

Clinical case presentation 2: Late response to treatment

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Background

- Therapy planning for patients with suboptimal response according to ELN criteria (Baccarani et al. 2006) has to be individual as late responses are possible
- In view of potential long-term adverse effects and potential non-response to following TKIs, are there patients who benefit from continuing imatinib?

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ELN recommendations

Time	Failure	Suboptimal response	Warnings
Dx	-	-	High risk Del9q+ ACA in Ph+ cells
3 months	No HR	< CHR	
6 months	< CHR No CgR	< PCgR	
12 months	< PCgR	< CCgR	< MMoIR
18 months	< CCgR	< MMoIR	
Anytime	Loss of CHR Loss of CCgR Mutation (IM-insensitivity)	ACA in Ph+ cells Loss of MMoIR Mutation (IM-sensitivity)	Any ↑ transcript level OCA in Ph- cells

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Patient

- Male patient, 61 years old
- June 2006
 - CML, Ph+, BCR/ABL+ (b3a2) chronic phase
 - Euro CML score: intermediate risk
 - No sibling donor



**400 mg/d imatinib
+ 3 x 1.5⁶ units IFN**

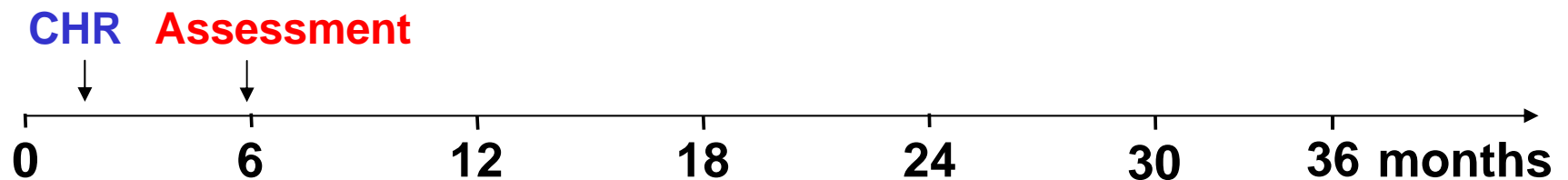
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Patient

- Male patient, 61 years old
- December 2006
 - CHR since July 2001 (after 1.5 months of therapy)
 - Declining Ph+ chromosomes from August 2006 (70%) to December 2006 (40%) (after 2 and 6 months on therapy)
 - No severe side effects



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Patient

What would you suggest?

- Continue 400 mg/d imatinib and IFN
- Stop imatinib and IFN and switch to dasatinib
- Stop imatinib and IFN and switch to nilotinib
- Check for unrelated donor

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Comments

- Suboptimal according to ELN criteria as partial cytogenetic response at 6 months was not achieved
- Suboptimal response implies that the patient may still substantially benefit from continuing IM treatment but that the long-term outcome is not likely to be optimal, so the patient becomes eligible for other treatments

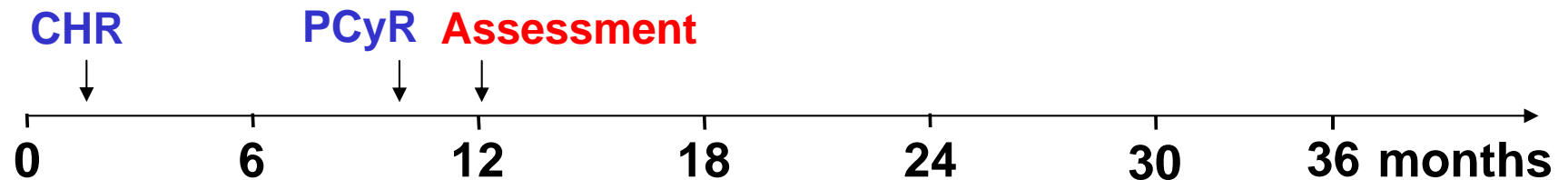
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Patient

- Male patient, 61 years old
- Imatinib and IFN was well tolerated and continued
- June 2007
 - Further declining of Ph+ chromosomes from December 2006 (40%) to April 2007 (10%) (after 6–10 months of therapy)
 - BCR-ABL/ABL ratio was 0.25% (IS) in June 2007 (after 12 months of therapy)



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Patient

What would you suggest?

