Risk of subsequent primary malignancies in patients with multiple myeloma

– before and after the introduction of novel therapies

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Disclosure

<u>Conflicts of interest:</u> None

Background

- Increased frequency of myeloid malignancies noted among myeloma patients since 1970s

- Although underlying biological mechanisms are poorly understood, treatment-related factors (e.g., melphalan) considered a main source

Aims of this population-based study

- **Define risk of primary hematologic and solid malignancies subsequent to myeloma, compared to general population**

- **For the first time, assess role of treatment and non-treatment related factors**

Mailankody et al., and Landgren (submitted)

Methods – patients and hospitals

- **High-quality population-based data from Sweden (1986-2005)**
  - **All incident myeloma pts**
  - **Nationwide MGUS cohort[1]**

- **Age- and gender-specific incidence rates for entire population during study period**

- **Risks before/after 1995 (intro high-dose melphalan/ASCT)**

Mailankody et al., and Landgren (submitted); [1]Landgren et al., Blood 2009

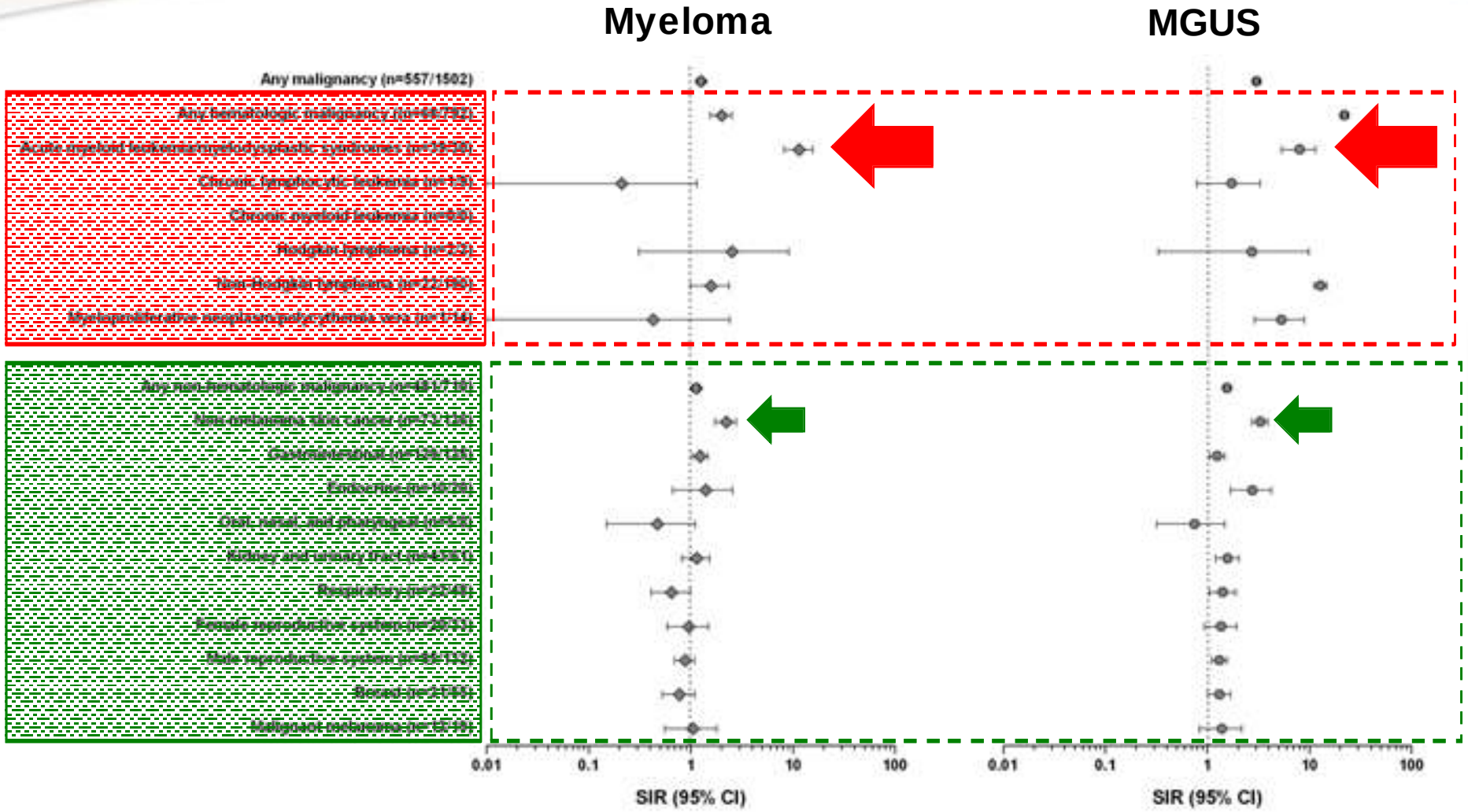
Results – patients' characteristics

Variable	Myeloma	MGUS
Total number, n (%)	8740 (100)	1652 (100)
≤65 yrs at dx, n (%)	2495 (29)	585 (28)
Male sex, n (%)	4811 (55)	845 (50)
Year of dx		
1986-1994, n (%)	4228 (48)	462 (24)
1995-2005, n (%)	4512 (52)	1190 (76)

Follow-up data (cancer and mortality) available until end of 2006

Mailankody et al., and Landgren (submitted)

Results – risk of any malignancy



Mailankody et al., and Landgren (submitted)

Results – hematologic malignancies

Subsequent malignancy	Multiple myeloma (N=8740)		MGUS (N=5652)	
	N	SIR (95% CI)	N	SIR (95% CI)
Any hematologic malignancy	68	**2.01 (1.56- 2.55)**	792	**22.07 (20.56-23.66)**
Multiple myeloma	-	-	447	**64.62 (58.77-70.90)**
Waldenstrom's/NHL	22	1.58 (0.99-2.39)	190	**12.85 (11.08-14.81)**
AML/MDS	**39**	**11.51 (8.19-15.74)**	**30**	**8.01 (5.4-11.43)**
Chronic lymphocytic leukemia	1	0.21 (0.01-1.15)	9	1.73 (0.79-3.28)
Chronic myeloid leukemia	0	–	0	–
Hodgkin lymphoma	2	2.53 (0.31-9.16)	2	2.74 (0.33-9.88)

Mailankody et al., and Landgren (submitted)

