European LeukemiaNet

# Response-related Prognostic Factors: The Molecular Response

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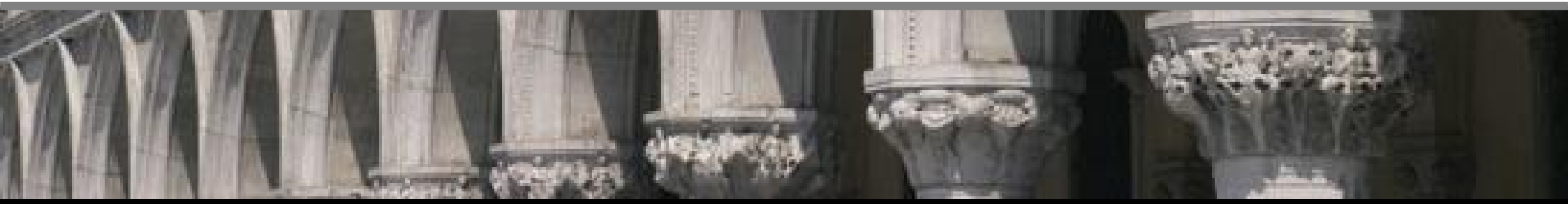
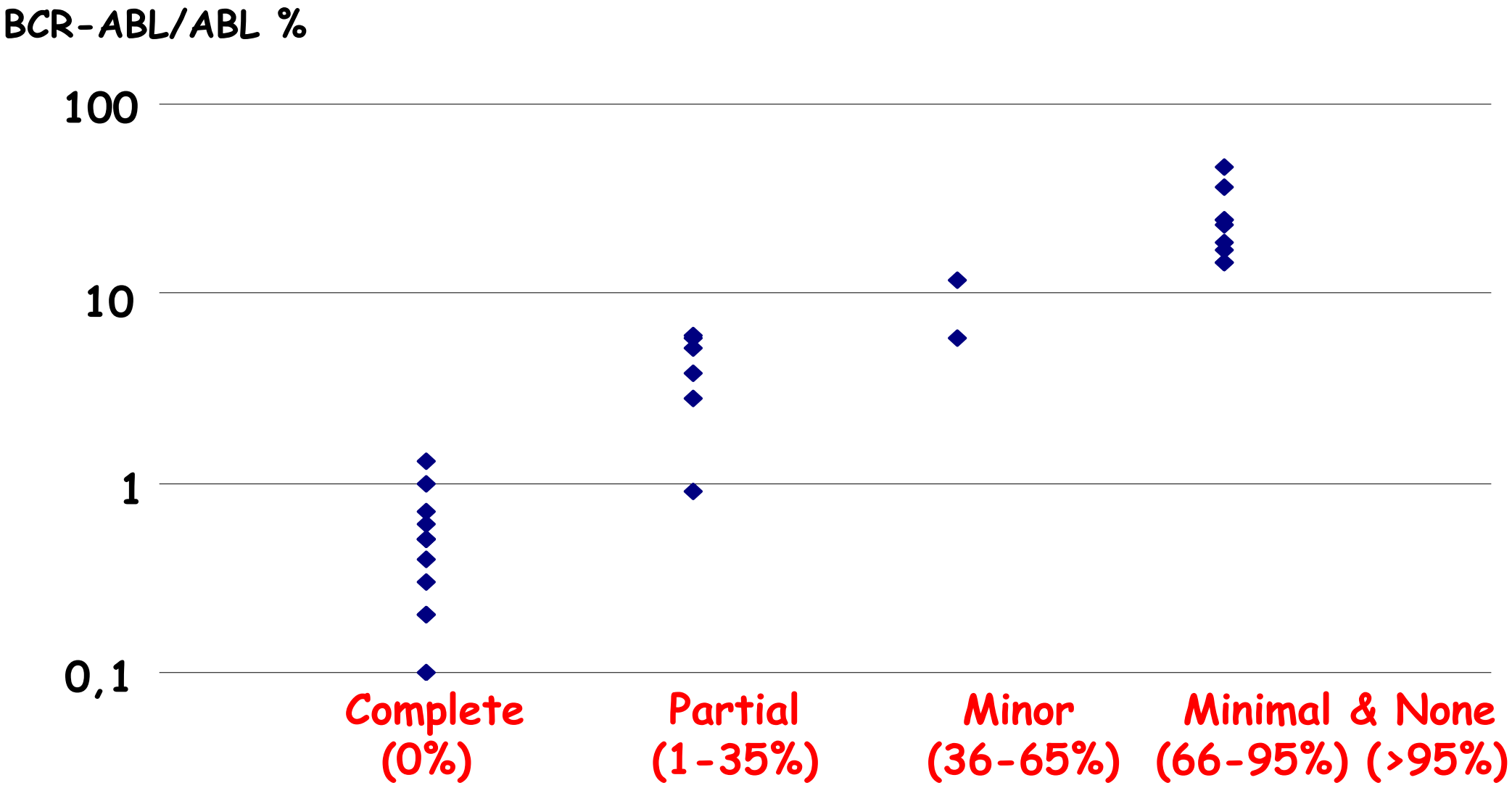
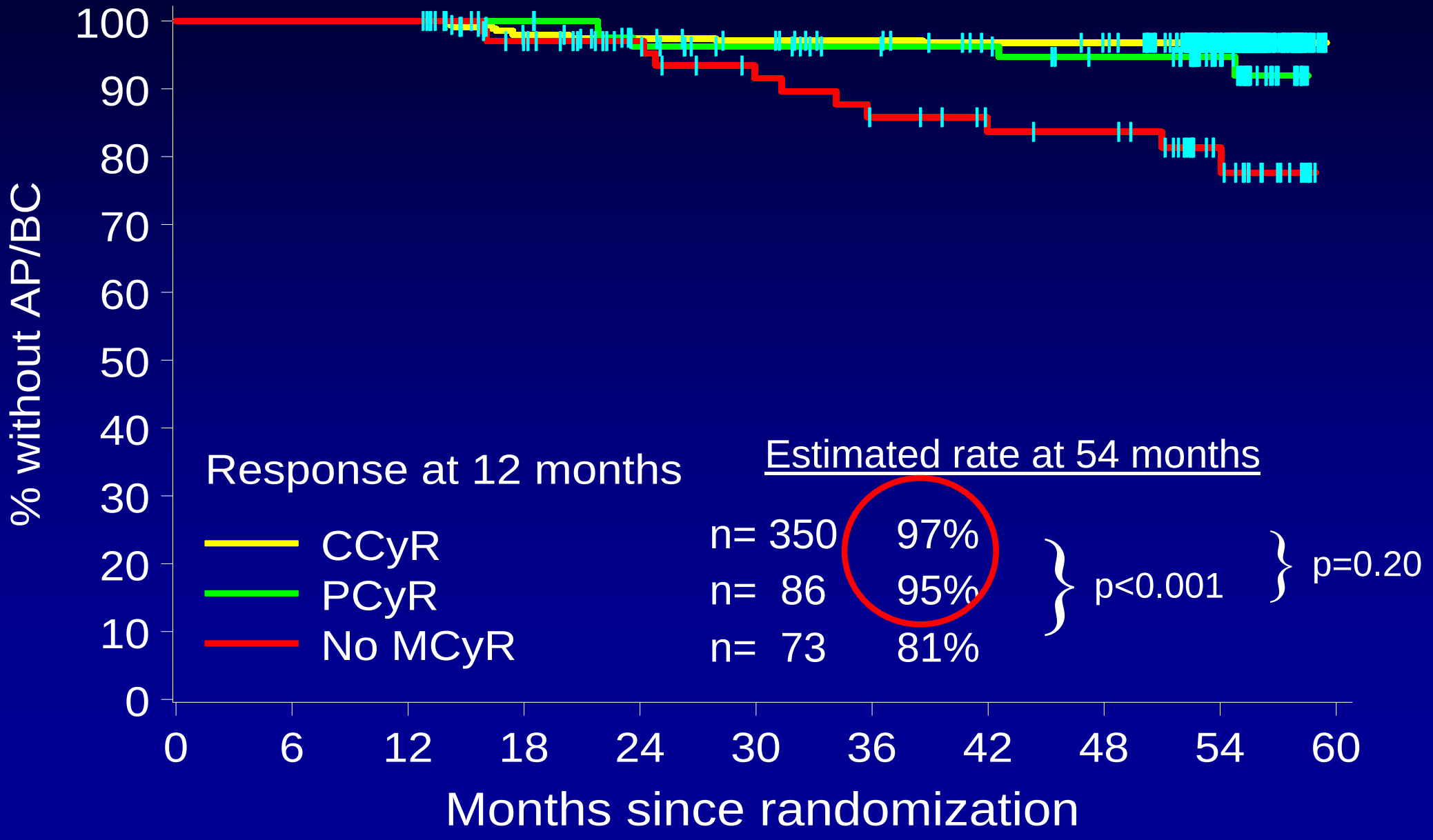


