



Relative Risk (Sokal & Hasford): Relationship with Treatment Results

Michele Baccarani





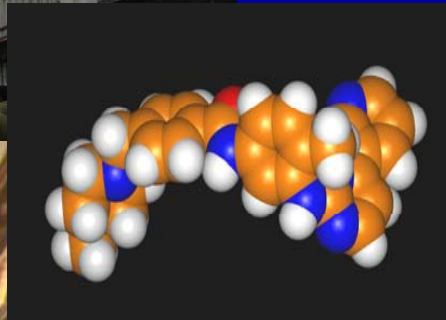
European LeukemiaNet

**EVOLVING CONCEPTS IN THE
MANAGEMENT OF CHRONIC
MYELOID LEUKEMIA**

VENICE 8 – 9 MAY 2006

Disease risk (Sokal and Hasford)

Michele Baccarani



- 1975 JACQUILLAT et al NOUV REV FR D'HEMAT: 15; 229 - 240**
- 1981 TURA et al BR J HAEMATOL: 47; 105 - 119**
- 1981 GOMEZ et al CANCER: 47; 2470 - 2477**
- 1981 OGUMA et al CANCER: 50; 2928 - 2934**
- 1982 CERVANTES et al BLOOD: 60; 1298 - 1304**
- 1985 KANTARJIAN et al BLOOD: 66; 1326 - 1335**
- 1990 KANTARJIAN et al AM J MED: 88; 1 - 8**

1984 **PROGNOSTIC DISCRIMINATION IN “GOOD RISK”
CHRONIC GRANULOCYTTIC LEUKEMIA.**

**- J.E. SOKAL, E.B. COX, M. BACCARANI, S. TURA,
G.A. GOMEZ et al, BLOOD 1984; 63: 789 - 799**

1998 **A NEW PROGNOSTIC SCORE FOR SURVIVAL OF
PATIENTS WITH CHRONIC MYELOID LEUKEMIA
TREATED WITH INTERFERON ALFA.**

**J. HASFORD, M. PFIRRMANN, R. HEHLMANN, N.C.
- ALLAN, M. BACCARANI et al, J NATL CANCER INST
1998; 90: 850 - 858**

	SOKAL⁽¹⁾	EUROPEAN⁽²⁾
AGE (YEARS)	0.116 (AGE-43.4)	0.666 WHEN AGE \geq50
*SPLEEN (Cm)	0.0345 (SPLEEN -7.51)	0.042 x SPLEEN
PLATELET COUNT (x10⁹/L)	0.188 [(PLT:700)²-0.563]	1.0956 WHEN PLT\geq1500
BLOOD MYELOBLASTS (%)	0.0887 (MB-2.10)	0.0584 x MB
BLOOD BASOPHILS (%)	/	0.20399 WHEN BASO >3%
BLOOD EOSINOPHILS (%)	/	0.0413Xeos
RELATIVE RISK	EXPONENTIAL OF THE TOTAL	TOTAL X 1000
LOW RISK	< 0.8	\leq 780
INTERMEDIATE RISK	0.8 – 1.2	781 – 1480
HIGH RISK	> 1.2	> 1480

* MAXIMUM DISTANCE FROM COSTAL MARGIN

(1) SOKAL et al. BLOOD 1984; 63: 789-799 (2) HASFORD et al. JNCI 1998; 90: 850-858

