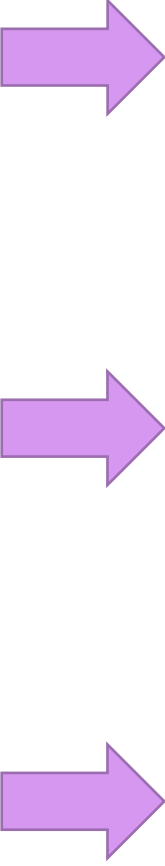




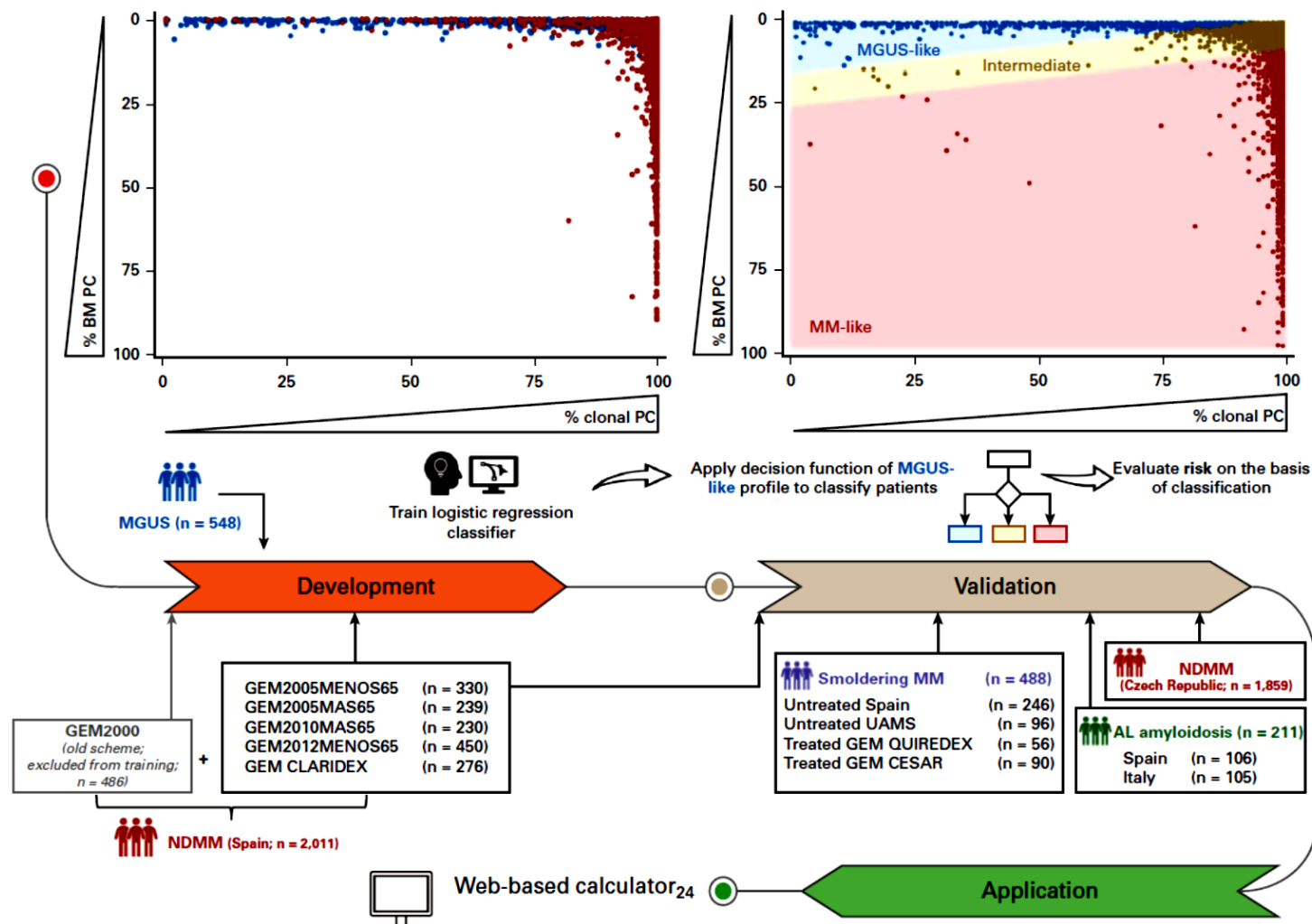
Definition and clinical significance of the monoclonal gammopathy of undetermined significance–like phenotype in patients with monoclonal gammopathies

