

# The Use of 2nd Generation TKIs as First Line Therapy Does Not Prevent CML Related Death: Results of an Italian CML Campus Prospective Study in 1277 Patients Treated First Line With Imatinib or 2nd Gen TKIs

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## BACKGROUND

In the last decades prognosis and survival of chronic myeloid leukemia (CML) patients have dramatically improved, thanks to a wider therapeutic armamentarium. Molecular responses are the milestones that guide clinical decisions; however, some information is still lacking and what we know derives mainly from investigational trials: it is still unclear if real-life management could lead to comparable results. For this reason, a prospective observational study was conducted by a CML Italian network to analyze molecular responses in a real-life setting.

## METHODS

- Web-based database ([www.epiclin.it/lmc](http://www.epiclin.it/lmc))
- newly diagnosed CML prospective patients
- 24 Italian Hematology Centers involved
- from January 2013 onwards



## RESULTS

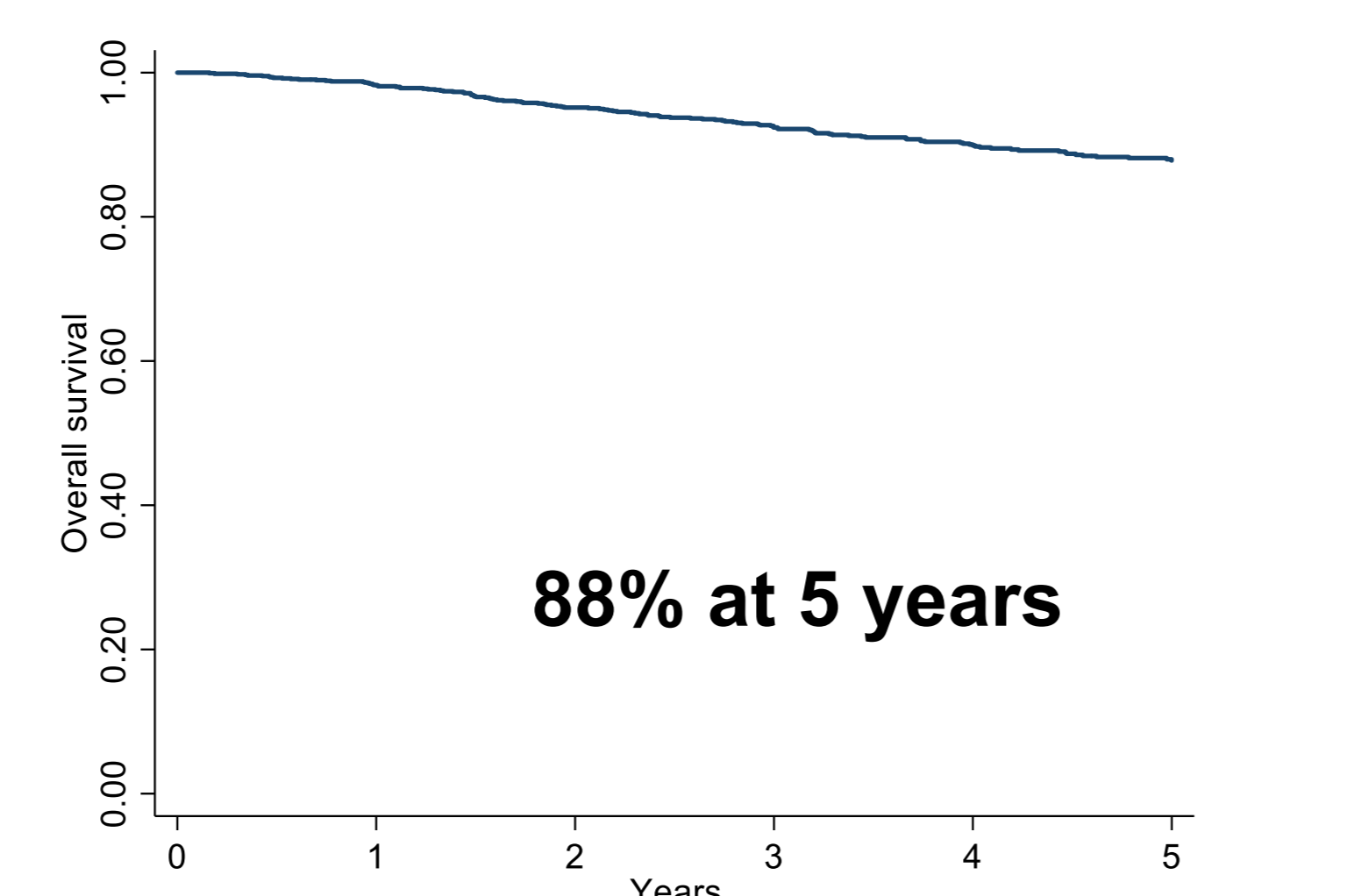
### Patients characteristics

		ALL 1277		IMA 607		II-TKI 670	
		n	%	n	%	n	%
Sex	Female	532	41.66	242	39.87	290	43.28
	Male	745	58.34	365	60.13	380	56.72
Age	Median	58		70		52	
	Low	761	59	305	50.25	456	68.06
	Intermediate	361	28	218	35.91	143	21.34
CCI	High	153	12	83	13.67	70	10.45
	Low (2)	908	71.10	341	56.18	567	84.63
ACA	Intermediate (3-4)	293	22.94	209	34.44	84	12.54
	High (>5)	72	5.64	53	8.73	19	2.84
ACA	all	179	14	79	13	100	14.9
	Major routes	80	6.3	26	4.3	54	8

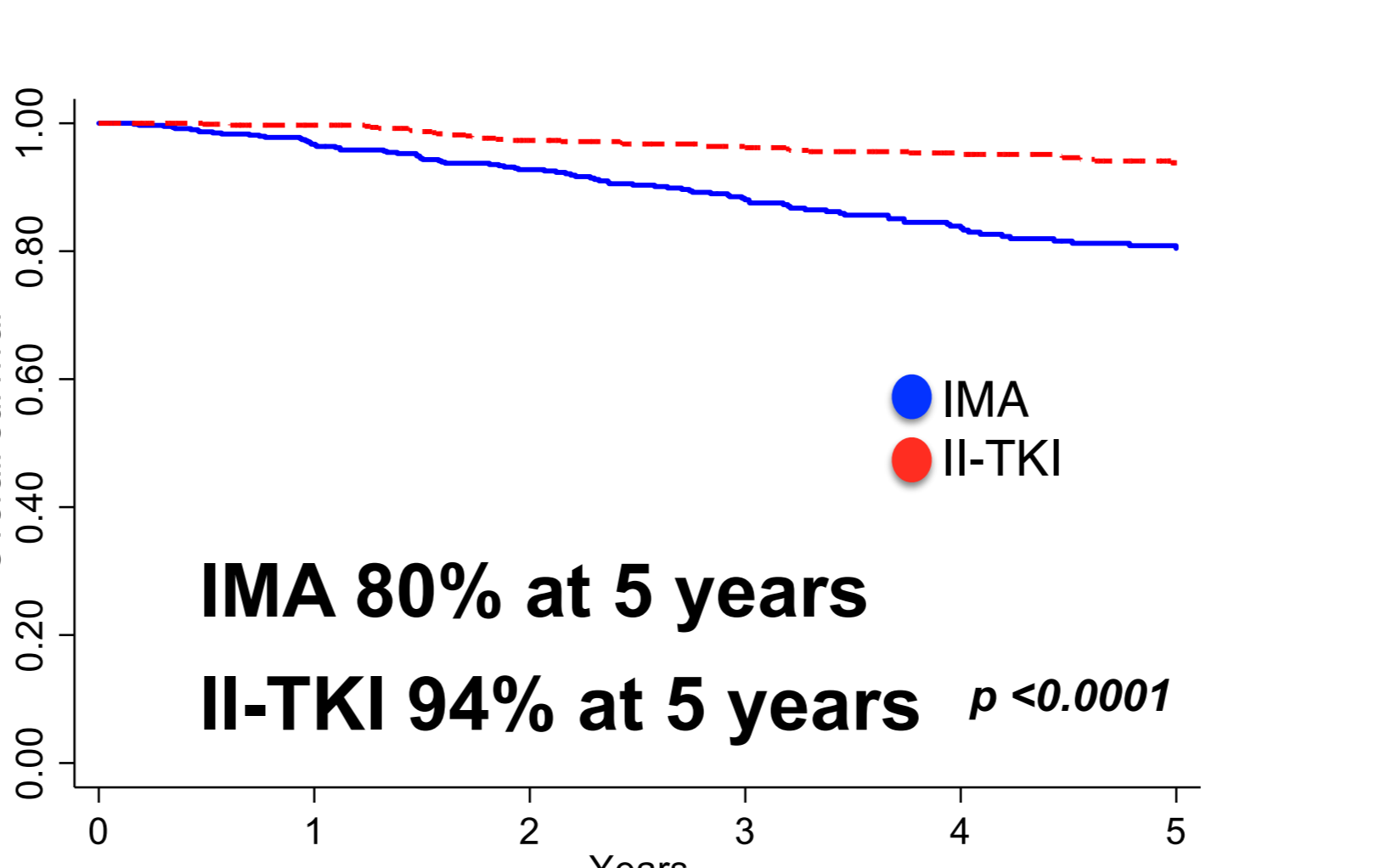
MEDIAN FOLLOW UP: 4,1 years  
CCI: Charlson Comorbidity Index; ACA: additional cytogenetic abnormalities