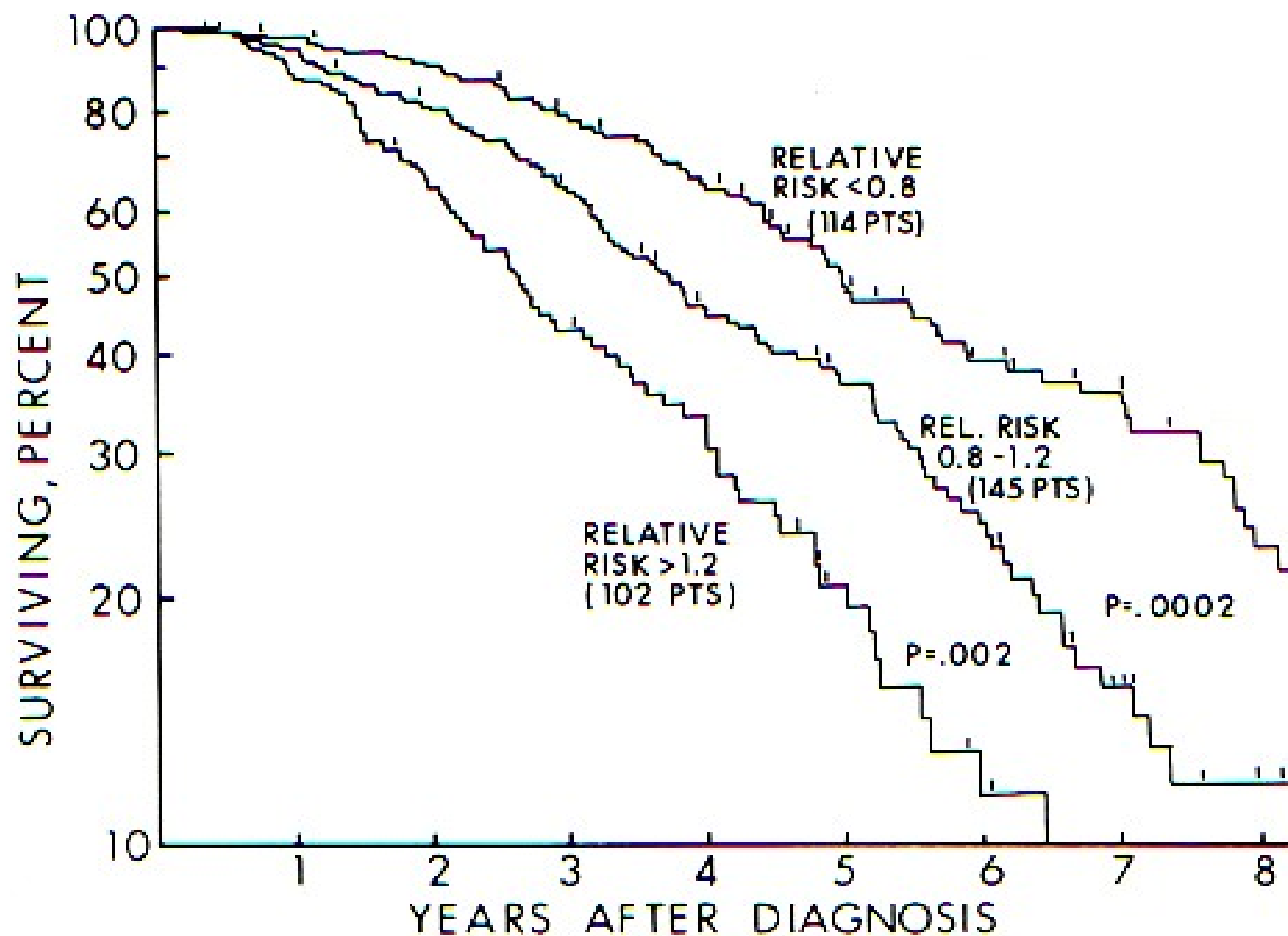
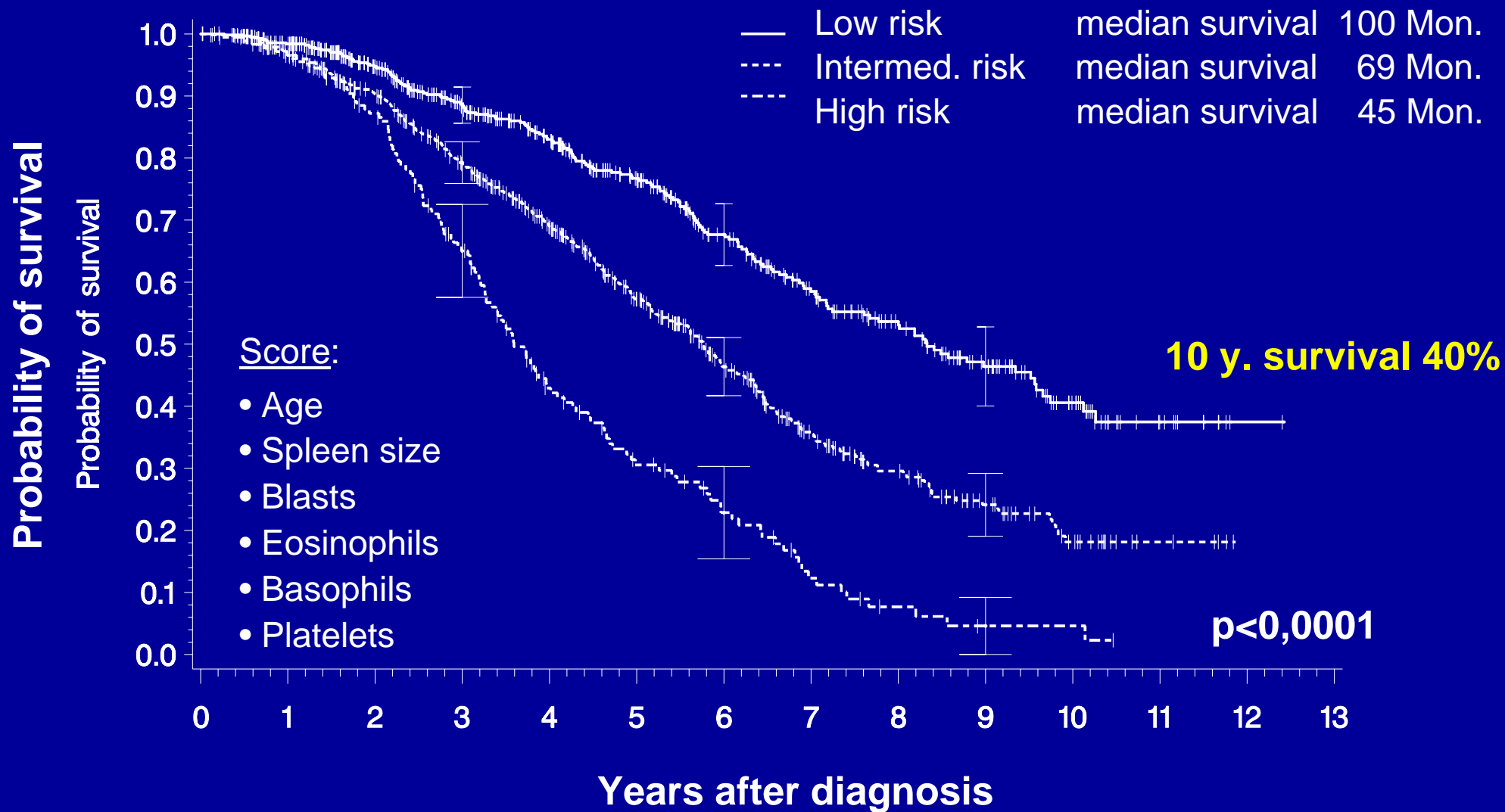