# The amount of BCR-ABL transcripts roughly mirrors the number of residual BCR-ABL positive cells.

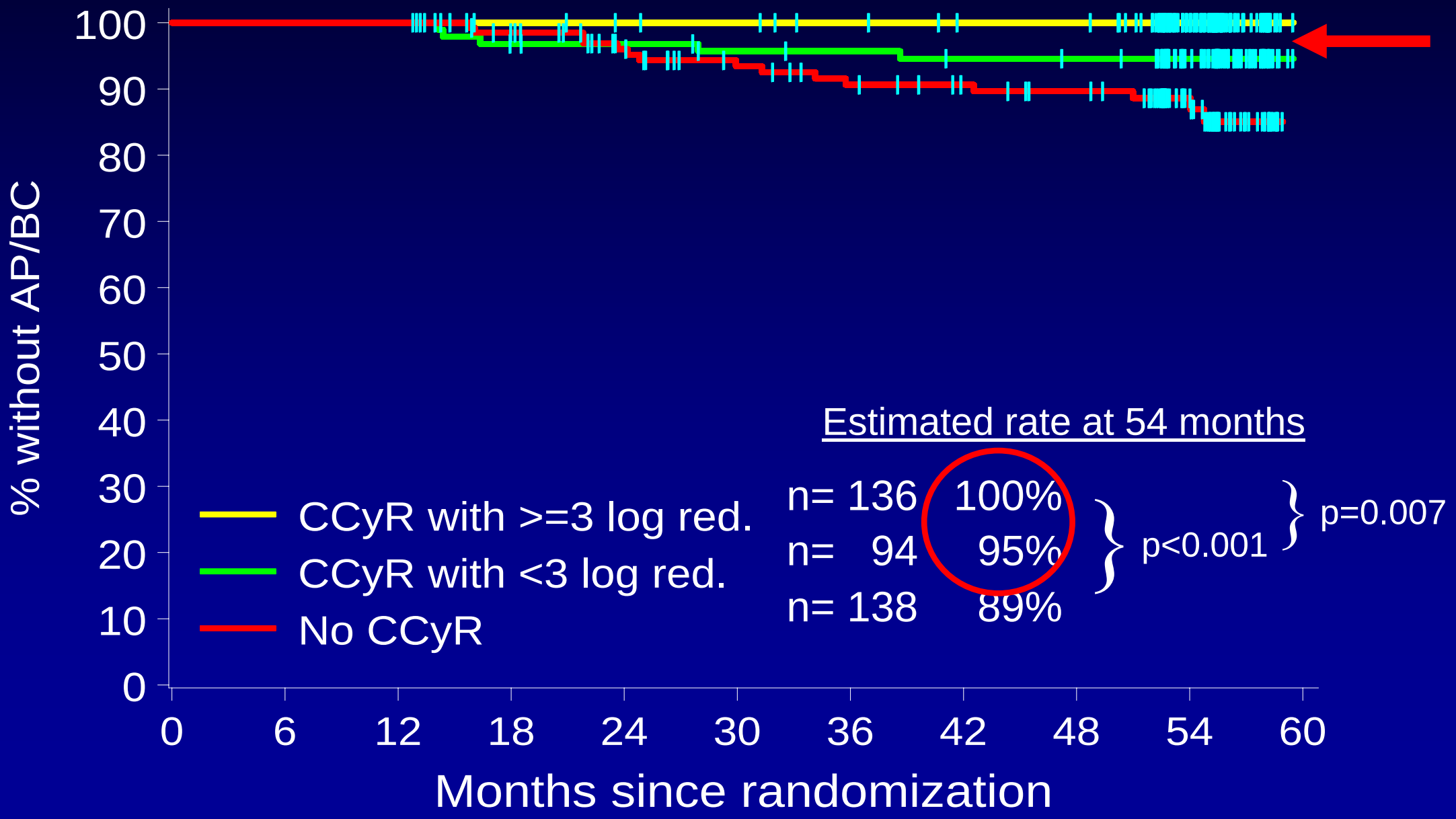



Amount of BCR-ABL in the PB after 3 months of imatinib therapy in the different cytogenetic-response groups

# Survival Without AP/BC by Level of CyR at 12 Months on First-line Imatinib



# Survival Without AP/BC by Molecular Response at 12 Months on First-line Imatinib



Possible explanation:

- the molecular analysis is more precise in discriminating between response subgroups than cytogenetic analysis

