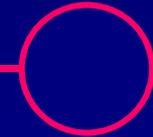


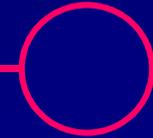
Chronisch myeloische Leukämie

- R. Weide-



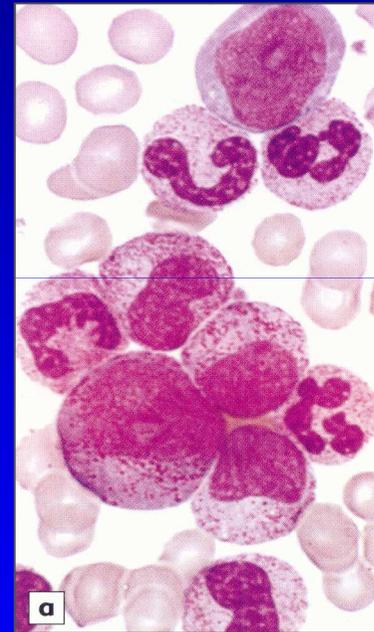
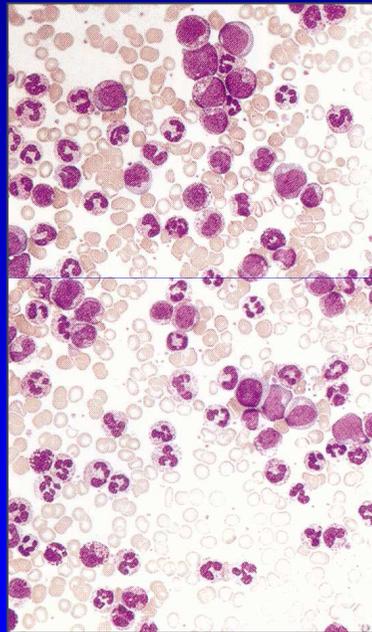


- **19 jährige Patientin, Erstvorstellung 03/05**
- **Leukozyten: 219 G/l (NW:4-10G/l),**
- **Thrombozyten: 1.132 G/l (NW:150-450G/l)**
- **Milz 3 QF unter Rippenbogen**