Fig. 7. Survival according to relative risk (Cox model analysis) for 361 patients in the "training" population.

New Prognostic Score



	SOKAL 1984 (INTERNATIONAL)	HASFORD 1998 (EUROPEAN)
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No. OF SERIES	6	14
No. OF PATIENTS	813	1303
EUROPE	435	1228
USA	378	0
YEARS OF DIAGNOSIS	1962-1981	1985-1996
MEDIAN AGE	43	49
TREATMENT	CONVENTIONAL CHEMOTHERAPY	IFNα-BASED REGIMES

	SOKAL (1984)	HASFORD (1998)
PTS. DISTRIBUTION		
- LOW RISK	48%	59%
- INT RISK	29%	32%
- HIGH RISK	23%	9%
MEDIAN SURVIVAL (mo)		
- LOW RISK	105	105
- INT RISK	76	65
- HIGH RISK	45	45
10-YEAR SURVIVAL		
- LOW RISK	34%	37%
- INT RISK	28%	16%
- HIGH RISK	8%	0

SOKAL FORMULATION WAS DERIVED FROM PATIENTS TREATED WITH CONVENTIONAL CHEMOTHERAPY (1962 – 1981)

HASFORD FORMULATION WAS DERIVED FROM PATIENTS TREATED WITH IFN α - BASED REGIMES (1985 – 1996)

NEITHER FORMULATIONS APPLY TO PATIENTS SUBMITTED TO ALLOGENEIC STEM CELL TRANSPLANTATION

DO THEY APPLY TO PATIENTS TREATED WITH IMATINIB?

