Raisa Gorbacheva Memorial Lecture

„Treatment of Acute Myeloid Leukemia: Present Status and New Directions III“

Thomas Büchner, MD PhD
Professor of Medicine and Hematology
University of Münster, Germany
buechnr@uni-muenster.de

1999

Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

- **Experience**
- **AML Biology**
- **Older Age AML**
- **Novel Approaches**
- **Cooperation**

Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

Complete remissions (CR) and 4-5-year continuous complete remissions (CCR) in multicenter randomized trials in the order of patients age :

Younger patients

Publication	Age	No. of Patients	% CR	% CCR at 4-5 Y
Hann et al. 1997 Burnett et al. 1998	0-55	1857	82	42
Mandelli et al. 1992	15-55	448	68	24
Cassileth et al. 1998	16-55	740	70	35-43
Rai et al. 1981	0-60	247	36-59	22 (not age specific)
Yates et al. 1982	1-60	427	57-72	not given
Büchner et al. 1985	16-60	255	68	8-24
Rees et al. 1986	0-60	740	73	18
Hayat et al. 1986	10-60	257	66	17 (not age specific)
Zittoun et al. 1995	11-59	941	66	44
Preisler et al. 1987	14-60	564	65	17
Hansen et al. 1991	17-60	135	60	34
Dillman et al. 1991	15-60	226	69	10 (not age specific)
Cassileth et al. 1992	15-60	376	71	16-27 (not age specific)
Mayer et al. 1994	16-60	742	71	24-44
Bishop et al. 1996	15-60	301	73	23-41
Weick et al. 1996	< 65	665	54	19
Büchner et al. 1999	16-60	725	68	32
Büchner et al. 2003	16-60	535	74	34
Löwenberg et al. 2003	18-60	640	81	39
Büchner et al. 2006	16-60	840	70	45

Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

ctt-journal 2008;1:7-17

Complete remissions (CR) and 4-5-year continuous complete remissions (CCR) in multicenter randomized trials in the order of patients age:

Older patients

Publication	Age	No. of Patients	% CR	% CCR at 4-5 Y
Löwenberg et al. 2003	18-60	640	81	39
Hayat et al. 1986	60-65	30	47	no age specific data
Hansen et al. 1991	60-65	39	46	30
Cassileth et al. 1992	60-65	73	52	no age specific data
Rowe et al. 1995	55-70	117	61	not given
Witz et al. 1998	55-75	132	62	23
Goldstone et al. 2001	56-80	1311	50-62	15-18
Anderson et al. 2002	56-84	328	38	15
Rai et al. 1981	60+	105	16-45	no age specific data
Yates et al. 1982	60-84	226	31-47	not given
Büchner et al. 1985	60-78	79	39	0-28
Büchner et al. 2003	60-82	297	60	13
Rees et al. 1986	60-83	305	48	9
Preisler et al. 1987	60+	104	41	17
Dillman et al. 1991	60-83	100	41	no age specific data
Mayer et al. 1994	60-86	346	47	15
Stone et al. 1995	60+	388	53	13
Büchner et al. 1997	60+	340	42-54	22
Dombret et al. 1995	65+	172	47-70	not given
Rees et al. 1996	1-79	923	63	26 (not age specific)
Bishop et al. 1990	15-70	264	58	14-37 (not age specific)
Löwenberg et al. 1998	60-88	489	38-47	7-13
Rowe et al. 2004	56-86	348	42	4
Büchner et al. 2006	60-85	930	53	16

Mean percent complete remissions

in 31 randomized multicenter trials and 19 882 patients

Publication Year

	1980-1990	1991-2006
Age (years)		
< 60	66 %	72 %
60+	42 %	51 %

Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

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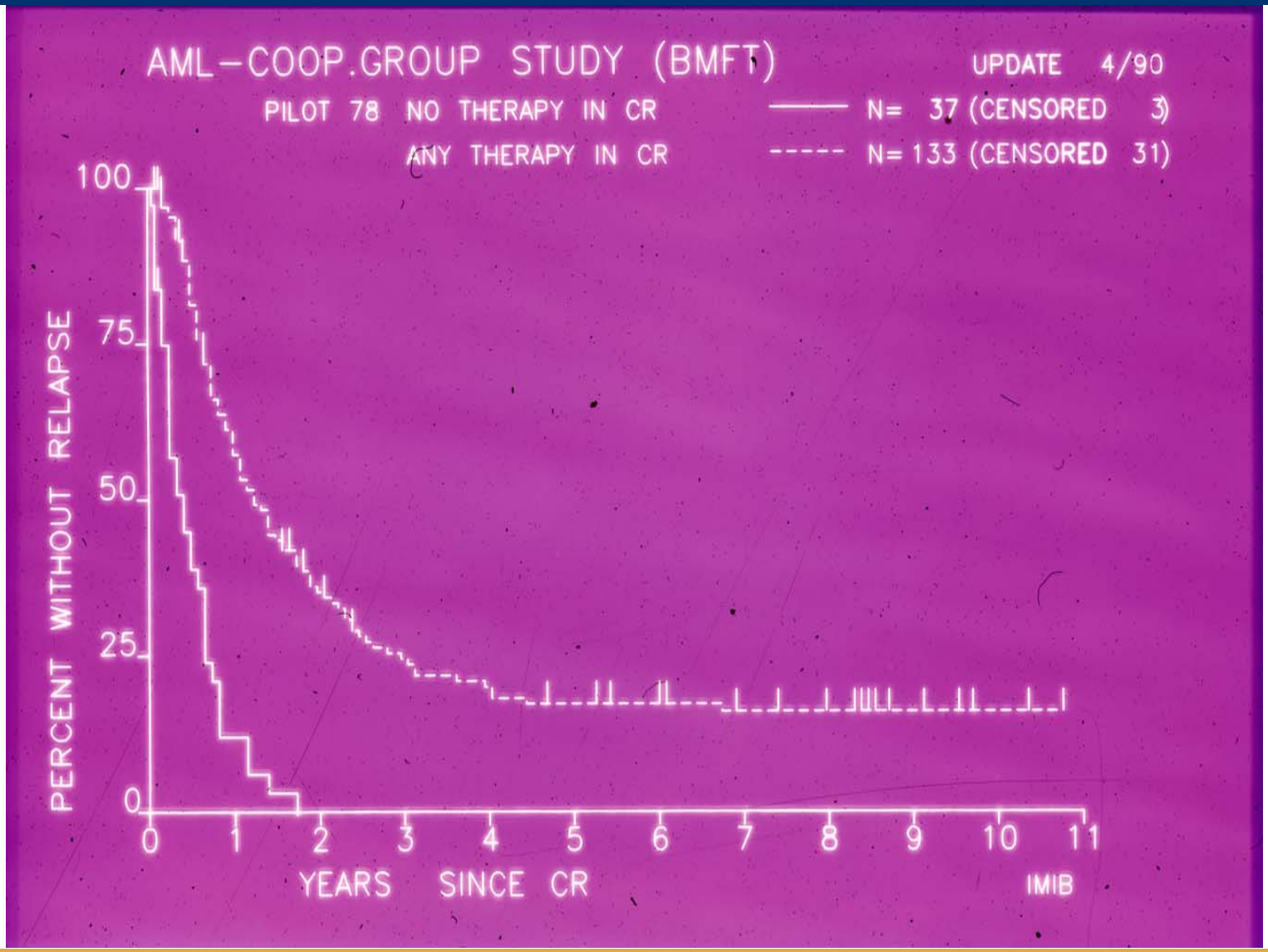
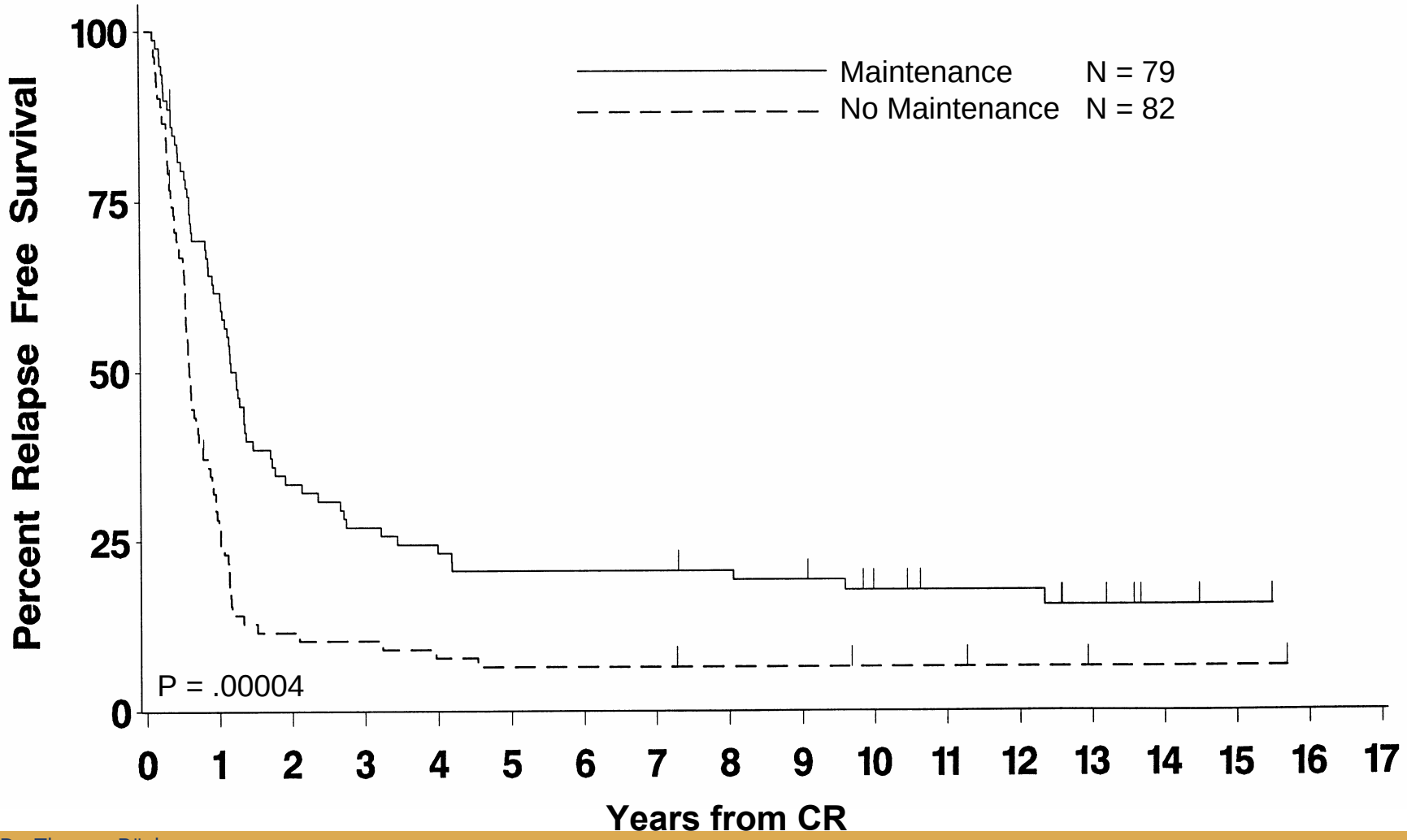
Mean percent continuous complete remissions at 4-5 years in 31 randomized multicenter trials

Publication Year

	1980-1990	1991-2006
Age (years)		
< 60	17%	34%
60+	11%	15%

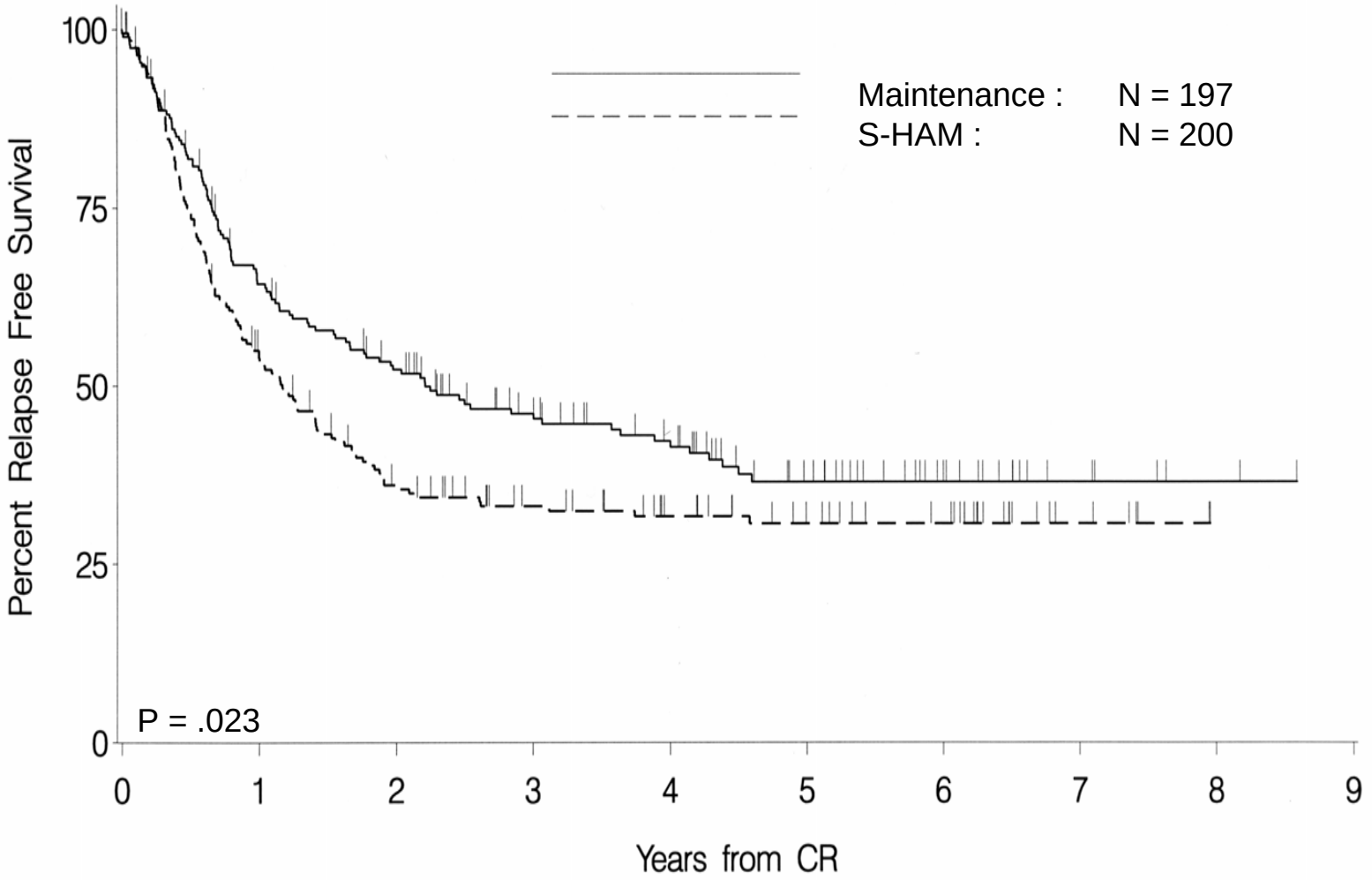

AML–COOP.GROUP STUDY (BMFT)
UPDATE 4/90
PILOT 78 NO THERAPY IN CR
N= 37 (CENSORED 3)
ANY THERAPY IN CR
N= 133 (CENSORED 31)
PERCENT WITHOUT RELAPSE
100
75
50
25
0
0 1 2 3 4 5 6 7 8 9 10 11
YEARS SINCE CR
IMIB