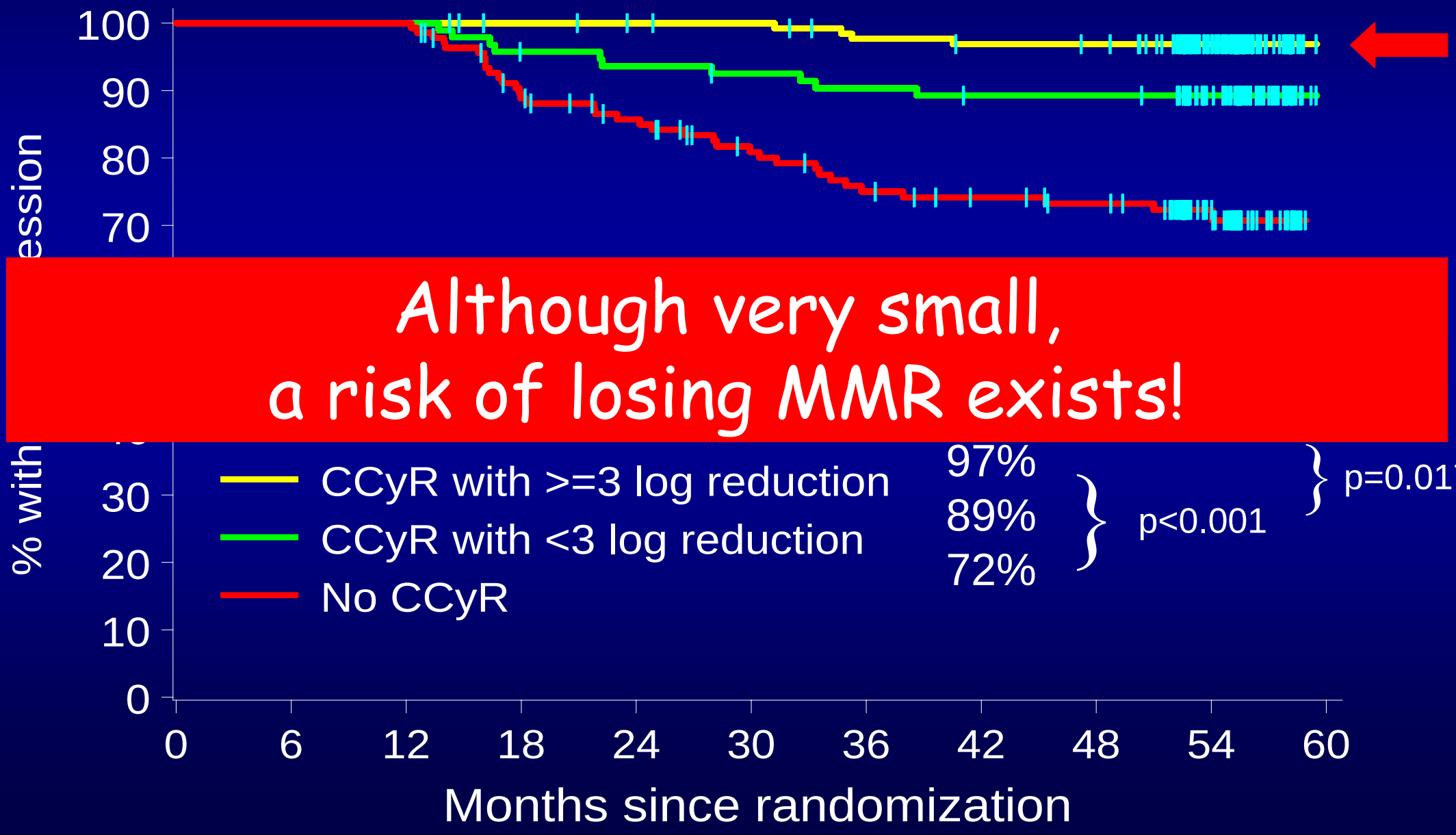
Consequence:

- The patient must be followed not only by cytogenetics but also by RQ PCR

# Question

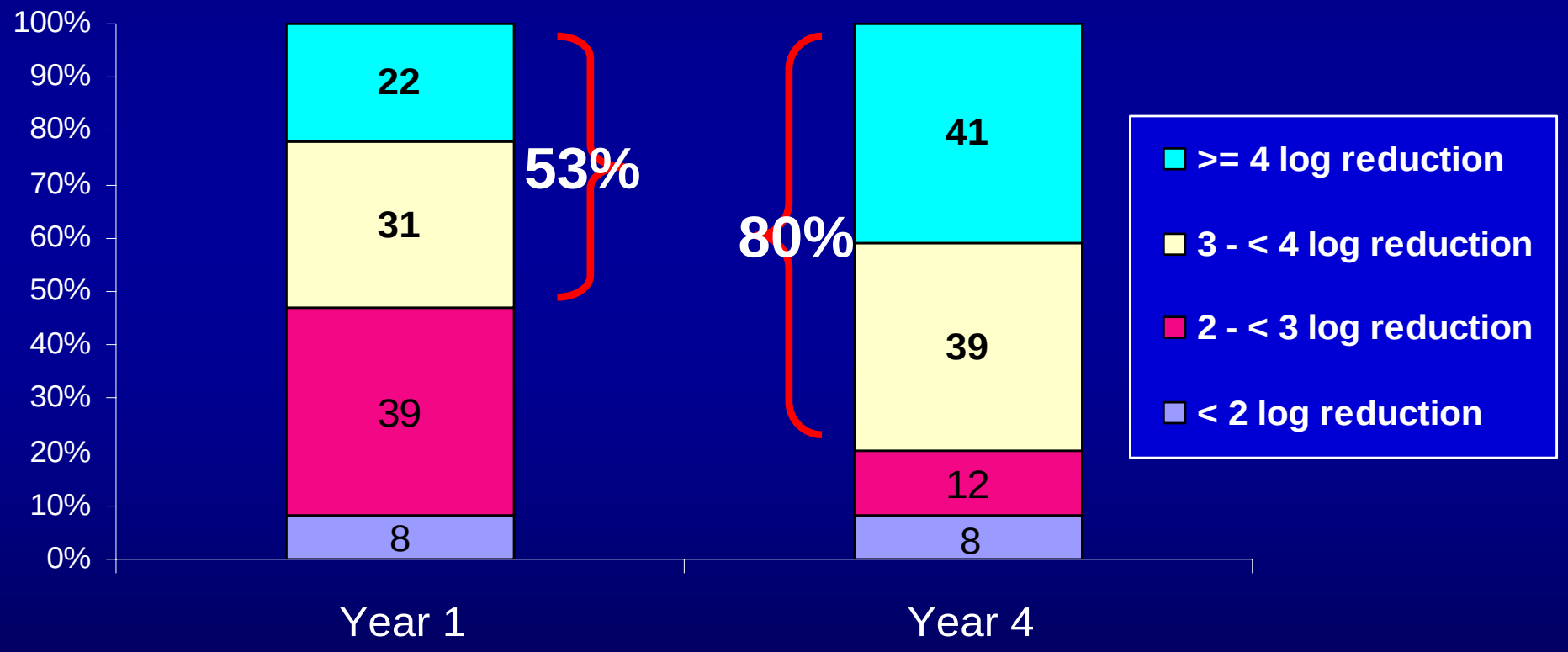
Once reached, is MMR stable over time?

