

Monoclonal gammopathy of undetermined significance and smoldering multiple myeloma

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MONOCLONAL GAMMOPATHIES

I. MALIGNANT

1. Multiple myeloma
2. Variants of myeloma
 - Smoldering myeloma
 - Non-secretor
 - Plasma cell leukemia
 - POEMS
3. Localized plasmacytomas
 - Solitary plasmacytoma (bone)
 - Extramedullary plasmacytoma
4. Waldenström's macroglobulinemia
5. Primary amyloidosis

II. NON-MALIGNANT

1. Monoclonal gammopathy of undetermined significance
2. Transient MG: HIV infection, bone marrow transplant, organ transplant (liver, kidney)

Monoclonal Gammopathy of Undetermined Significance (MGUS) Diagnostic Criteria*

- Serum M protein size <3g/dL
- Bone marrow plasma cells <10%
- No clinical manifestations or other laboratory abnormalities attributable to the monoclonal gammopathy

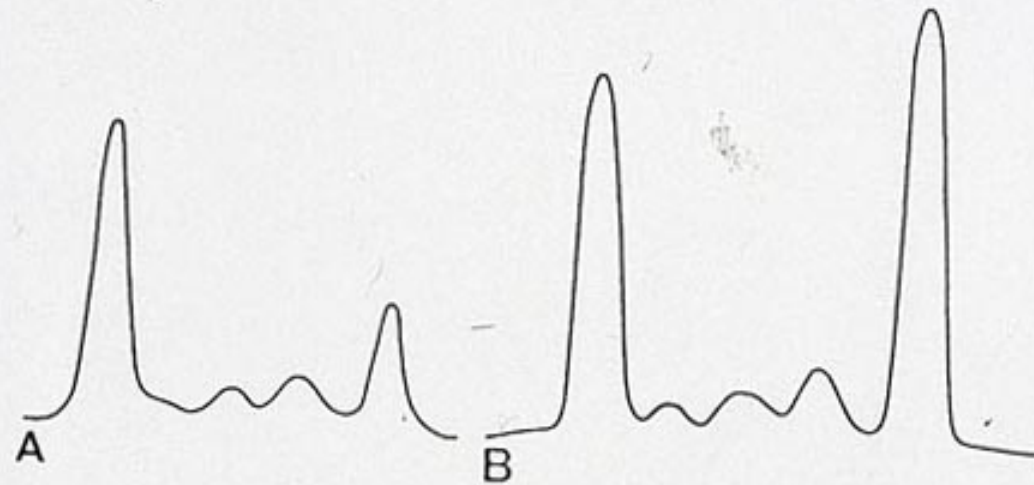


Fig. 22.2 Serum electrophoresis: (A) from a patient with IgG monoclonal gammopathy of undetermined significance showing a modest M-component in the γ region; (B) from a patient with an overt IgG multiple myeloma.

MGUS. Actuarial Probability of Malignant Evolution *

Author, yr.	N ^o of patients	% probability at		
		10 yrs.	20 yrs.	25 yrs.
Kyle et al, 2004**	241	17	34	39
Pasqualetti et al, 1997	263	15	31	--
Cesana et al, 2002	1104	14	--	--
Kyle et al, 2002	1384	12	25	30
Montoto et al, 2002	434	15	34	--

* Only series with long-term follow-up are included.