Bruno Paiva

Introduction

- Early intervention is being investigated in patients with smoldering MM having high-risk of transformation
 - Treatment de-escalation or intensification are being explored in patients with active MM according to the depth of response
 - The presence of patients with MM with MGUS-like phenotype has been hypothesized in studies using gene expression profiling and flow cytometry
- 
- Paramount to define patients with smoldering MM with a benign clinical behavior resembling that of MGUS to avoid unnecessary treatment
 - The possibility of having MGUS-like disease deserves consideration in patients with persistent M-component after treatment but low risk of progression, and in whom achievement of a suboptimal response may not require additional treatment for prolonged survival
 - The former technique remains investigational whereas the latter is available in most clinical laboratories and is part of the routine diagnostic examination of patients with MM

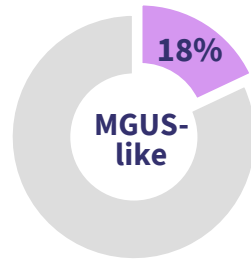
Study design



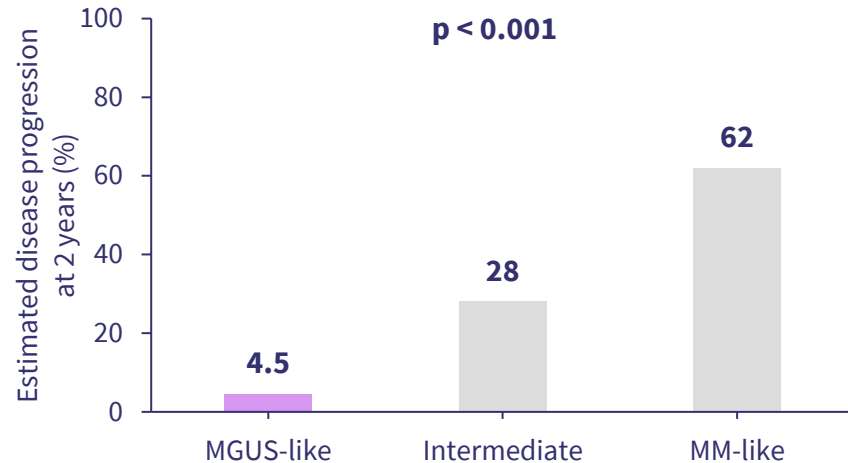
Bruno Paiva. Personal Communication; Apr 12, 2023.

Patients with MGUS-like smoldering MM have very low risk of transformation

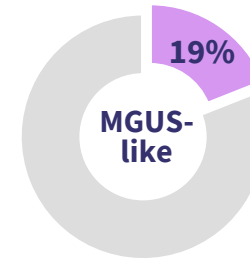
Untreated patients with smoldering MM in Spain
(n = 246)



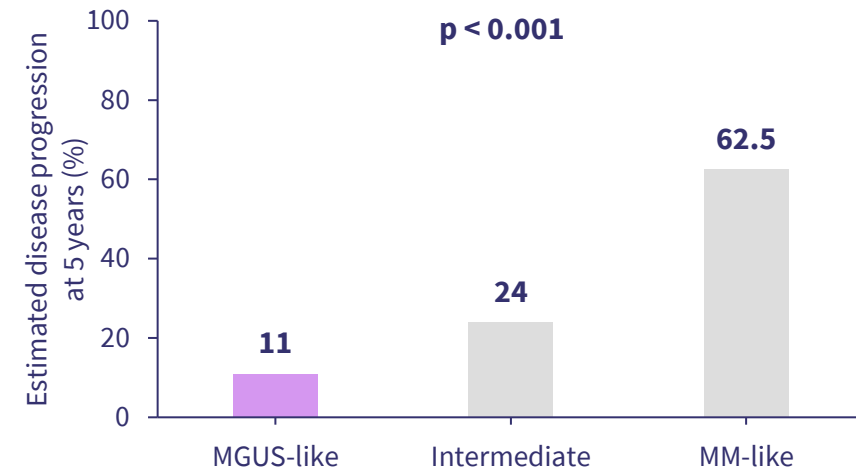
Estimated rate of disease progression at 2 years after a median follow-up of 2.5 years