# PFS by Molecular Response at 12 Months on First-line Imatinib




Although very small,
a risk of losing MMR exists!

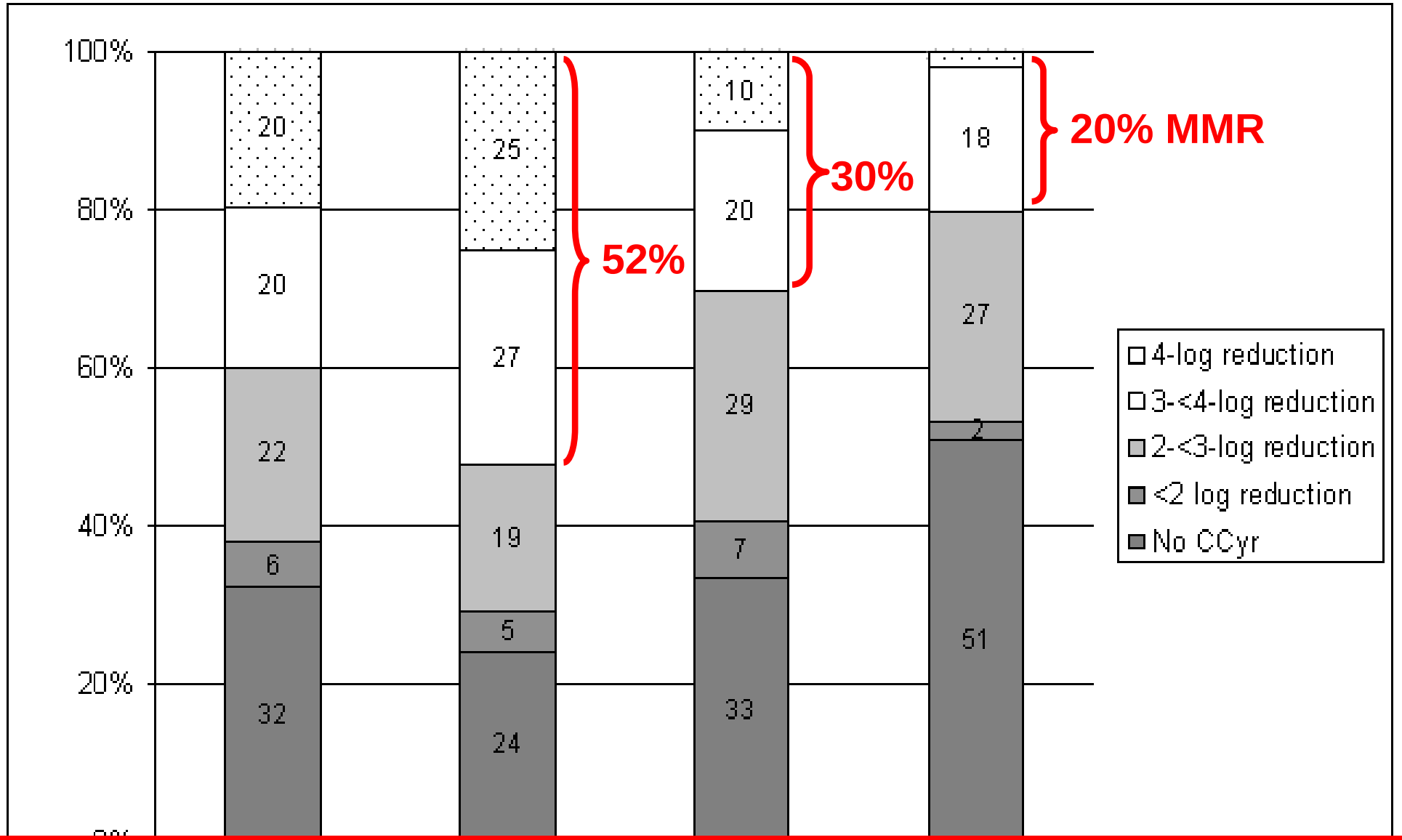
# % *BCR-ABL* log reduction in 124 CCyR pts at 1 and 4 years: IRIS Trial



# Question

Are all molecular remissions the same?