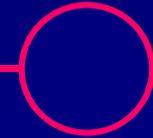


Diagnostische Charakteristika der CML

(1) Leukozytose, Granulozytose, „buntes Bild“



(2) Häufig Thrombozytose + milde Anämie



Diagnostische Charakteristika der CML

(3) Häufig Splenomegalie



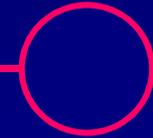
(4) Eosinophilie

(5) Basophilie

(6) Alkalische Leukozytenphosphatase ↓

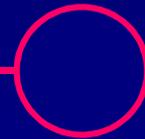
(7) Hyperplastisches Knochenmark

(8) Philadelphia-Chromosom / BCR/ABL-Rearrangement

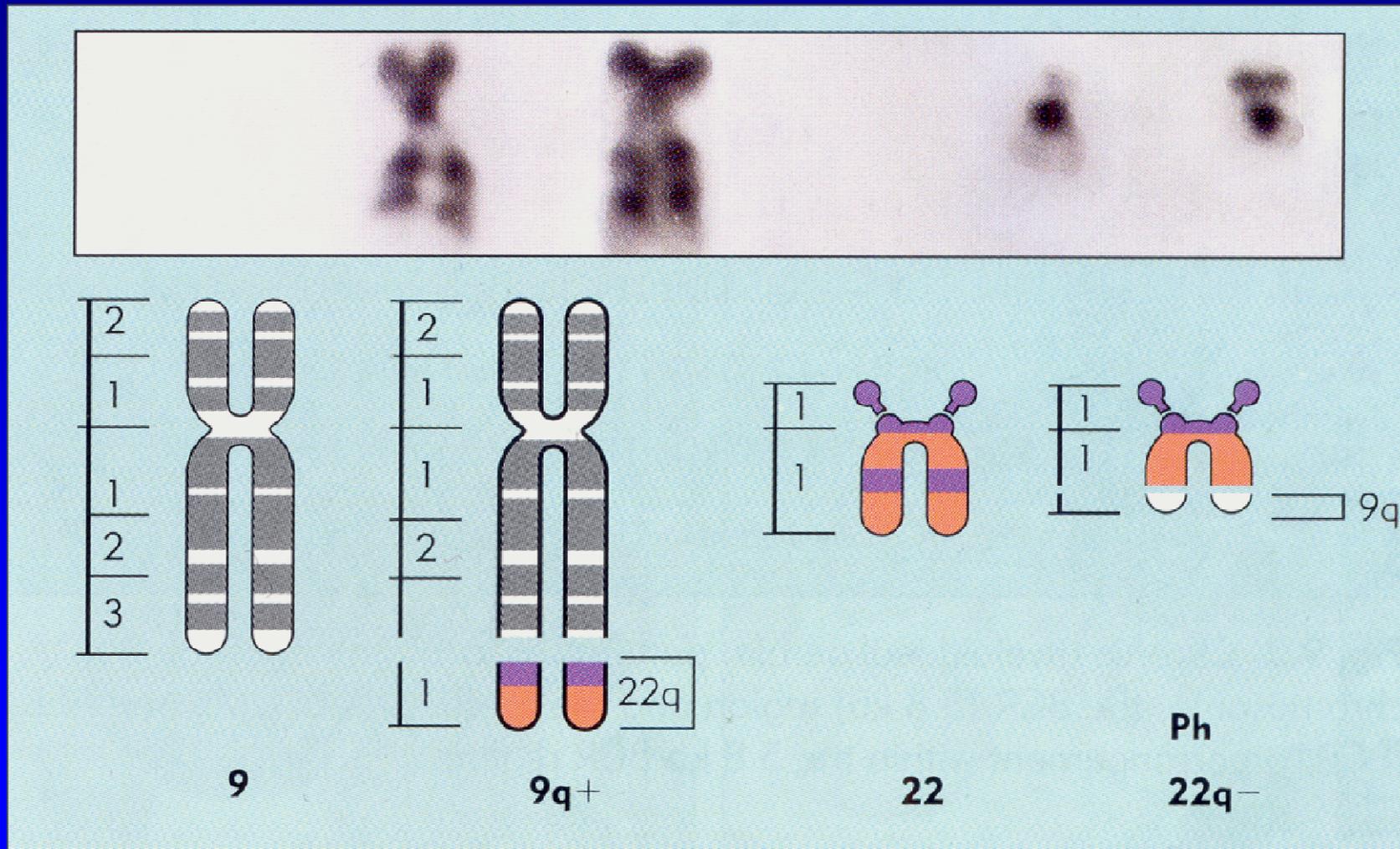


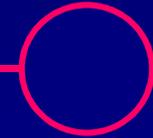
Krankheitsphasen der CML

- **Chronische Phase**
- **Akzelerierte Phase**
- **Blastenschub**