AMLCG 81: All Ages



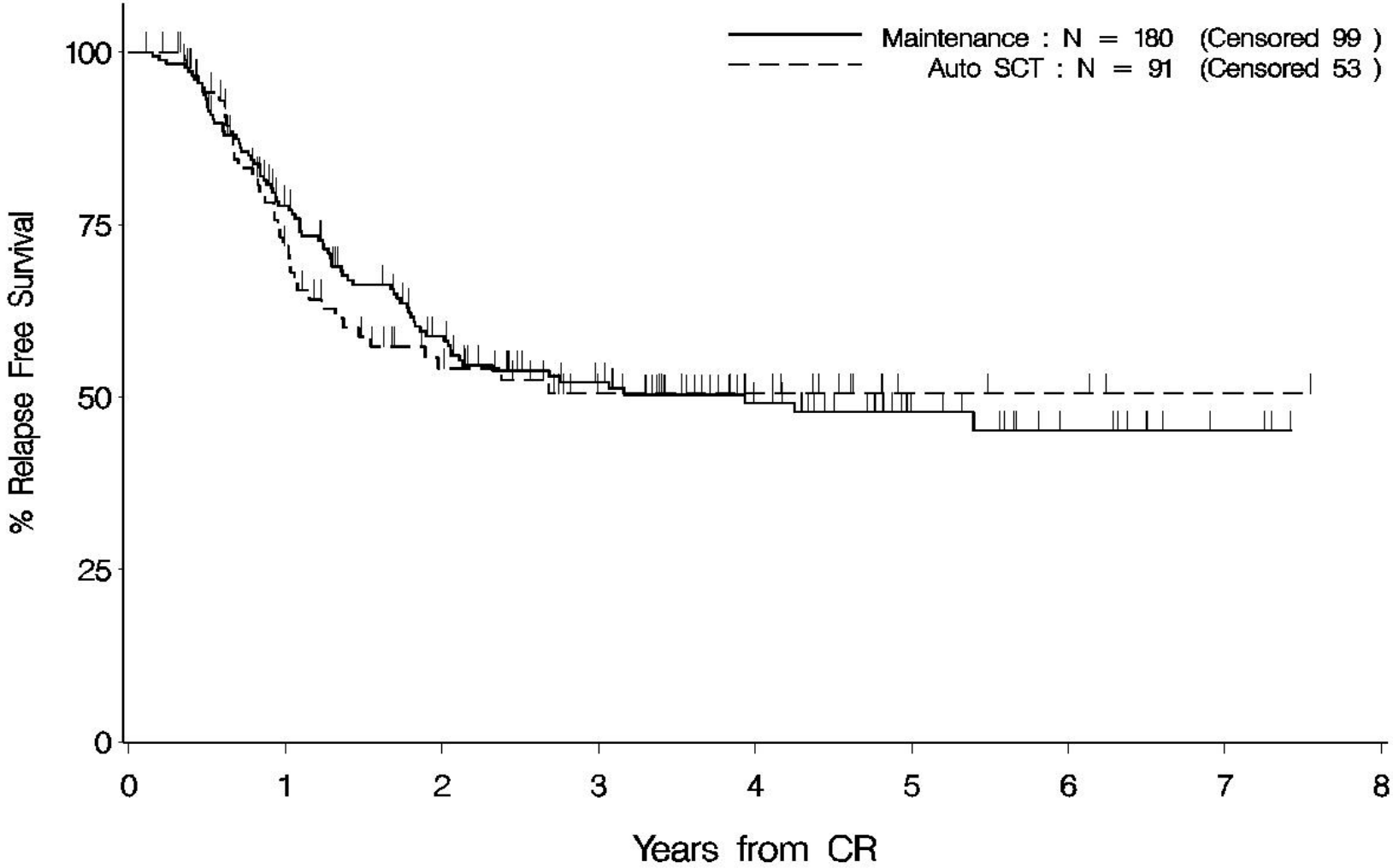
Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

AMLCG 92



Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

Auto SCT Age < 60 Y: As Treated

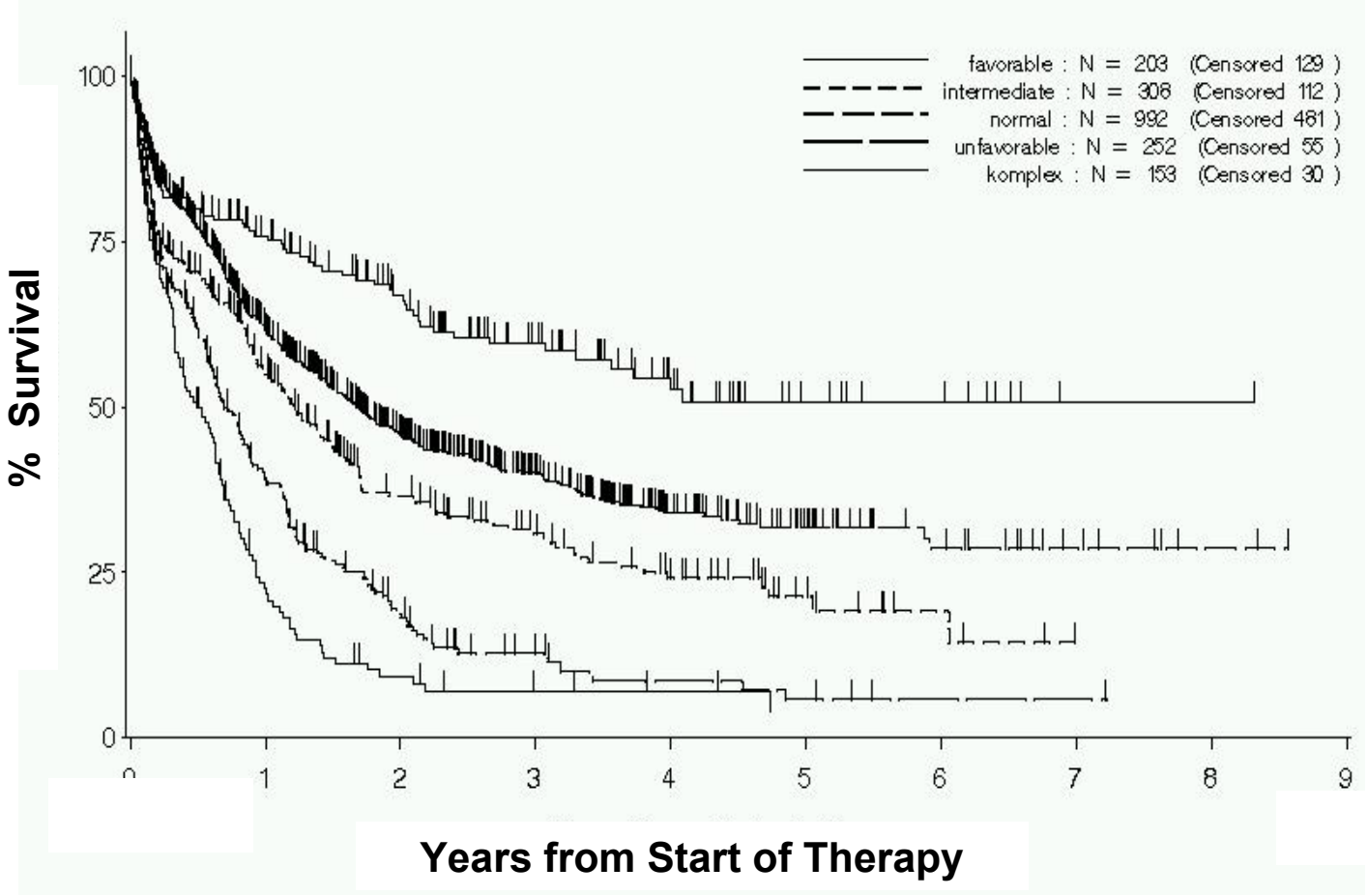


Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

- Experience
- AML Biology
- Older Age AML
- Novel Approaches
- Cooperation

Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

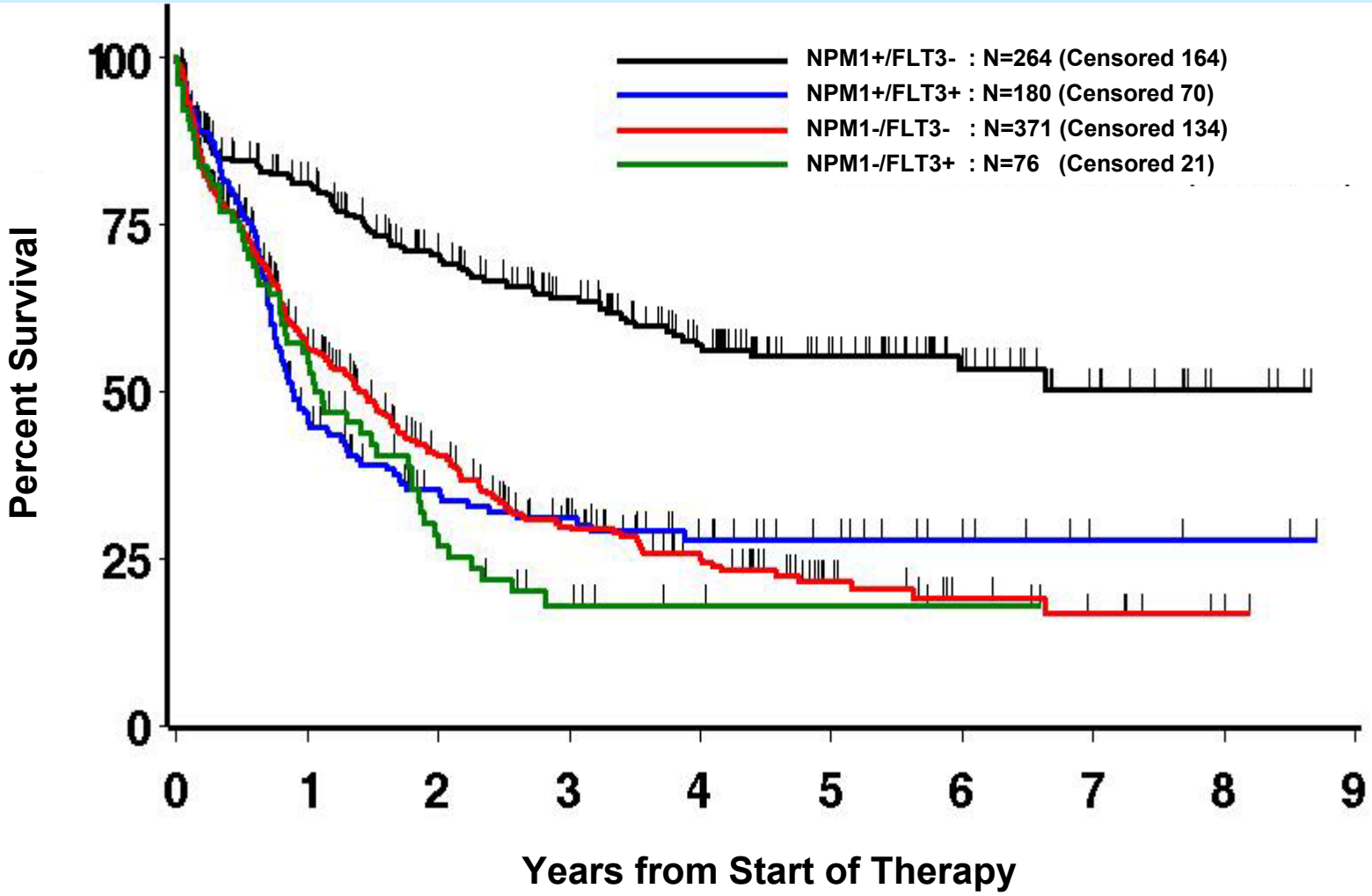
AMLCG 92 + 99



Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

Schoch C et al., Haferlach C et al.

