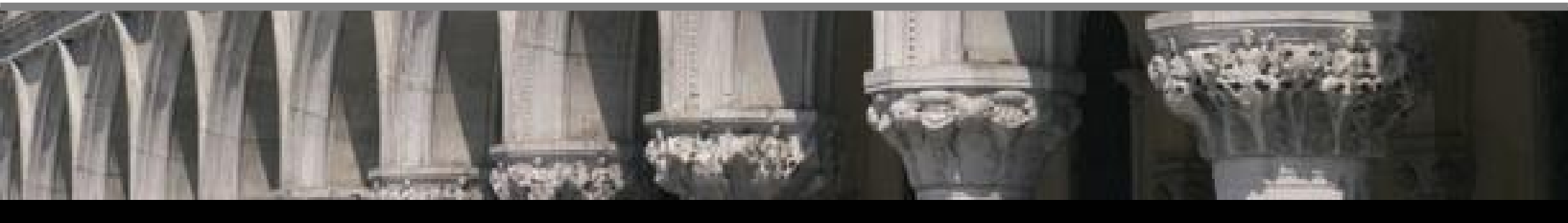




# Response-related Prognostic Factors: The Cytogenetic Response

**Michael Deininger**

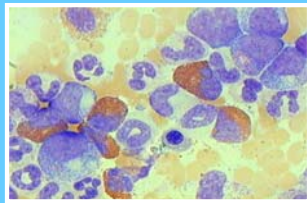


What is the role of cytogenetic monitoring in the era of quantitative RT-PCR?