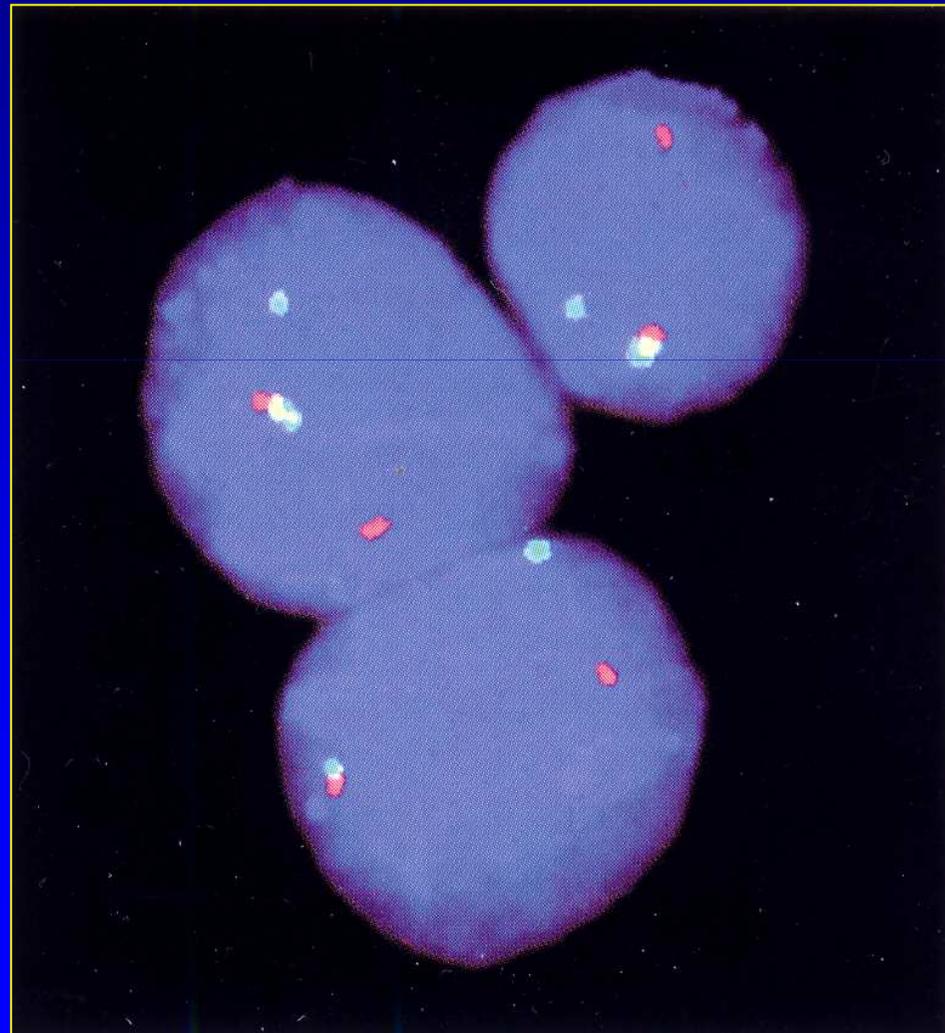


Pathogenese der CML



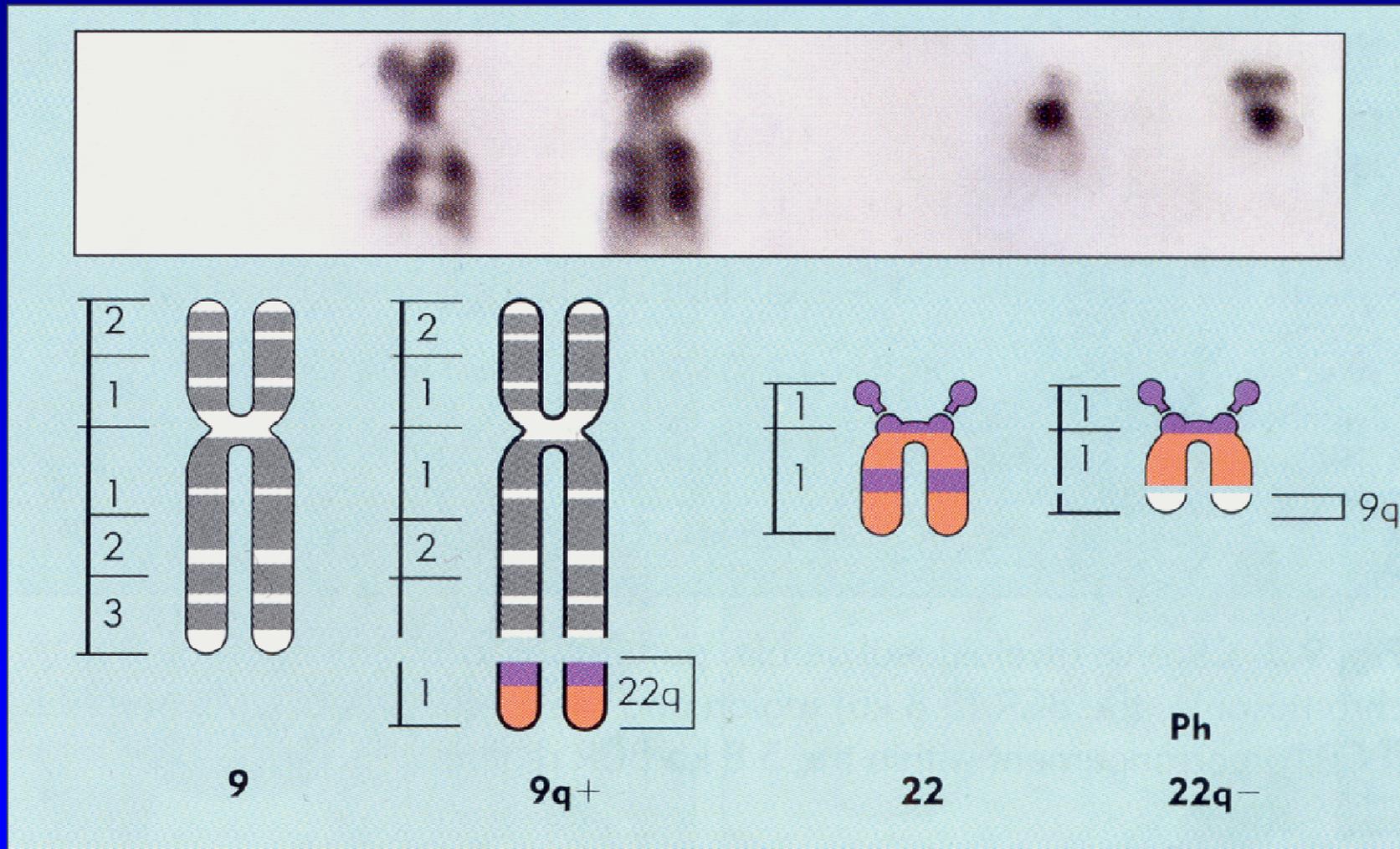


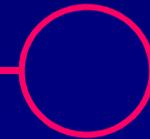
Pathogenese der CML



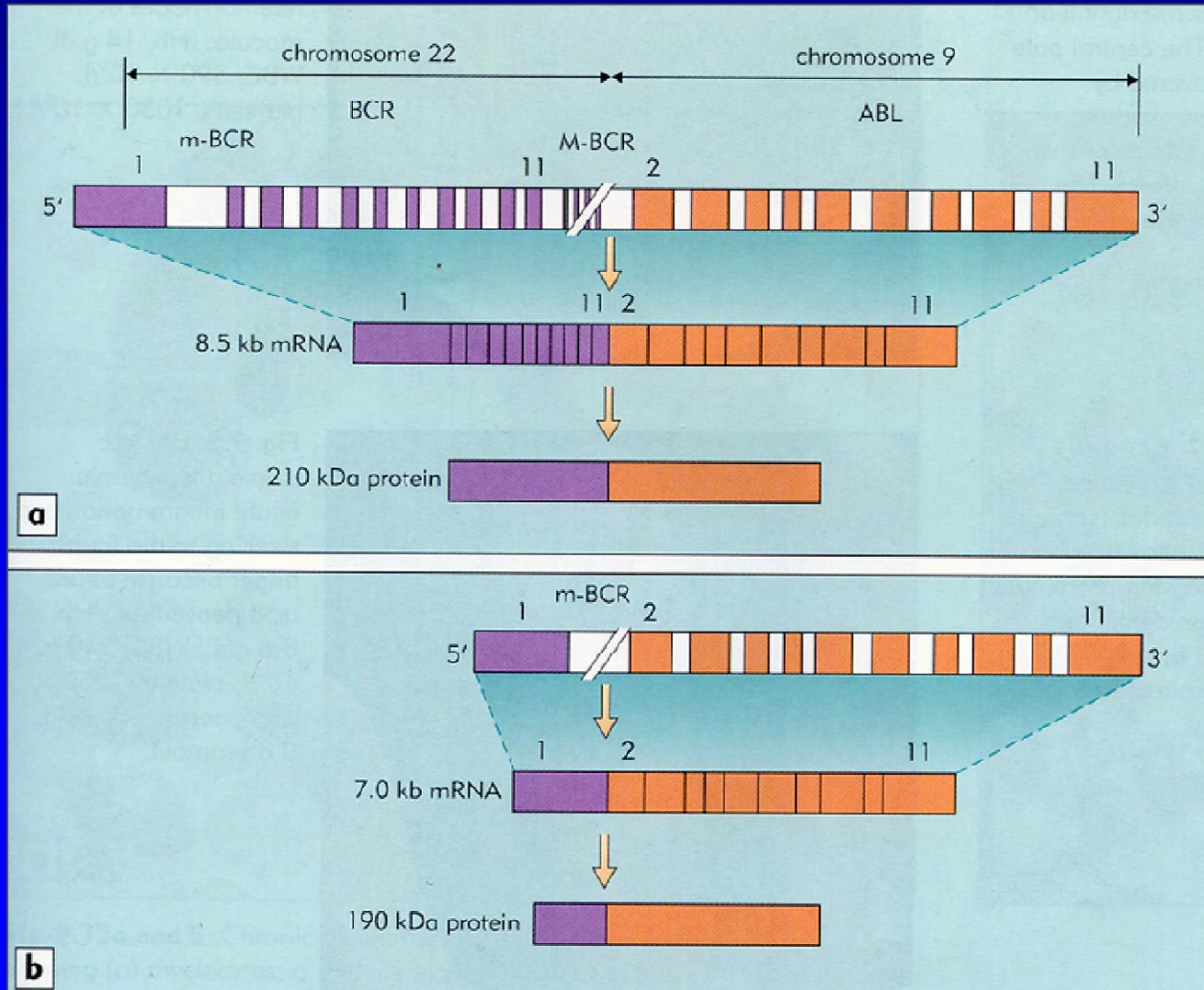


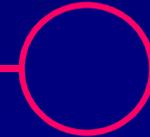
Pathogenese der CML



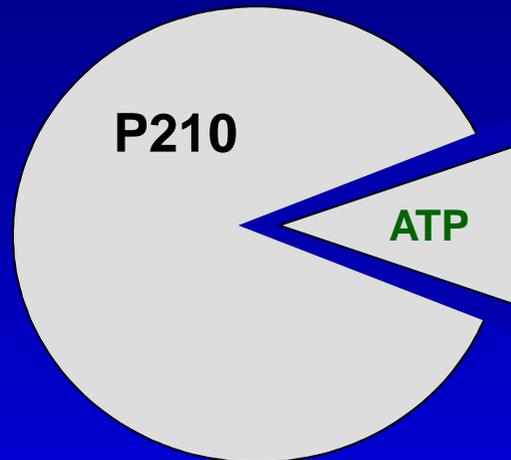