# Molecular response at 12 months by Sokal risk category




The probability to achieve MMR correlates to the Sokal risk

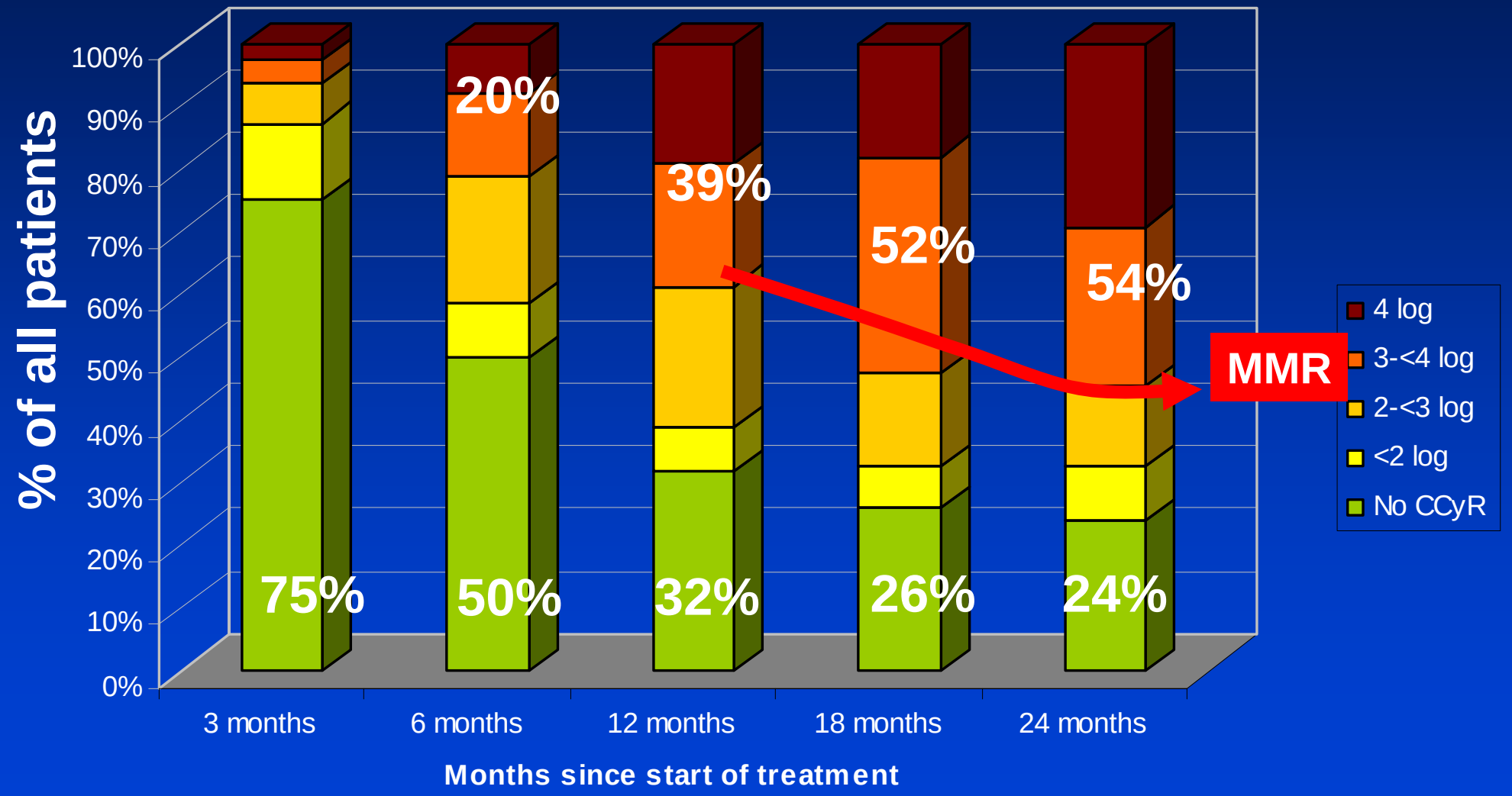
However, when a high or intermediate risk patient achieves a Major Molecular Remission, the risk of subsequent progression is as small as that of low risk patients.

(Goldman J et al., ASH 2005)