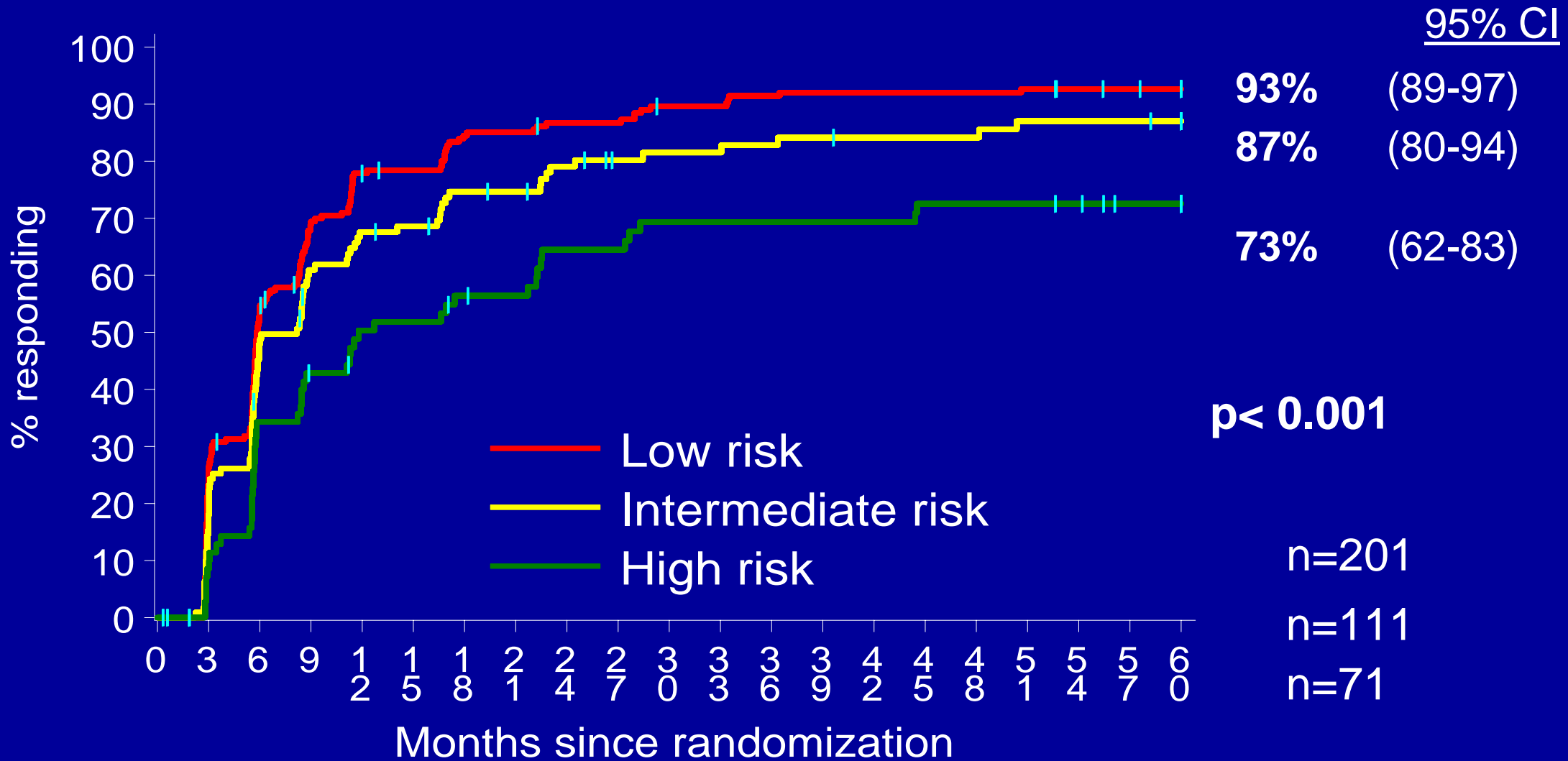
COMPLETE CYTOGENETIC RESPONSE

SOKAL RISK	LOW	INTERM.	HIGH
ITALIAN MULTICENTER STUDY, 77 PTS, 400 MG, 6 MONTHS ⁽¹⁾	70%	41%	8%
IRIS STUDY, 383 PTS, 400 MG			
- 12 MONTHS ⁽²⁾	76%	67%	49%
- 42 MONTHS ⁽³⁾	91%	84%	69%
HOUSTON STUDY, 187 PTS, 400-800 MG, OVERALL RESPONSE	84%	85%	69%

