Discontinuation of Imatinib in Patients with Chronic Myeloid Leukemia Who Have Maintained Complete Molecular Response: Update Results of the STIM

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on behalf of the STIM Investigators

Disclosures for François-Xavier Mahon, MD, PhD, Hematologist

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Presentation includes discussion of the following off-label use of a drug or medical device: [N/A]

Background

- Imatinib treatment significantly improves survival in pts with CML.

- We previously demonstrated that Imatinib could be safely discontinued in pts with a sustained CMR, i.e., of at least 2 years duration.

- Little is known about whether treatment can safely be discontinued in the long term.

- We present the updated results from the first 100 pts included in the STIM study with a longer follow up.

1. Rousselot *et al. Blood* 2007;109:58–60
2. Mahon FX, et al. Lancet oncology, 2010;11: 1029-1035 (an interim analysis on 69 pts having at least 12 months of follow-up)

STop **IM**atinib TRIAL: Key Issues

- What is the risk of molecular recurrence after discontinuation with a longer follow up?
- Which category of patients may most benefit from treatment discontinuation?
- Is it safe to stop therapy?

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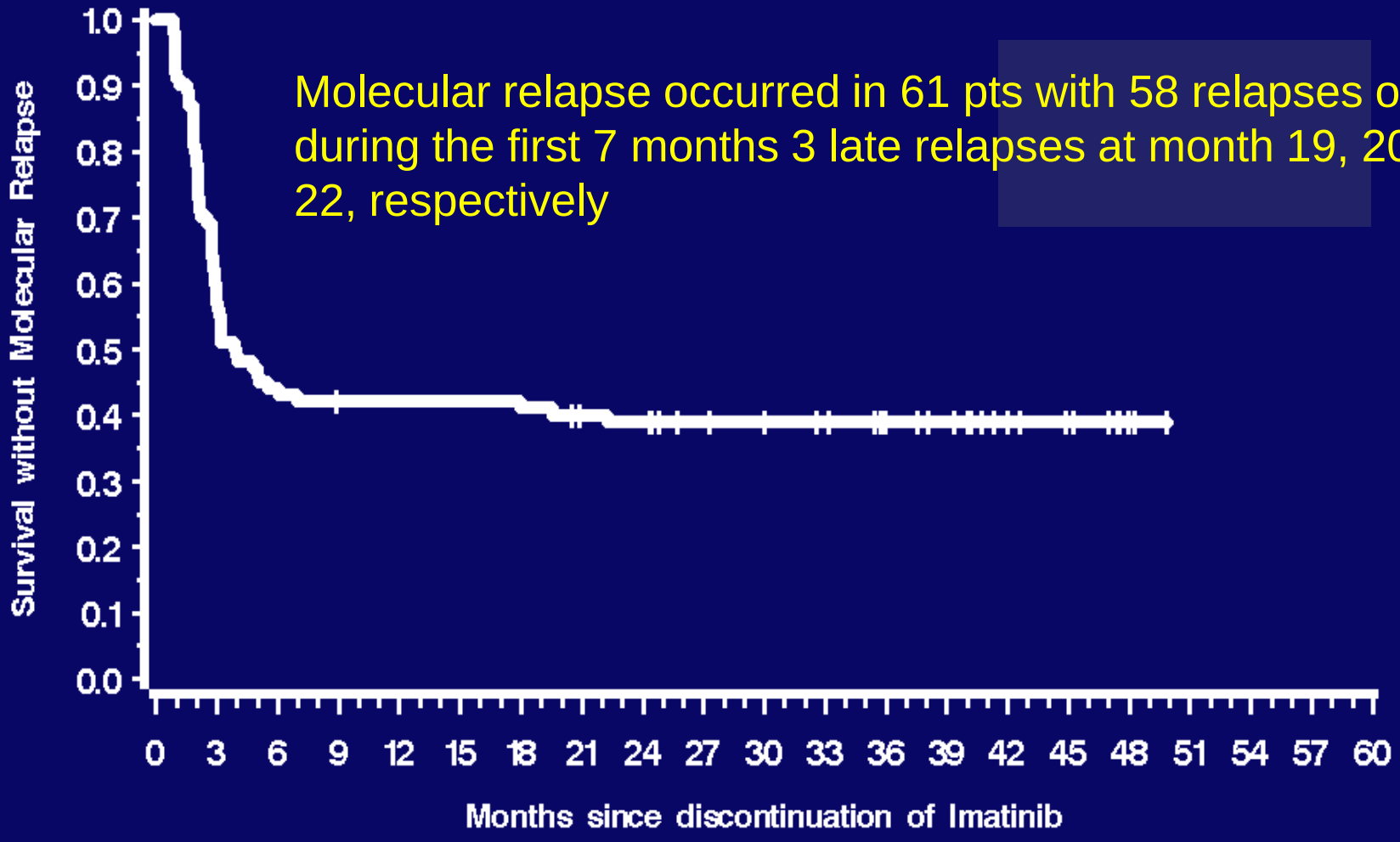
Baseline characteristics of the 100 pts