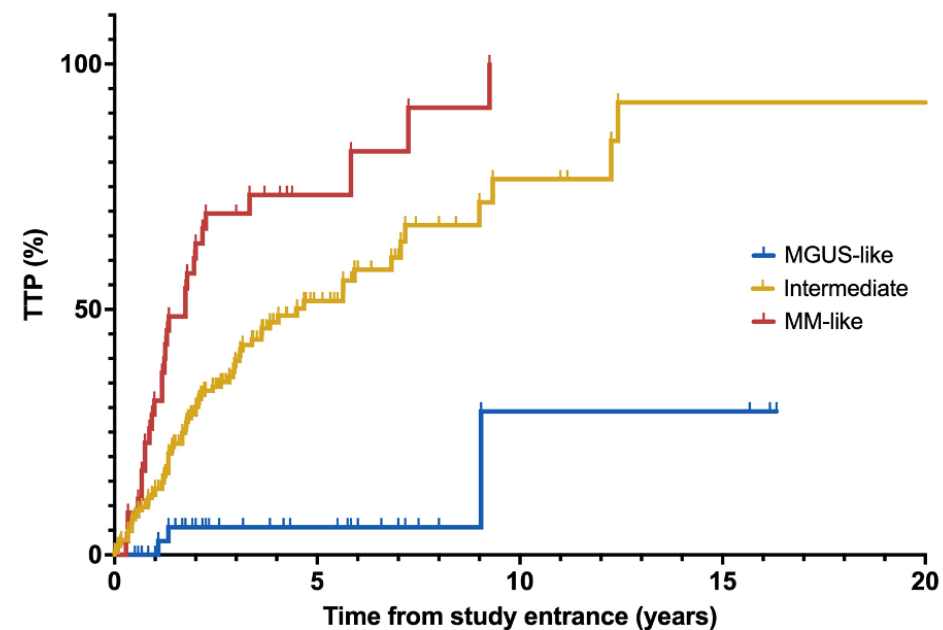
Untreated patients with smoldering MM at UAMS
(n = 96)



Estimated rate of disease progression at 5 years after a median follow-up of 5 years



Patients with MGUS-like smoldering MM have very low risk of transformation



MGUS-like	44	14	4	4	1
Intermediate-like	167	30	6	2	2
MM-like	35	4	1	1	1

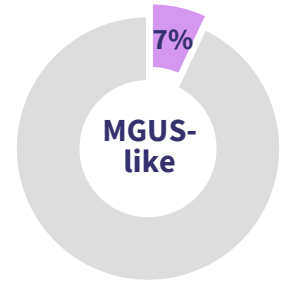
Numbers at risk

Bruno Paiva. Personal Communication; Apr 12, 2023.

No statistically significant differences in TTP between treatment versus observation in patients with MGUS-like smoldering MM

MGUS-like phenotype predicts favorable prognosis in active MM

Patients with active MM enrolled in the PETHEMA/GEM clinical trials (n = 1,525)



Median follow-up = 6 years

	Median PFS	p value
MGUS-like	Not reached	< 0.001
Intermediate	3.9 years	
MM-like	2.8 years	

	Median OS	p value
MGUS-like	Not reached	≤ 0.005
Intermediate	9.2 years	
MM-like	3.6 years	

Patients with transplant-eligible active MM with MGUS-like phenotype showed PFS and OS rates at 5 years of 79% and 96%, respectively

The MGUS-like classifier complements the revised ISS in active MM

Patients with active MM enrolled in the PETHEMA/GEM clinical trials (n = 1,525)