Patients with Normal Cytogenetics in AMLCG 99



Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

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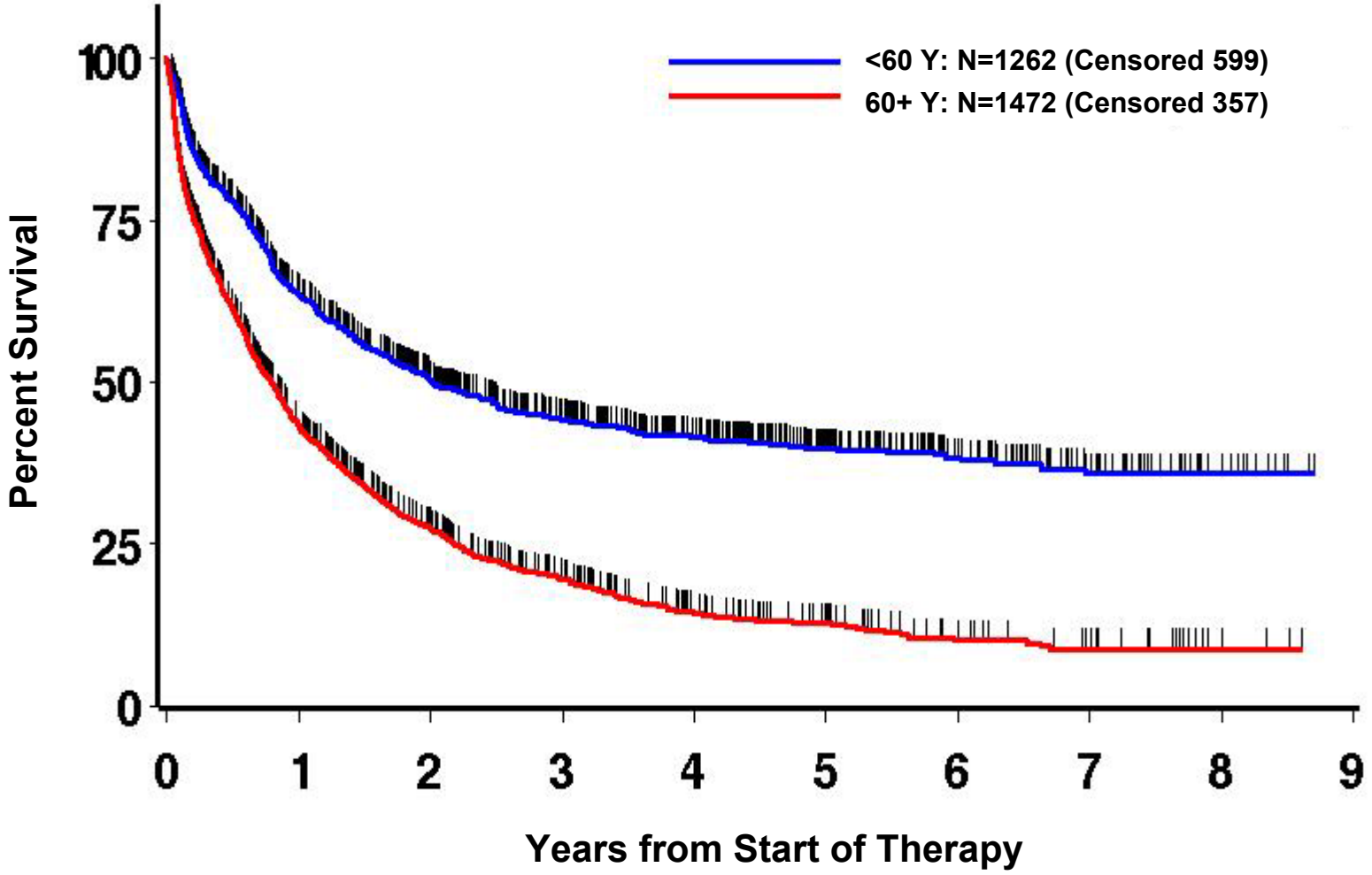
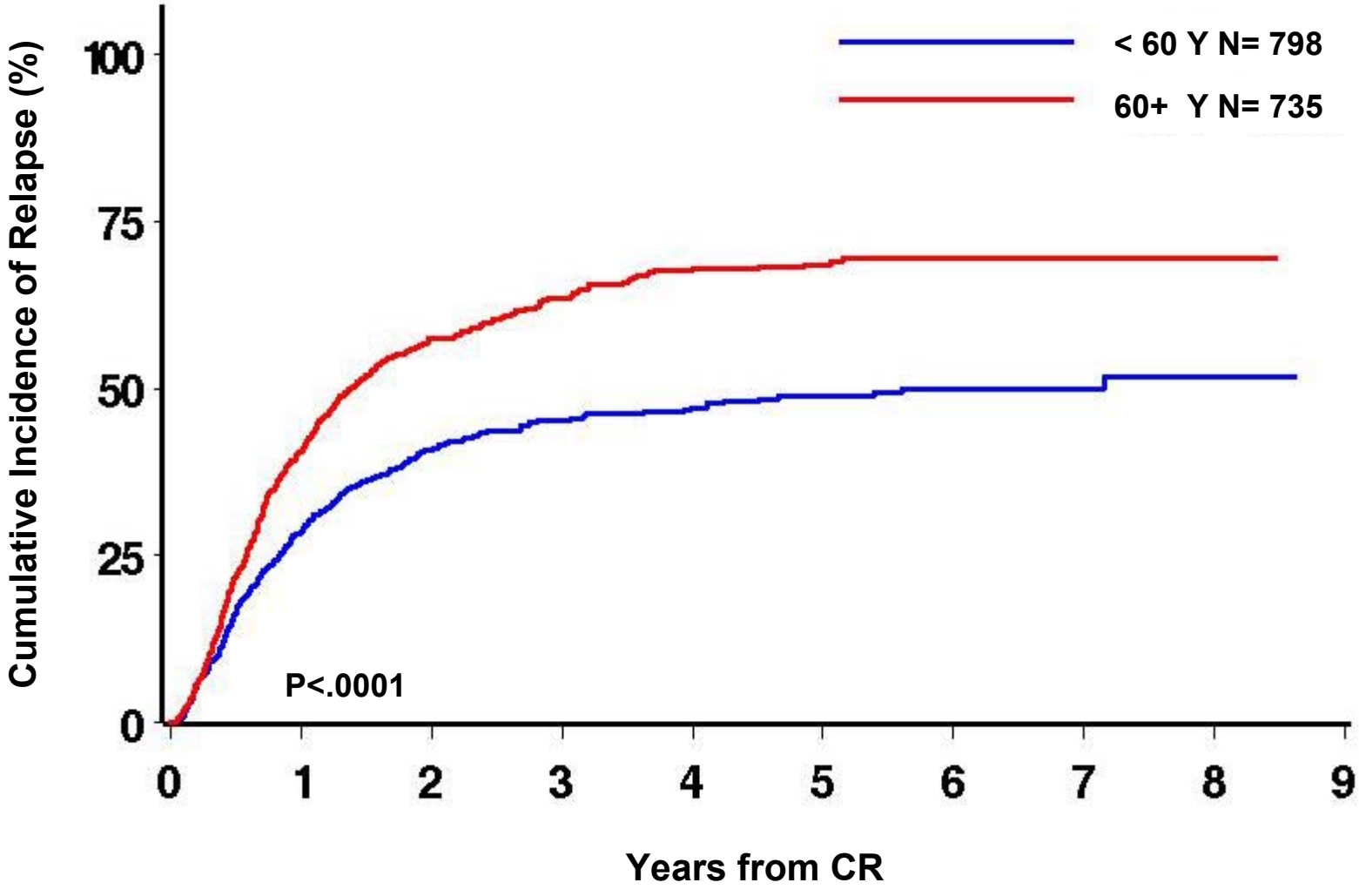
AMLCG 99: All Patients (N=2734)