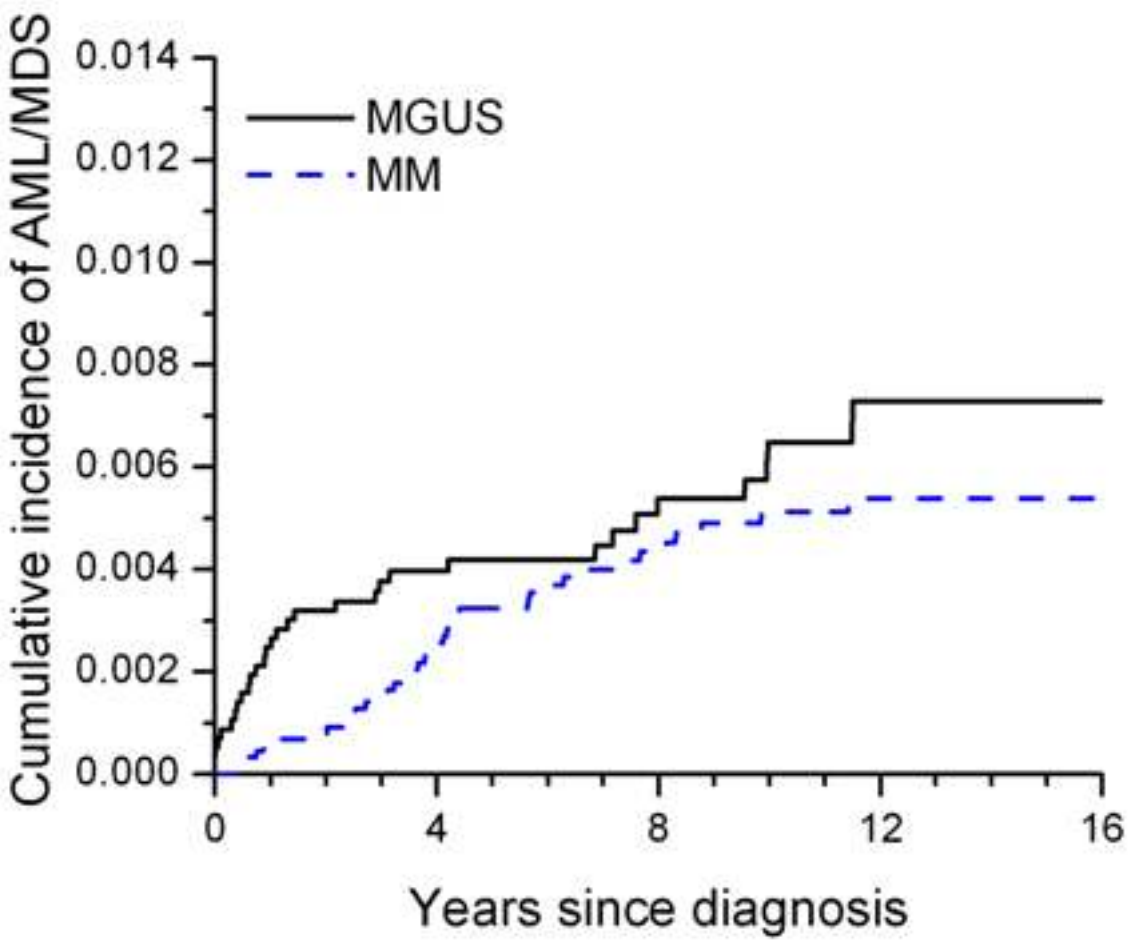
Results – MGUS and risk of AML/MDS, by isotype and M-spike (g/dL)

MGUS isotype	AML/MDS cases, n	SIR (95% CI)
IgG and IgA, n=1880	10	7.44 (3.57-13.69)
IgM, n=425	0	-
Missing, n=2113	11	8.24 (4.12-14.75)

M-protein concentration	AML/MDS cases, n	SIR (95% CI)
≥1.5g/dL, n=551	3	8.50 (1.75-24.85)
<1.5g/dL, n=1442	5	4.57 (1.48-10.66)
Missing, n=2426	13	8.17 (4.35-13.96)

Mailankody et al., and Landgren (submitted)

Results – cumulative incidence of AML/MDS



Mailankody et al., and Landgren (submitted)

Results – risk of AML/MDS following myeloma, by calendar period

In myeloma patients*, AML/MDS risk was very similar before/after 1995 (intro of high-dose melphalan/ASCT)

Before 1995	SIR=33.34 (95%CI: 12.23-72.57)
1995 or later	SIR=23.19 (95%CI: 11.98-40.50)

*≤65 years at diagnosis

Mailankody et al., and Landgren (submitted)

Results – solid malignancies

Subsequent malignancy	Multiple myeloma (N=8740)		MGUS (N=5652)	
	N	SIR (95% CI)	N	SIR (95% CI)
Any non-hematologic malignancy	481	**1.13 (1.03-1.24)**	710	**1.56 (1.44-1.68)**
Non-melanoma skin cancer	**73**	**2.23 (1.74-2.80)**	**136**	**3.30 (2.76-3.90)**
Gastrointestinal	129	**1.24 (1.03-1.47)**	135	1.25 (1.05-1.48)
Endocrine	10	1.40 (0.67-2.56)	20	**2.76 (1.69-4.27)**

Mailankody et al., and Landgren (submitted)

Summary and conclusions (1 of 2)