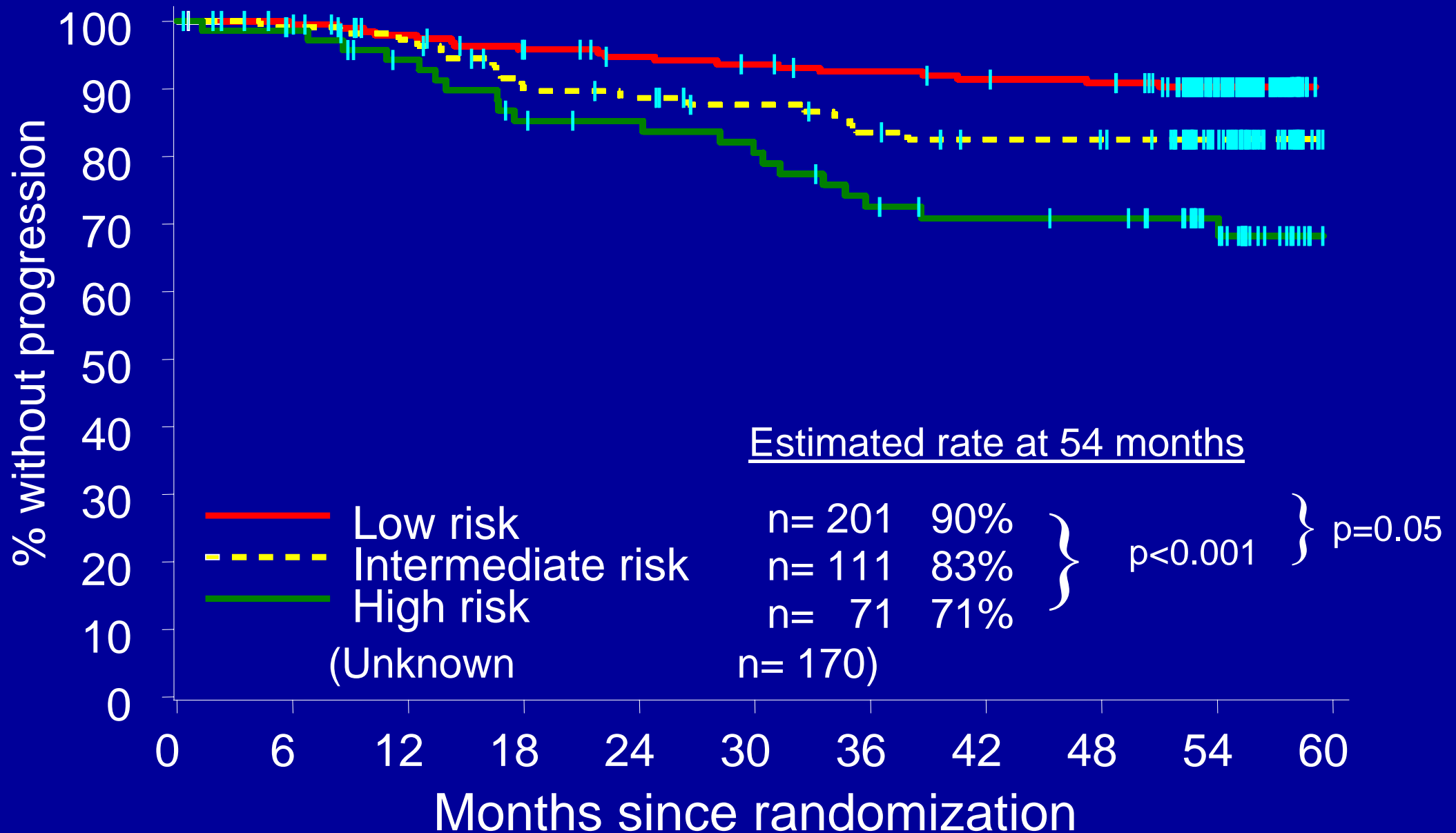
(1) ROSTI et al, HAEMATOLOGICA 2003, 88: 256-259 (2) HUGHES et al, NEJM 2003; 349: 1421-1432

(3) GUILHOT et al, BLOOD 2004; 104: 10a (ASH 2004) (4) SIMONSSON et al, BLOOD 2005; 106: 52a (ASH 2005)