# Sensitivity of monitoring strategies

## Leukemia cells

$>10^{12}$



Blood counts – 2%

CHR

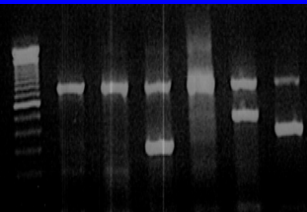
$10^{10}$



Cytogenetics – 14%

CCR

$10^8$



PCR – 84%

CMR

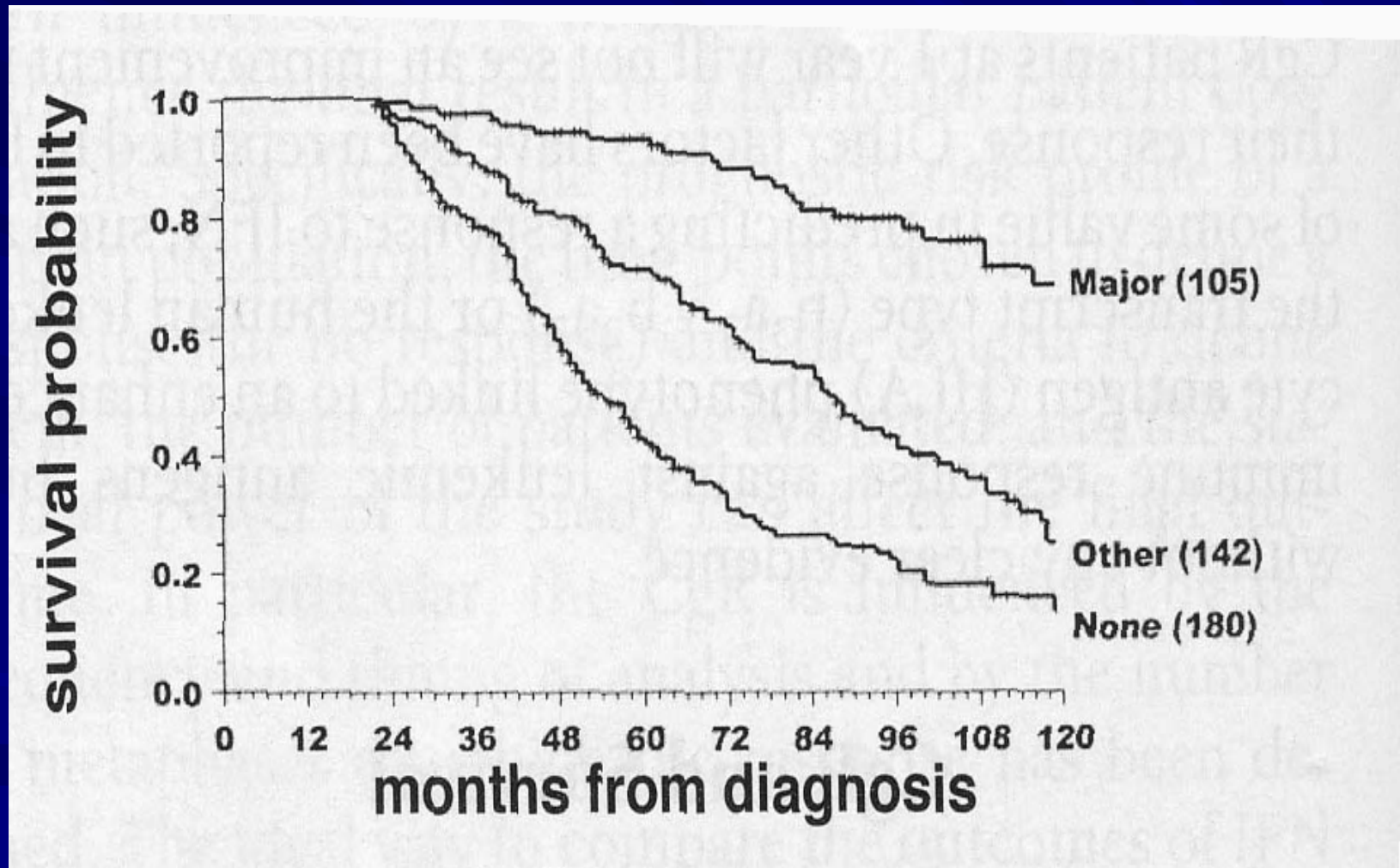
$10^6$

Undetectable range

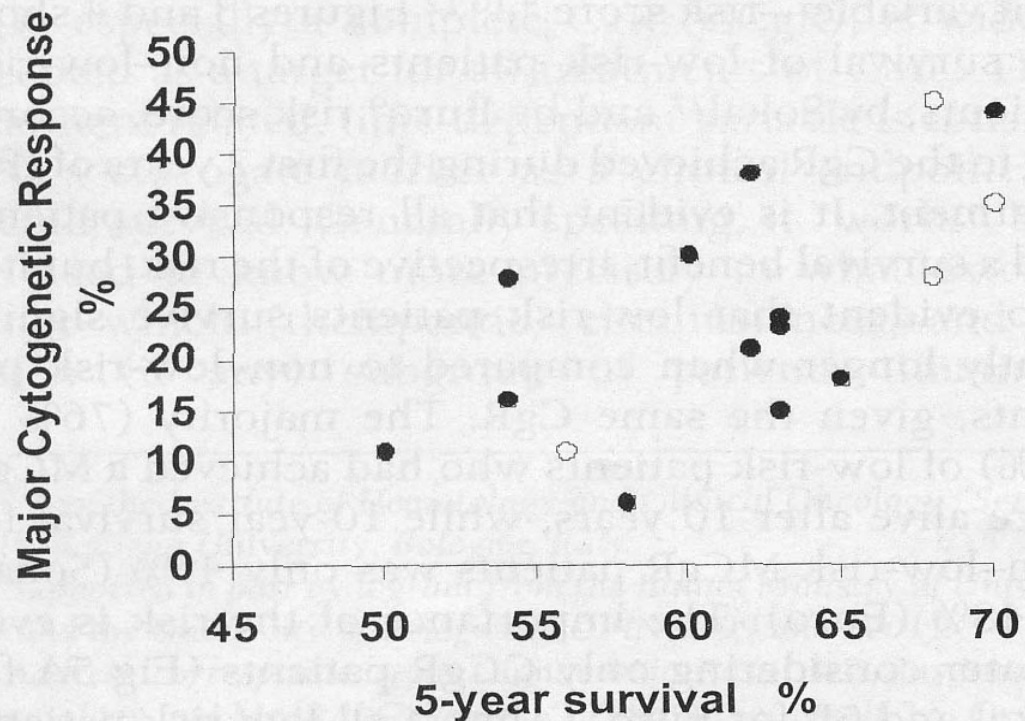
## Historical reminder

Cytogenetic response as a prognostic marker in patients treated with interferon- $\alpha$