Multivariate analysis of PFS

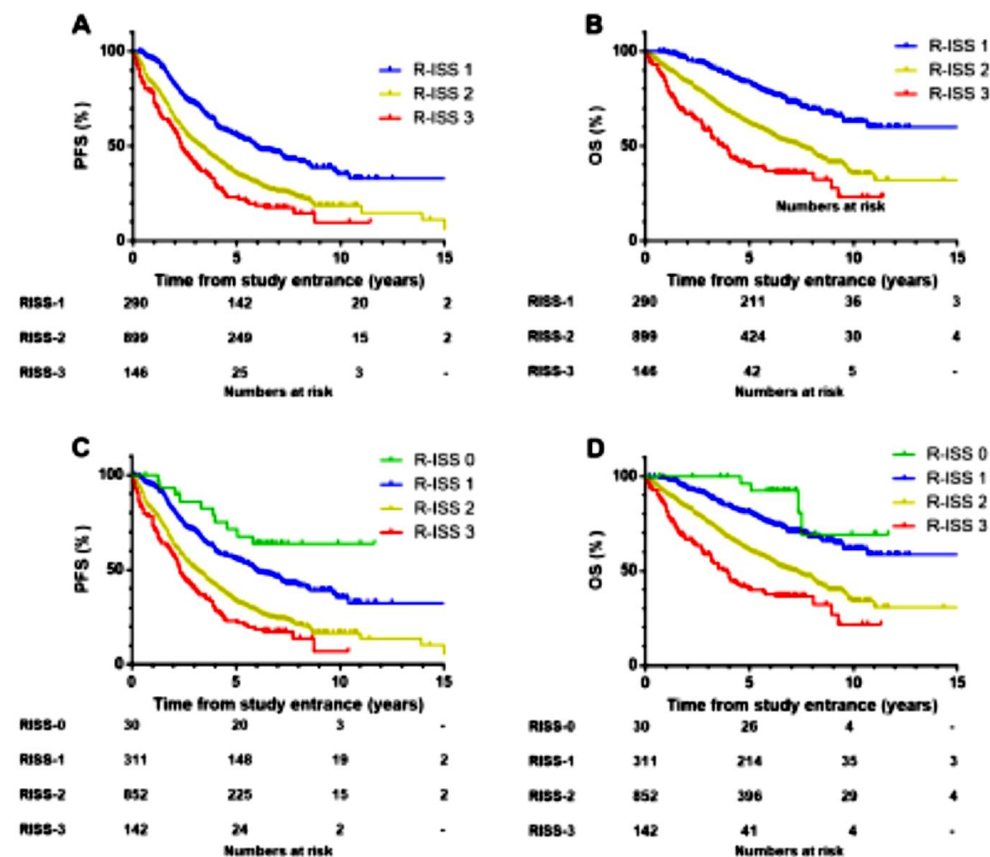
Variable	HR	95% CI	p value
MGUS-like	0.49	0.32–0.74	0.001
ISS	0.80	0.68–0.94	0.008
LDH	0.63	0.51–0.78	<0.001
Cytogenetics	0.72	0.61–0.85	<0.001
CR status	0.53	0.46–0.62	<0.001
HDT/ASCT	0.53	0.46–0.62	<0.001

Multivariate analysis of OS

Variable	HR	95% CI	p value
MGUS-like	0.56	0.32–0.97	0.039
ISS	0.67	0.55–0.83	<0.001
LDH	0.54	0.42–0.70	<0.001
Cytogenetics	0.61	0.50–0.75	<0.001
CR status	0.54	0.44–0.66	<0.001
HDT/ASCT	0.43	0.35–0.53	<0.001