- Number of patients included: 100
- Median age (range): 63 years (29–80)
- Gender distribution: 48 males, 52 females
- Patients with previous IFN treatment: 51
- *De novo* patients: 49
- Median Follow up : 34 months (range 9-50)

Kaplan-Meier estimates of CMR after discontinuation of imatinib

The overall probability of maintenance of CMR at 24 and 36 months was 39% (95% CI 29-48).



Molecular relapse occurred in 61 pts with 58 relapses occurring during the first 7 months 3 late relapses at month 19, 20 and 22, respectively

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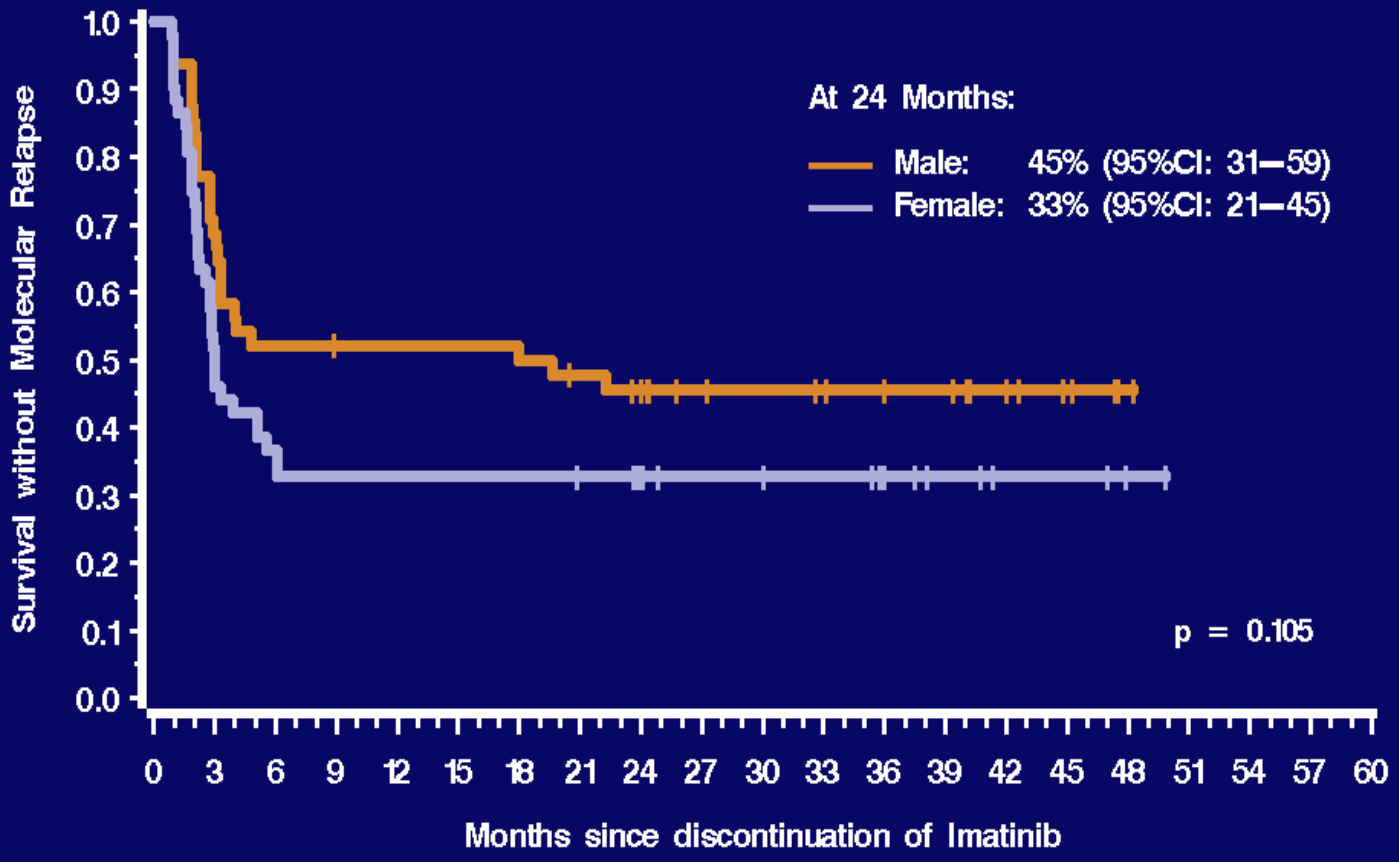
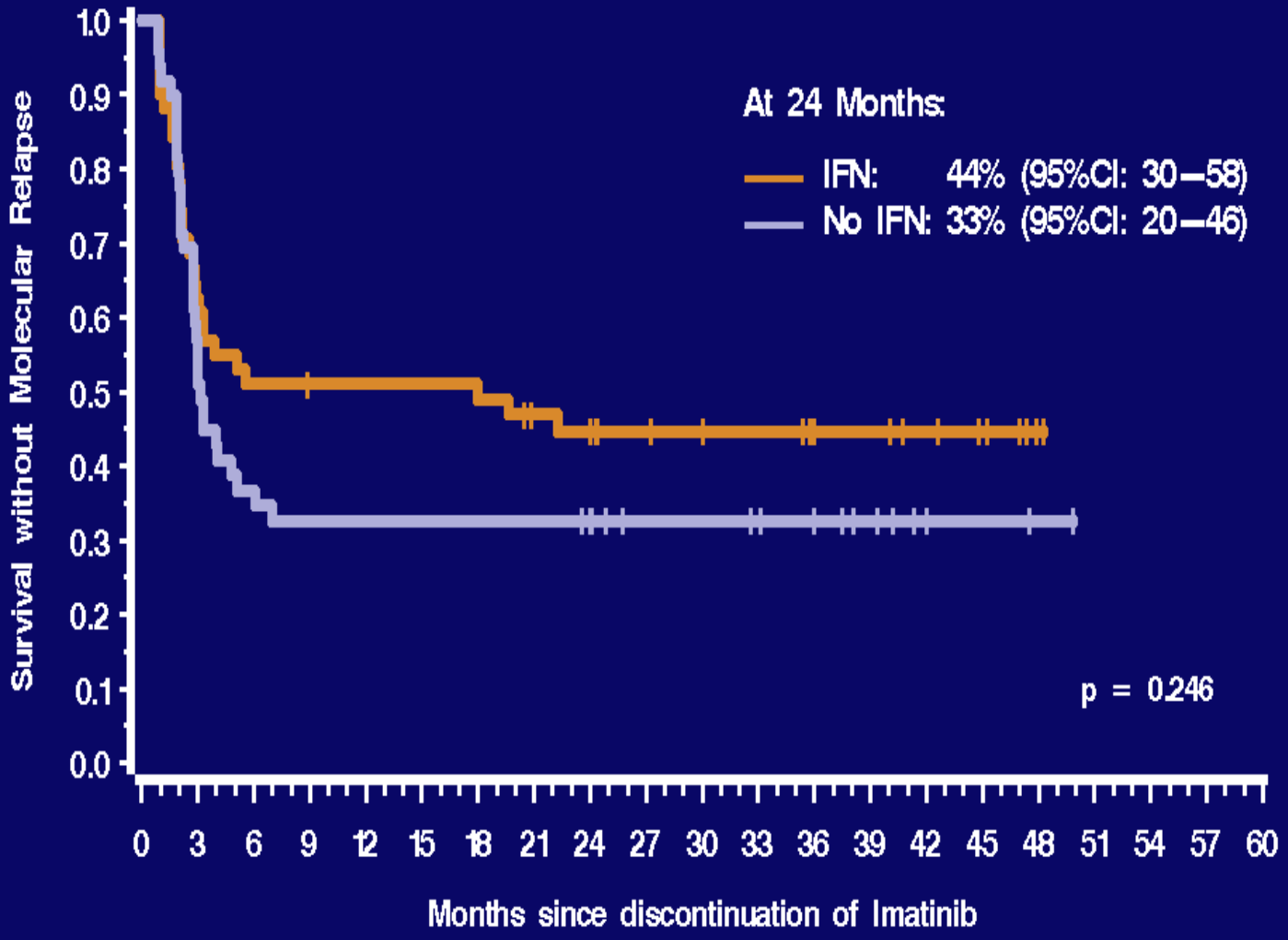
Kaplan-Meier estimates of CMR after discontinuation of imatinib in 100 patients with CML according to factor