Pathogenese der CML

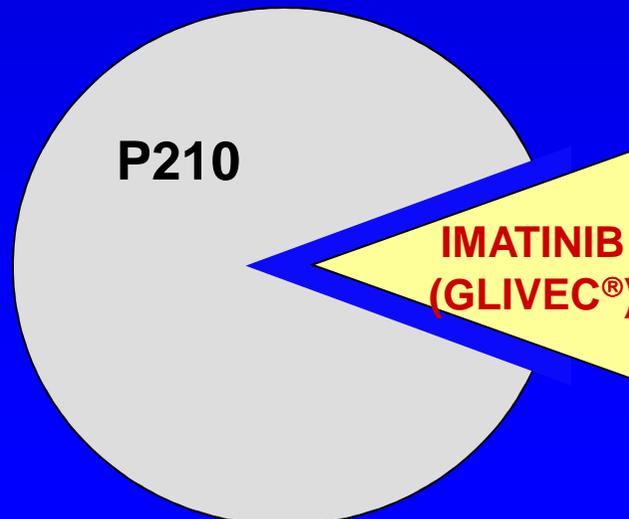


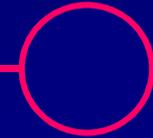


Therapieprinzipien in chronischer Phase



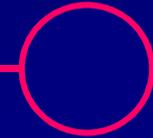
Thyrosinkinaseinhibition





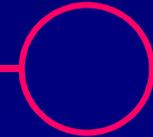
Definition von Risikogruppen bei der CML in der Glivec®-Ära