- Continue 400 mg/d imatinib and IFN
- Stop imatinib and IFN and switch to dasatinib
- Stop imatinib and IFN and switch to nilotinib
- Check for unrelated donor

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Commentary

- According to ELN criteria warning (no MMR at 12 months) and suboptimal response (no CCR at 12 months)
- Warnings imply that the patient should be monitored very carefully and may become eligible for other treatments

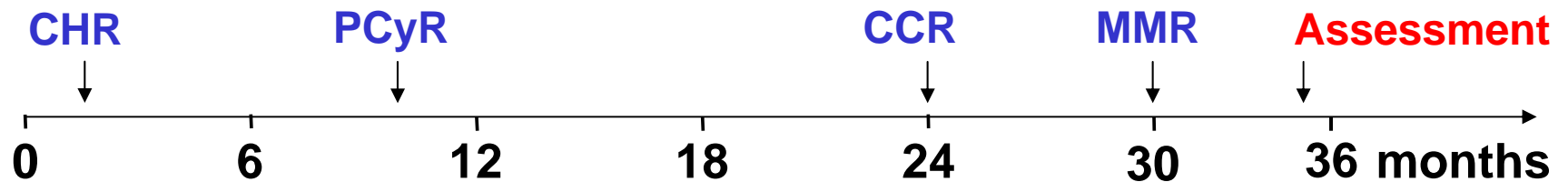
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Patient

- Male patient, 61 years old
- Imatinib and IFN was well tolerated and continued
- June 2009
 - CCR achieved June 2008 (24 months of therapy)
 - BCR-ABL/ABL ratio < 0.1% (IS) (30 months of therapy)
 - Stable disease since then