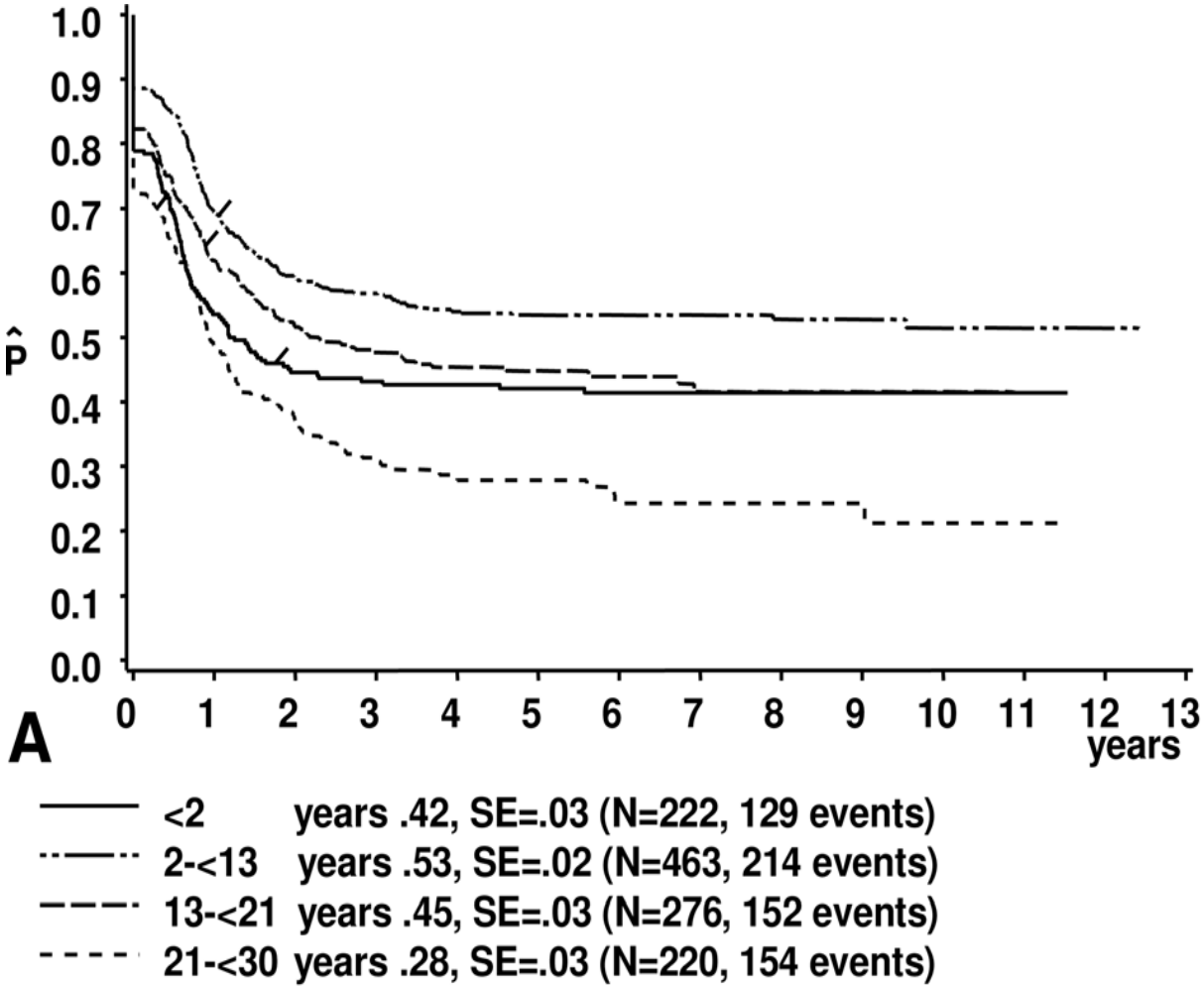


Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

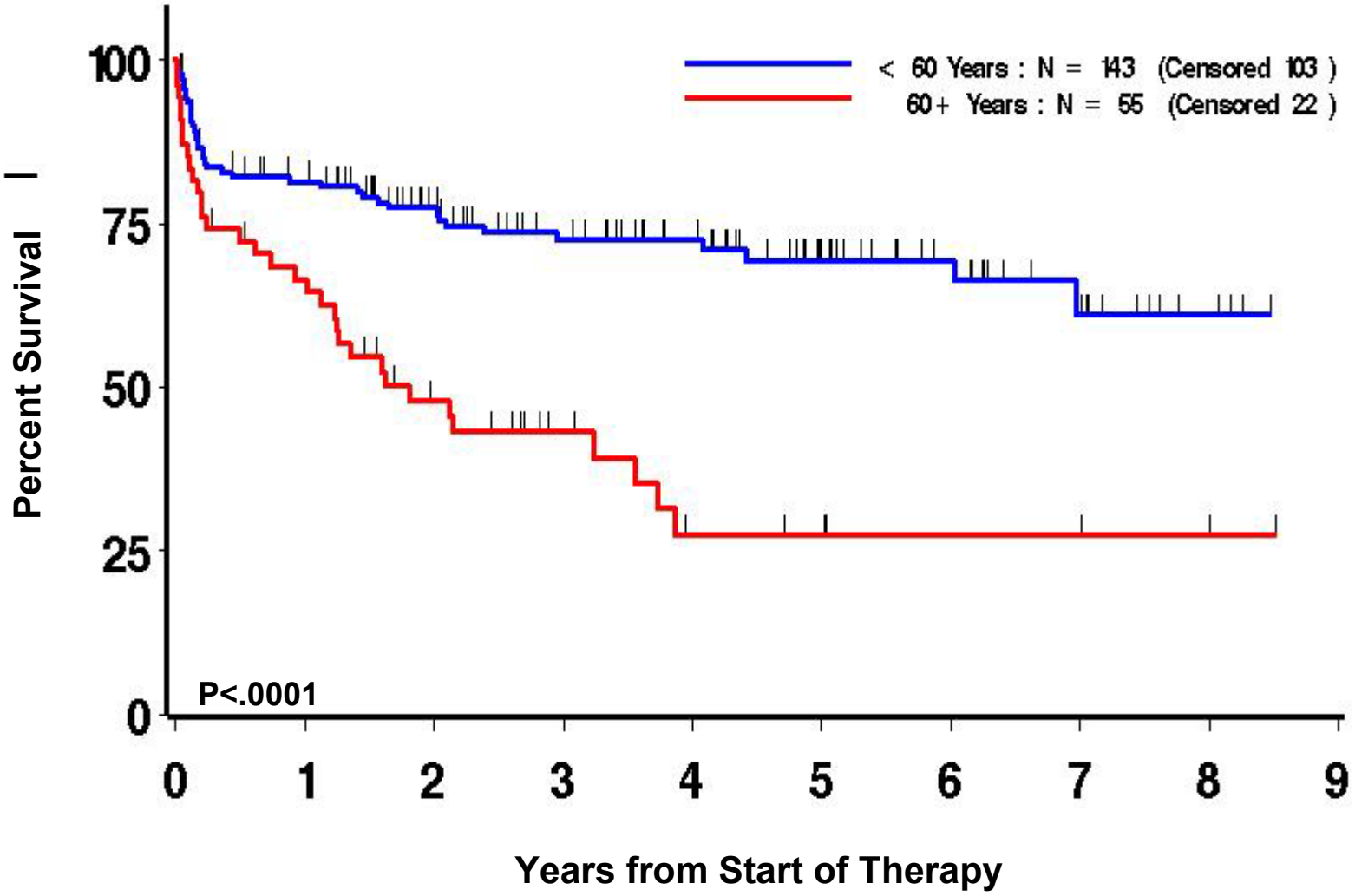
CR Patients



Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

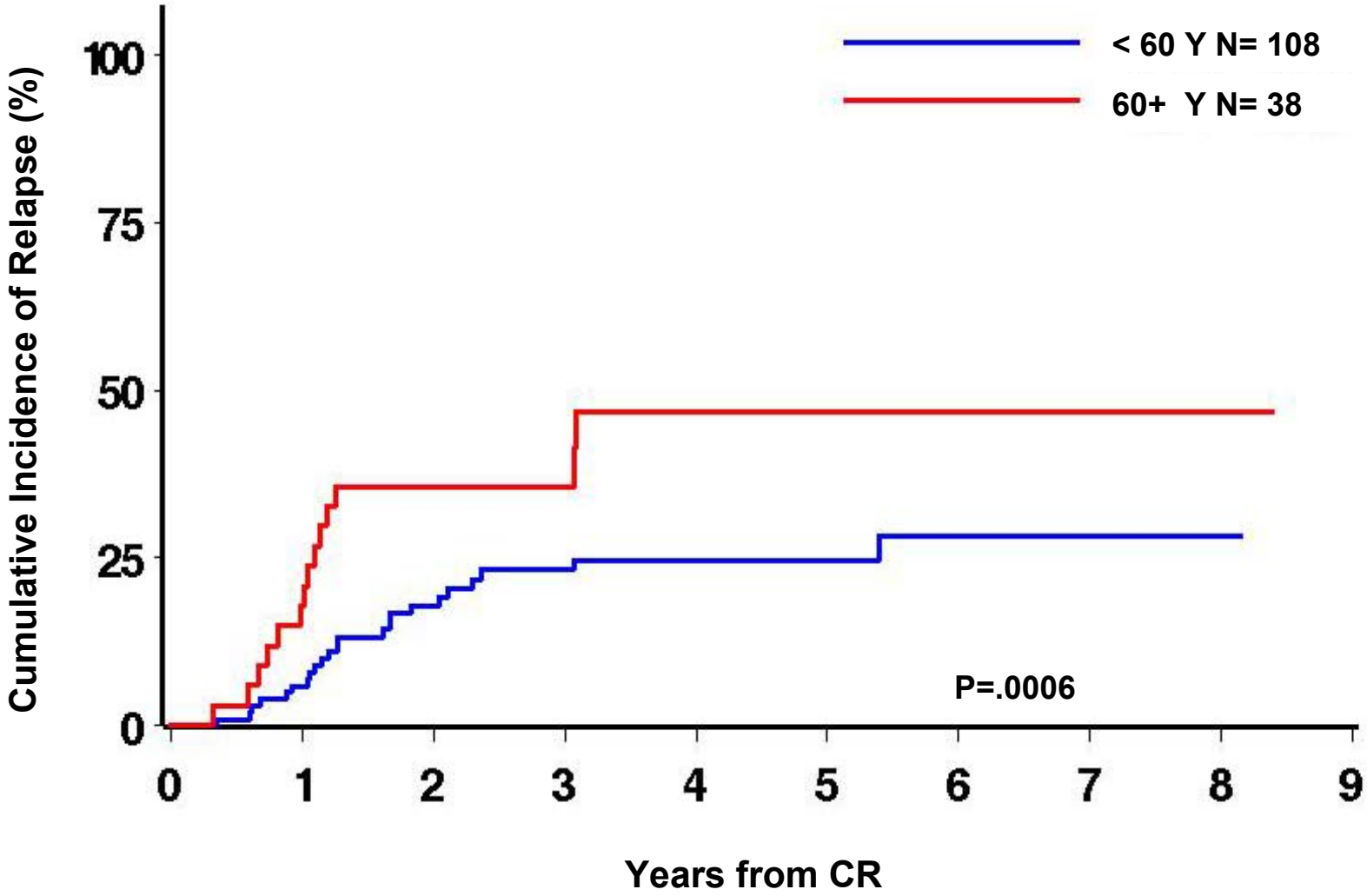

1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
P̂
0 1 2 3 4 5 6 7 8 9 10 11 12 13
years
A
<2 years .42, SE=.03 (N=222, 129 events)
2-<13 years .53, SE=.02 (N=463, 214 events)
13-<21 years .45, SE=.03 (N=276, 152 events)
21-<30 years .28, SE=.03 (N=220, 154 events)

Patients with CBF Leukemia



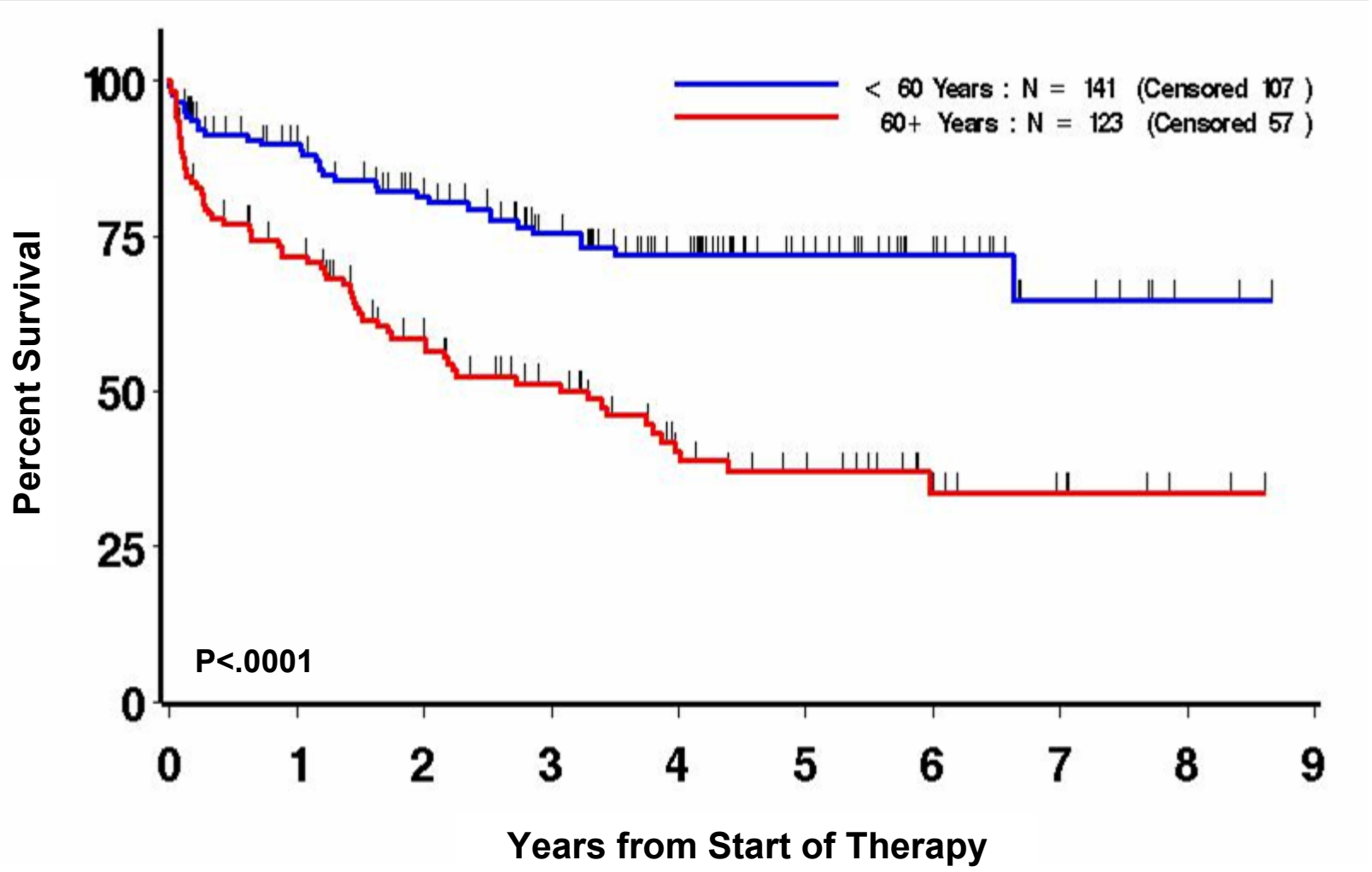
Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

CR Patients with CBF Leukemia



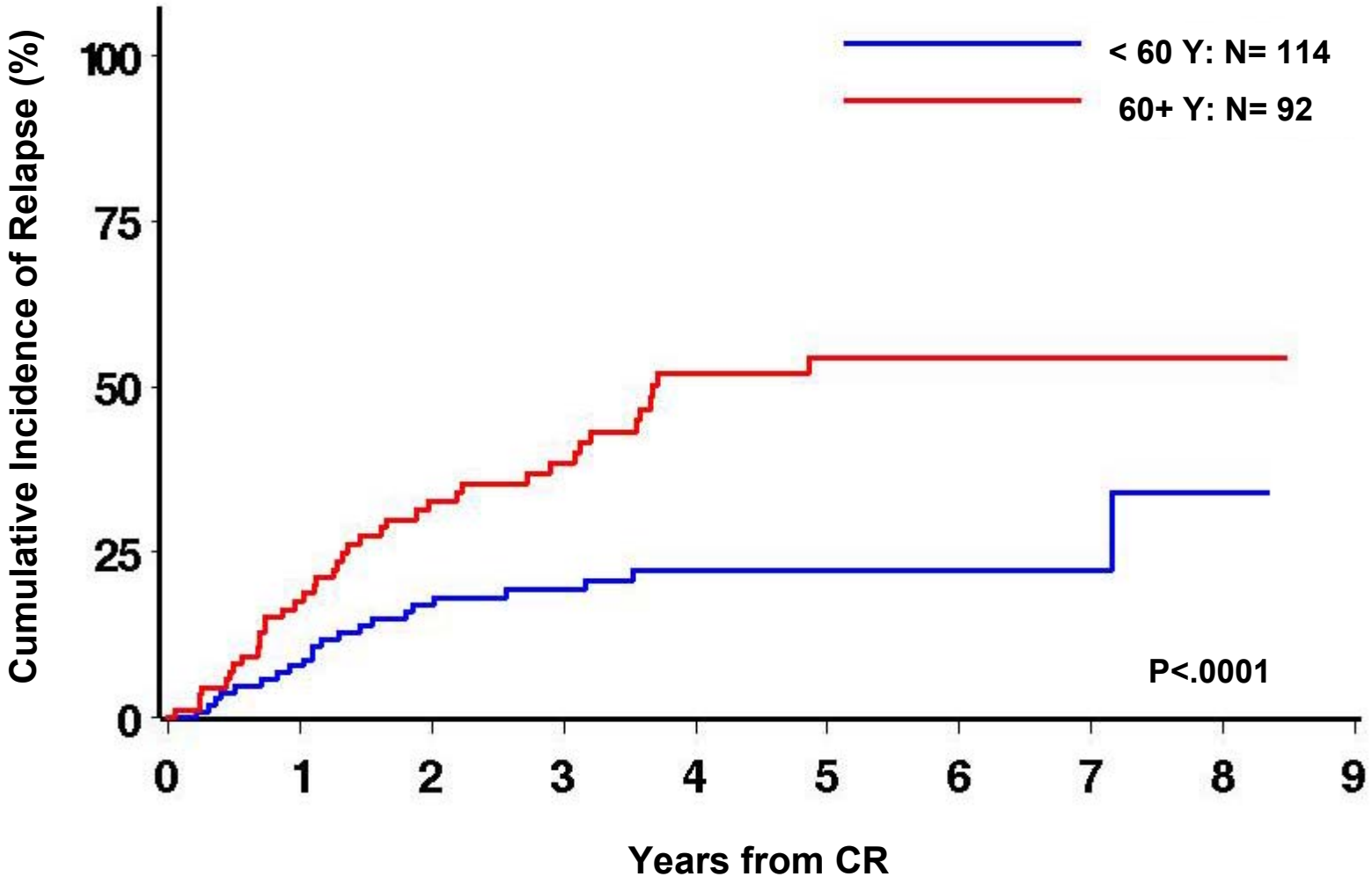
Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