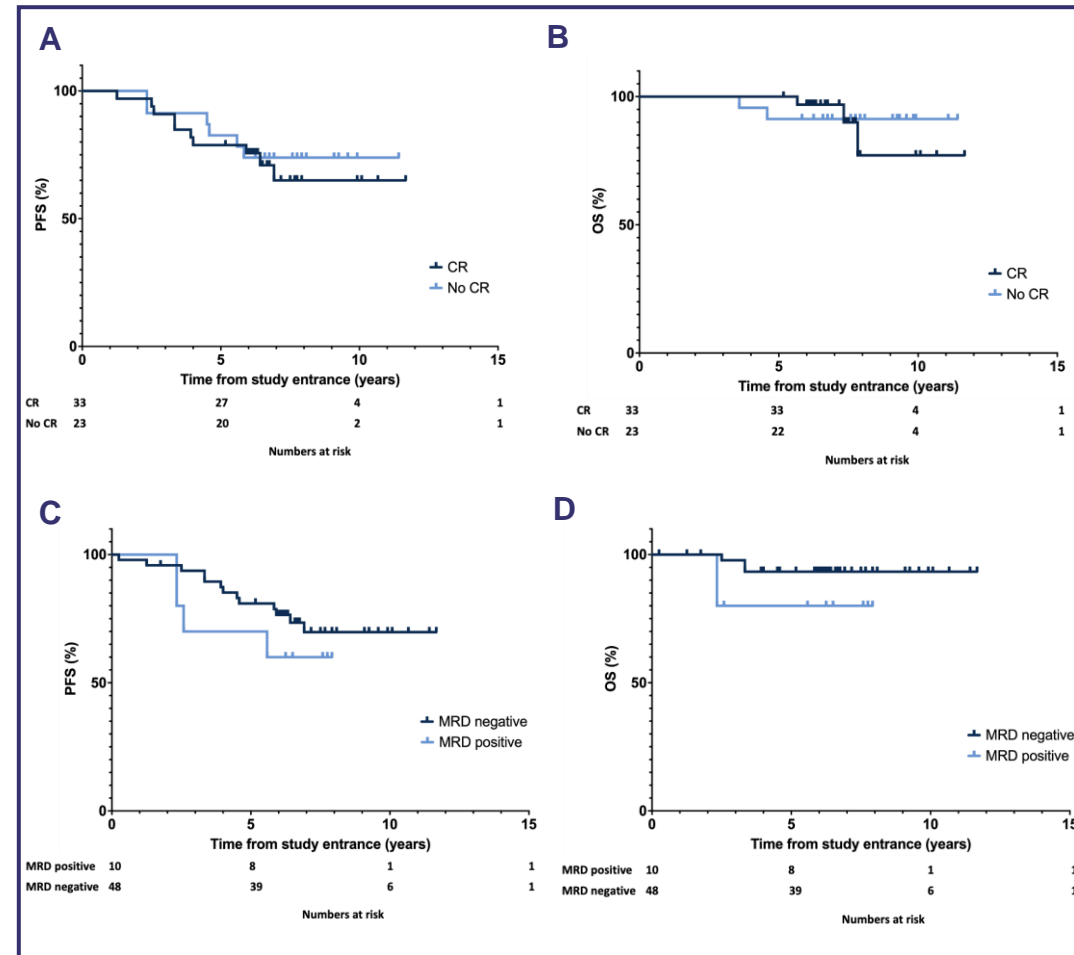
The MGUS-like classifier complements the revised ISS in active MM

Patients with active MM enrolled in the PETHEMA/GEM clinical trials (n = 1,525)



Bruno Paiva. Personal Communication; Apr 12, 2023.

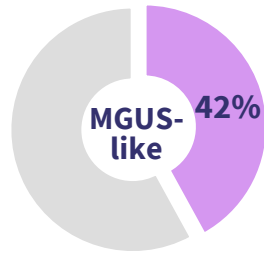
MGUS-like phenotype and prolonged survival in patients with transplant-eligible active MM achieving suboptimal response