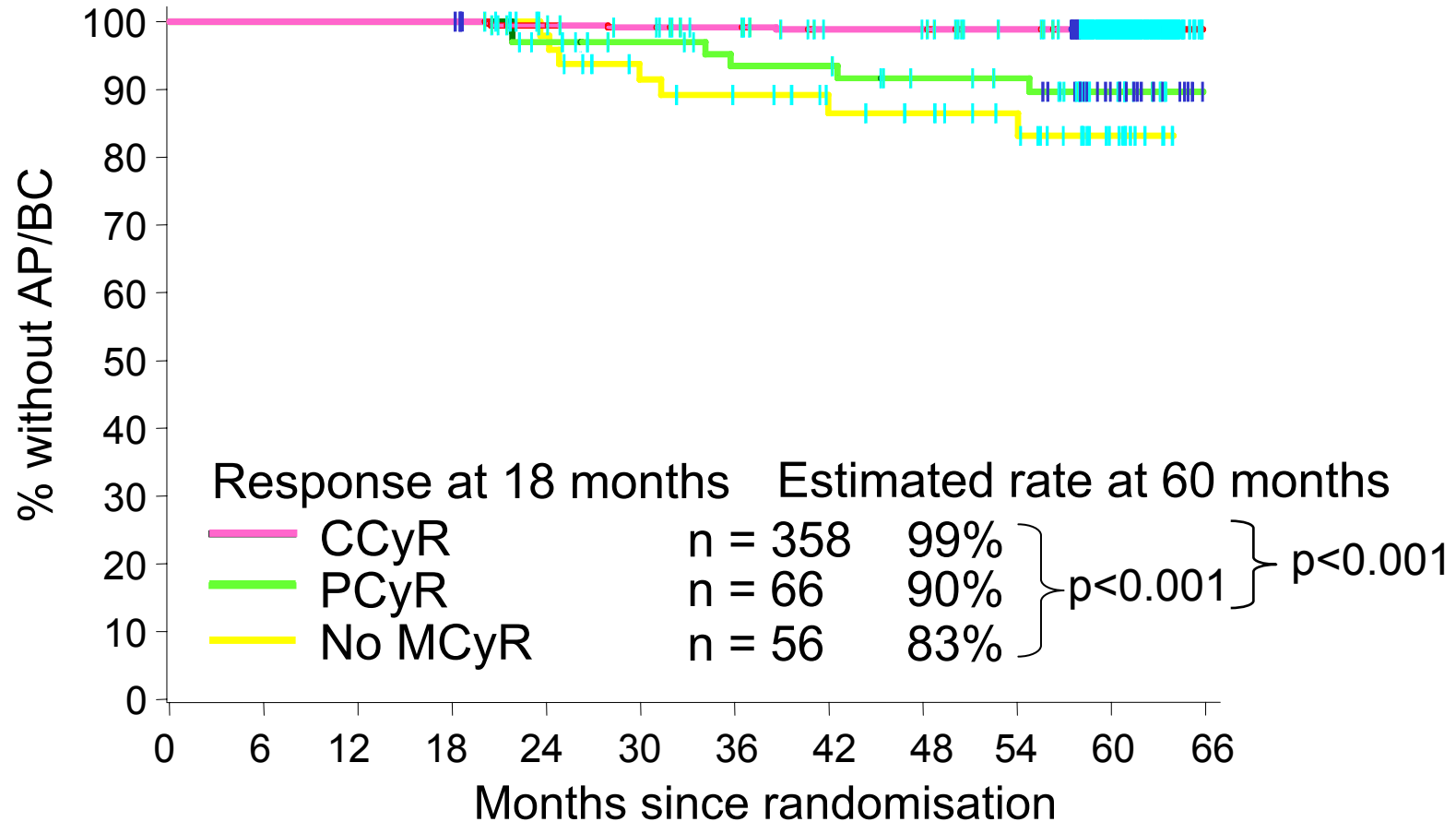


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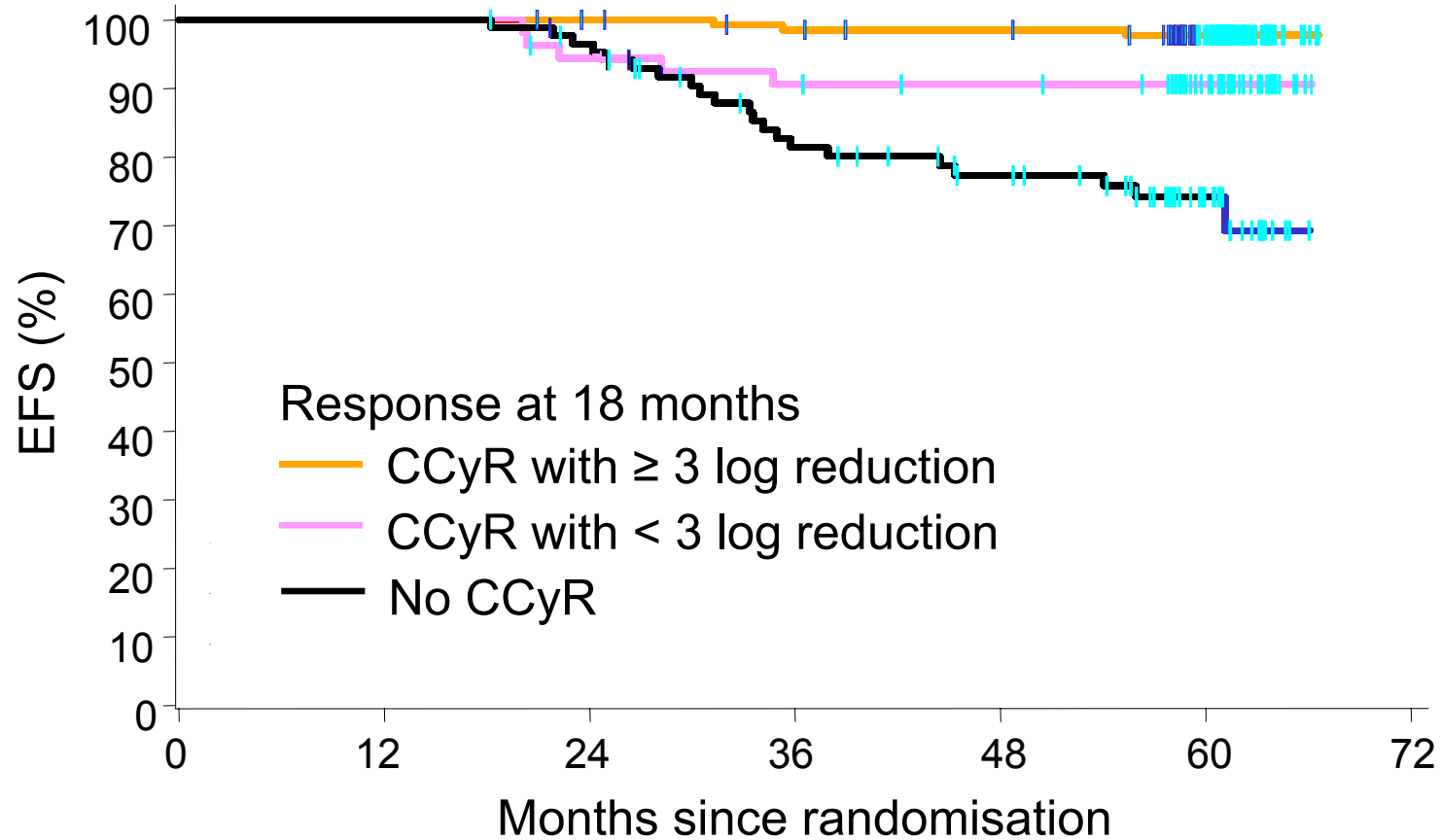
Survival without progression to AP/BC by level of CyR at 18 months



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Event-free survival by response at 18 months



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Conclusion: think twice about switching therapy

- ELN criteria are helpful tools in managing therapy of CML patients
- A substantial amount of patients not achieving a CCyR or MMR at 18 months showed good survival at 60 months
- Switching to other treatments should be carefully reviewed especially in patients with declining parameters

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