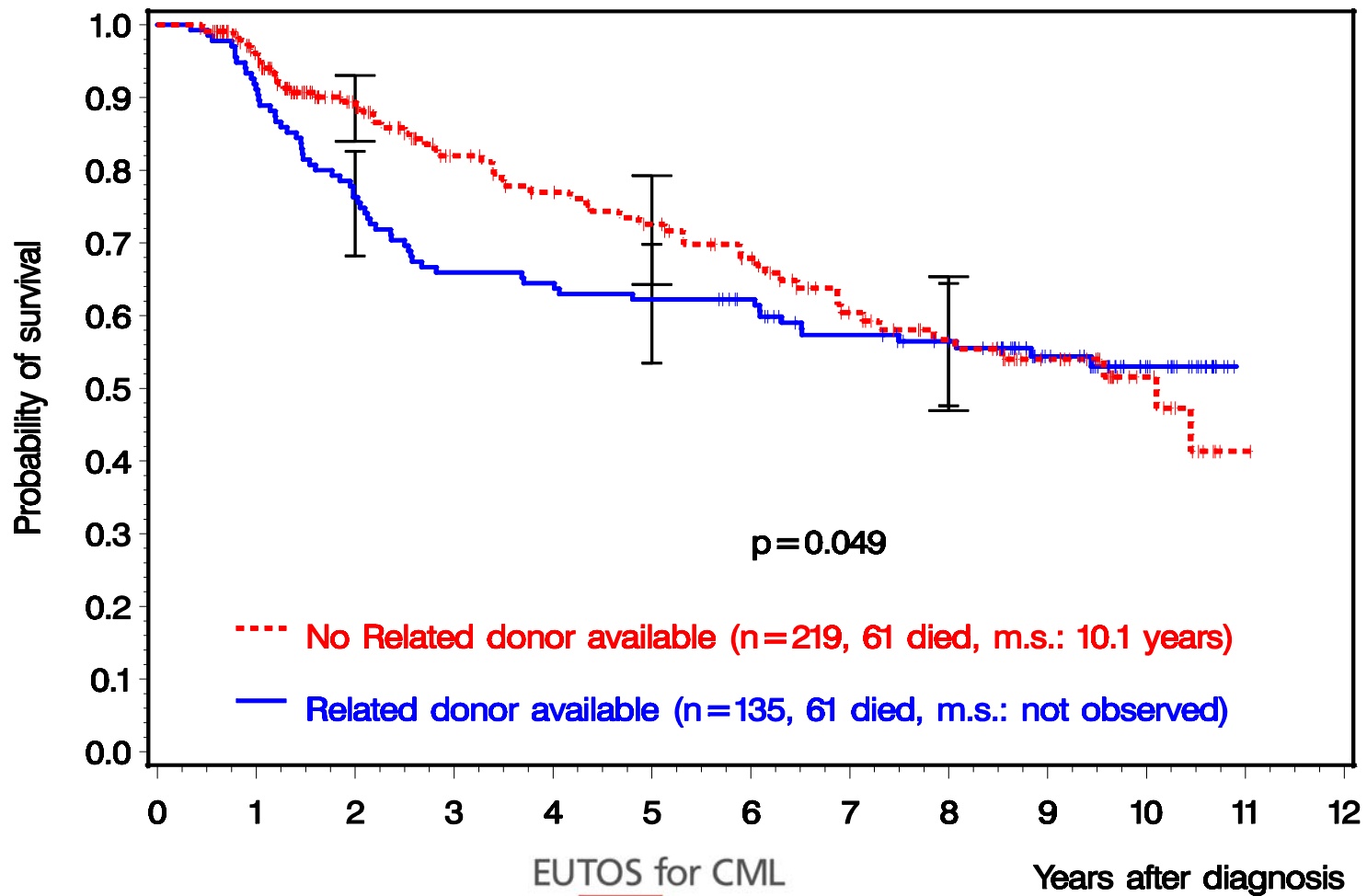
- Randomised (genetic) comparison of SCT and best drug treatment
  - CCR: > 90% vs 48%
  - MMR: > 80% vs 45%
  - Relapse < 1% per year
  - > 80% without drug treatment after transplantation

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# CML study III (Hehlmann, Blood 2007)



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# SCT in the imatinib era

- Declining transplantation numbers
  - In Germany, between 1998 and 2004, the annual SCT numbers decreased from 357 to 98 (28% of initial transplantations), predominantly due to the decrease in first CP from 223 to 45 (20%)