** First reported in 1978, 1984 and 1993.

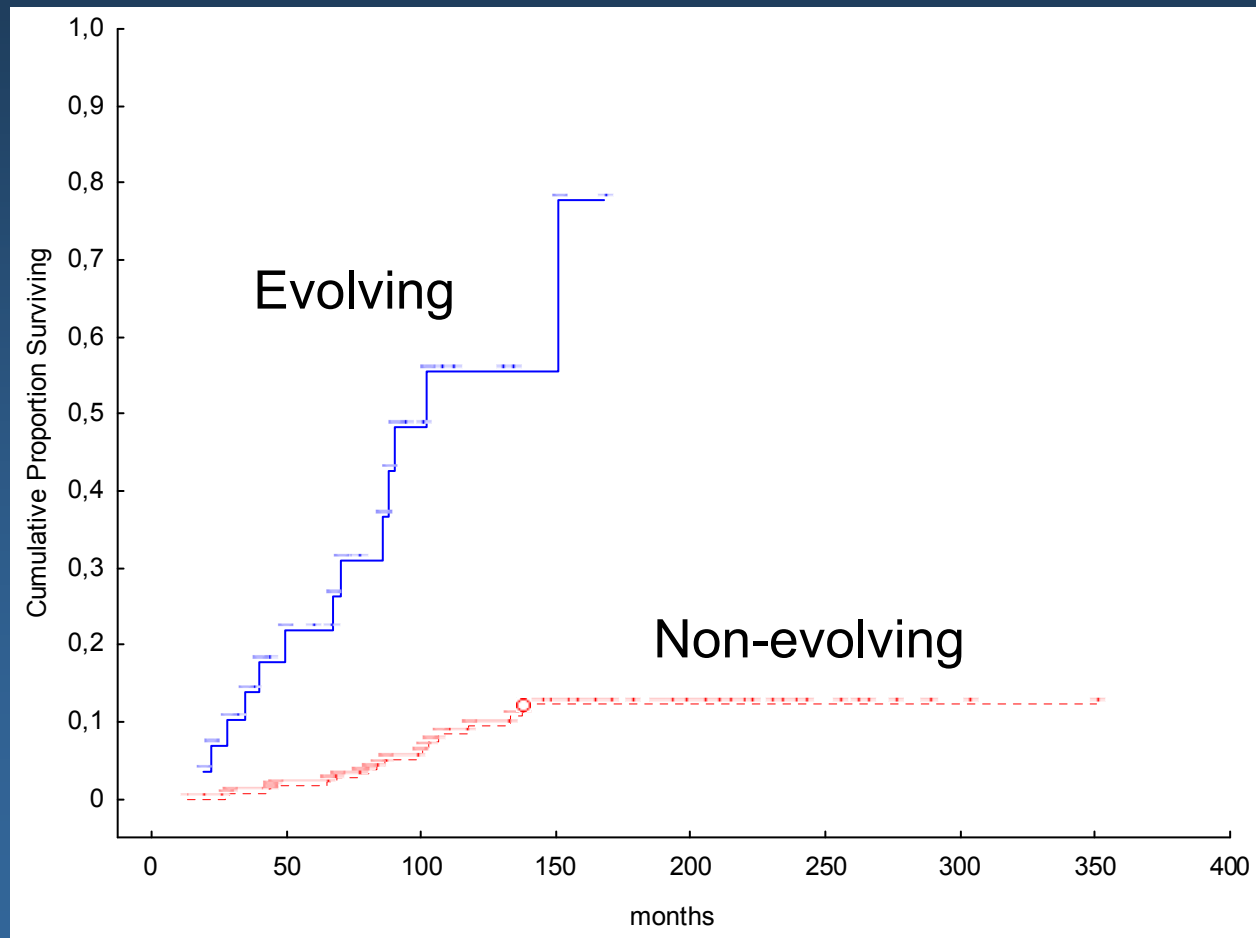
MGUS. Predictors of Malignant Transformation

Author, yr	N° of patients	M-protein size	BMPC (%)	M-protein type	Others
Kyle et al, 2004	241	--	--	--	--
Bladé et al, 1992	128	--	--	IgA > IgG, IgM	--
Baldini et al, 1996	386	+	+	--	↓ Polyclonal Igs
Pasqualetti et al, 1997	263	--	--	--	--
Gregersen et al, 2001	1247	+	ND	IgA > IgG, IgM	Female
Cesana et al, 2002	1104	+	+	IgA, IgM > IgG	LC proteinuria, ↑ESR, ↓ polyclonal Igs
Kyle et al, 2002	1384	+	--	IgA, IgM > IgG	--
Montoto et al, 2002	434	+	+	IgA > IgG, IgM	κ light chain

MGUS. Predictors of Malignant Transformation

Feature	RR	95% Confidence Interval	<i>p</i> -value
Evolving vs non-evolving	12.14	5.80-25.40	<0.0001
IgA vs others	2.92	1.36-6.28	0.006
M-protein (≥15 g/L)	2.18	1.02-4.66	0.044

Evolving vs. Non-evolving MGUS



MGUS Serum Free Light Chain (FLC) Ratio: an Independent Risk Factor for Progression

	Risk at 20 years
HIGH-RISK	
Abnormal FLC ratio, non-IgG and M-protein ≥ 15 g/L	58%
LOW-RISK	
Normal FLC ratio, IgG-type and M-protein < 15 g/L	5%

Rajkumar et al. *Haematologica / The Hematology Journal* 2005; S1: 194.

Rajkumar et al. *Blood* 2005; 106: 812-817.