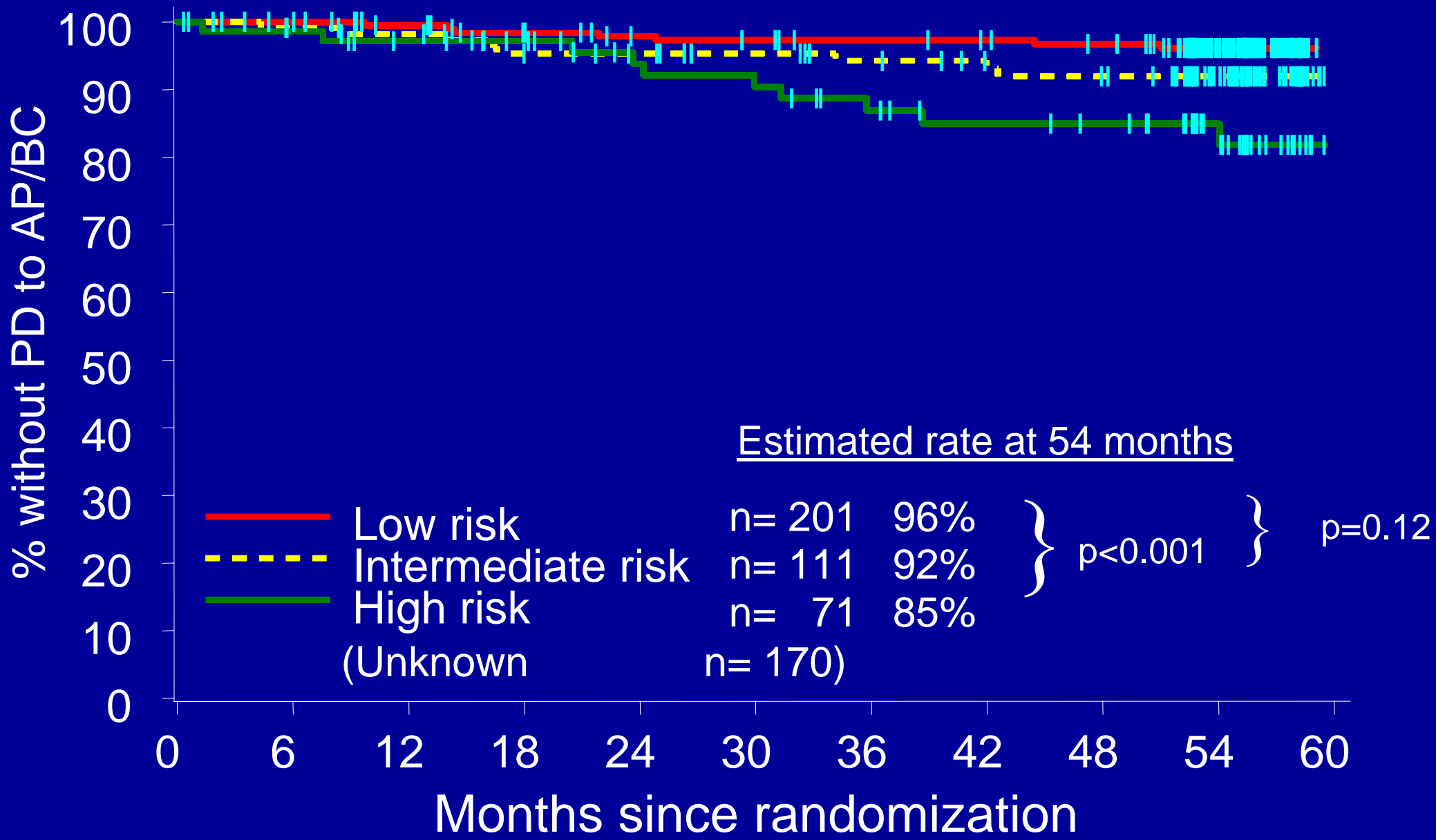
Estimated CCyR to First-line Imatinib by Sokal Group



