

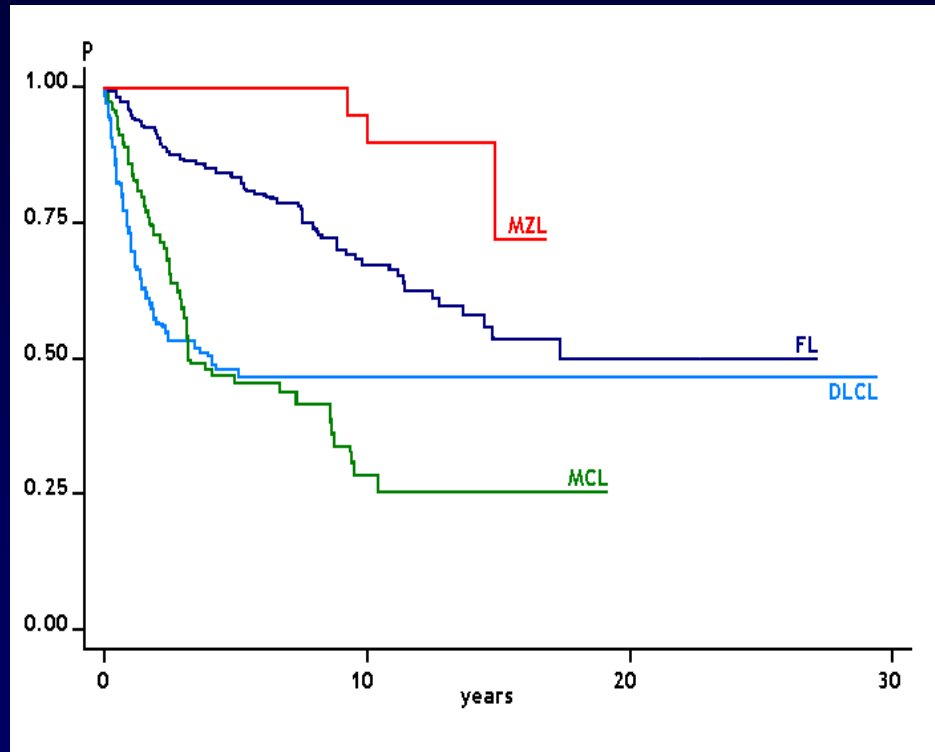
Conservative Treatment for Mantle Cell Lymphoma

Michele Ghielmini, MD

**Oncology Institute of Southern Switzerland
Ospedale San Giovanni
Bellinzona, Switzerland**

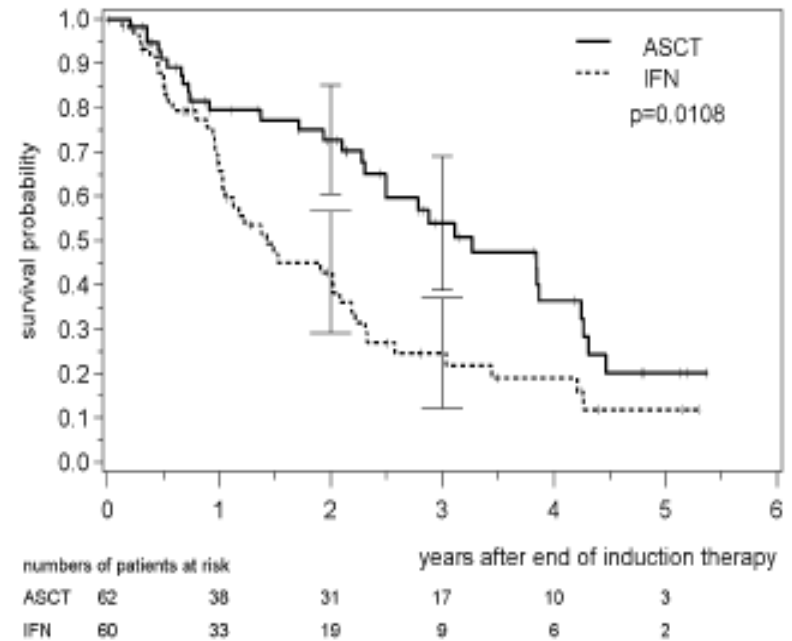
MCL: An Incurable Disease

Overall Survival



Zucca, IOSI database 2009

Progression Free Survival N = 122



Median PFS, 39 mos. (ASCT) vs. 17 mos (IFN)

Dreyling M, et al. *Blood*. 2005;105(7):2677-2684.