Smoldering Multiple Myeloma (Asymptomatic Myeloma) Diagnostic Criteria*

- Serum M protein size $\geq 3\text{g/dL}$

and / or

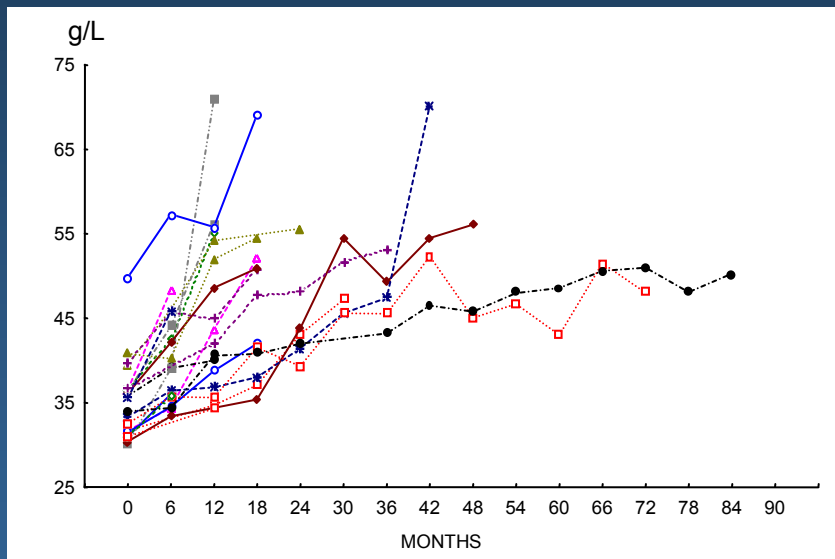
Bone marrow plasma cells $\geq 10\%$

- No clinical manifestations or other laboratory abnormalities due to the monoclonal gammopathy

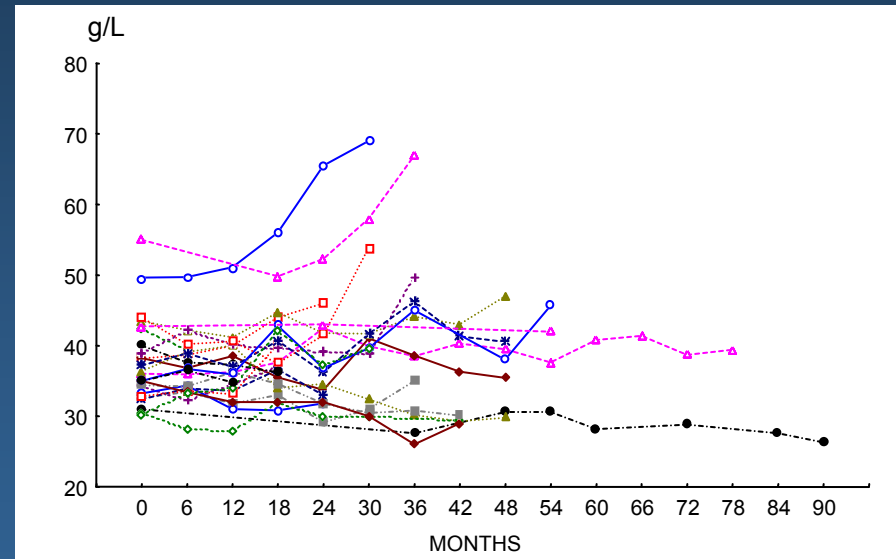
“Smoldering Multiple Myeloma: Natural History and Recognition of an Evolving Type”

Rosiñol L et al. *Br J Haematol*, 2003; 123: 631-636.