By gender



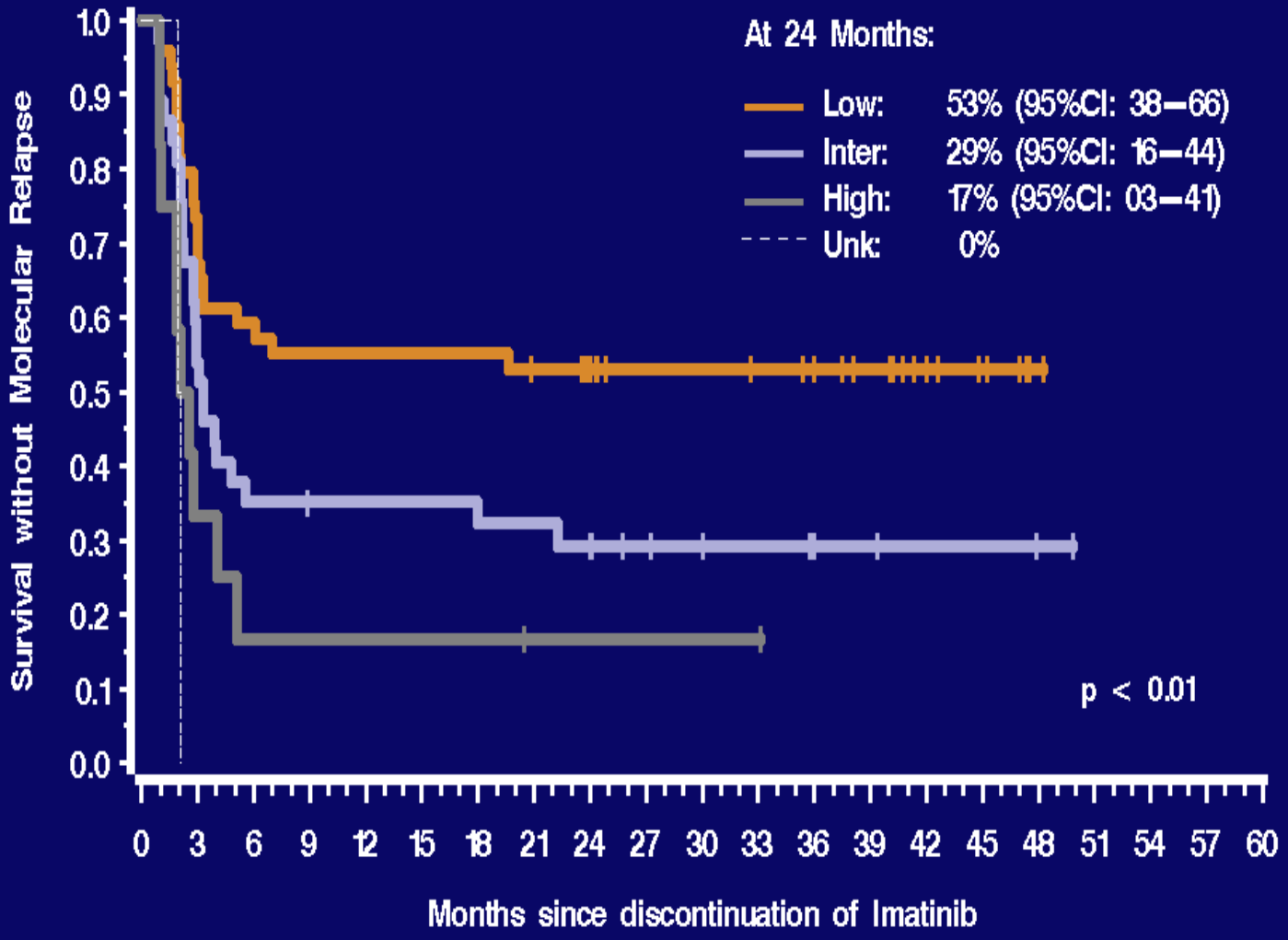
Kaplan-Meier estimates of CMR after discontinuation of imatinib in 100 patients with CML according to factor