- Kein adäquates Ansprechen auf Glivec®
- Verminderung des Ansprechens auf Glivec®
im Verlauf
- Blastenkrise



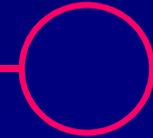
Monitoring des Therapieansprechens auf Imatinib (Glivec®)

- Komplette hämatologische Remission
- No cytogenetic response: 100% Ph⁺
- Minimal cytogenetic response: 35 - 90% Ph⁺
- Major cytogenetic response: 1 – 34% Ph⁺
- Complete cytogenetic response: 0% Ph⁺
- Major molecular response: BCR/ABL $\leq 10^{-3}$



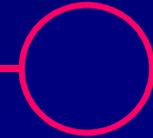
IRIS-Studie: (ASH 2005, # 163 + 166)
(Mediane Behandlungsdauer mit (Glivec®: 54 Monate)

- Komplette hämatologische Remission: 96%
- Major cytogenetic response: 88%
- Complete cytogenetic response: 81%
- Gesamtüberleben: 91%
 - (Niedriger Sokal score: 94%)
 - (Hoher Sokal score: 91%)
 - (Major molecular response: 100%)



Ziel der Glivec[®]-Therapie

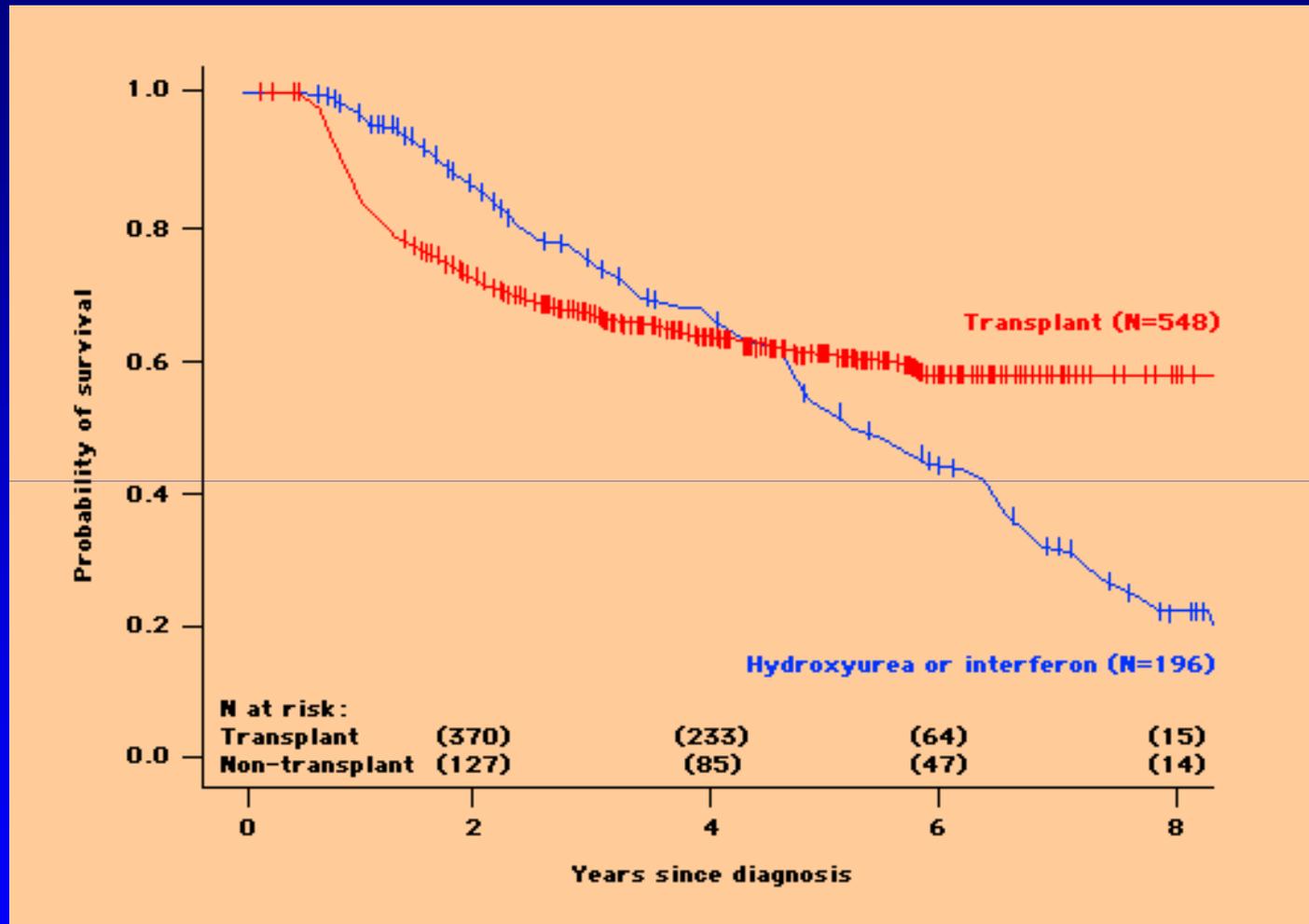
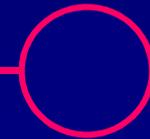
- Nach 3 Monaten: Komplette hämatologische Remission
- Nach 6 Monaten: Major cytogenetic response (< 35% Ph⁺)
- Nach 12 Monaten: Complete cytogenetic response (0% Ph⁺)
- Danach: Major molecular response (BCR/ABL-Transcriptlevel $\leq 10^{-3}$)