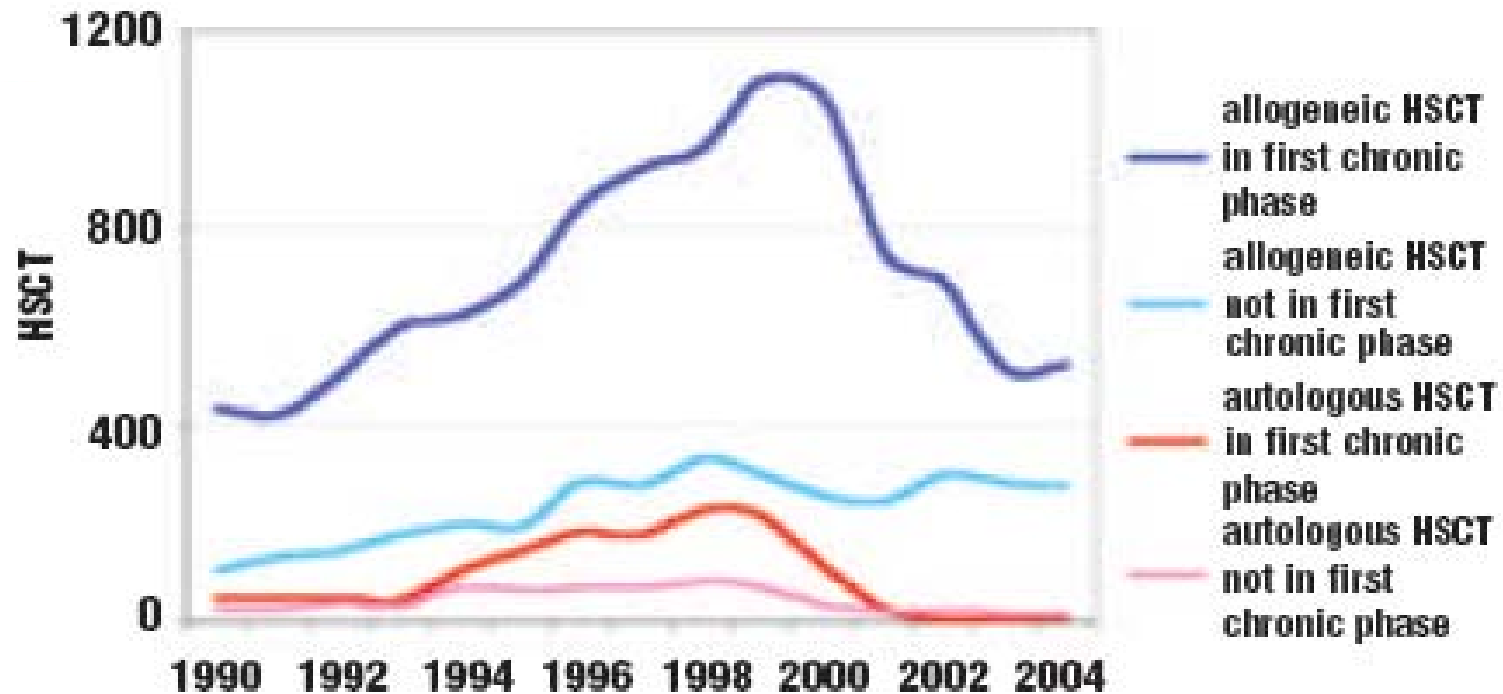
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Bacher. Ann Hem 2009

# SCT in the imatinib era



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Gratwohl et al. Haematologica 2006;91:513

# SCT in the imatinib era

- Better transplantation procedures
  - Allele matching
  - Management of infections and supportive care
  - Immunosuppression
- Studies focusing on the potential negative effect of imatinib
  - Lee. Blood 2008
  - Deininger. Haematologica 2006
  - Jabbour. Cancer 2007
  - Oehler. Blood 2007
- Imatinib prior to Allo-SCT did not increase TRM or morbidity

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# CML study IV: outcome of transplanted patients (n = 84)

	HSCT in first CP			HSCT in advanced phases
	Elective HSCT	HSCT after IM failure	Total	
<b>n</b>	<b>19</b>	<b>37</b>	<b>56</b>	<b>28</b>
<b>Probability of survival at 3 yrs after HSCT</b>	<b>88%</b>	<b>94%</b>	<b>91%</b>	<b>59%</b>