Patients with Normal Cytogenetics and NPM1mut/FLT3-ITDneg



Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

CR Patients with Normal Cytogenetics and NPM1mut/FLT3-ITDneg



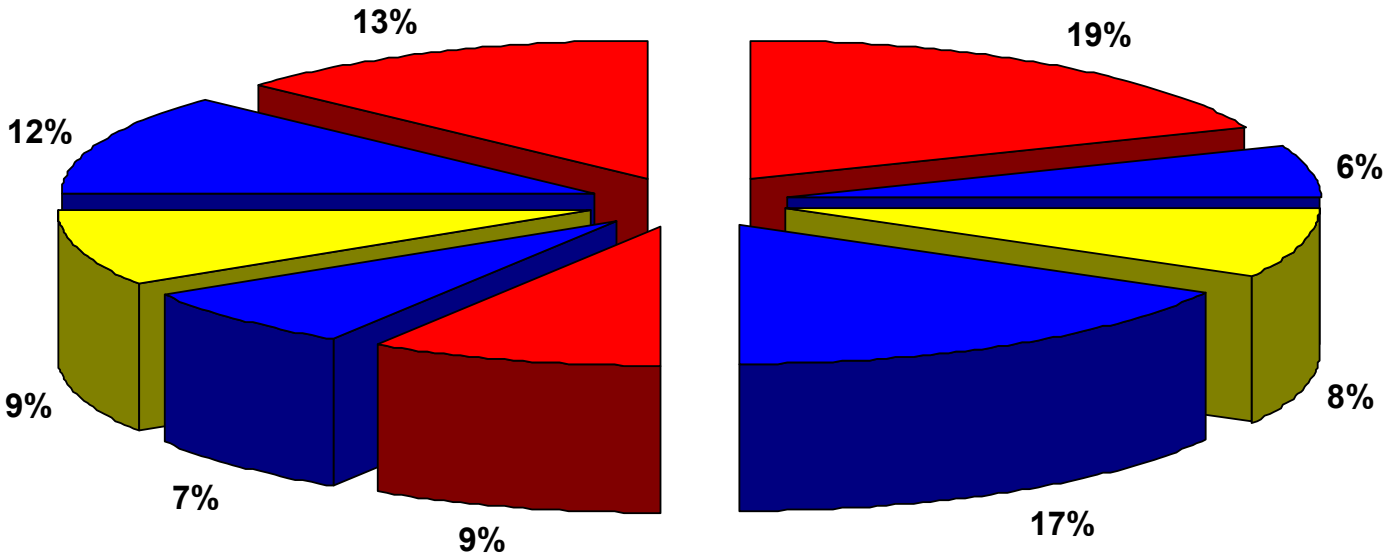
Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

Cytogenetic Groups

Mutations NPM1/FLT3

Age 60+

ABNORMAL CYTOGENETICS

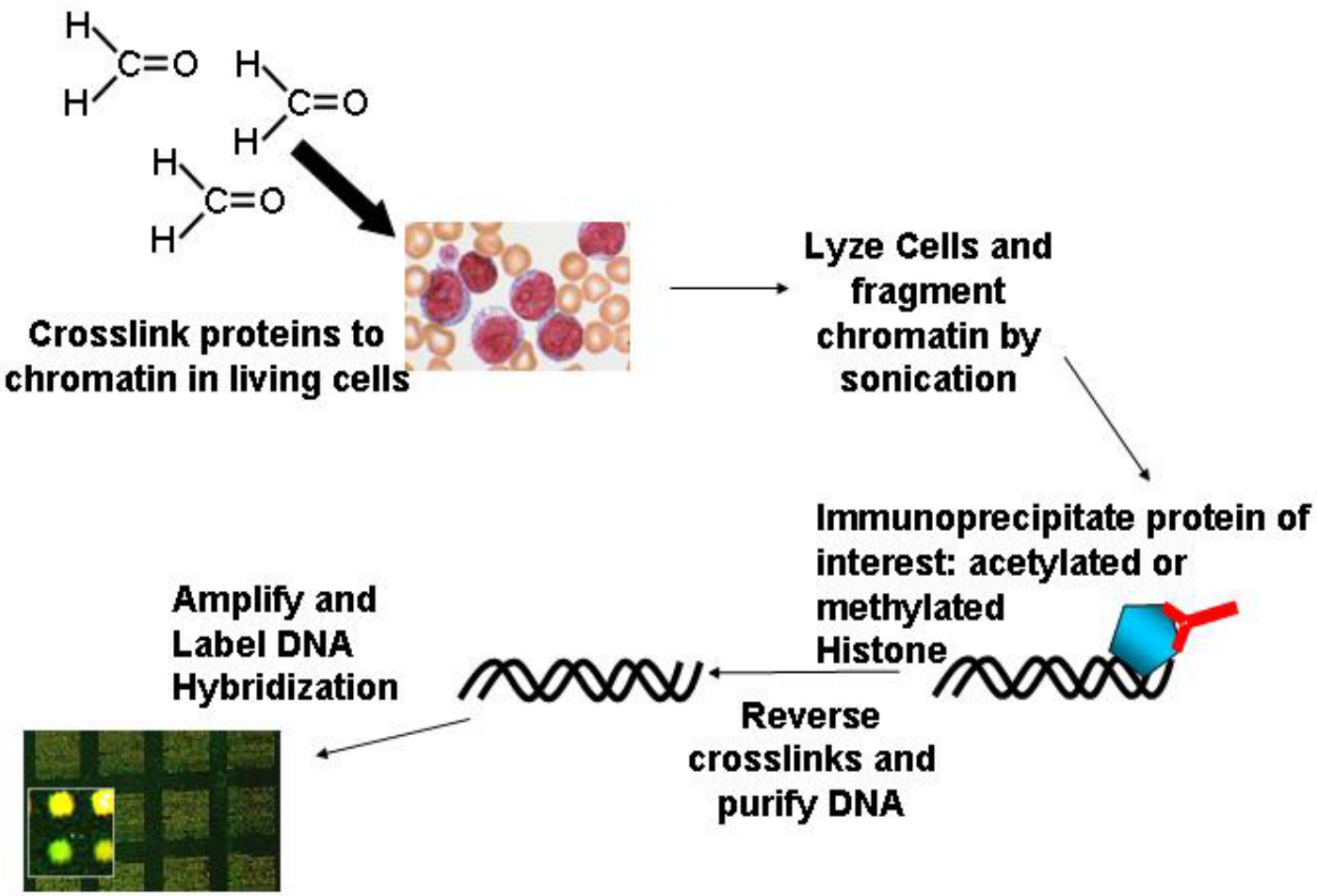


NORMAL CYTOGENETICS

Age < 60

favorable intermediate unfavorable

Principle of ChIP-Chip



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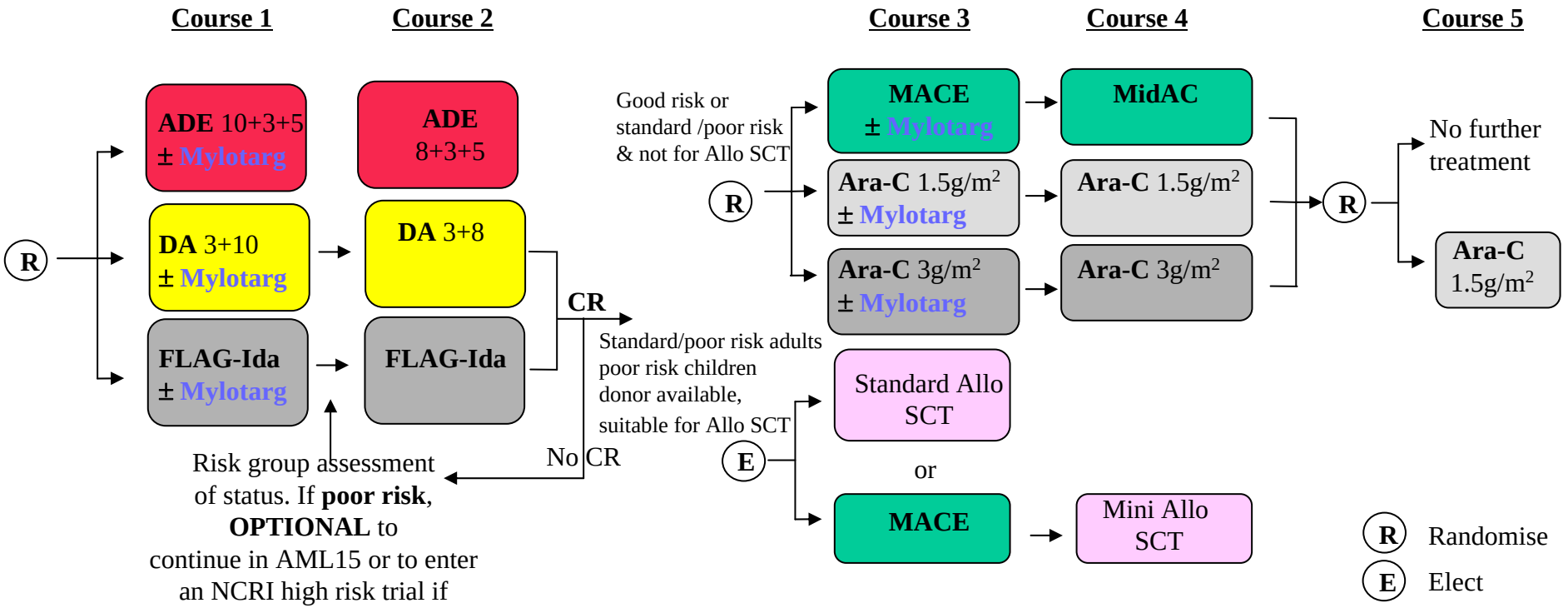
Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

Novel Approaches in AML

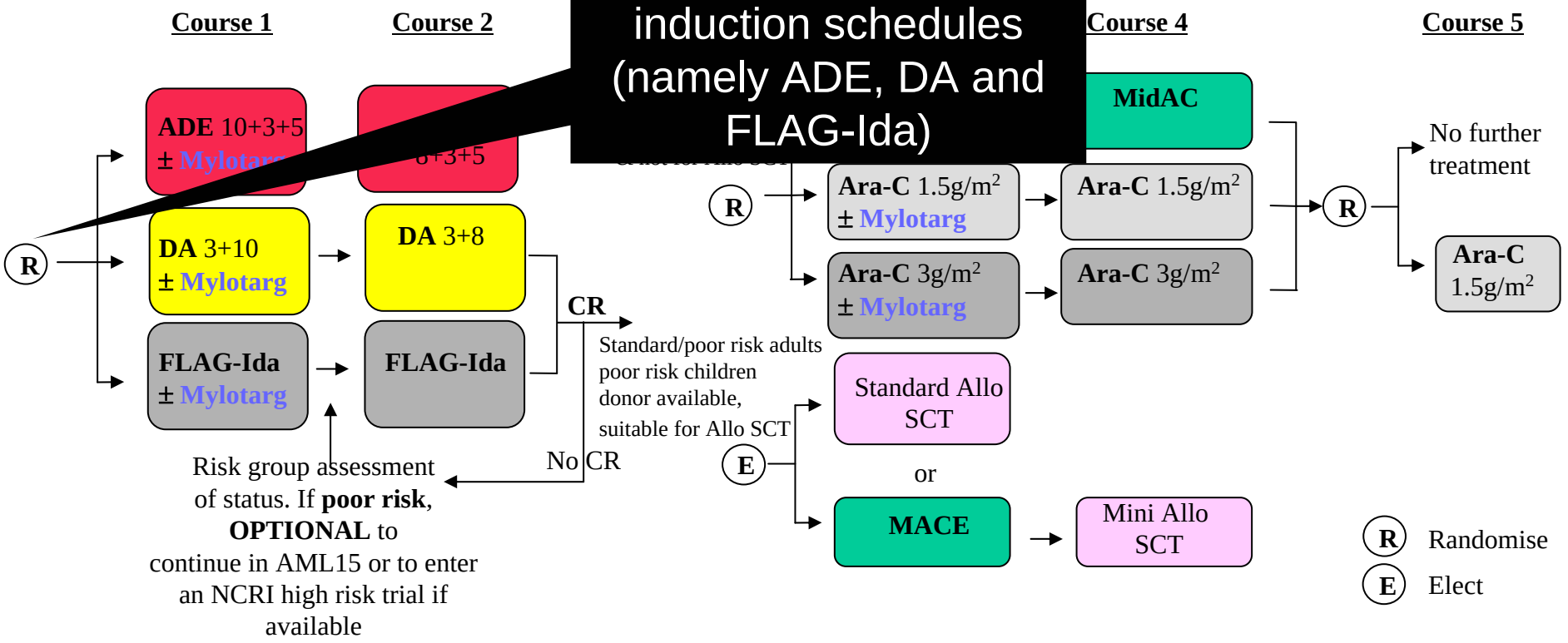
Targets	Approach
GvL target	Allo SCT (MRD, MUD)
RARA	ATRA
PML	Arsenic trioxide
BCR/ABL, c-kit	Imatinib, Dasatinib, Nilotinib
FLT3 (wild type and mutated)	Sorafenib, Midostaurin
Tyrosin Kinase	SU5416
Farnesyl-Transferase	Tipifarnib
DNA synthesis	Clofarabine
Histone deacetylation (HDAC)	Valproic acid
Hypermethylation (DNMT)	5-azacytidine, Decitabine
CD33	GO (Mylotarg)