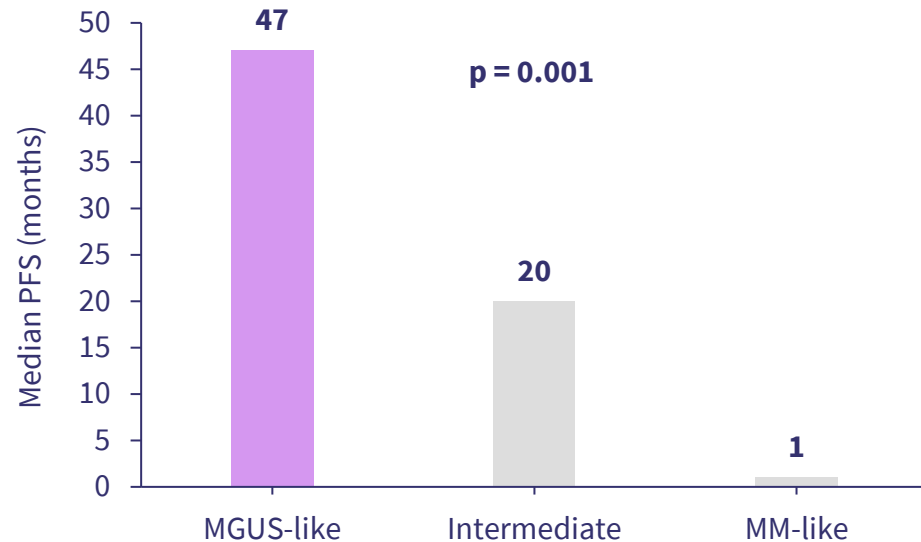
Bruno Paiva. Personal Communication; Apr 12, 2023.

Phenotypic classification, PFS, and OS of patients with AL amyloidosis

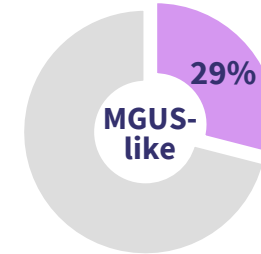
Patients with AL amyloidosis in Spain
(n = 106)