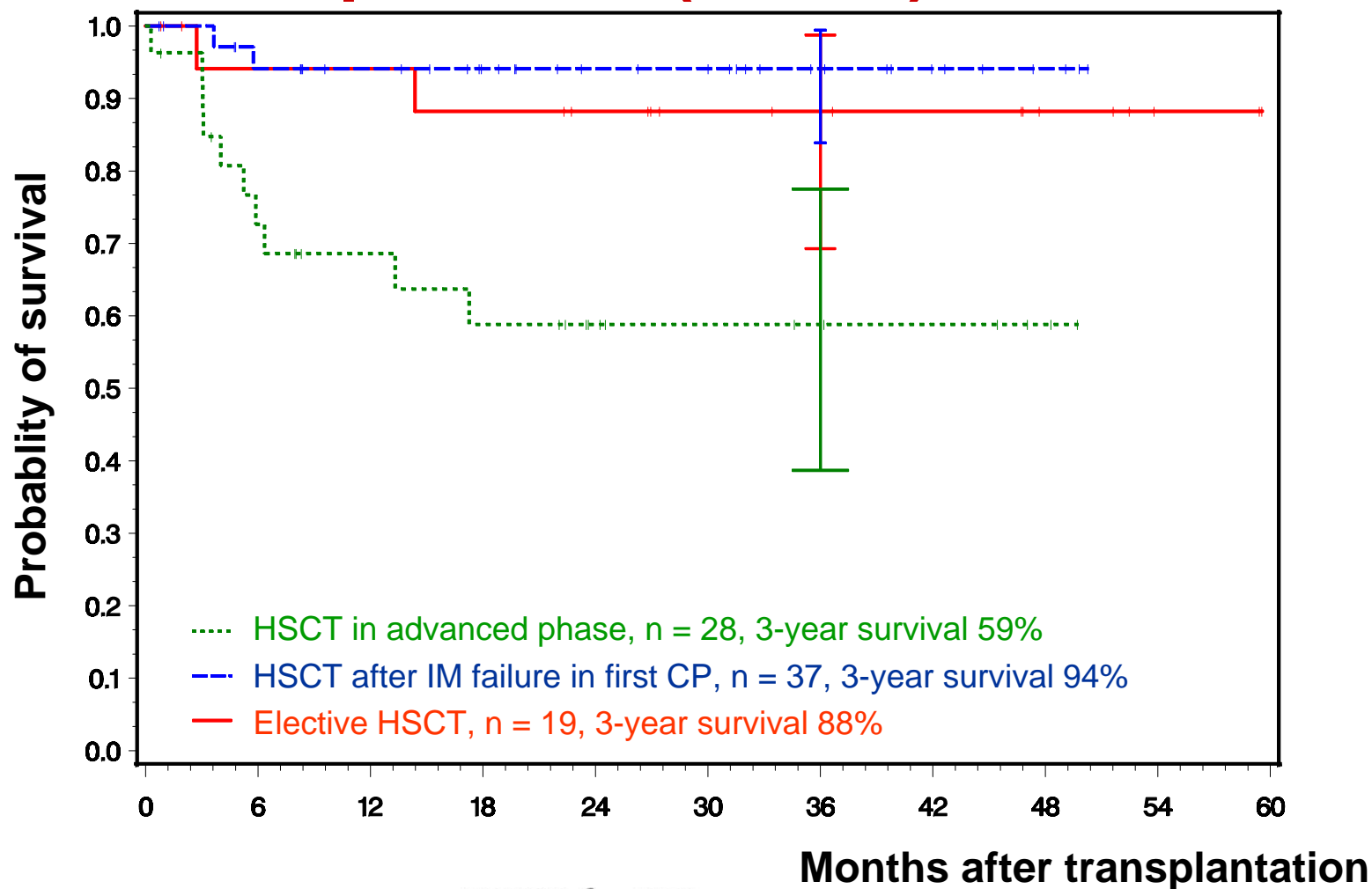
Saussele et al., Blood (ASH Abstracts), Nov 2008; 112: 448

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# CML study IV: outcome of transplanted patients (n = 84)



Saussele et al.,  
Blood (ASH Abstracts), Nov 2008; 112: 448

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# CML study IV: matched pair analysis