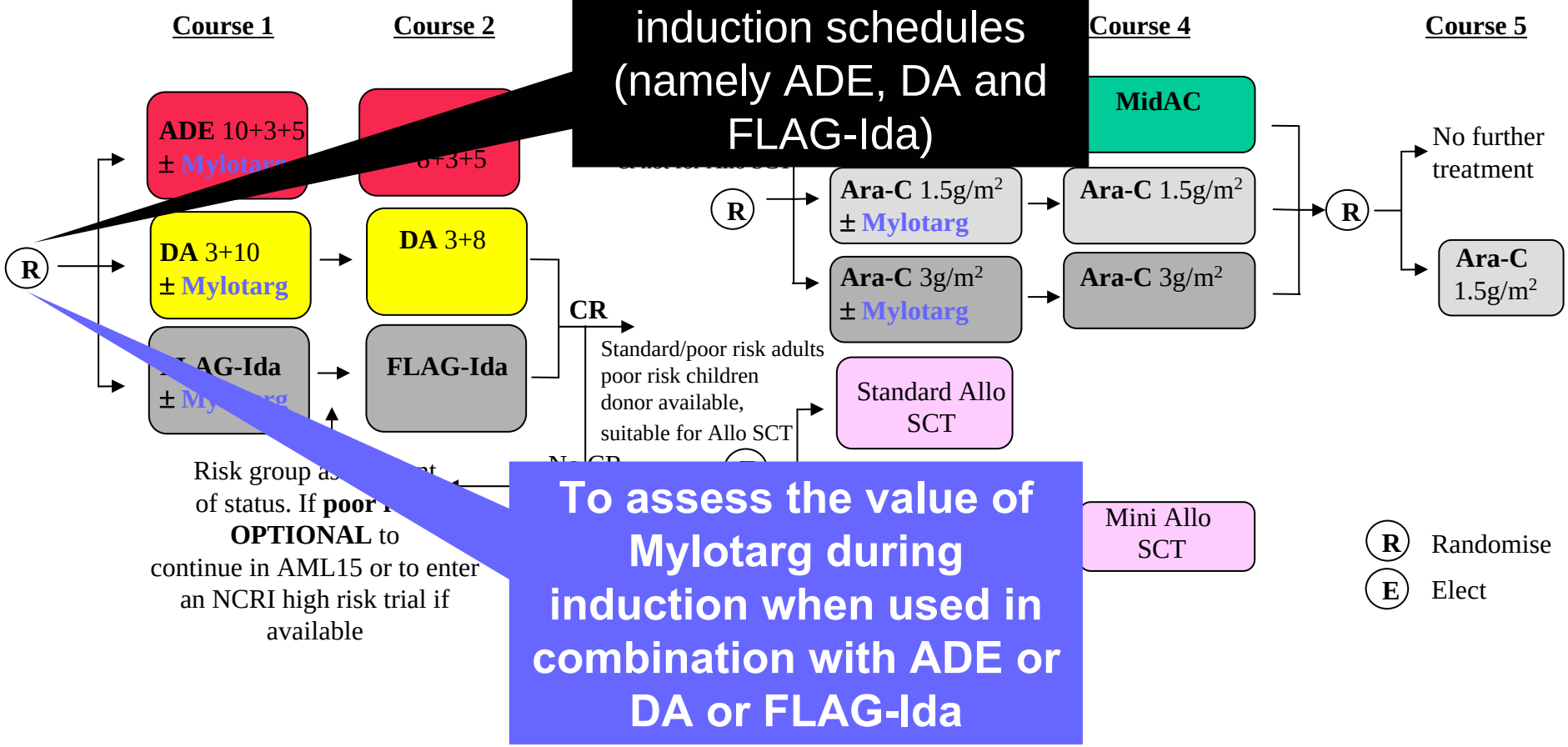
Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

From A. Burnett 2007

To compare three induction schedules (namely ADE, DA and FLAG-Ida)

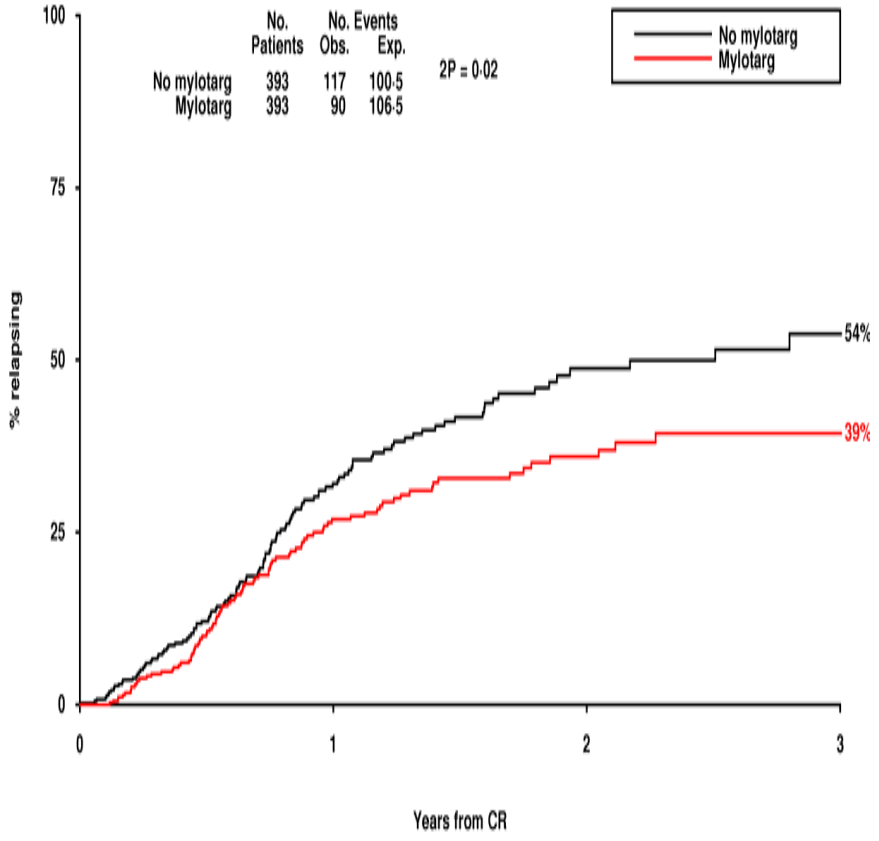


To compare three induction schedules (namely ADE, DA and FLAG-Ida)

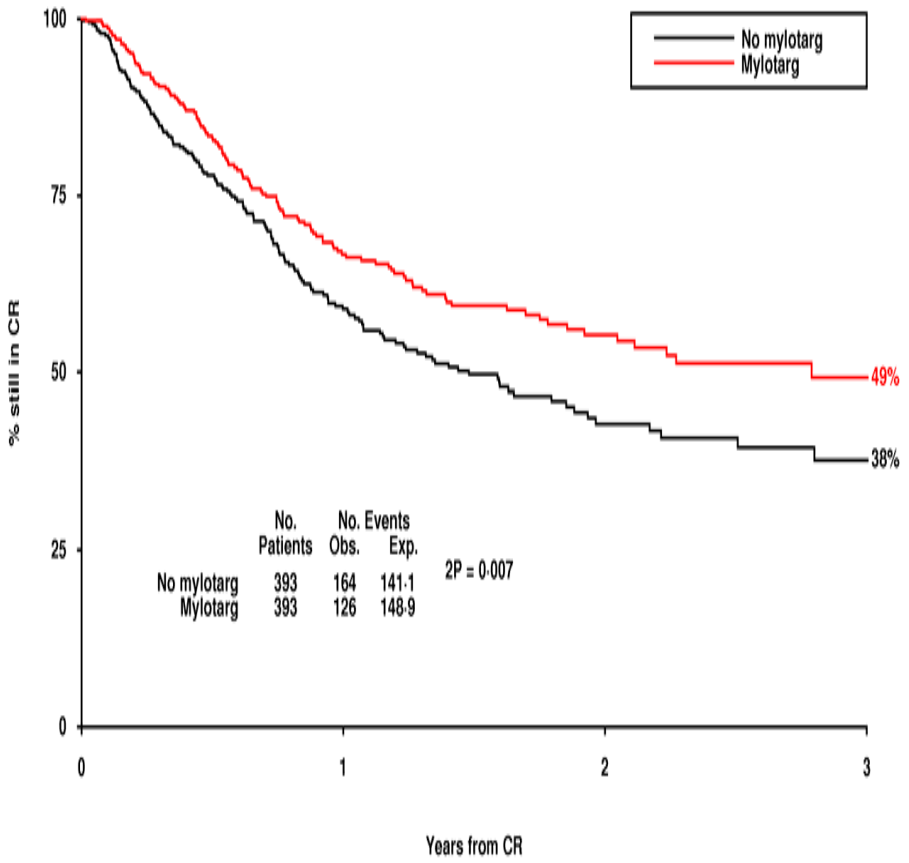


To assess the value of Mylotarg during induction when used in combination with ADE or DA or FLAG-Ida