# Survival of IFN-treated patients according to cytogenetic response at 24 months

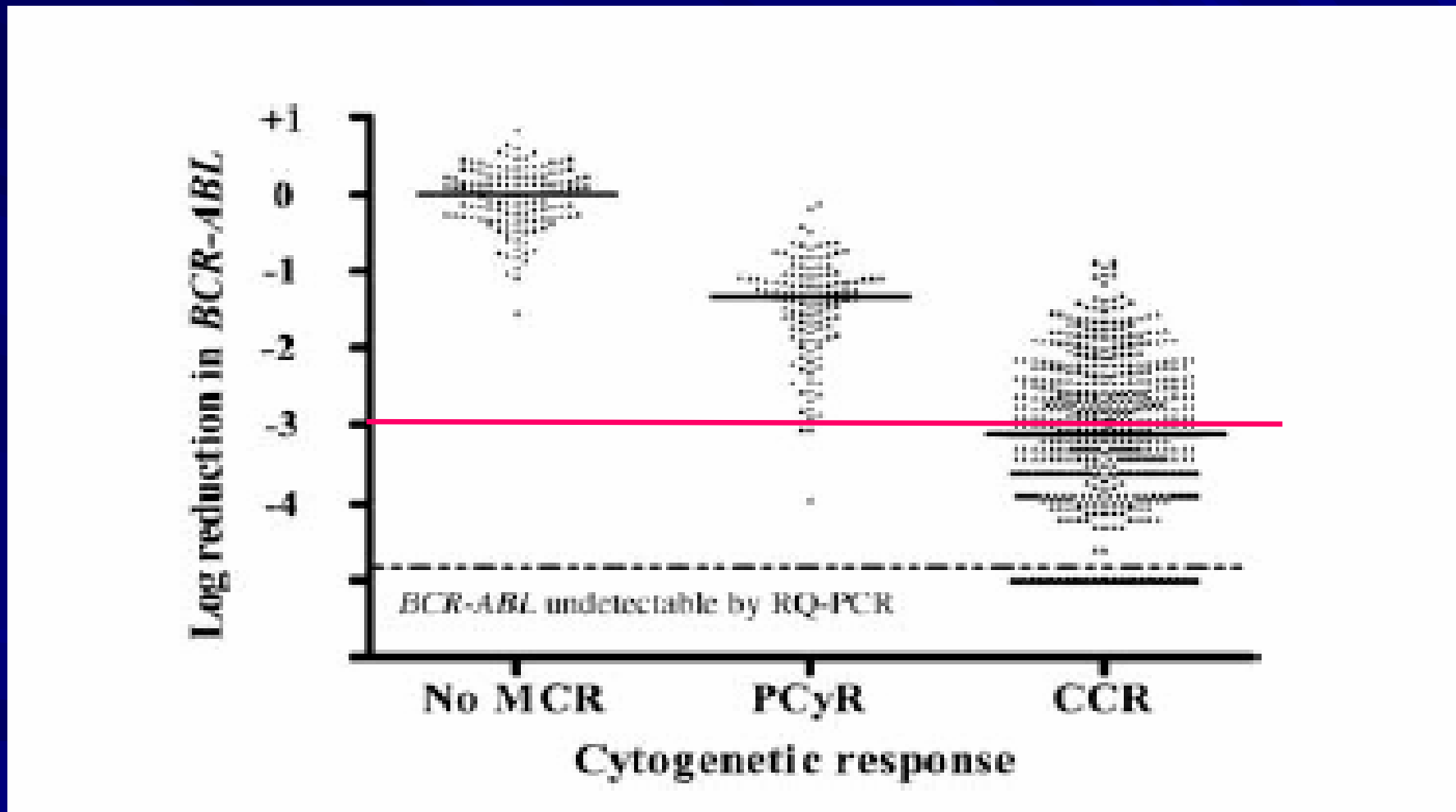


# Correlation between the incidence of major cytogenetic response and survival

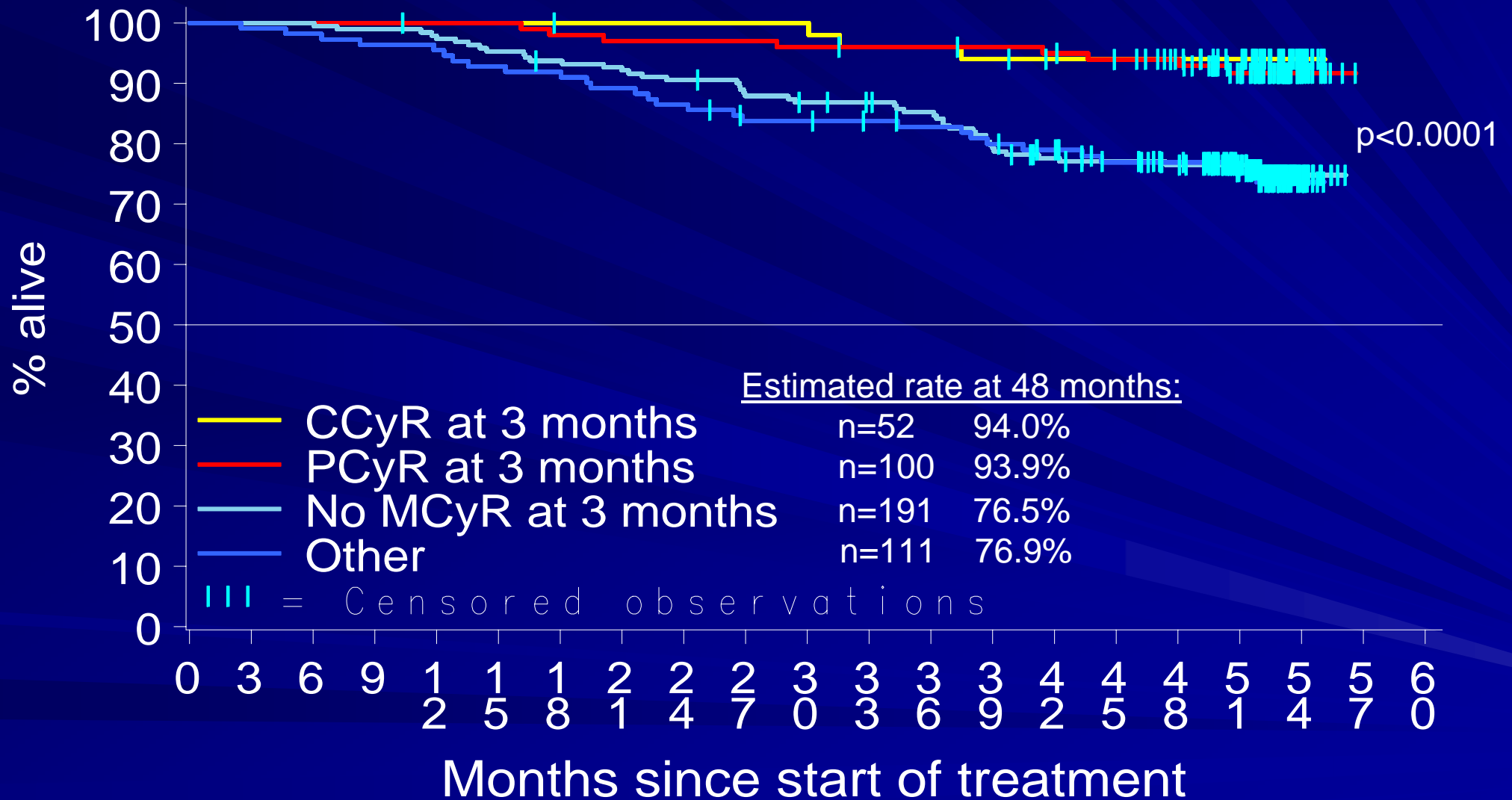


**Figure 1.** MCgR rates reported from 12 studies of IFN alone (●) and four studies of IFN + LDAC (○) plotted v 5-year survival. The relationship is significant ( $r = 0.662$ ,  $r^2 = 0.439$ ,  $P = .005$ ).