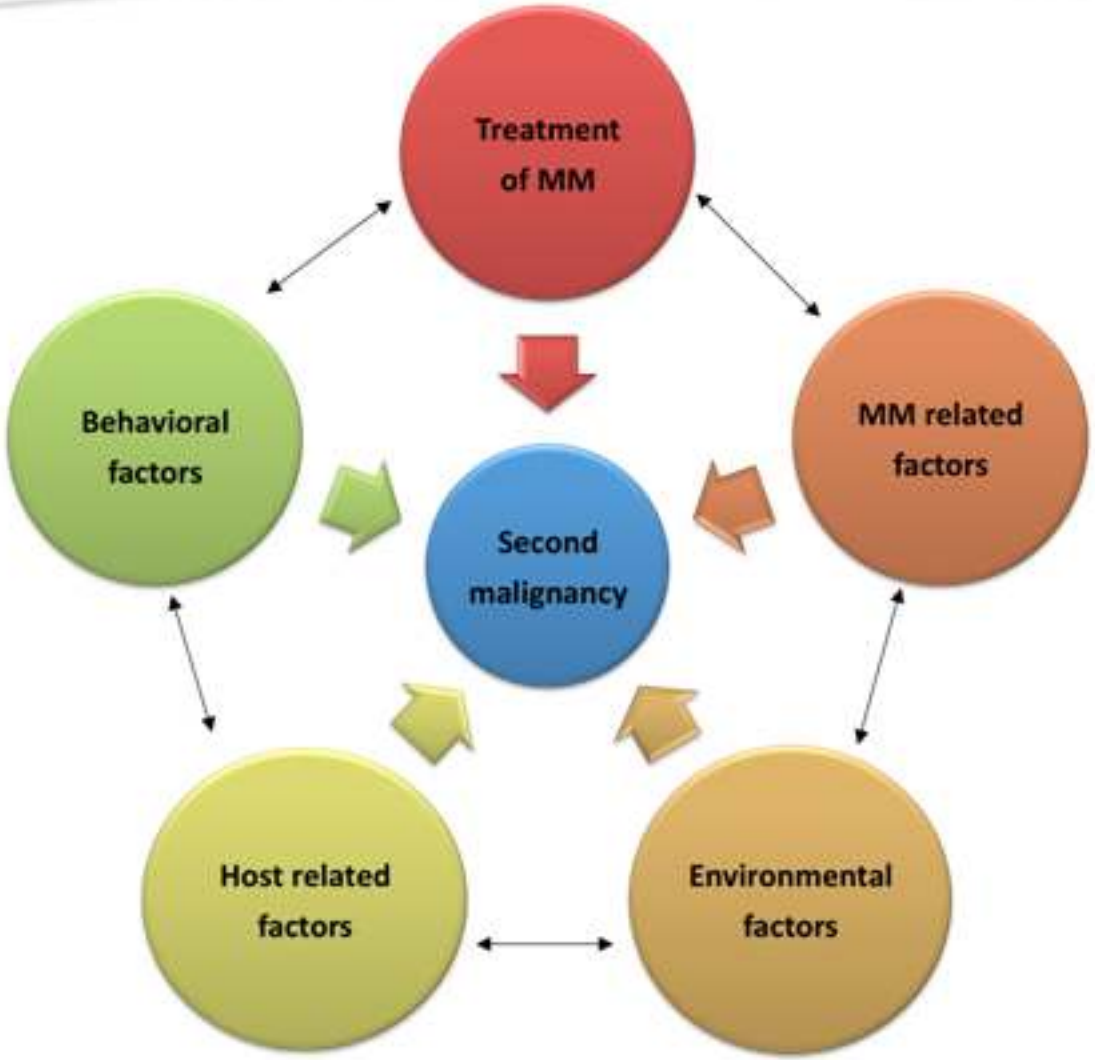
- **Our novel finding that MGUS is associated with AML/MDS risk supports a role for non-treatment related factors**

Summary and conclusions (2 of 2)

- **AML/MDS risk similar before/ after intro of HDM-ASCT suggests "high-dose and low-dose melphalan = similar risk?"**

- **Longer follow-up needed to better define secondary tumor risks in the IMiD-era**

Proposed model for second malignancies following myeloma



Thomas and Landgren (in manuscript)

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