SMM. Evolution of the M-protein

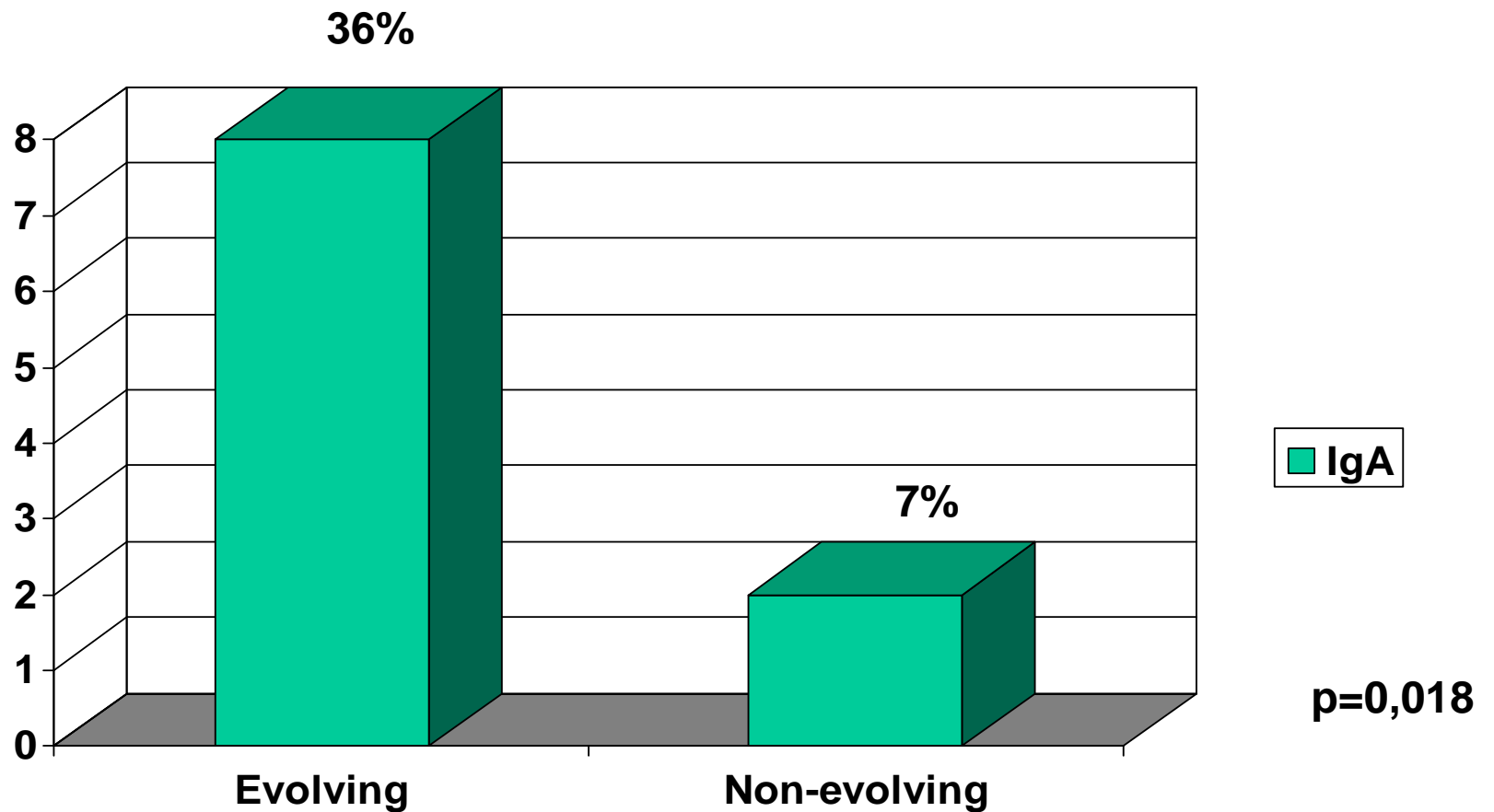


Evolving

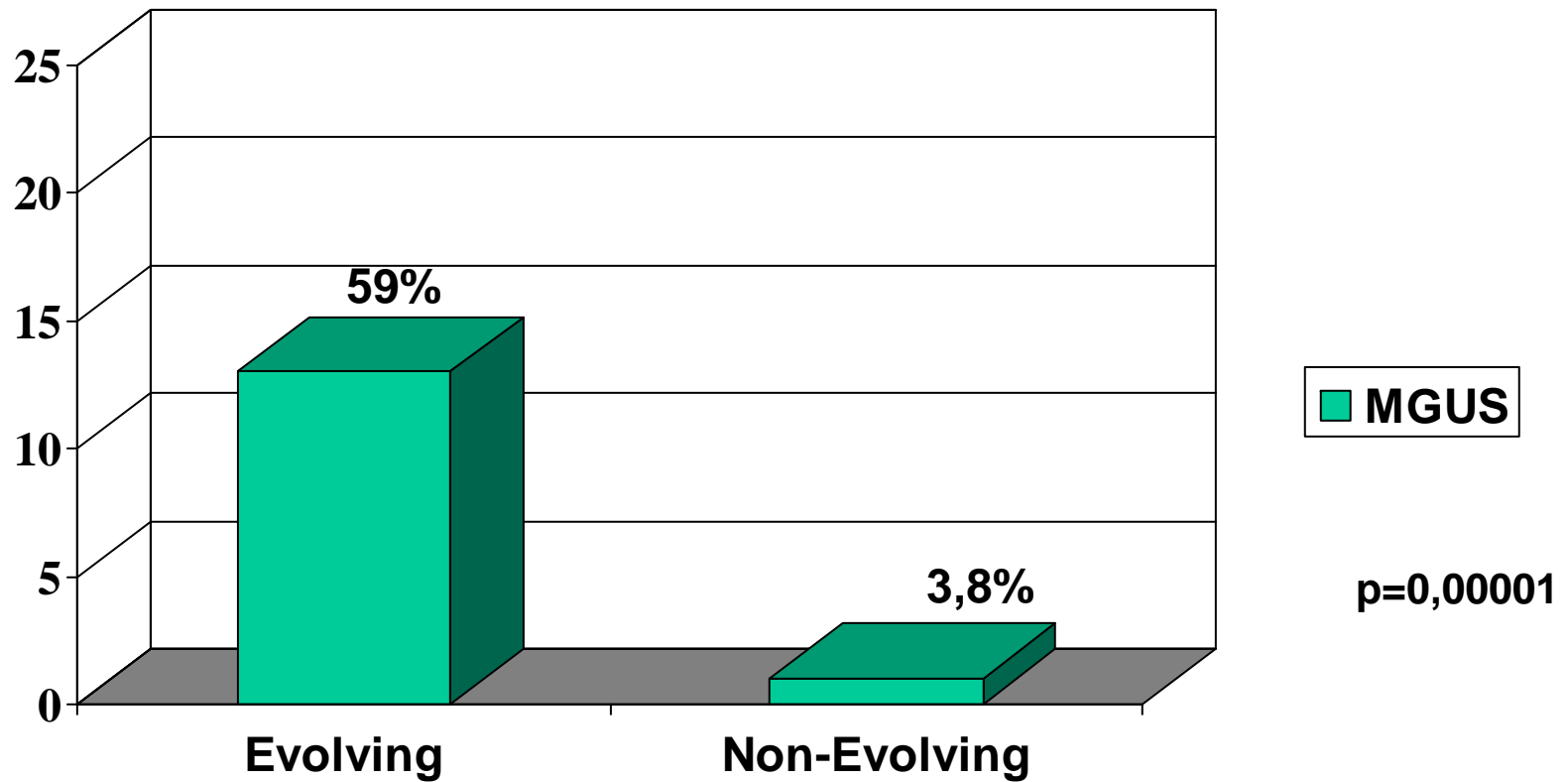


Non-evolving

Isotype IgA