# Correlation between cytogenetics and qPCR



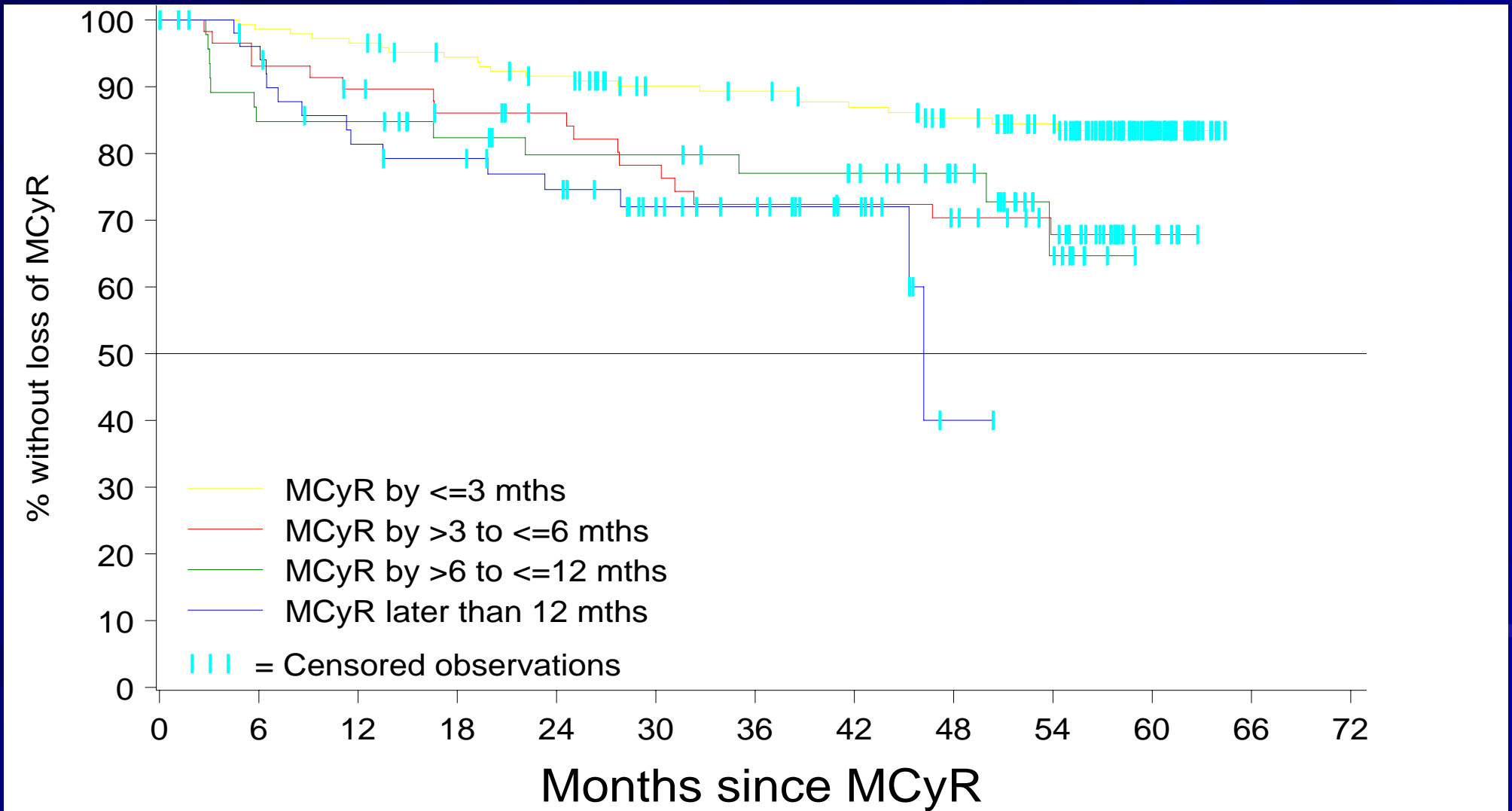
# Overall survival at 48 months – CML late CP