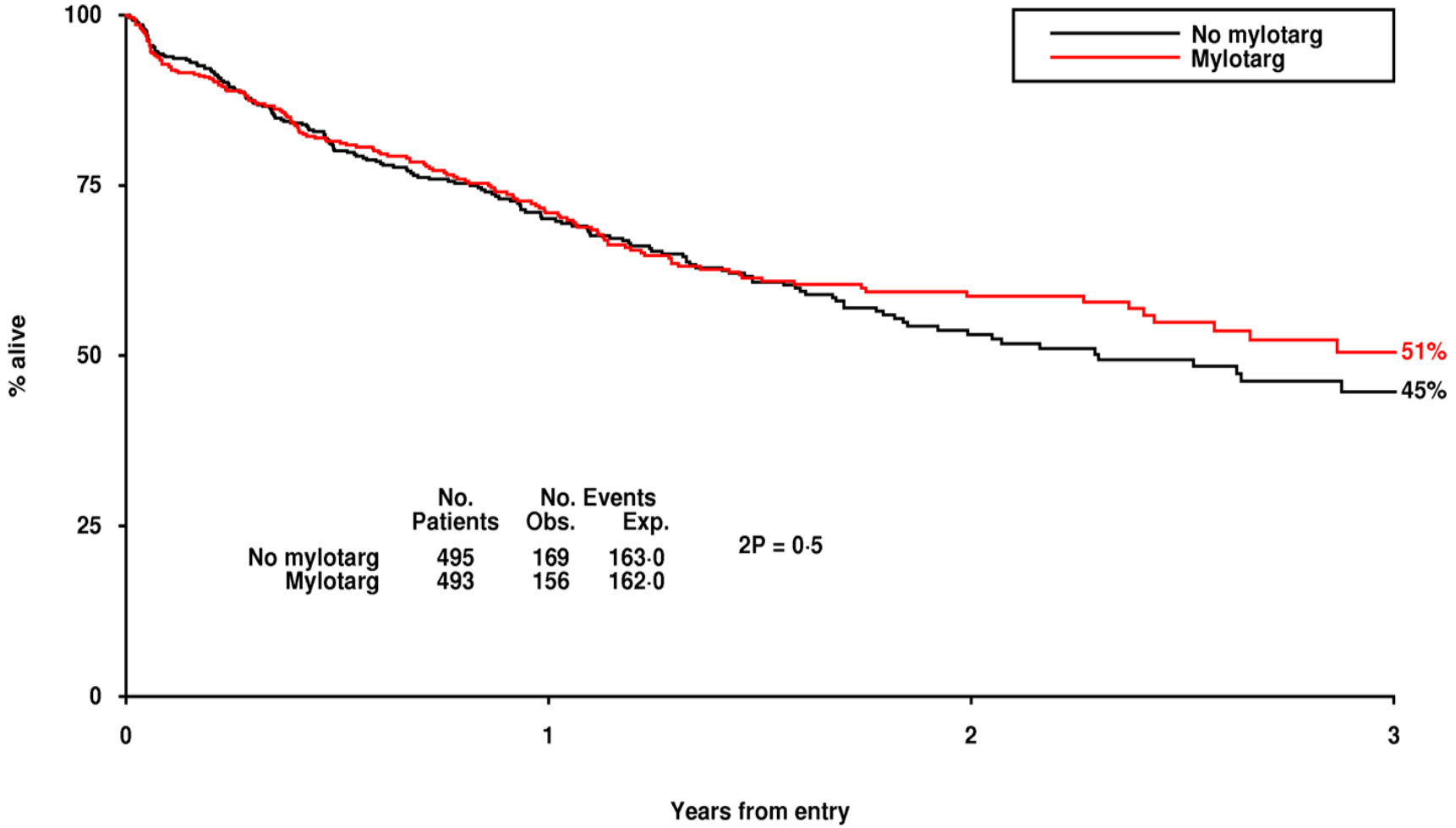
AML15: Relapse



AML15: Disease-free survival



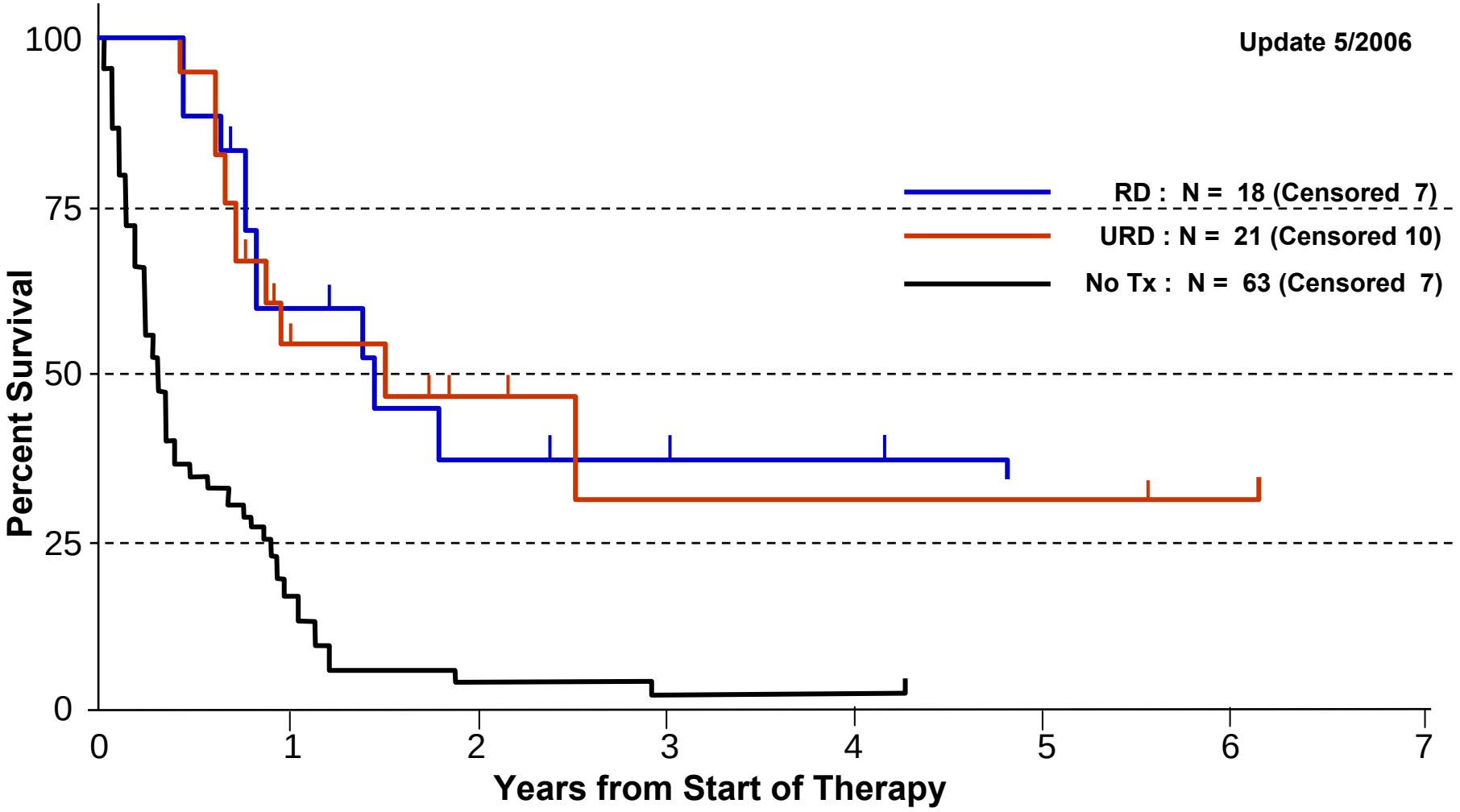
AML 15: Overall Survival



Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

AMLCG 99

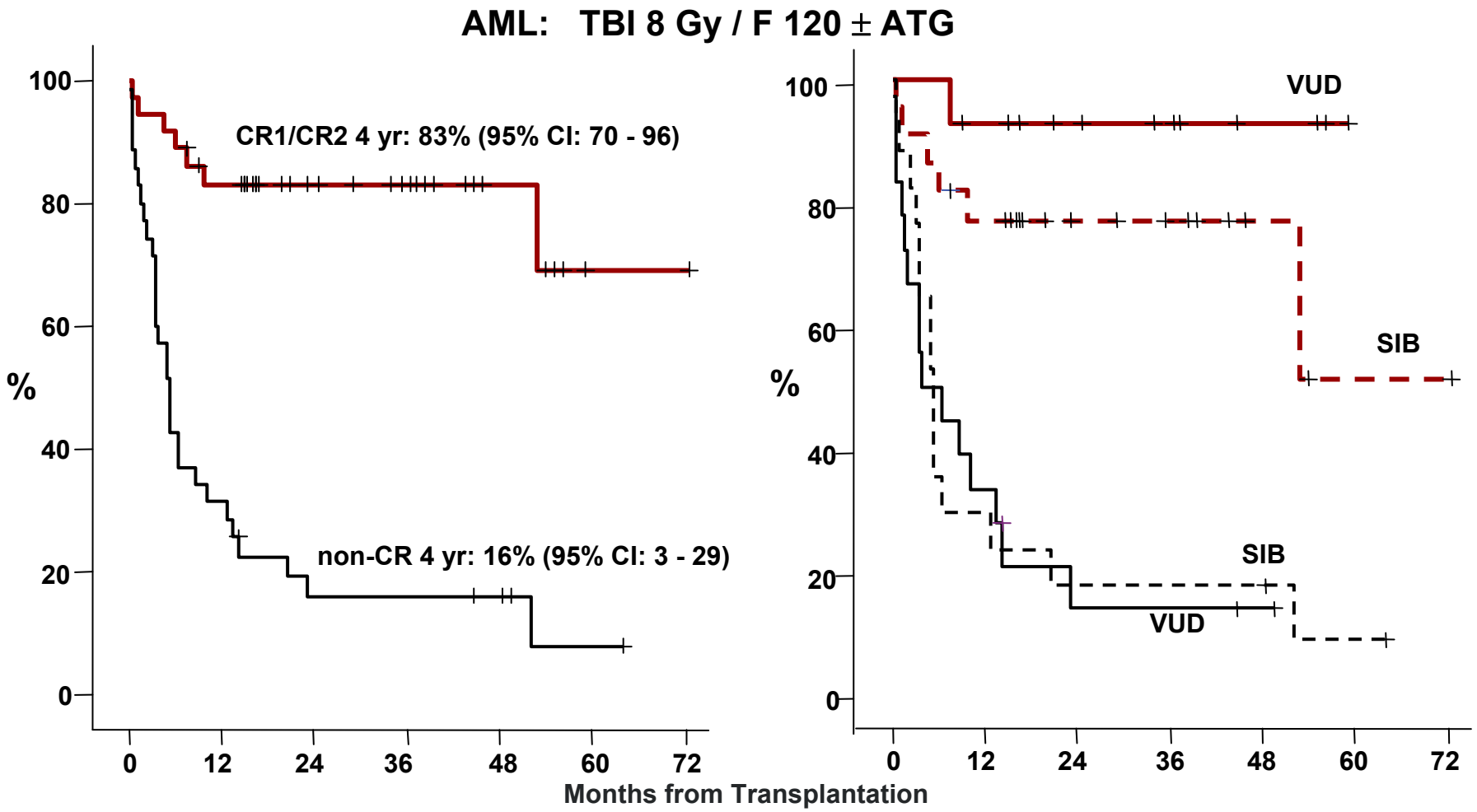
All Patients < 60 Years with Complex Karyotypic Abnormalities



Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

Prof.Dr.
Joachim Kienast

Related versus Unrelated Donors: Overall Survival



Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

M. Stelljes & J. Kienast et al. Blood 106: 3314-3321; 2005

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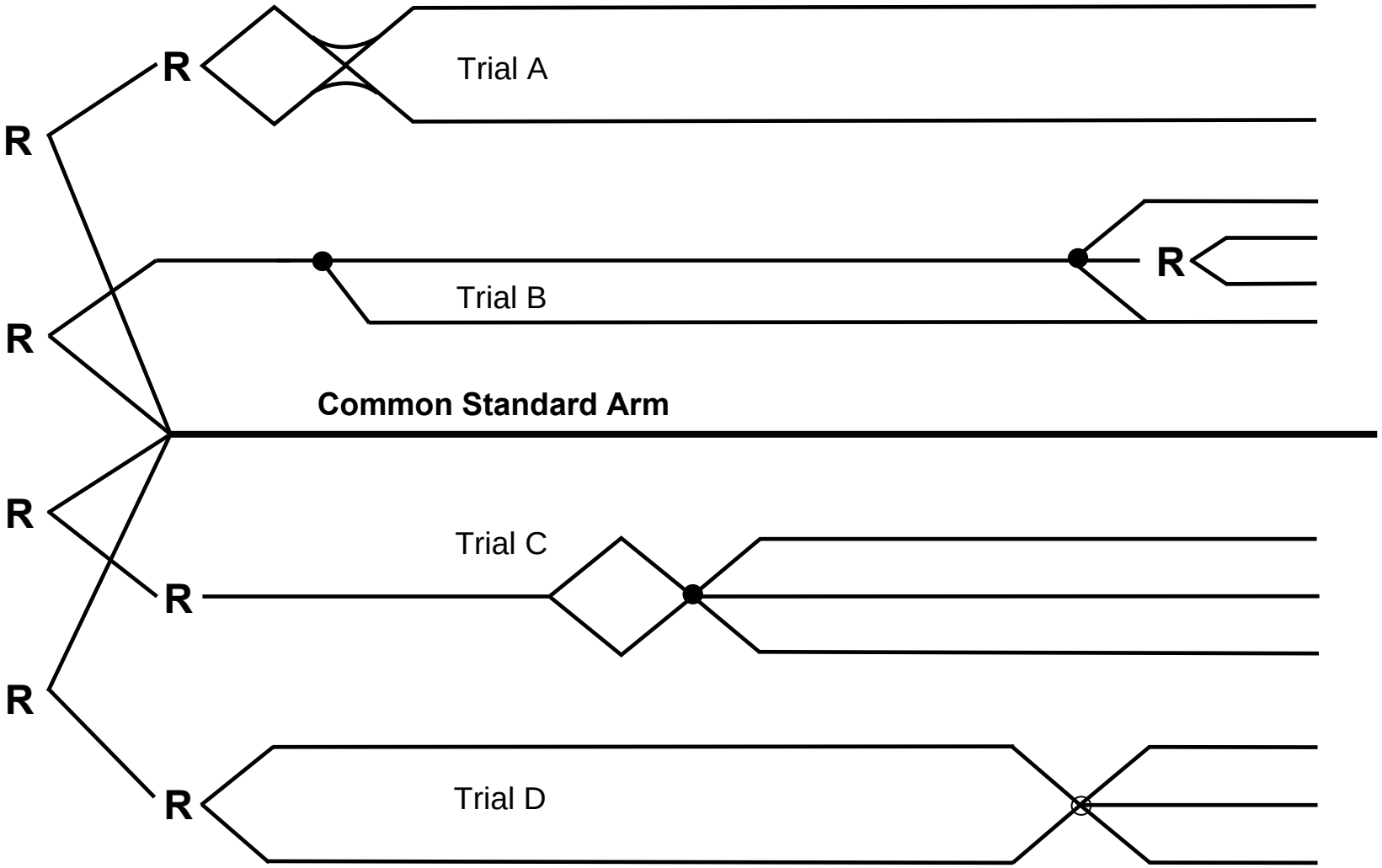
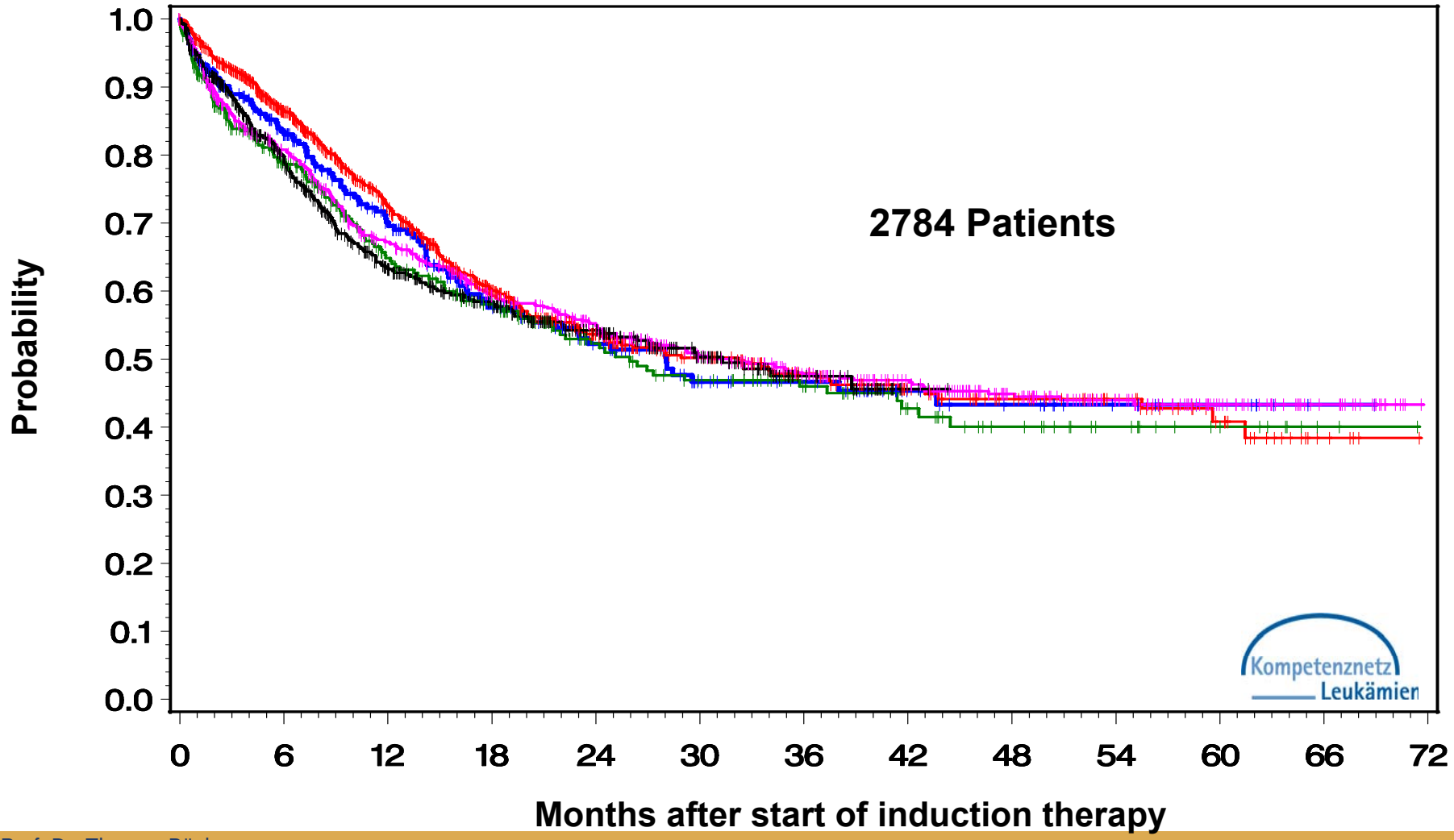
Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