- In 53 transplanted patients 2 imatinib-treated patients (n = 106) in first CP were matched according to
  - Sex
  - Age
  - Risk score
- Survival times were matched for time between diagnosis and transplantation of corresponding partner

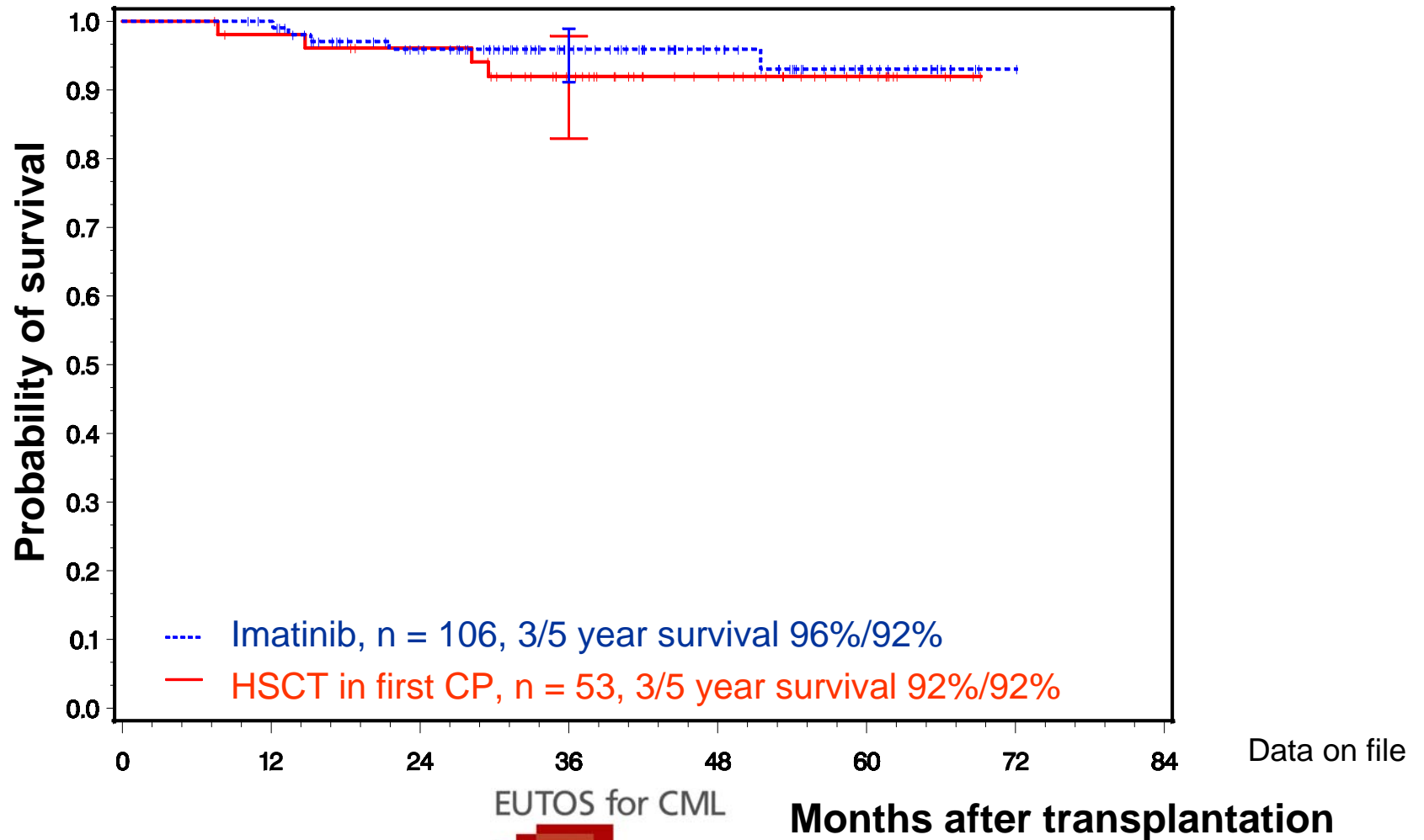
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Data on file

# CML study IV: matched pair analysis



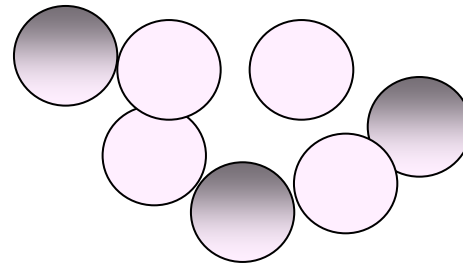
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# Blast crisis