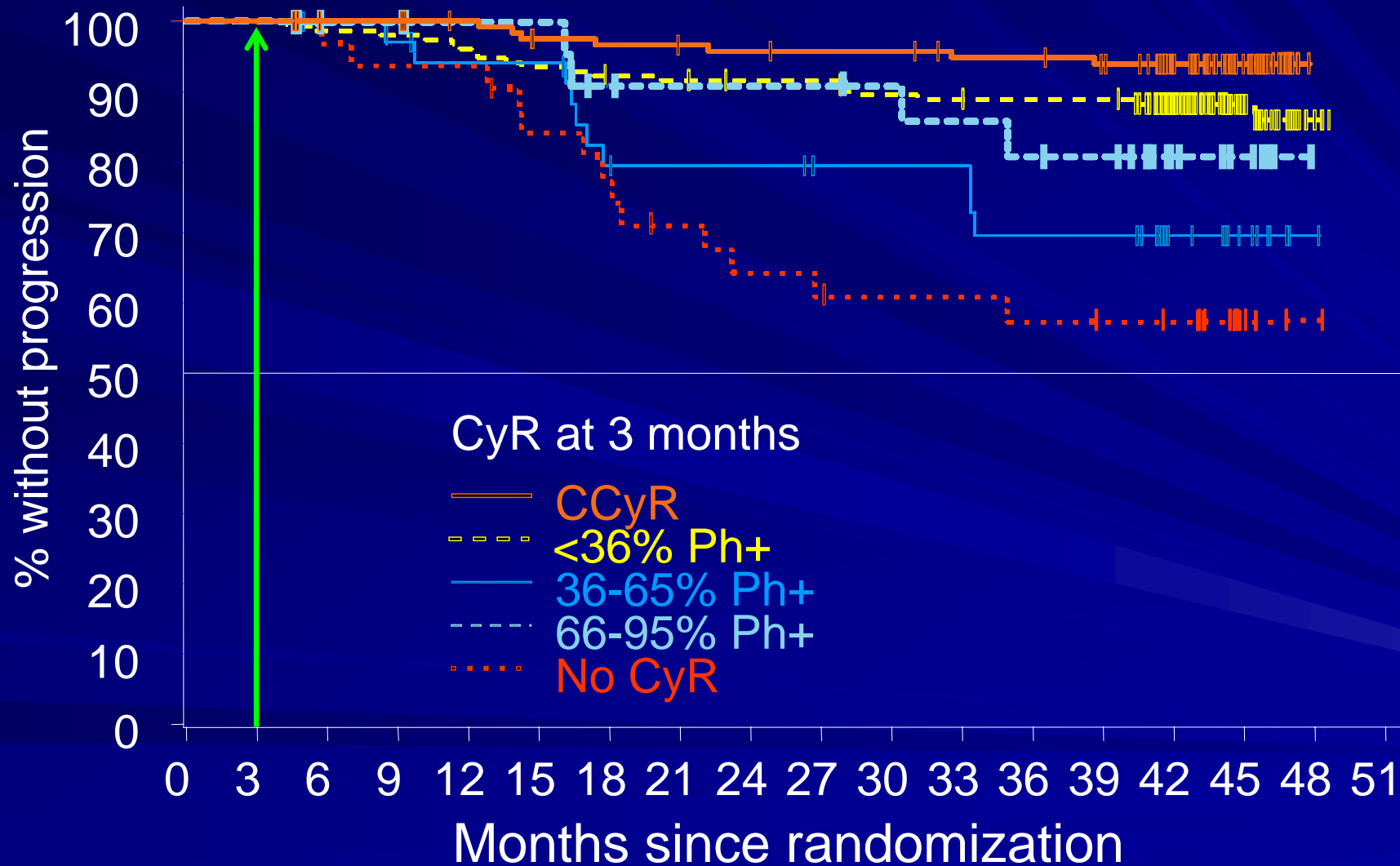
MCyR = CCyR + PCyR



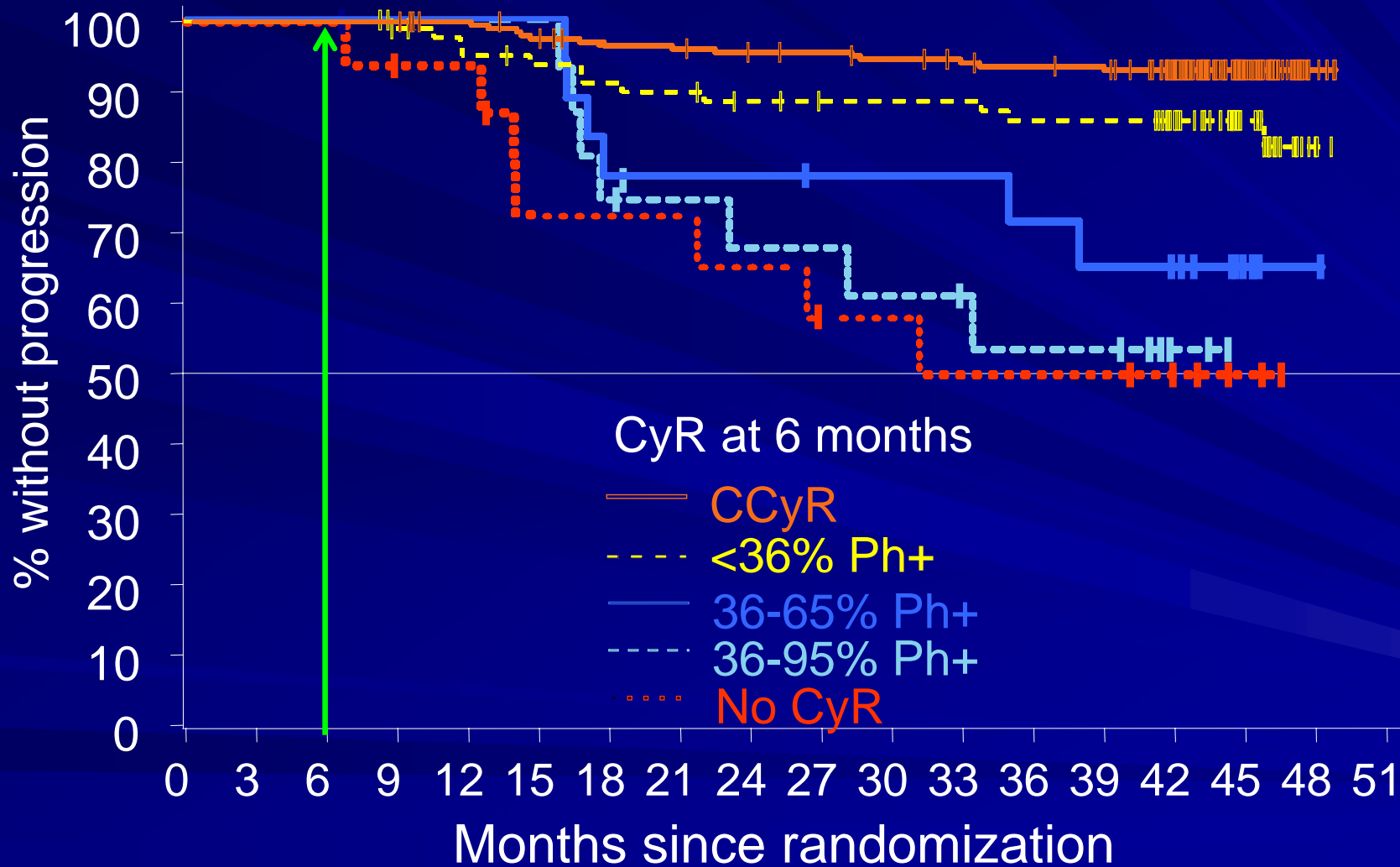
# Risk of MCR loss according to time to MCR achievement