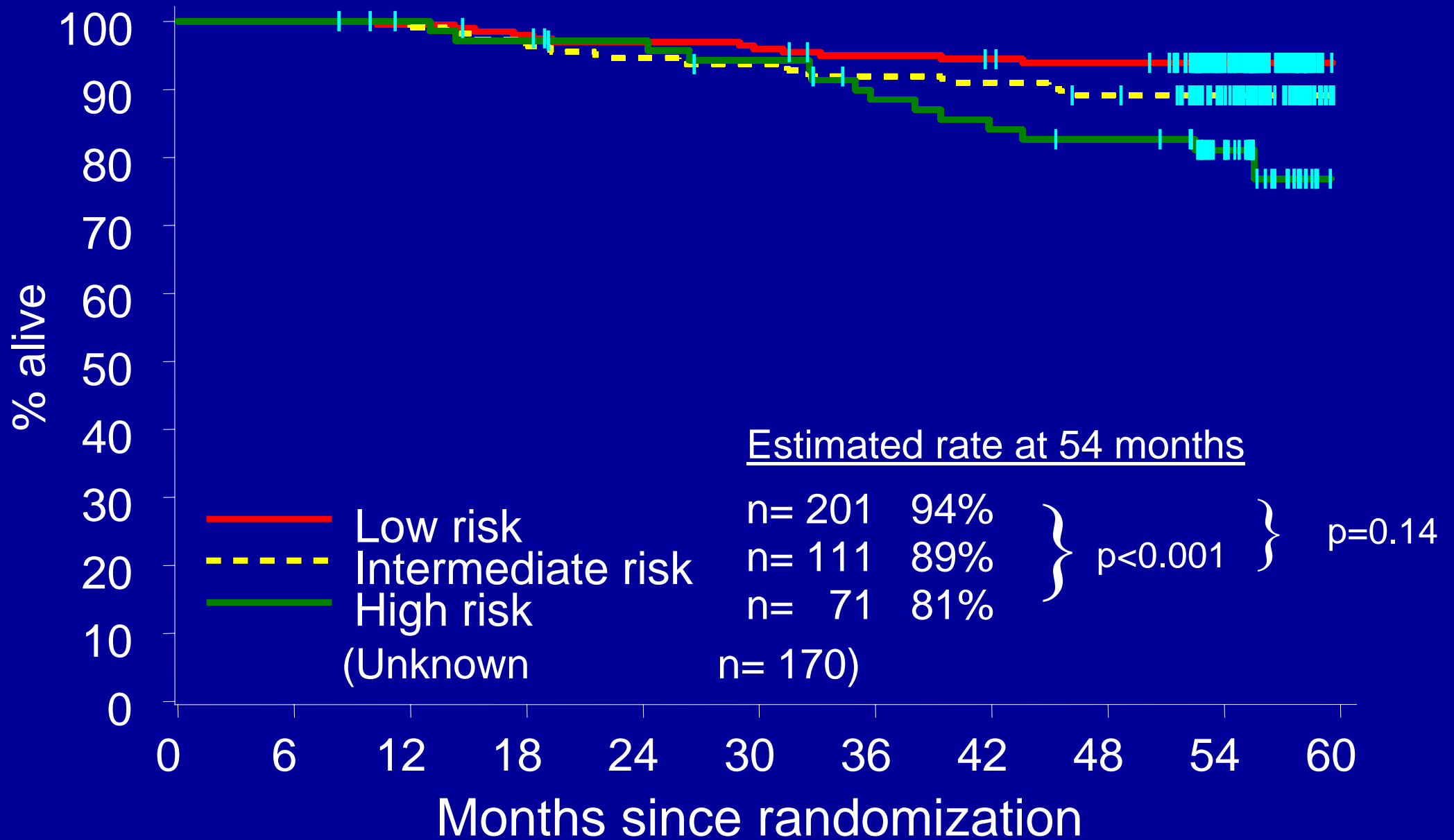
Progression-free Survival by Sokal Group