By previous treatment



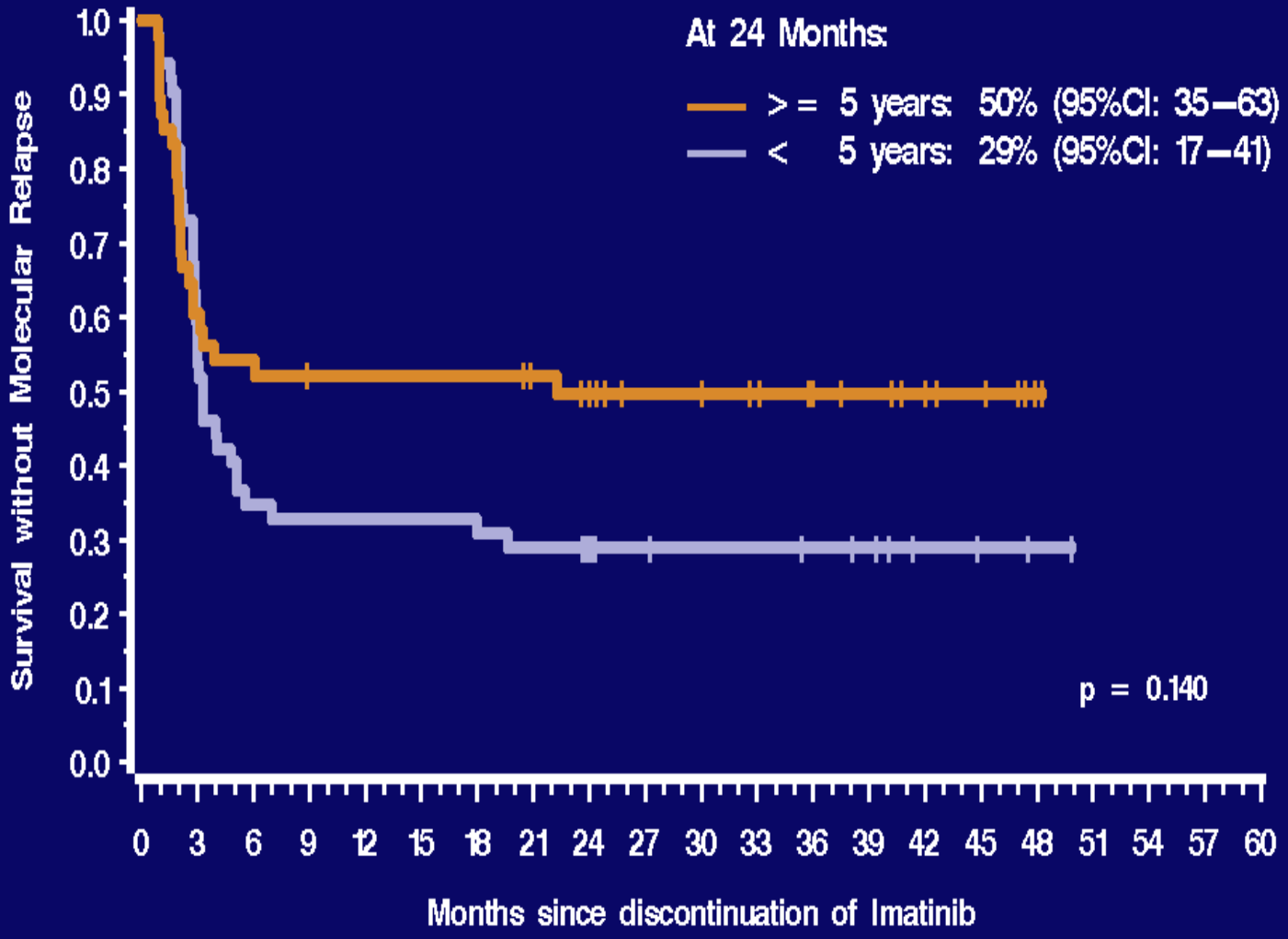
Kaplan-Meier estimates of CMR after discontinuation of imatinib in 100 patients with CML according to factor