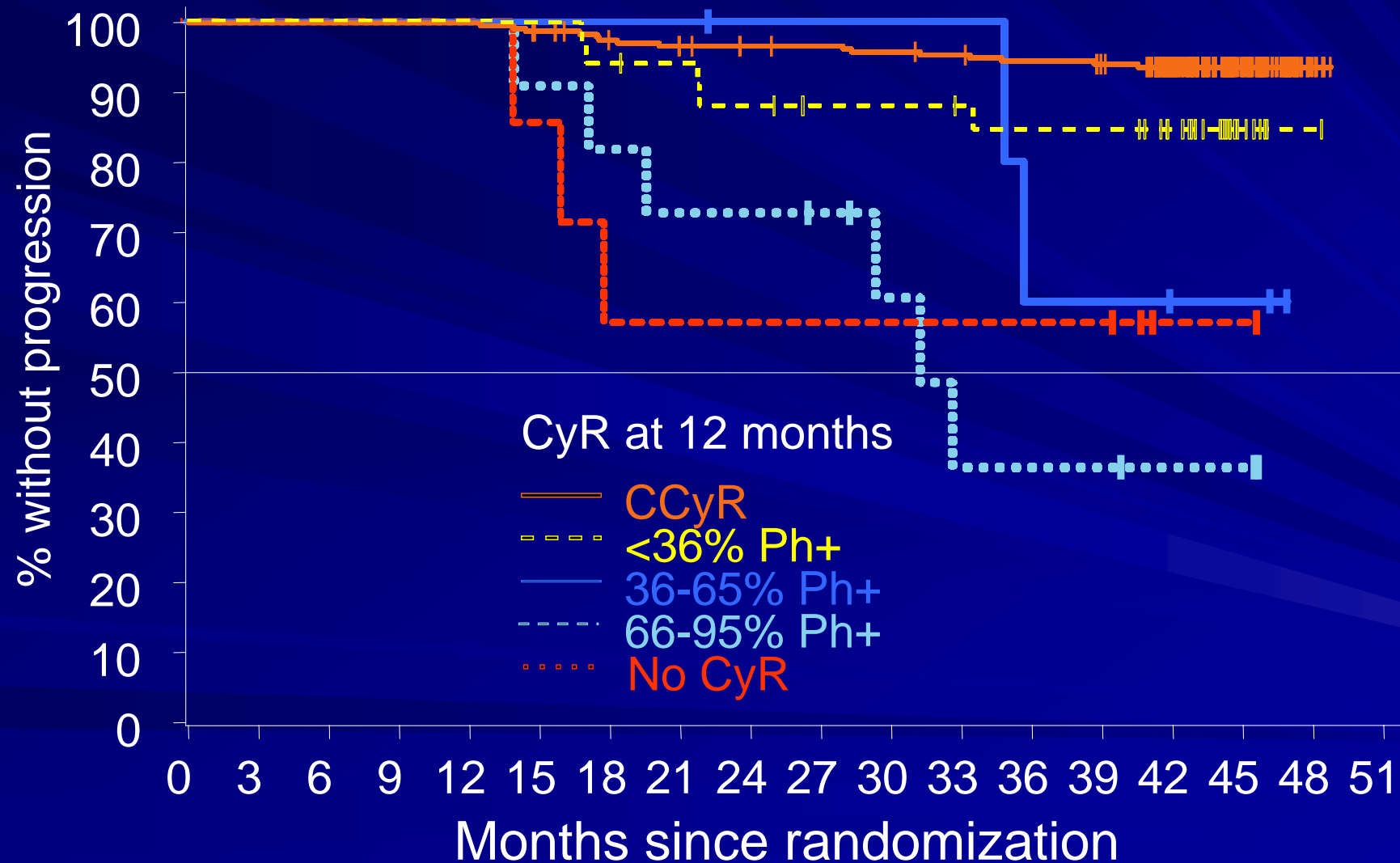
# Progression free survival according to cytogenetic response at 3 months