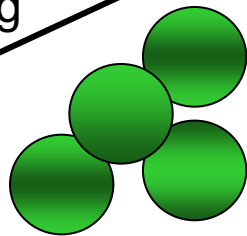
Proliferation, decreased apoptosis, increased myeloid compartment



CP

Stimulation of signaling

**BCR-ABL**



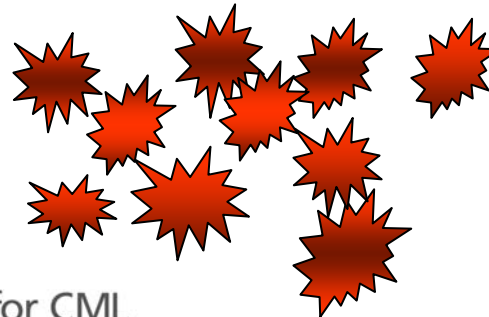
ROS



DNA-damage



Genetic instability, mutations, gene doubling, chromosome breakage, translocation



Progression to BC

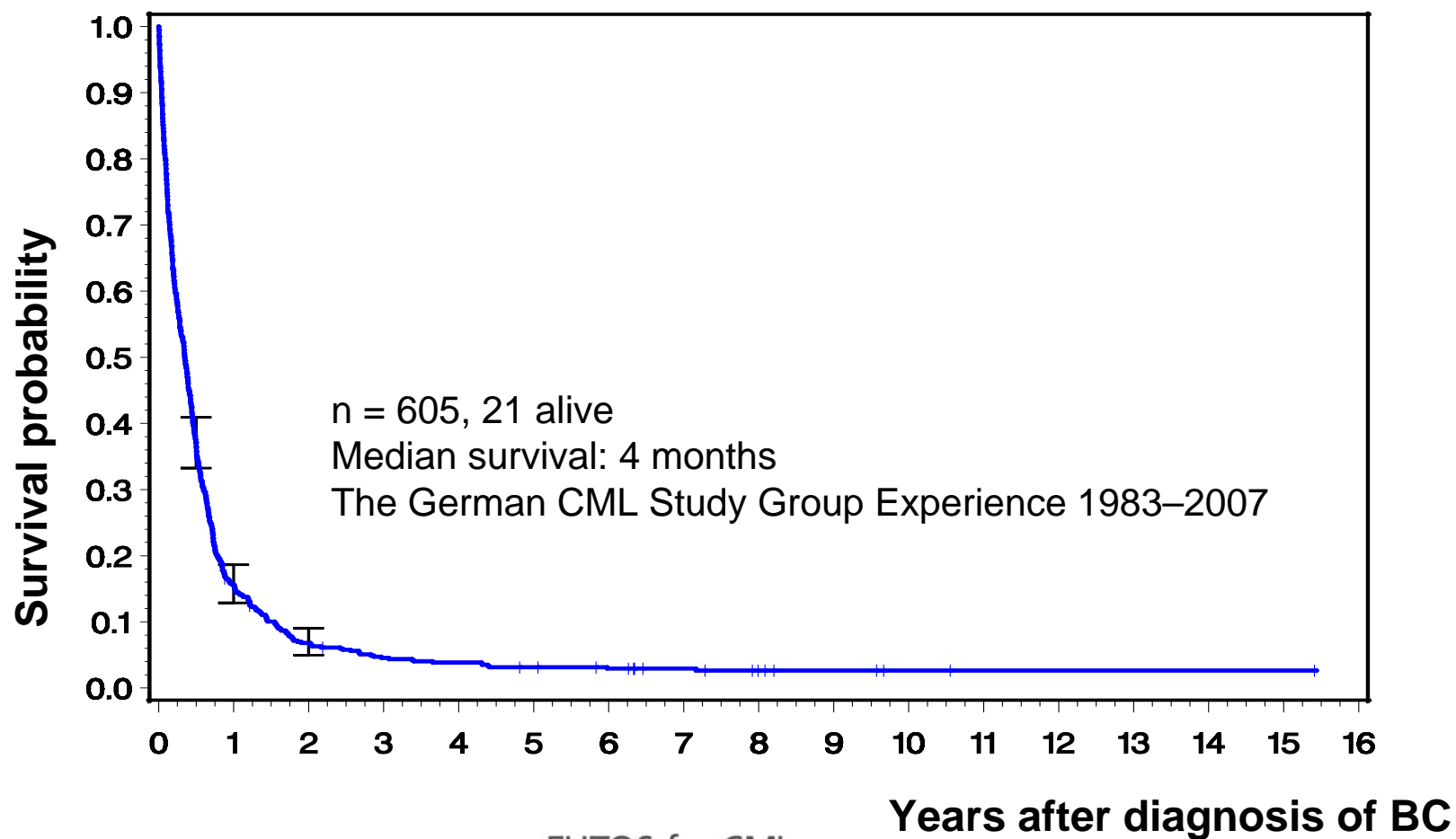
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Hehlmann and Saussele. Haematologica 2008