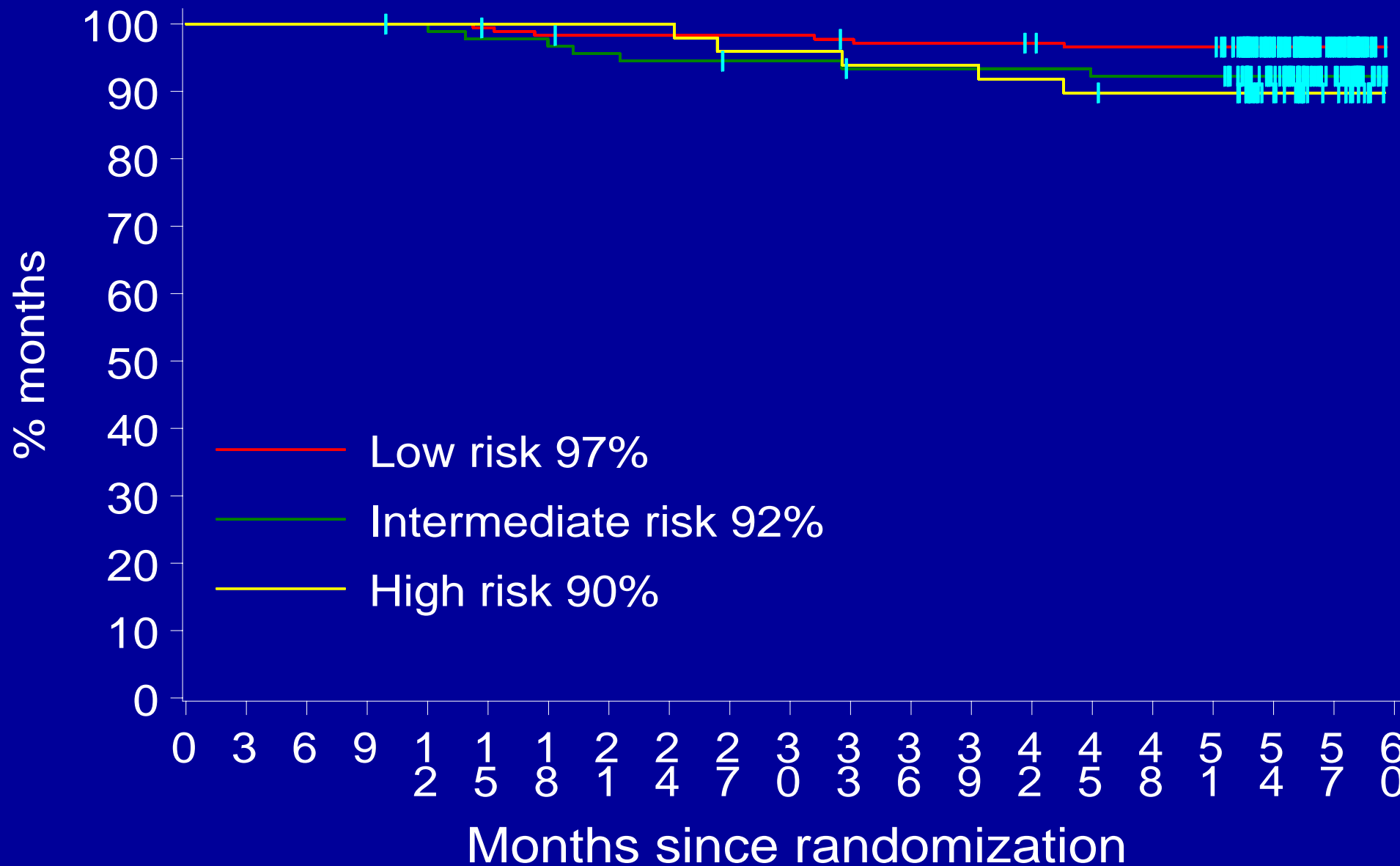
Survival without AP/BC by Sokal Group



Overall Survival by Sokal Group



Survival by Sokal Score given by CCyR Firstline Imatinib



CANDIDATE (PUTATIVE) BIOLOGIC PROGNOSTIC FACTORS

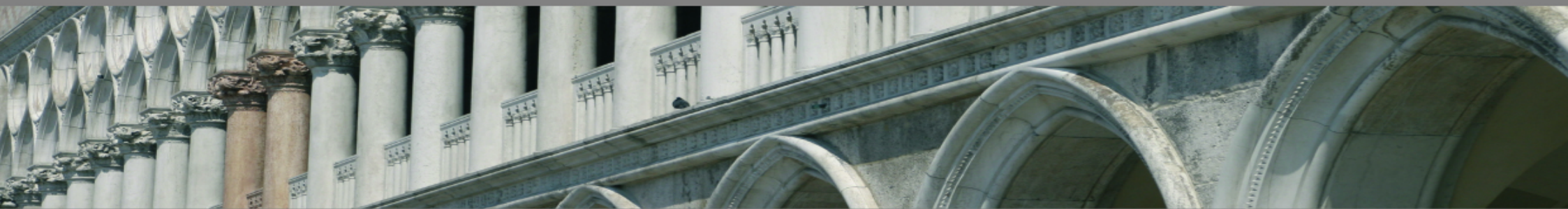
- **GENOMIC PROFILE**
- **GENETIC
POLYMORPHISMS**
- **WILM'S TUMOR GENE
EXPRESSION**
- **TOTAL
PHOSPHOTYROSINE
LEVEL IN CD34+ CELLS**
- **CrKI PHOSPHORILATION
DURING TREATMENT**
- **BCR-ABL TRANSCRIPT
LEVEL**
- **ADDITIONAL
CHROMOSOME
ABNORMALITIES (Ph
AMPLIFICATION, DEL
9q+, etc)**
- **PRE-EXISTING ABL KD
MUTATIONS IN CD34+
CELLS**

**CELLULAR AND MOLECULAR BIOLOGY STUDIES WILL
HELP IMPROVE PROGNOSIS AND TREATMENT**

BUT

**DON'T FORGET THAT TODAY SOKAL / HASFORD RISK
DEFINITION IS REQUIRED TO PLAN THE TREATMENT OF A
CML PATIENT. ALL WHAT YOU NEED IS SPLEEN SIZE,
BLOOD COUNTS AND BLOOD DIFFERENTIAL **PRIOR TO ANY
TREATMENTS****

EVOLVING CONCEPTS IN THE MANAGEMENT OF CHRONIC MYELOID LEUKEMIA



RECOMMENDATIONS FROM AN EXPERT PANEL ON BEHALF OF THE EUROPEAN LEUKEMIANET