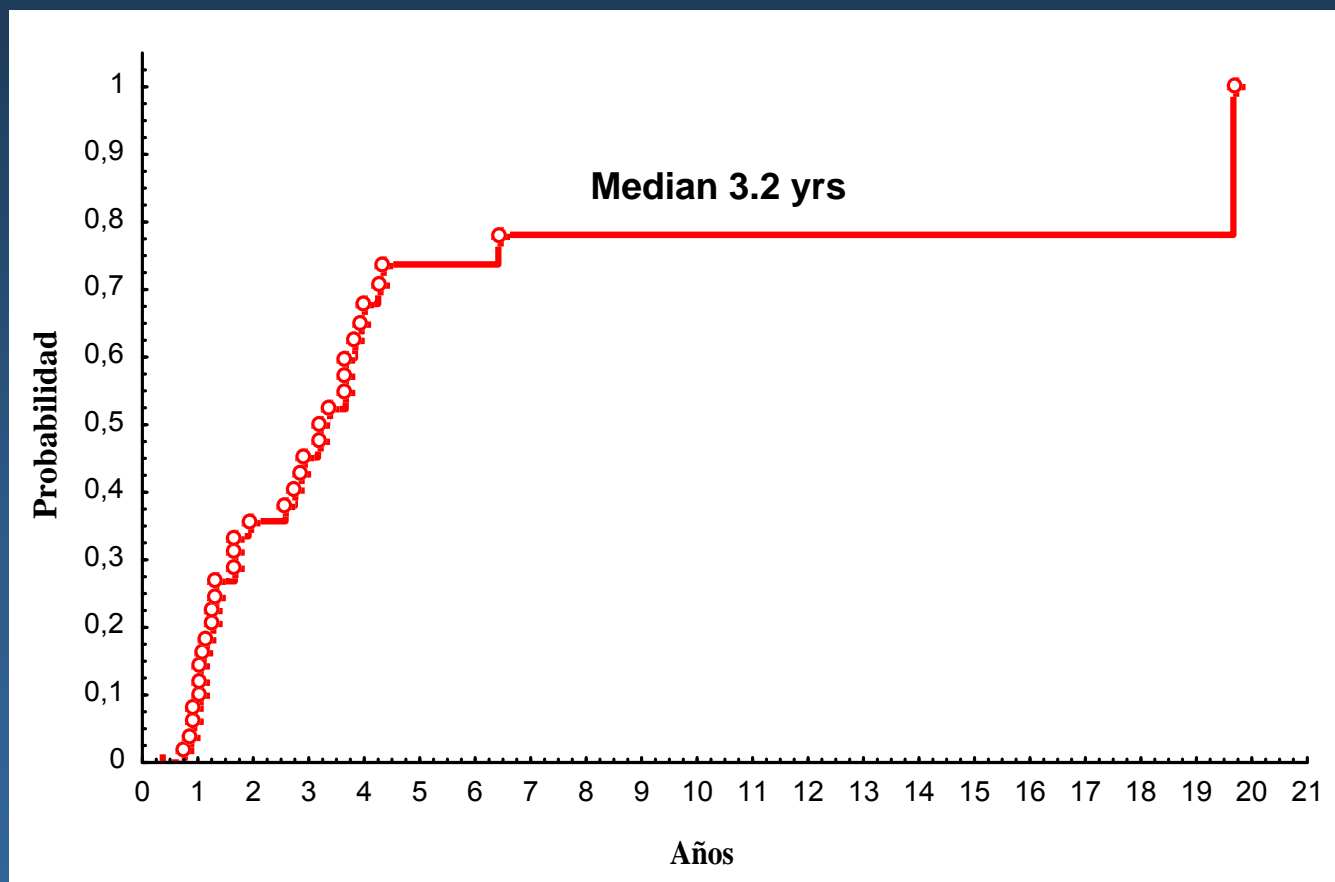
SMM and previous MGUS



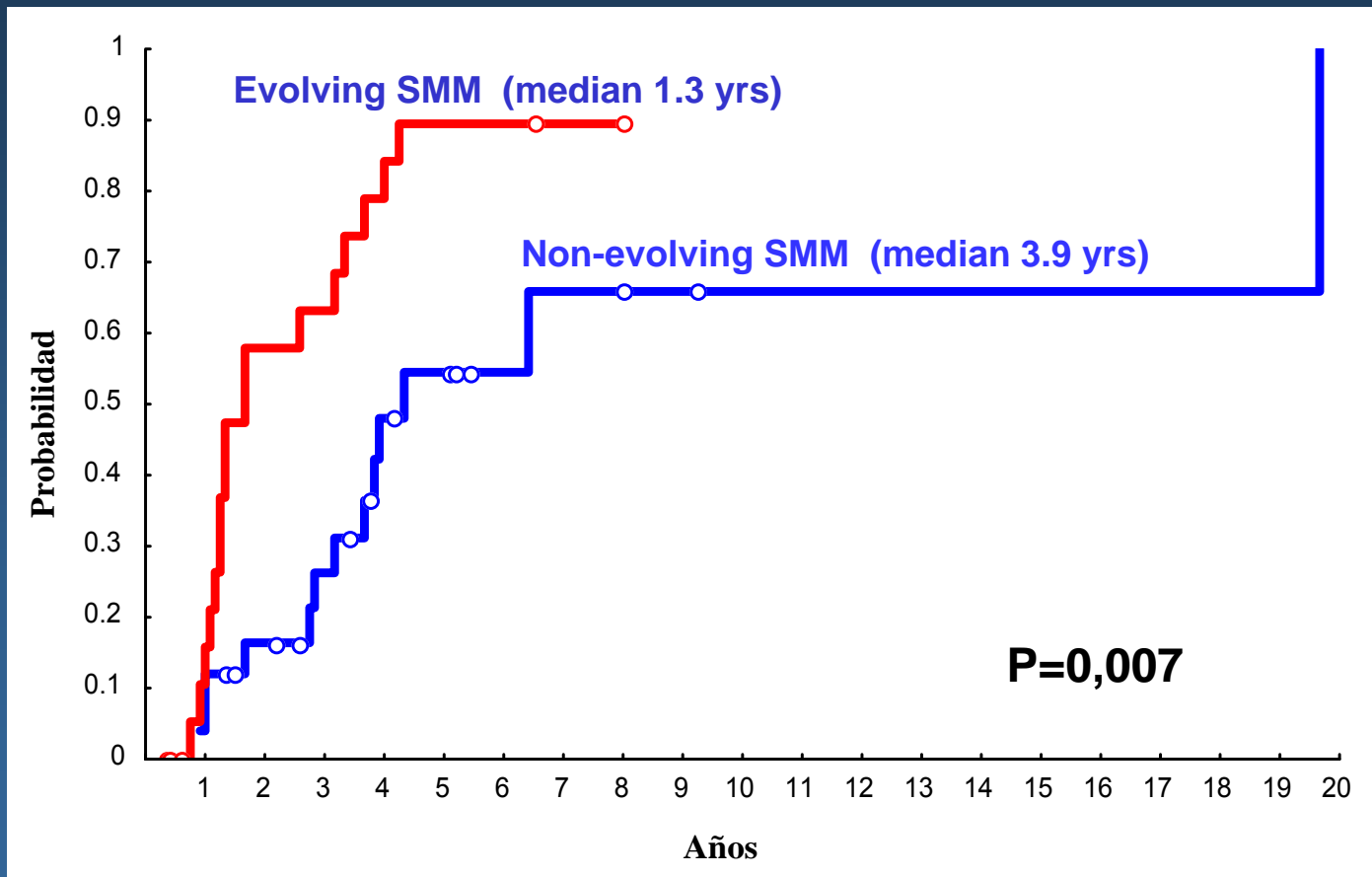
SMM. PATTERN OF PROGRESSION

	Overall (n=34*)	Evolving SMM (n=16)	Non- evolving SMM (n=14)
Pattern of progression:			
Anemia	11	6	5
Lytic lesions	6	4	2
Anemia and lytic lesions	12	5	6
Others (bone pain, unknown)	5 (3, 2)	1	1