## RESULTS

### OS of ALL POPULATION (n: 1277)

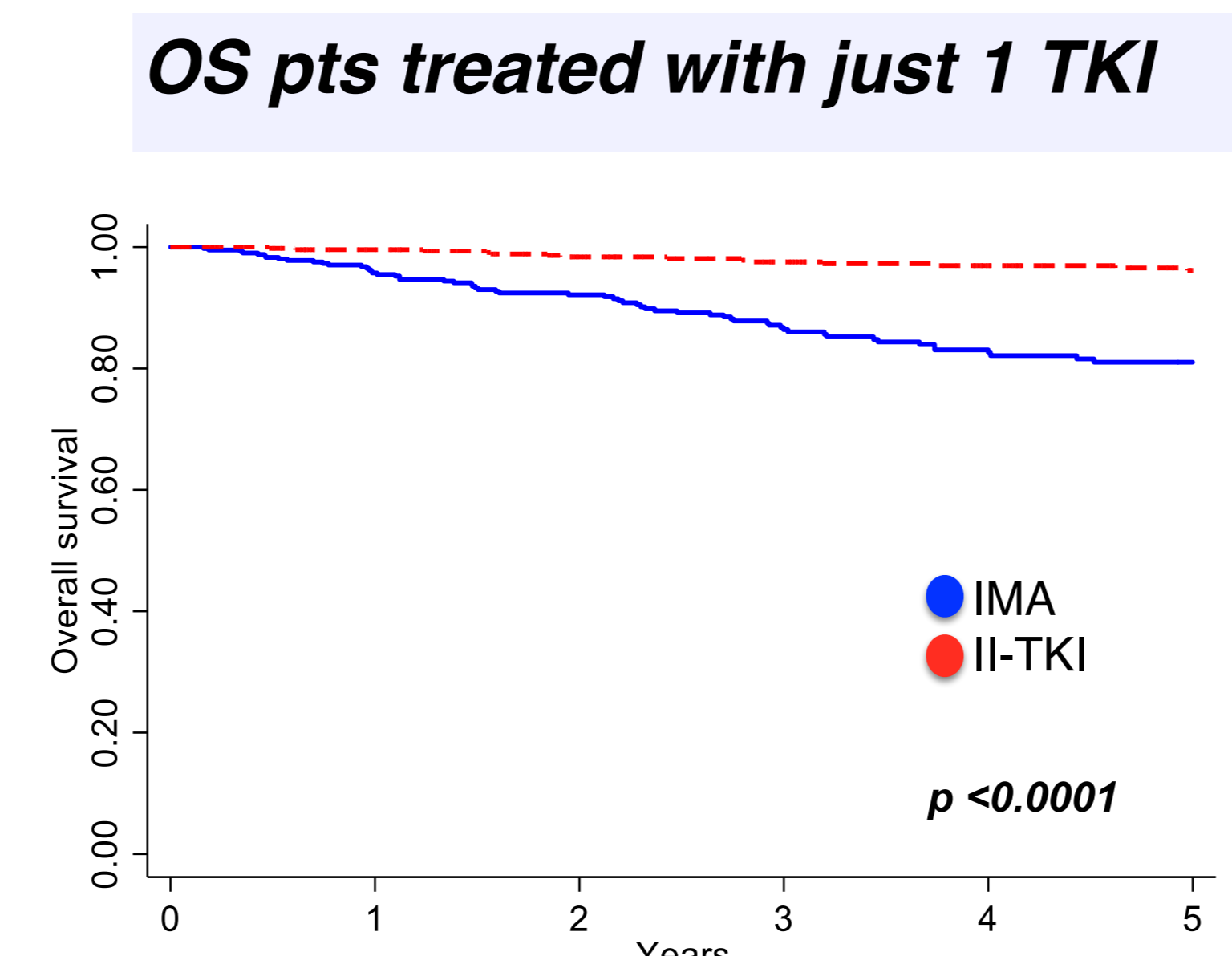


### OS according to first line TKI

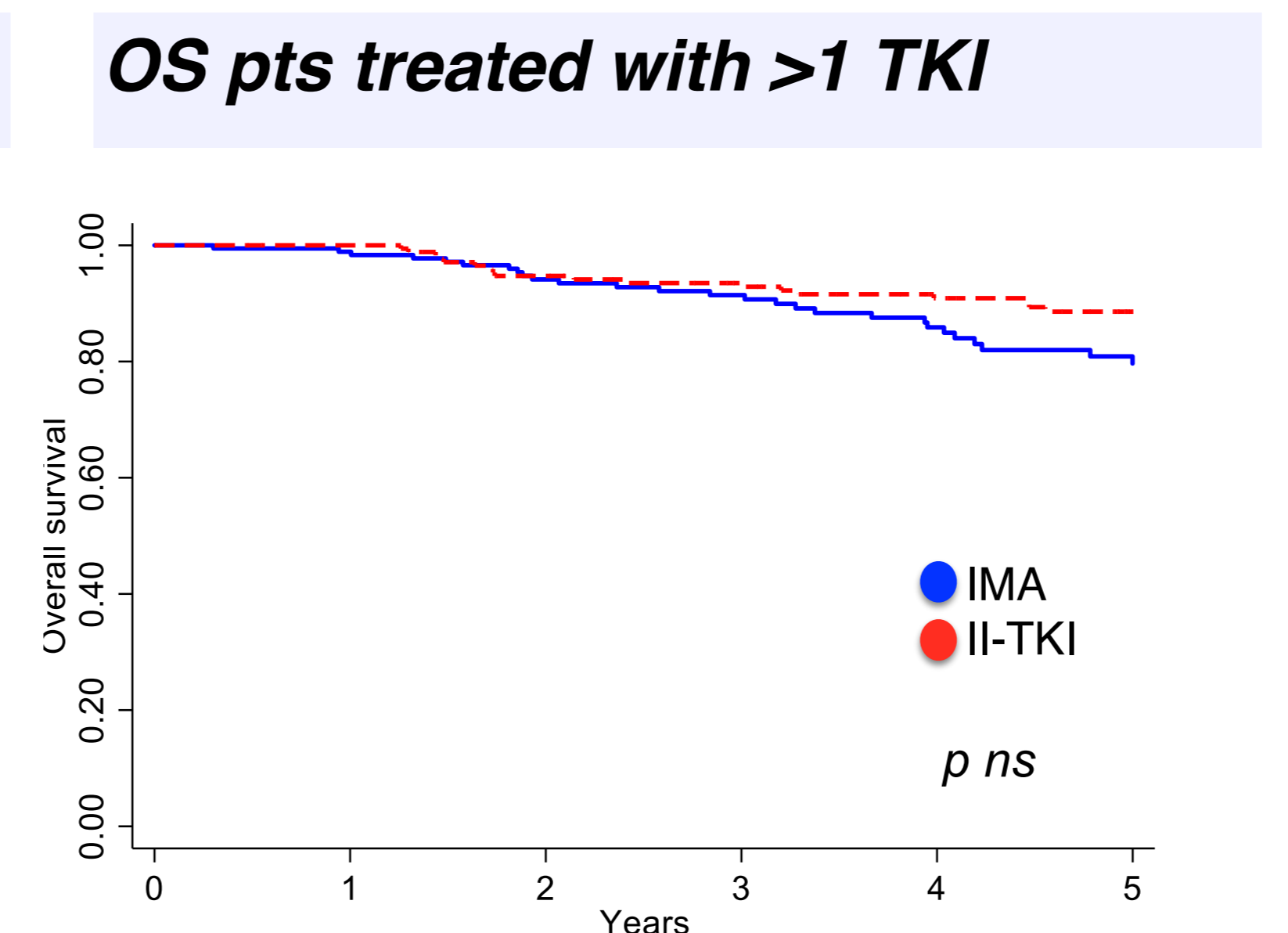


5 years OS	First line TKI			
	IMA n: 607		II-TKI n: 670	
	Stayed on IMA	Switched to other	Stayed on II-TKI	Switched to other
	422/607 (69%)	185/607 (31%)	492/670 (73%)	178/670 (27%)
	81%	80%	96%	89%