By SOKAL score



Among the 11 patients with high sokal risk score 9 patients relapsed

Freedom from Molecular Relapse by Median Duration of Imatinib Treatment



Logistic regression at 8 months : all early relapses included n = 58

		Univariate analysis *P value*		Multivariate analysis # (final model)
Age at Discontinuation §	**: No relapse**	60		-
	Relapse	61	*0.315*	
Gender £	**Male**	48%		-
	Female	67%	*0.050*	
Sokal score £	**Low**	**45%**		
	Intermediate	**65%**		
	High	**83%**	***0.026***	***0.005***
Interferon	**Yes**	49%		-
	No	67%	*0.060*	
Time to CMR §	**: No relapse**	19	*0.378*	-
	Relapse	17		
CMR duration §	**: No relapse**	38		-
	Relapse	35	*0.363*	
IM duration §	**: No relapse**	66		
	Relapse	55	***0.080***	***0.028***
				-

§ Median (months)
£ Percentage relapsing

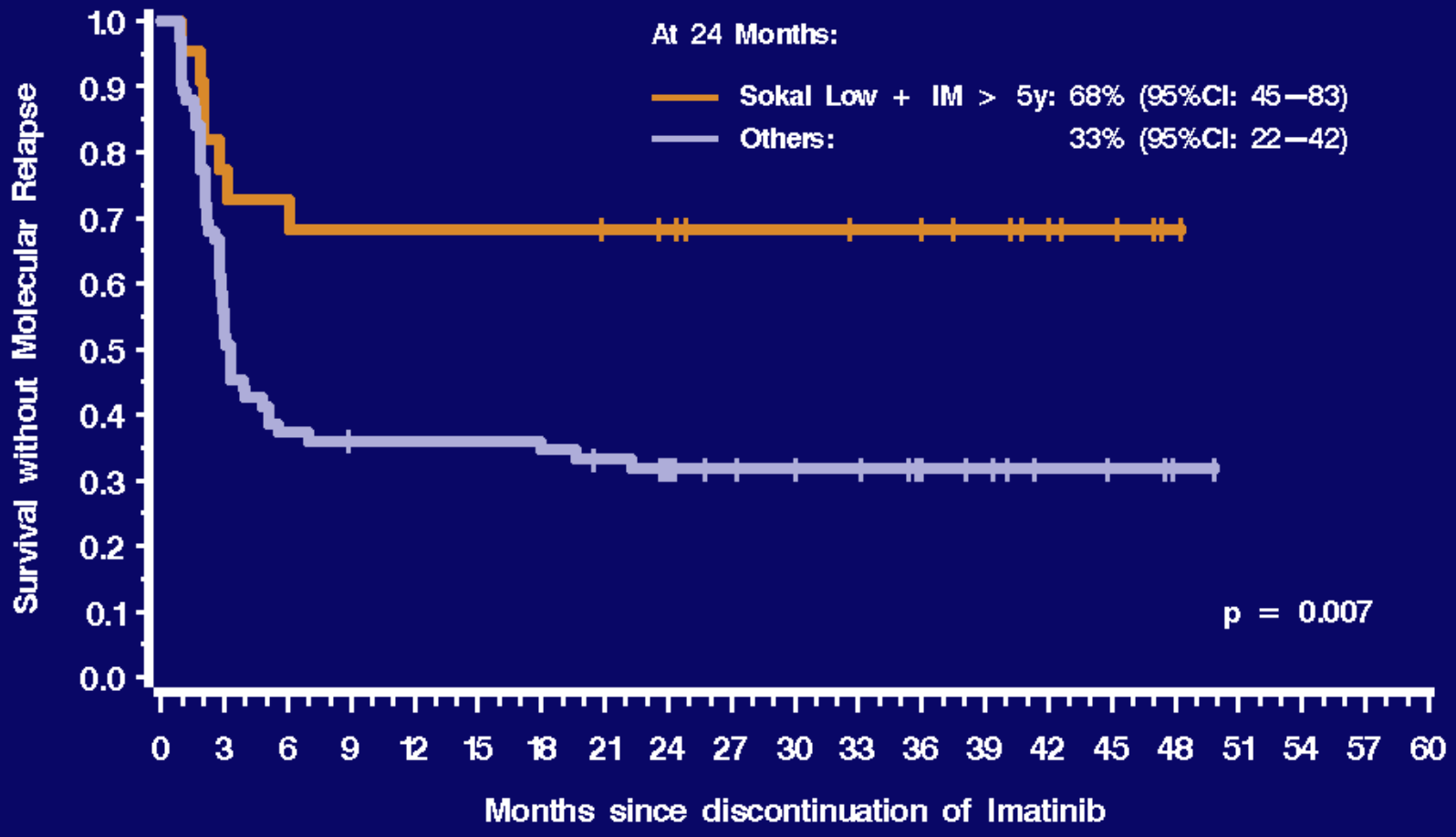
Logistic regression

Multivariate Analysis Cox model over all patients and all relapses

	Multivariate analysis Cox model	
	Hazard ratio (95% CI)	p value
Sokal score	2.555 (1.278 -5.119)	0.008
IM duration >60 months vs ≤60 months	0.582 (0.340 -0.995)	0.047

Final Model => 2 independent prognostic factors

Kaplan-Meier estimates of CMR after discontinuation imatinib in 100 pts according to combined factors



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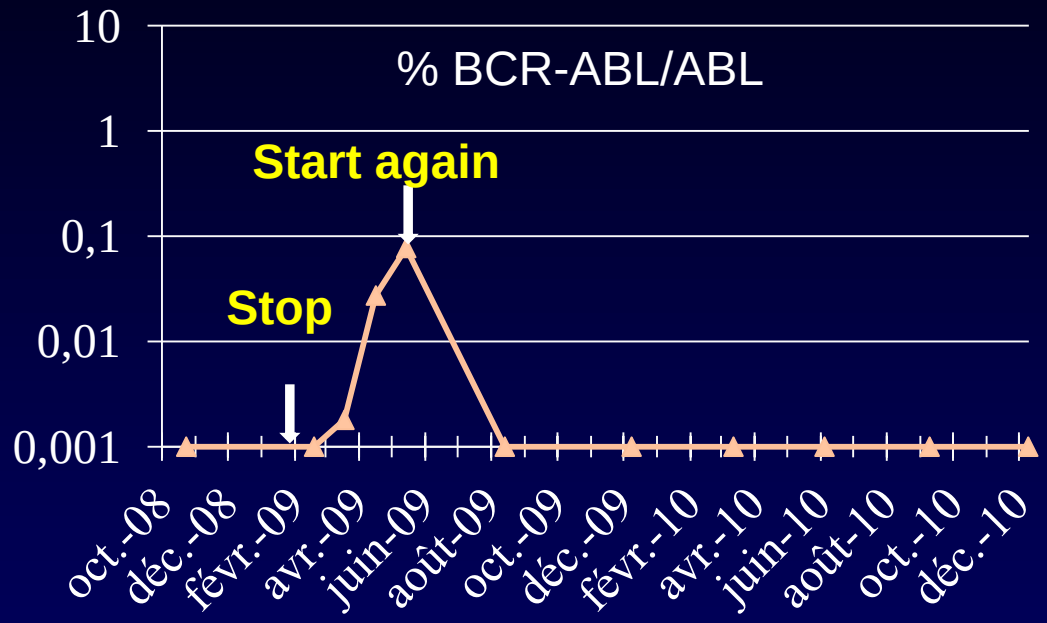
All patients are sensitive after imatinib re-challenge