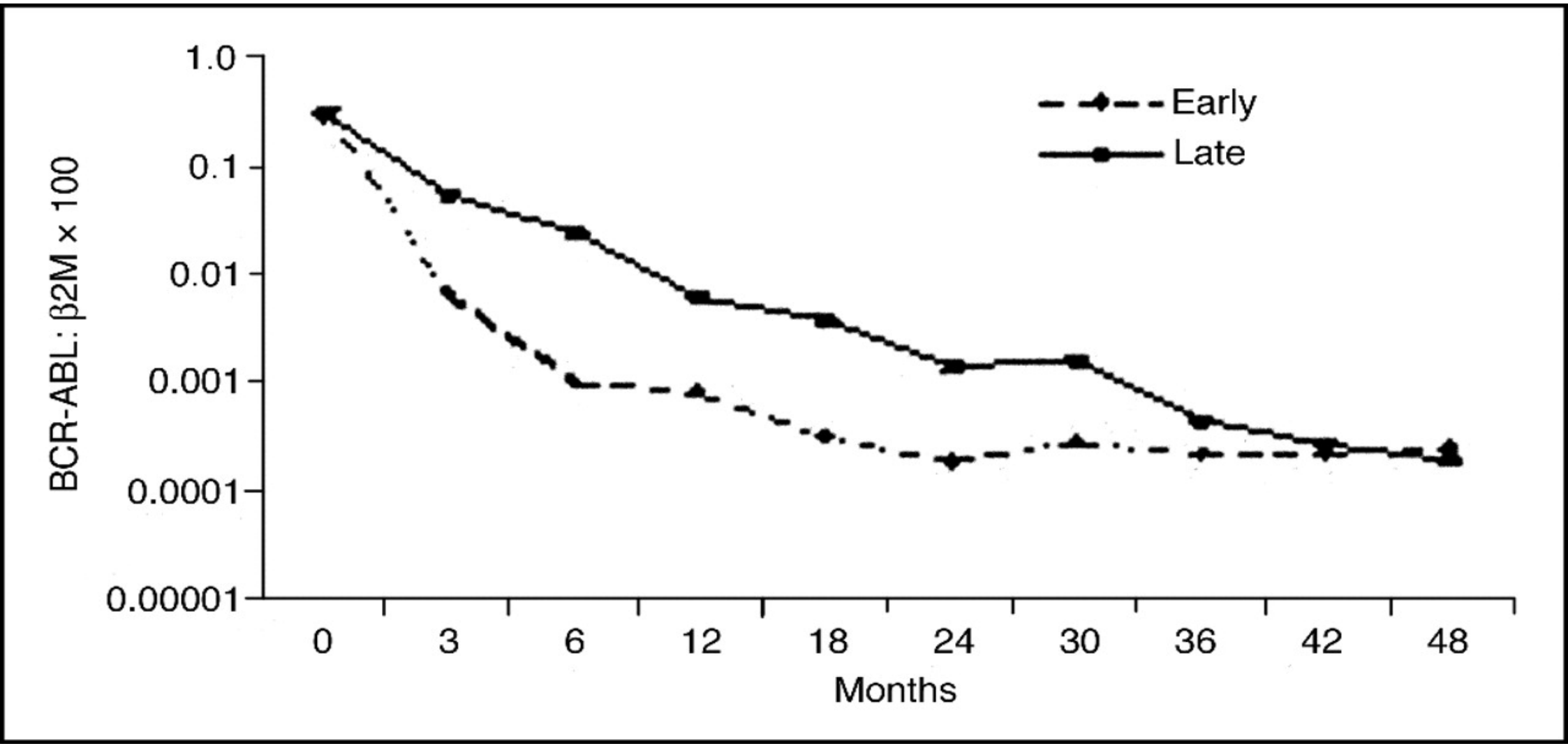
# Question

Is the time to reach MMR relevant in terms of prognosis?