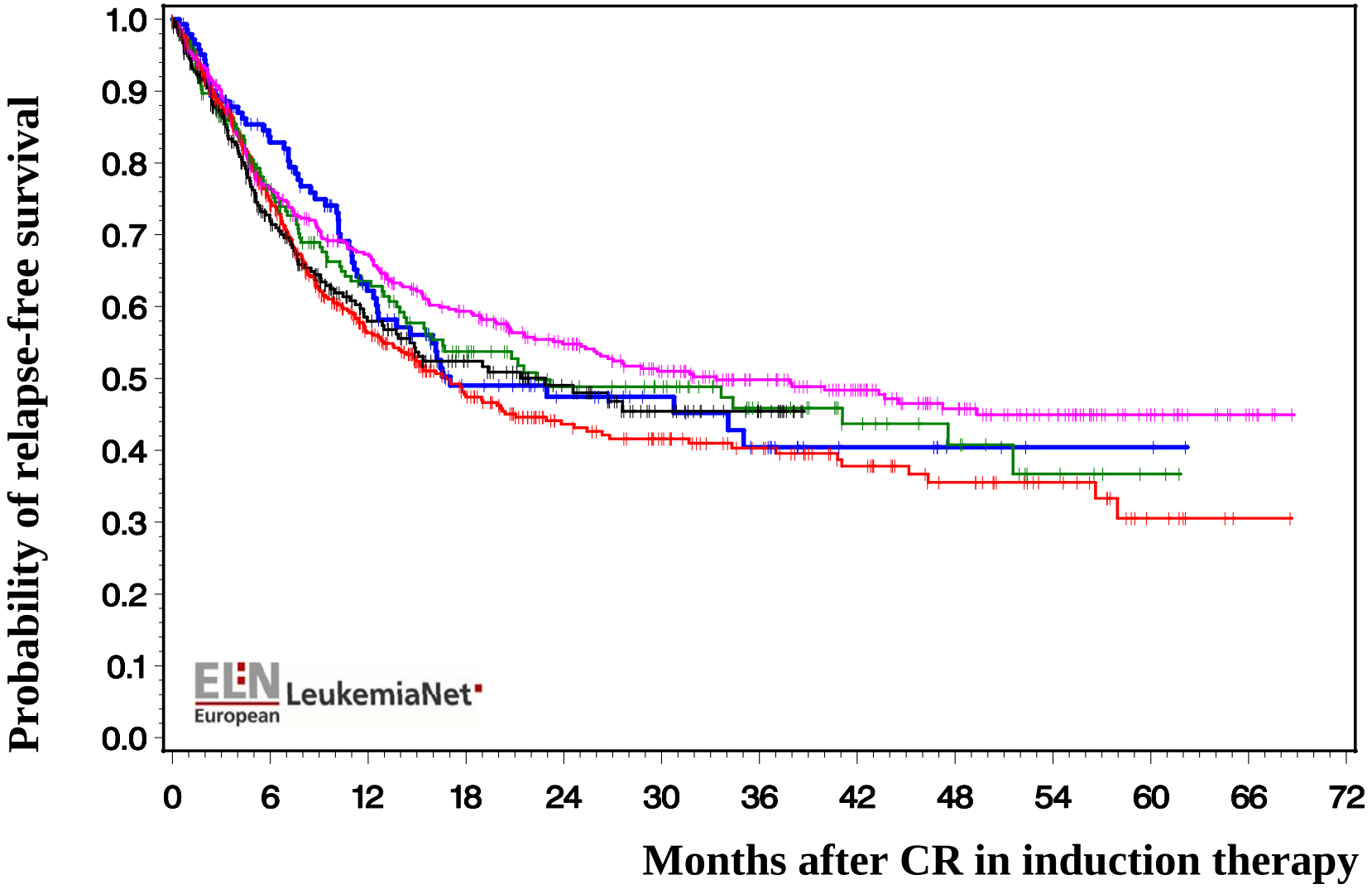


Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

Overall Survival



Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de



Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

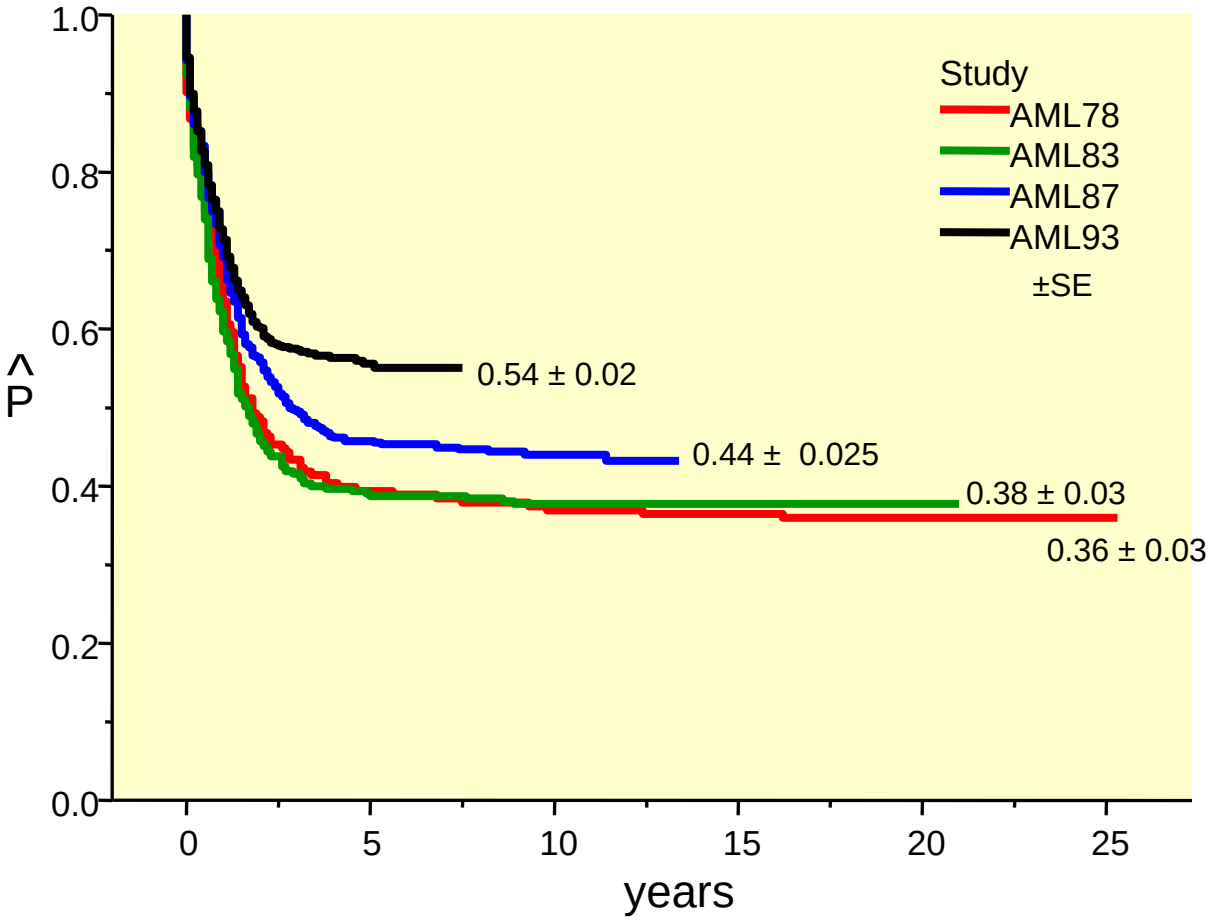
Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

Prof. Dr. Jörg Ritter

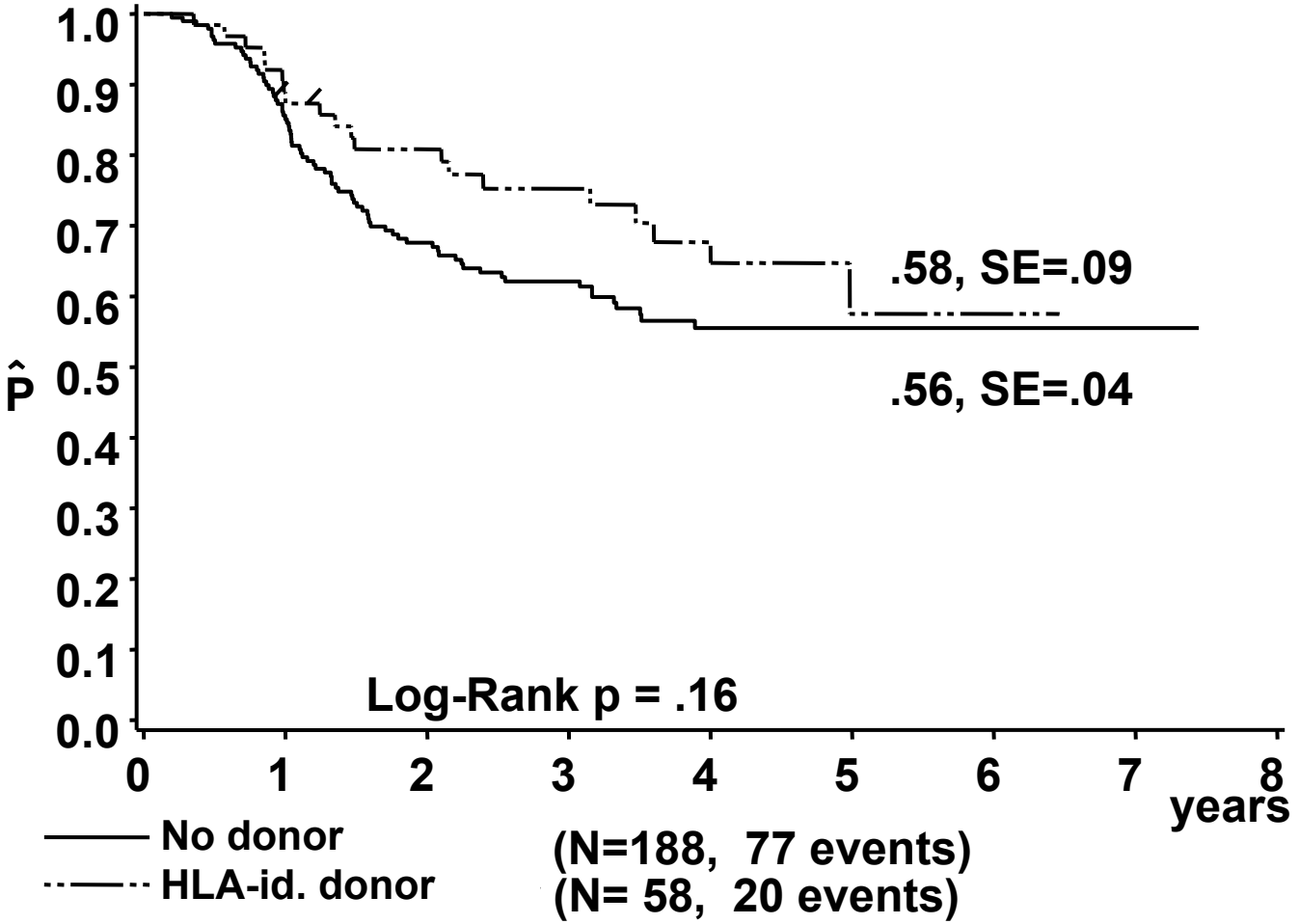
Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

AML-BFM Studies 78- 93 - event free survival-



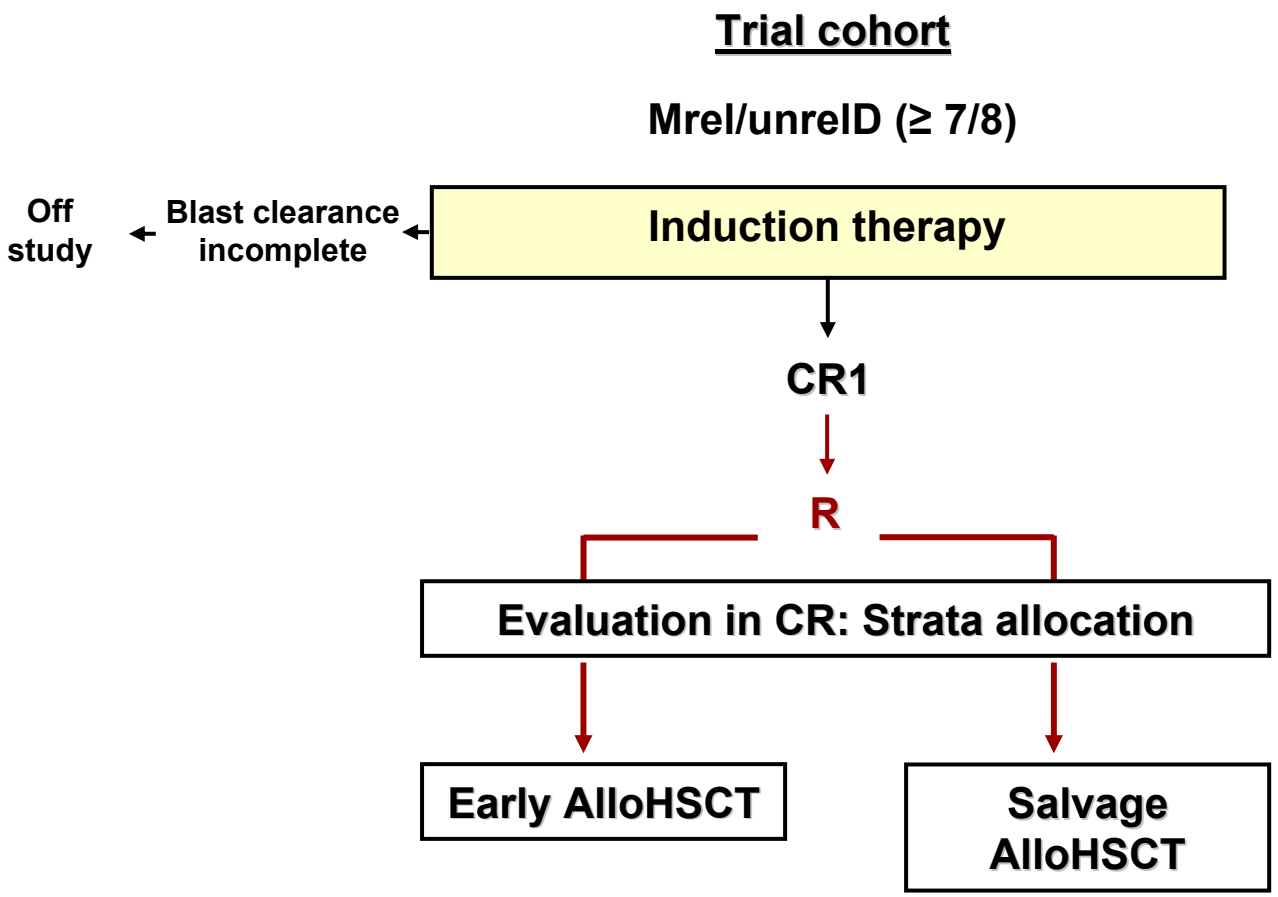
Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

AML-BFM 98 Intent-to-treat analysis overall- survival



Prof. Dr. Thomas Büchner
Dept. of Medicine, Hematology and Oncology
Email: buechnr@uni-muenster.de

CTSG ETAL-1 Trial



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