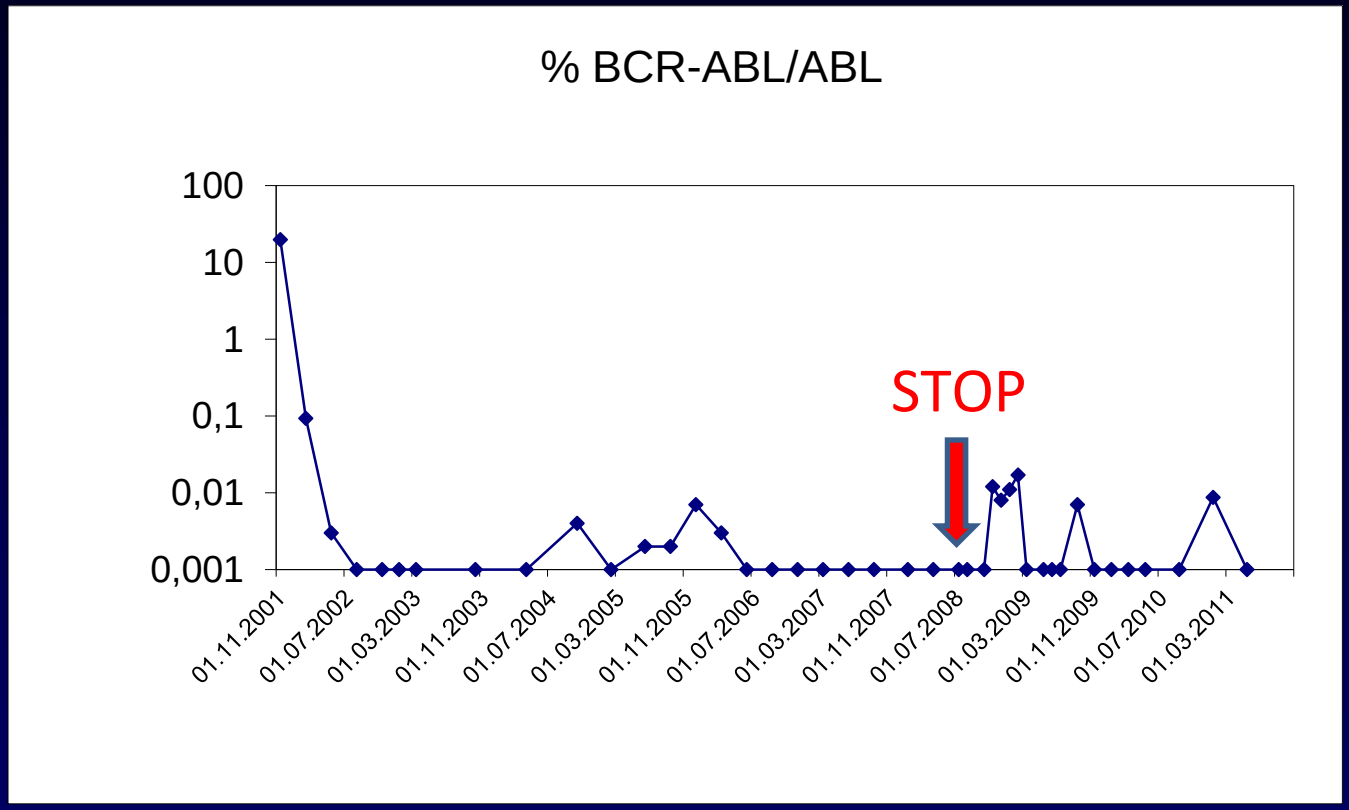


- Among the 61 with molecular recurrence 10 are not in sustained CMR

- Five return to CMR after imatinib rechallenge but exhibited a fluctuation in BCR-ABL transcripts.

- Five pts did not return to CMR, with a median values of BCR-ABL level of 0.19% (0.005-0.8) because they did not want to take a treatment as soon as they relapsed.

Fluctuation of BCR-ABL detection after discontinuation



Among the 39 pts without confirmed molecular relapse,
5 exhibited clearly a fluctuation in BCR-ABL transcript detection

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- What is the risk of molecular recurrence after discontinuation with a longer follow up?
- Which category of patients may most benefit from treatment discontinuation?
- Is it safe to stop therapy?
- Shall we speculate that we will increase the numbers of patients who stop treatment?

Discontinuation of Dasatinib or Nilotinib in Chronic Myeloid Leukemia (CML) Patients (pts) with Stable Undetectable Bcr-Abl Transcripts: Results From the French CML Group (FILMC)

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Conclusions

- I will recommend to propose discontinuation only in

a clinical trial with close molecular monitoring

- The most important factors to predict recurrence after discontinuation

i) **the inherent nature of the disease** (illustrate by the Sokal score)

ii) **the duration of therapy**

- Taking into account the number of months without treatment in the study at last analysis, **the savings within the STIM trial were estimated at 4 millions Euros.**

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