### OS pts treated with just 1 TKI



### OS pts treated with >1 TKI

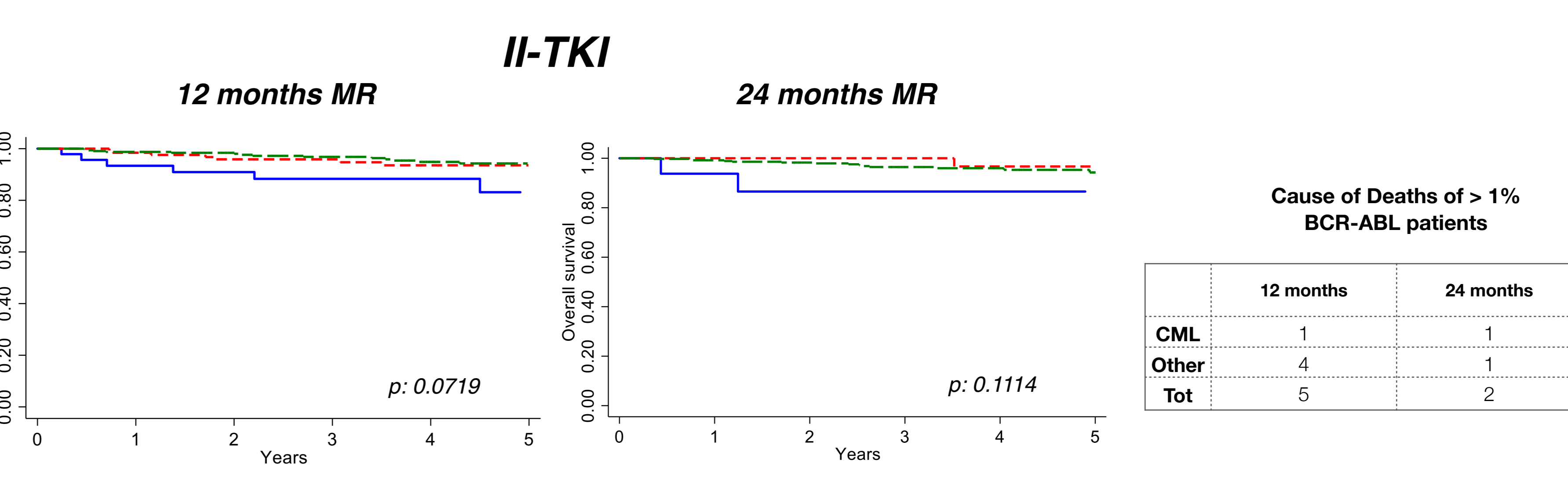
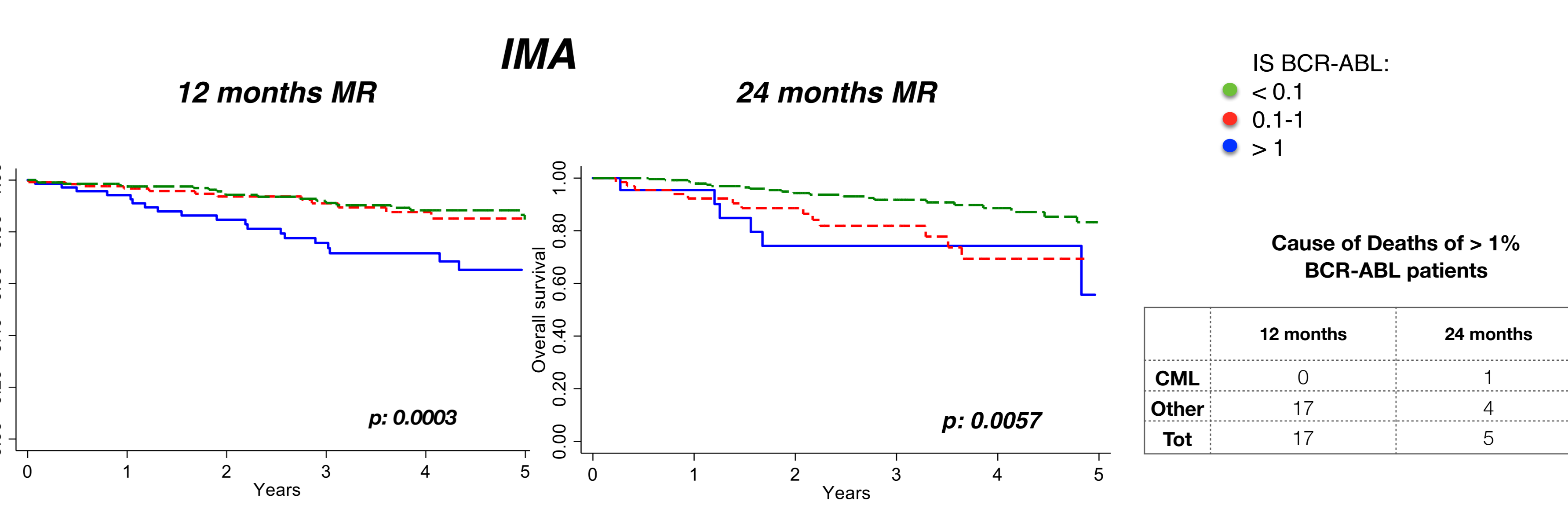


### CML related deaths

Total CML-rel	IMA total deaths: 86/607		II-TKI total deaths: 32/670	
	Stayed on IMA	Switched to other	Stayed on II-TKI	Switched to other
	8/58 (14%)	3/28 (10%)	1/15 (7%)	11/17 (65%)
	11/86 (13%)		12/32 (37%)	

- 73 deaths were observed in the group of patients treated with just 1 TKI (n: 914): 9/73 were CML related.
- 45 deaths were observed in the group of patients treated with > 1 TKI (n: 363): 14/43 were CML related.

### OS according to MOLECULAR RESPONSES



## CONCLUSIONS

- good prognosis obtained independently by the TKI used in 1st line
- most of the deaths are due to CML unrelated causes
- the use of II-TKIs does not seem to prevent the CML related deaths
- OS is similar in pts in IMA therapy versus to those who switch: presence of unfavorable prognostic factors at diagnosis not controlled by IMA nor by II-TKIs?
- better OS in IMA patients with BCR ABL <1% at 12 months and with MMR at 24 months (association rather than a determining factor?)
- early NGS study could give helpful information for identifying patients that, even if treated 1st line with II-TKIs, could benefit of an early switch, since 11 of the 12 progressions were observed in this group.

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