# Survival of blast crisis patients



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## Treatment of blast crisis in the era of TKI

Study	Drug	Patients	Survival (overall)	
			At 12 months	Median
Palandri 2008	Imatinib 600mg	92 (20 LBC)	29 %	7 mo
Druker 2001	Imatinib 300–600 mg	58 (20 LBC)	NA	NA
Sawyers 2002	Imatinib 400–600 mg	229	30 %	6.9 mo
Kantarjian 2002	Imatinib 300–1000 mg	75 (10 LBC)	22 %	6.5 mo
Sureda 2003	Imatinib 600mg	30	36 %	10 mo
Talpaz 2006	Dasatinib 50–100 mg bid	33 (10 LBC)	~ 22%	~ 6 mo
Cortes 2008 and Gambacorti 2007	Dasatinib 70–100 mg bid	157 (48 LBC)	49% / 30%	11.8 mo (5.3 mo)
Giles 2008	Nilotinib 400–600 mg bid	136 (31 LBC)	42 %	~ 10 mo

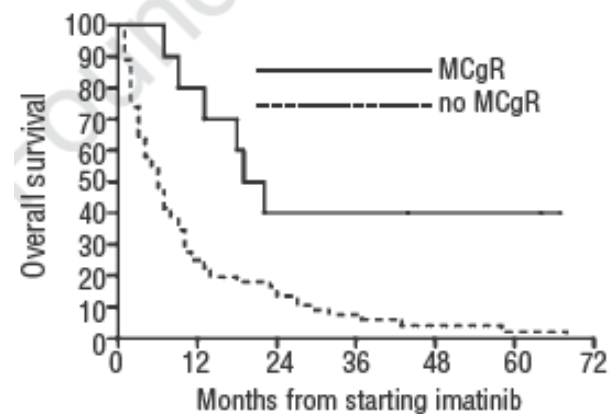
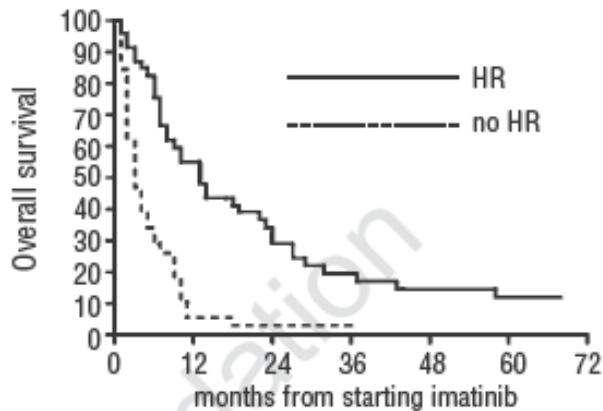
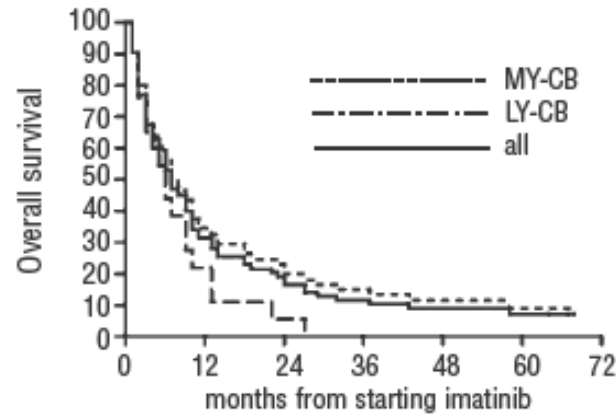
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# Management of blast crisis