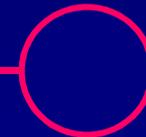
Diagnostische Maßnahmen zur Verlaufsbewertung

- (1) Klinische Untersuchung
- (2) Sonographie (Milzgröße)
- (3) Blutbild + klinische Chemie
- (4) Zytogenetik aus Knochenmark
- (5) Quantitative PCR aus Blut

Chronische myeloische Leukämie



Survival in CML: transplant versus hydroxyurea or interferon This graph plots the probability of survival versus years since diagnosis of chronic myelogenous leukemia (CML) for patients treated with hematopoietic cell transplantation (red) and those treated with either hydroxyurea or interferon. Data from Gale, RP, et al. Blood 1998; 91:1810.



EGBMT Risk Assessment Score for Allogeneic Transplantation in CML[†]

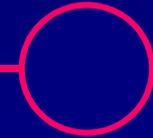
Item	Score	Category
Donor	0	HLA Identical sibling donor
	1	Matched unrelated donor
Stage	0	First chronic phase
	1	Accelerated phase
	2	Blast crisis or ≥2nd chronic phase
Age	0	<20 years
	1	20 to 40 years
	2	>40 years
Sex matching (donor/recipient)	0	All other matches
	1	Female donor, male recipient
Time to HCT from diagnosis	0	<12 months
	1	>12 months

Score	Treatment-related mortality (%)	5-year Overall Survival (%)
0	20	72
1	23	70
2	31	62
3	46	48
4	51	40
5	71	18
6	73	22
7	--	--

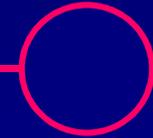
Scoring: Scoring is from zero to a maximum of seven, with points scored for each of the five risk categories, as shown in the upper table. Treatment-related mortality and five-year overall survivals as a function of the score are shown in the lower table. There were too few patients with a score of seven to adequately assess TRM and OS.

Abbreviations: EGBMT: European Group for Blood and Marrow Transplantation; CML: chronic myelogenous leukemia; HCT: hematopoietic cell transplantation

[†] Data from Gratwohl, A, et al. *Lancet* 1998; 352:1087.



- **19 jährige Patientin, Erstvorstellung 03/05**
- **Leukozyten: 219 G/l, Thrombozyten: 1.132 G/l**
- **Milz 3 QF unter Rippenbogen**



- **CML, 1. chronische Phase**
Philadelphia-Chromosom-positiv
- **Hasfordscore 284 (Niedrigrisiko)**
- **seit 04/05: Glivectherapie**
- **Stand 10/05: Komplette zytogenetische**
Remission + Major cytogenetic response (5% Ph⁺)
- **Stand 03/09: Major molecular response (ideales**
Ansprechen, keinerlei Nebenwirkungen)