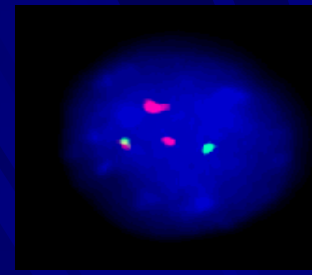
# Progression free survival according to cytogenetic response at 6 months



# Progression free survival according to cytogenetic response at 12 months

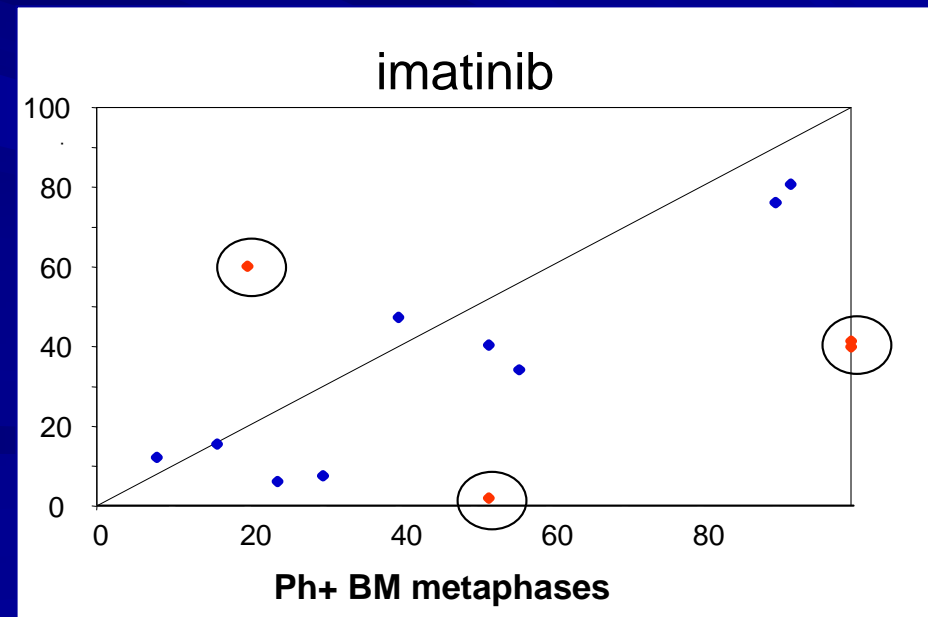
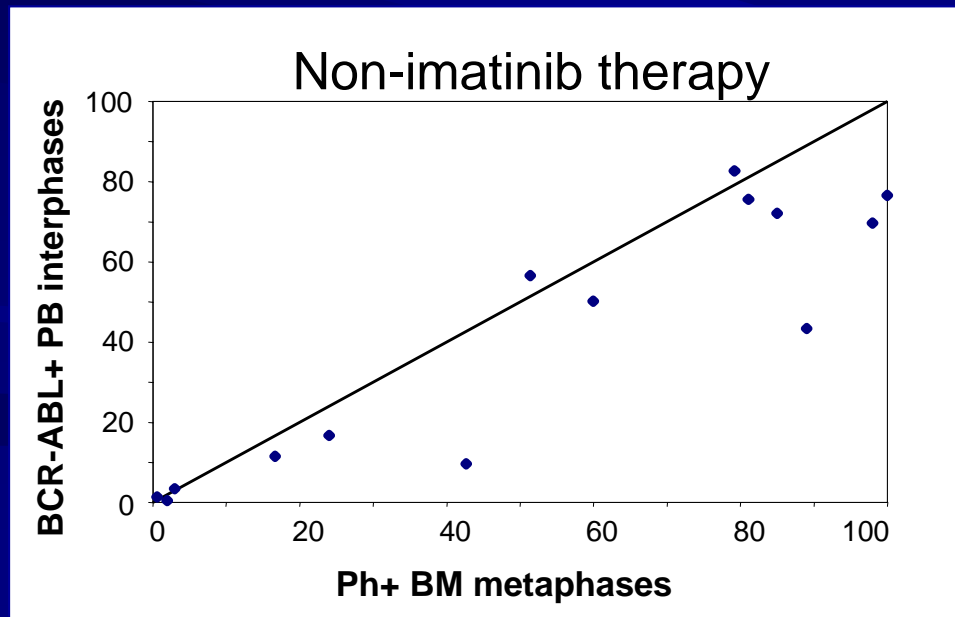