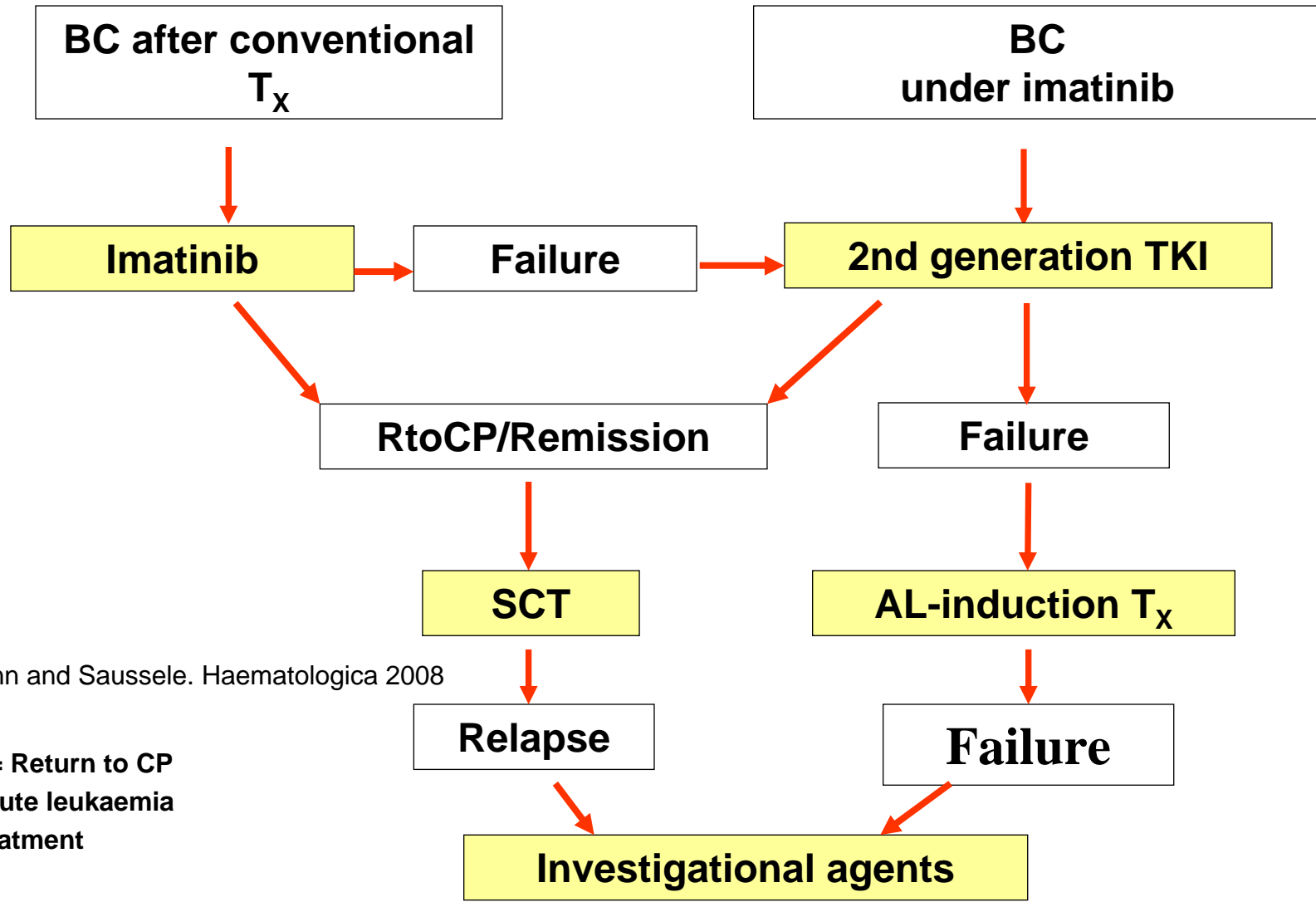
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Palandri, Haematologica 2008

# Treatment of blast crisis



Hehlmann and Saussele. Haematologica 2008

RtoCP = Return to CP  
AL = Acute leukaemia  
Tx = Treatment

# Summary

- SCT was and still is the only curative therapy option in CML
- Imatinib has no negative effect on outcome after SCT; in contrast it seems to ameliorate outcome
- Promising results (CML study IV) indicate that SCT could be offered second line to patients with an available donor and should be considered as a more important treatment alternative than currently perceived
- Management of BC include TKI, chemotherapy to achieve HR; SCT should be performed whenever possible

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