# IRIS Q-PCR Study: Overall Estimated Log Reduction of *bcr-abl* with First-line Imatinib

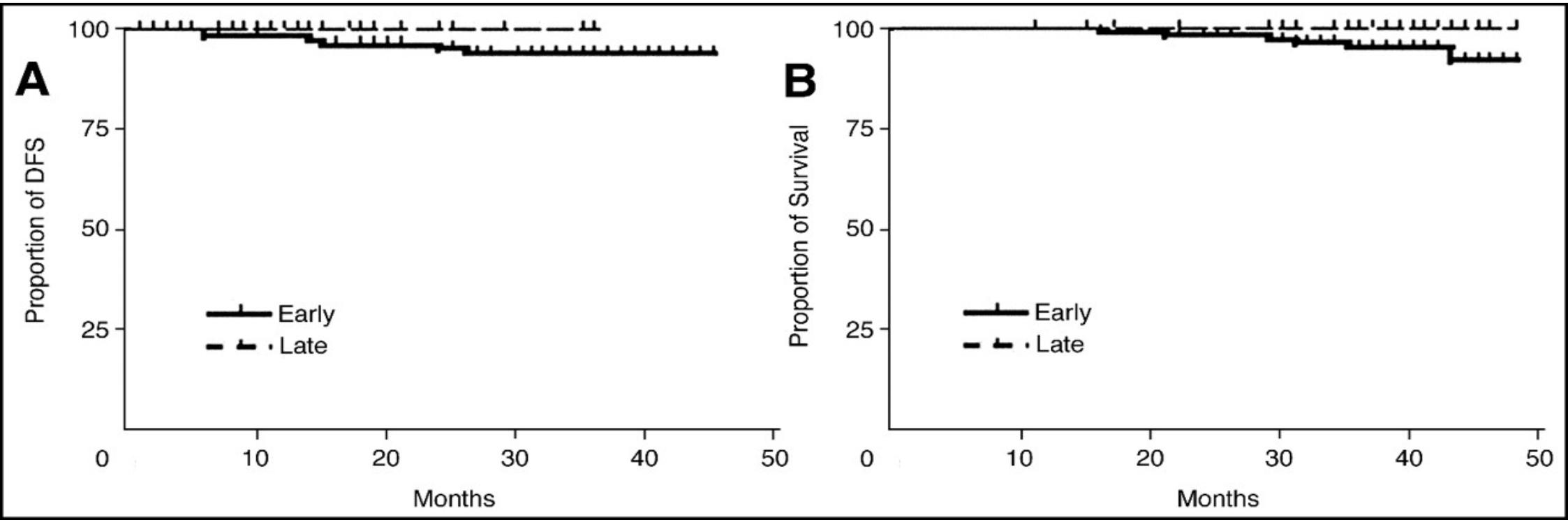



Radich J, et al. *Blood.* 2003;102:181a. Abstract 635 and oral presentation.




Iacobucci, I. et al. J Clin Oncol; 24:454-459 2006

# Association of early and late cytogenetic response with progression-free (A) and overall (B) survival

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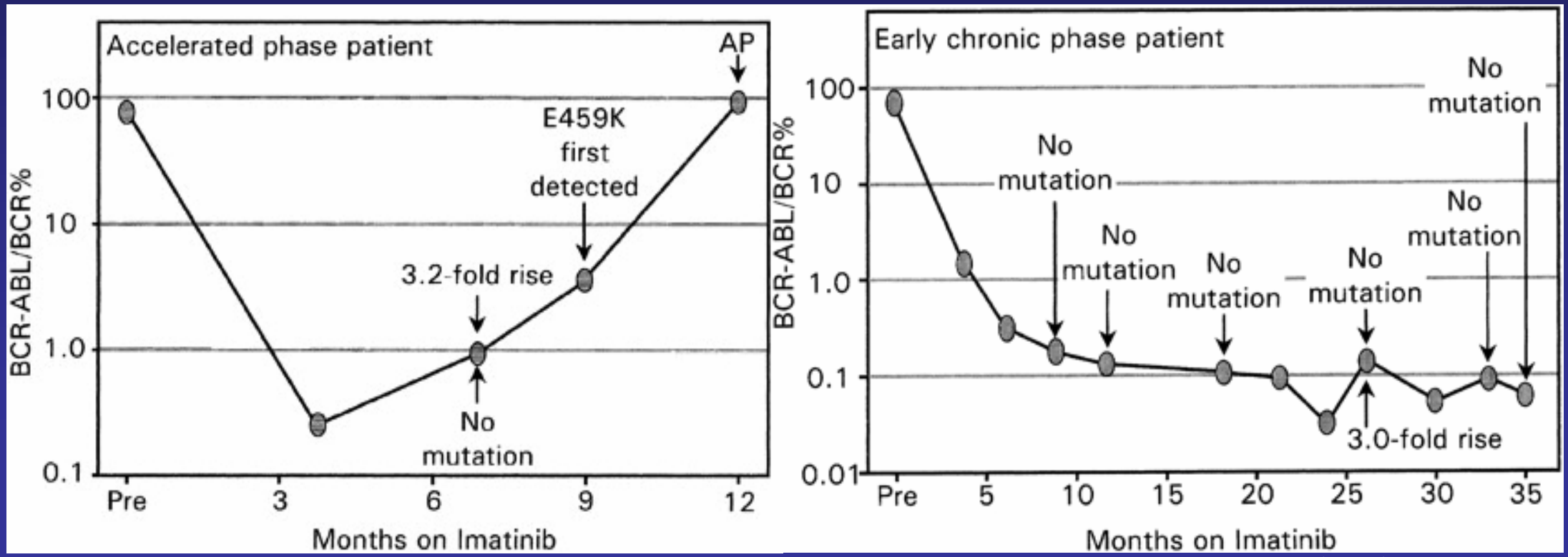
# RISE in BCR-ABL

- A rise in BCR-ABL of more than 2-fold identifies patients at high risk to become imatinib resistant
- In 60% of these cases, presence BCR-ABL mutations
- Mutation detection can be important




Branford S et al. Blood 2004

# Question

Which increase in BCR-ABL transcript level must trigger search for mutation?

Still an open question!

- 2 fold rise (Branford et al., Blood 2004)

- consecutive rises (Wang et al., Haematologica 2006)

# Timing


- RQ PCR during the first year:
  - To assess the response

- RQ PCR on PB every 3 months after the first year:
  - to identify the late responders (continously decreasing BCR/ABL%)
  - to detect a possible rise in BCR-ABL

# EVOLVING CONCEPTS IN THE MANAGEMENT OF CHRONIC MYELOID LEUKEMIA

RECOMMENDATIONS FROM AN EXPERT PANEL ON BEHALF OF THE EUROPEAN LEUKEMIANET

EXIT