# Is there a role for FISH in monitoring response?

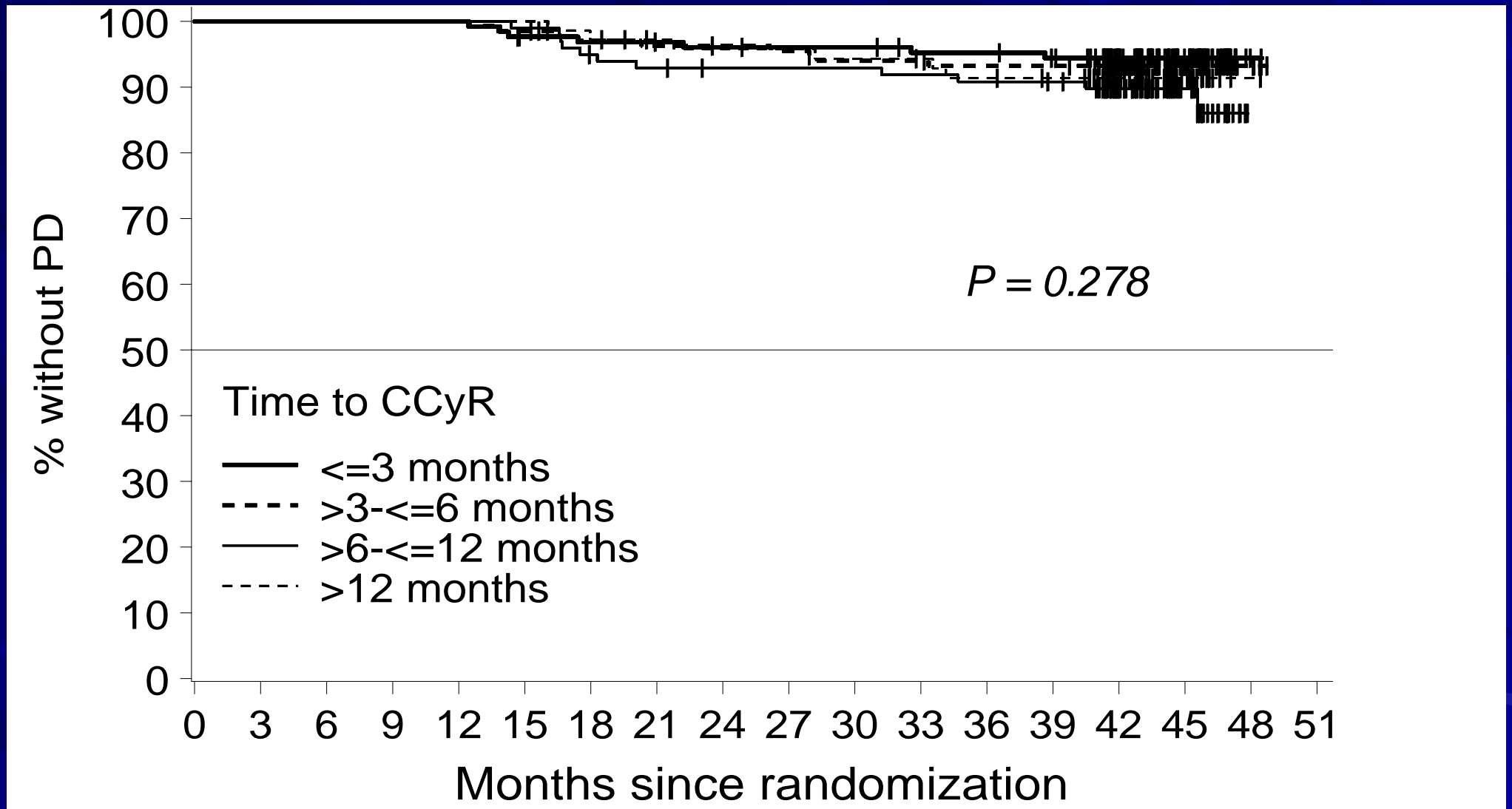


Conveniently done on peripheral blood but

- gain of sensitivity over conventional cytogenetics max. 1 log
- not validated in prospective trials
- misleading in individual cases



# PFS by time to CCR

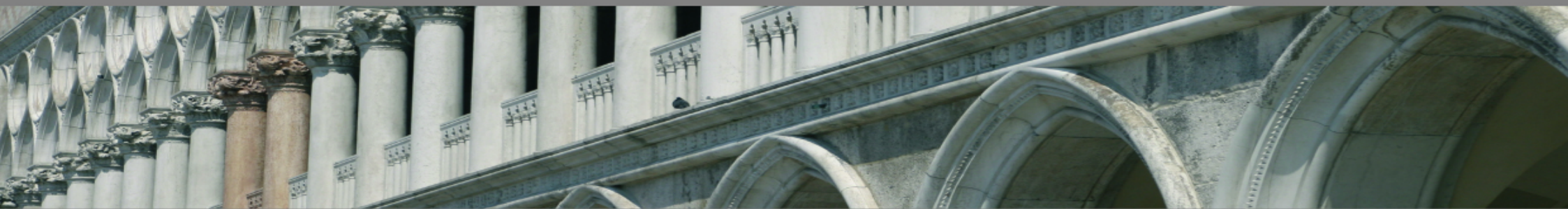


# Conclusions

## Early chronic phase

- Cytogenetic response at 6 months: first relevant cytogenetic prognosticator
- CCR at 12 months: accurately predicts freedom from progression to AP/BC in >95% of patients → cytogenetics preferable if *reliable* qPCR is unavailable
- CCR seems to override pretherapeutic Sokal risk

EVOLVING CONCEPTS IN THE MANAGEMENT OF CHRONIC MYELOID LEUKEMIA



RECOMMENDATIONS FROM AN EXPERT PANEL ON BEHALF OF THE EUROPEAN LEUKEMIANET