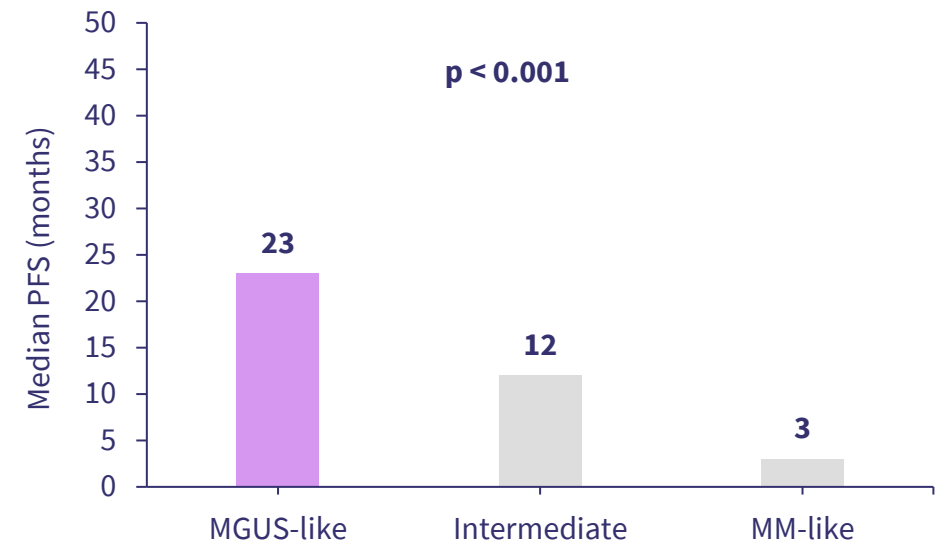
Median PFS



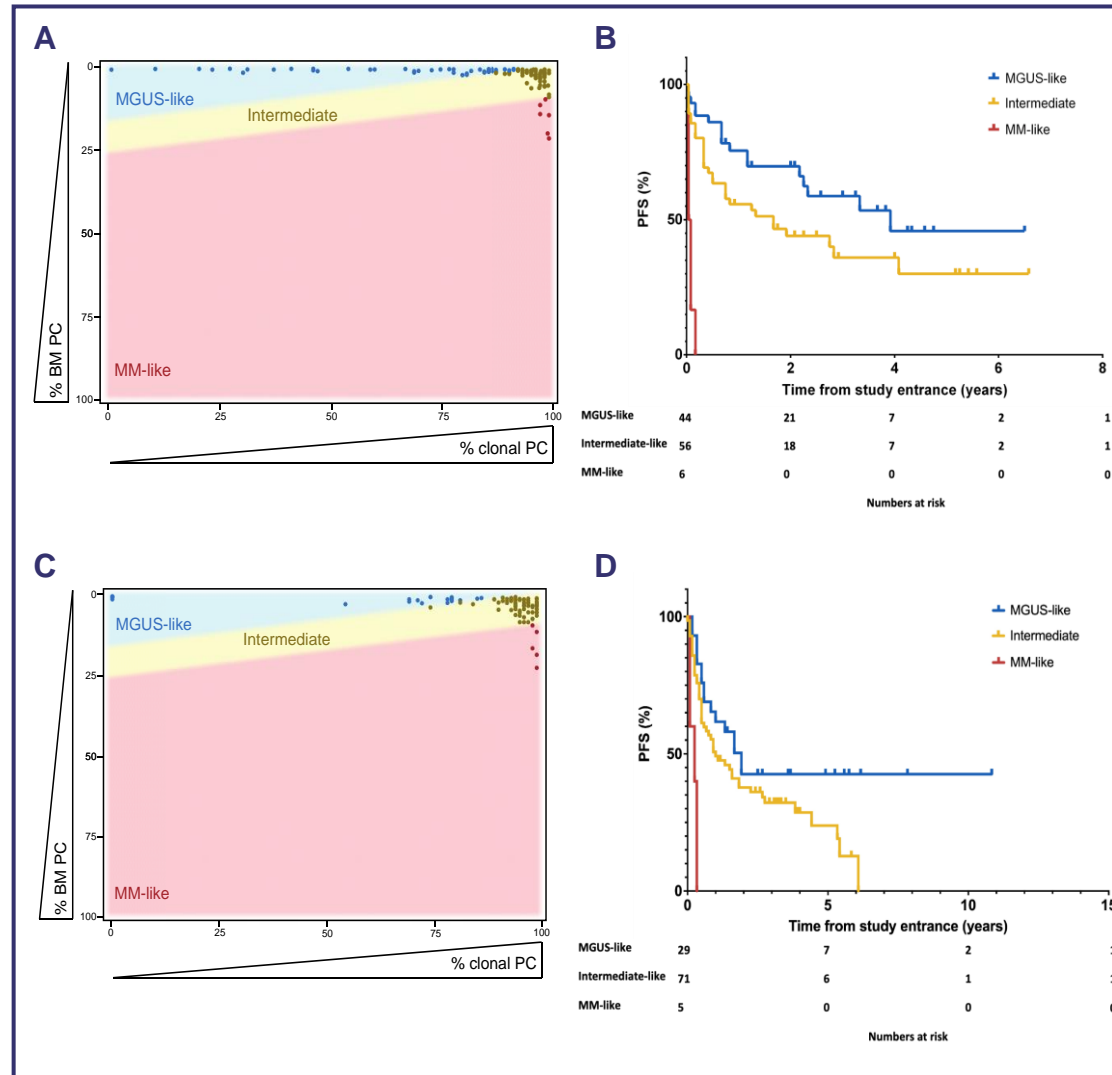
Patients with AL amyloidosis in Italy
(n = 105)



Median PFS



Phenotypic classification, PFS, and OS of patients with AL amyloidosis



Bruno Paiva. Personal Communication; Apr 12, 2023.

Conclusions

- A more personalized approach to therapy demands the identification of distinct subgroups of patients with singular clinical behavior, using routine tests to guarantee a real and wide translation of research into clinical practice.
- Here, we provide an open-access tool based on flow cytometry parameters that are routinely assessed in clinical laboratories.
- The MGUS-like classifier identifies a subset of patients with smoldering and active MM having unprecedented outcomes.
- In AL amyloidosis, the same tool uncovers a subgroup of patients with MM-like BM involvement and dismal survival.
- This phenotypic classification of monoclonal gammopathies may help individualizing treatment and should be part of standard laboratory examinations.

Acknowledgements