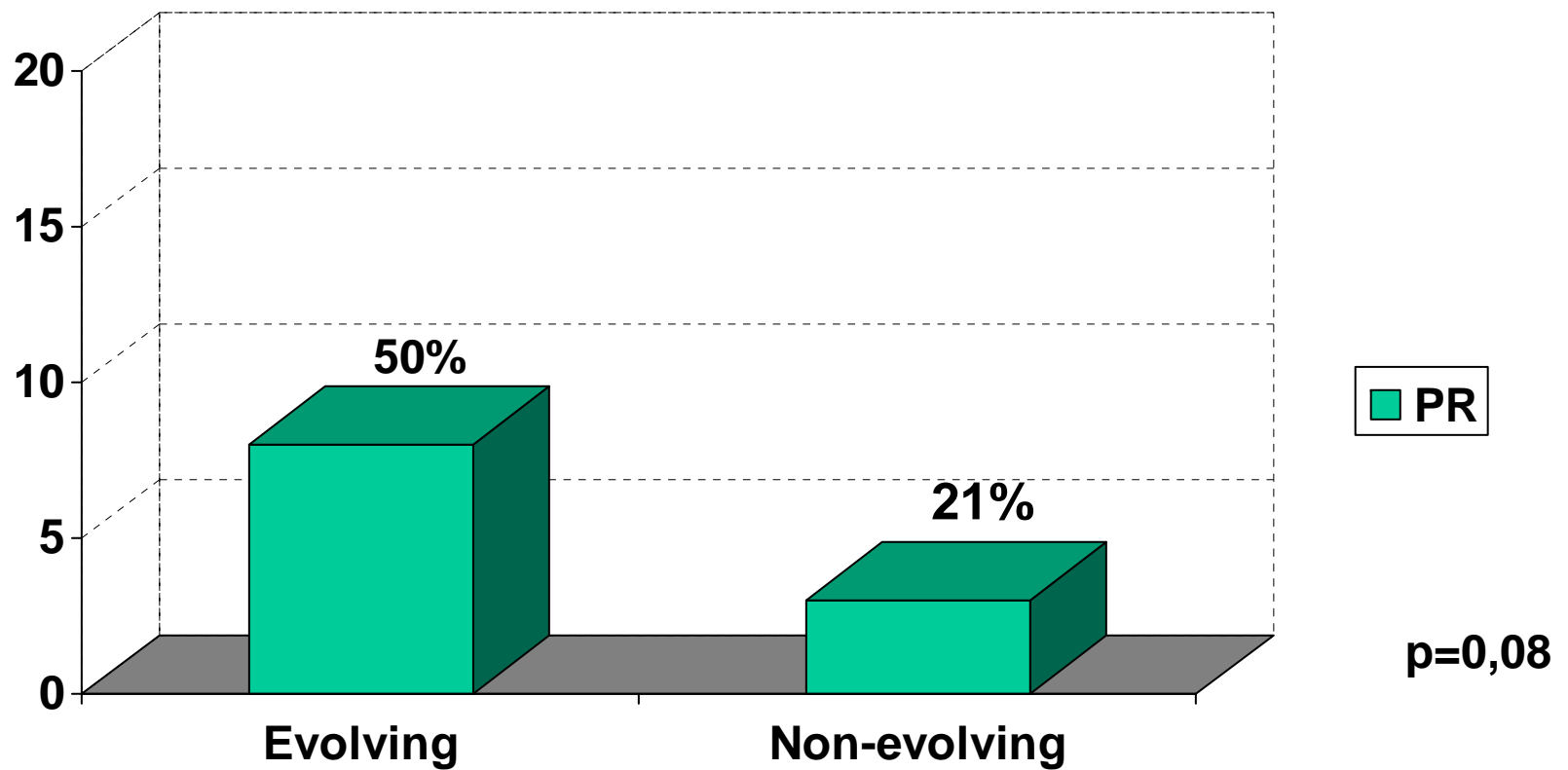
Time to progression to symptomatic MM



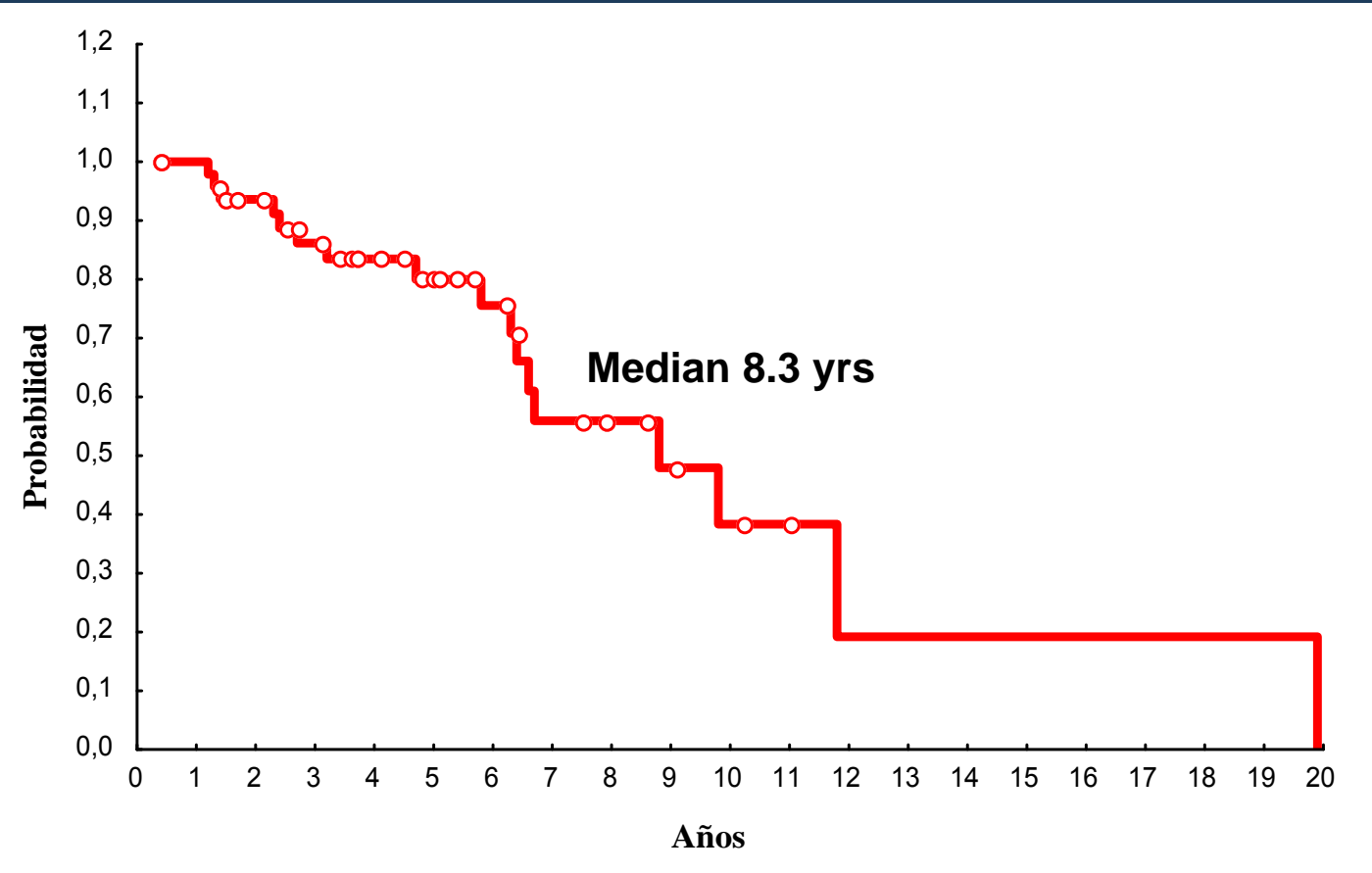
Time to progression to symptomatic MM according to the type of SMM



RESPONSE TO TREATMENT ACCORDING TO THE TYPE OF SMM



SURVIVAL FROM DIAGNOSIS OF SMM



MONOCLONAL GAMMOPATHIES