MCL: Hints of Curability?

n = 160

Age < 66

MCL 1

maxi CHOP



BEAM

MCL 2

R-maxi CHOP



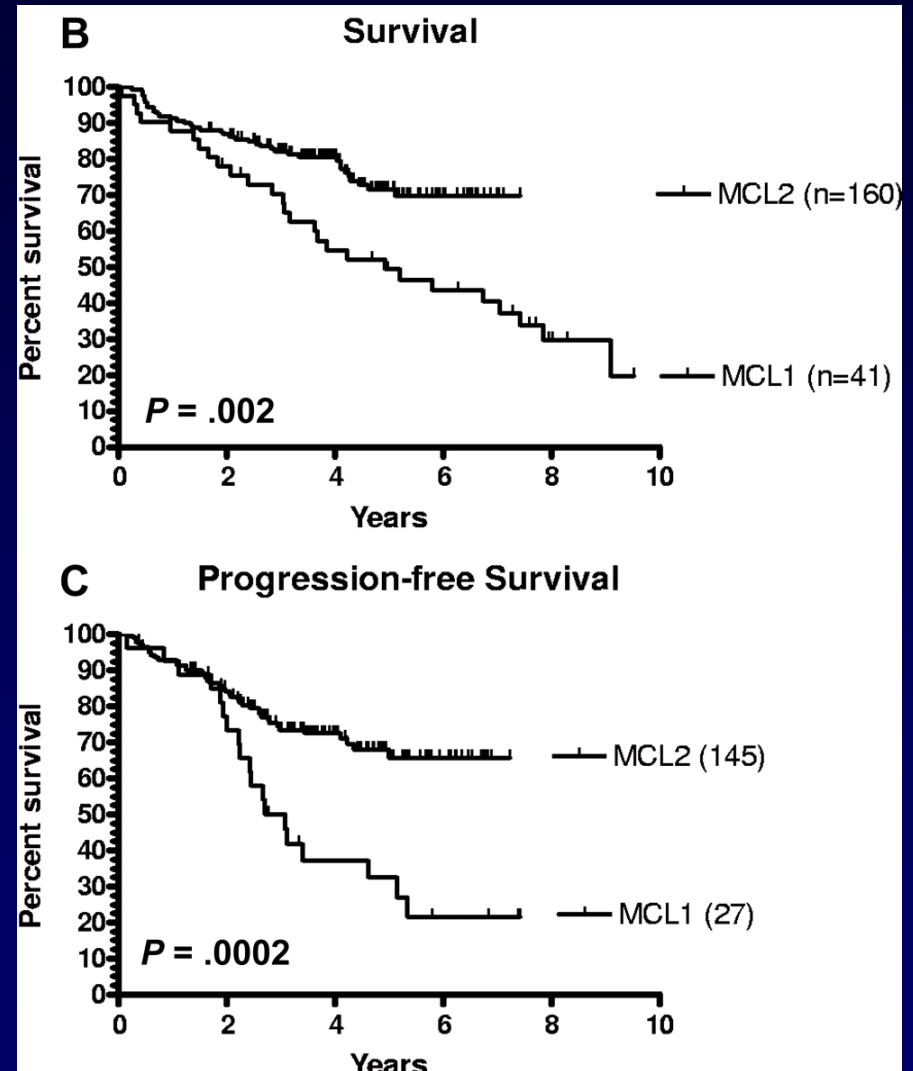
R-HD-AraC



R-in-vivo purging



BEAM



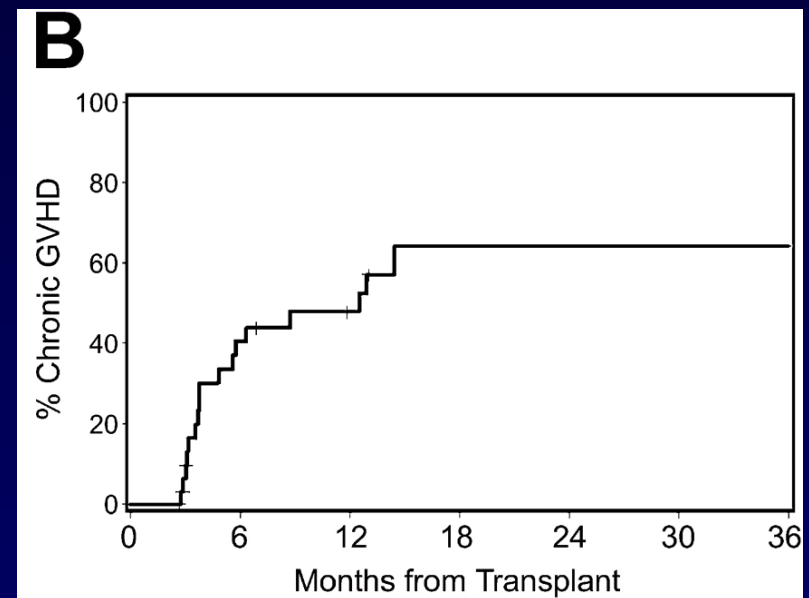
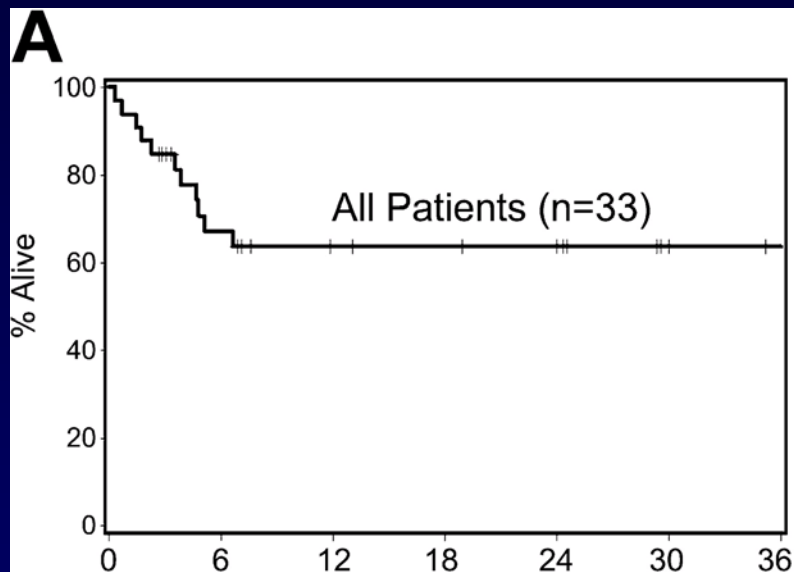
SWOG Lymphoma Group Trial

- R-Hyper CVAD as per MDACC protocol (first-line)

	n	CR	RR	2y PFS
MDACC	97	87%	97%	90%
SWOG	49	58%	88%	63%

Allo-BMT in MCL: More Cure or More Toxic Deaths?

RIT in 6 USA centres: Fludarabine + 2 Gy TBI



Maris MB, et al. *Blood*. 2004;104(12):3535-3542.

RIT in EBMT registry

n = 144

PFS 26% at 2y

OS 31% at 2y

Robinson SP, et al. *Blood*. 2002;100(13):4310-4316.

Aggressive Treatment: For Whom?

- MCL is not an indolent nor a curable disease
- Retrospective series suggest that the addition of
Rituximab
HD-AraC
PBSCT
could be beneficial
- The majority of patients are aged > 60: not eligible for HD-AraC nor for PBSCT

Combination Chemotherapy

(series with n = 26-62)

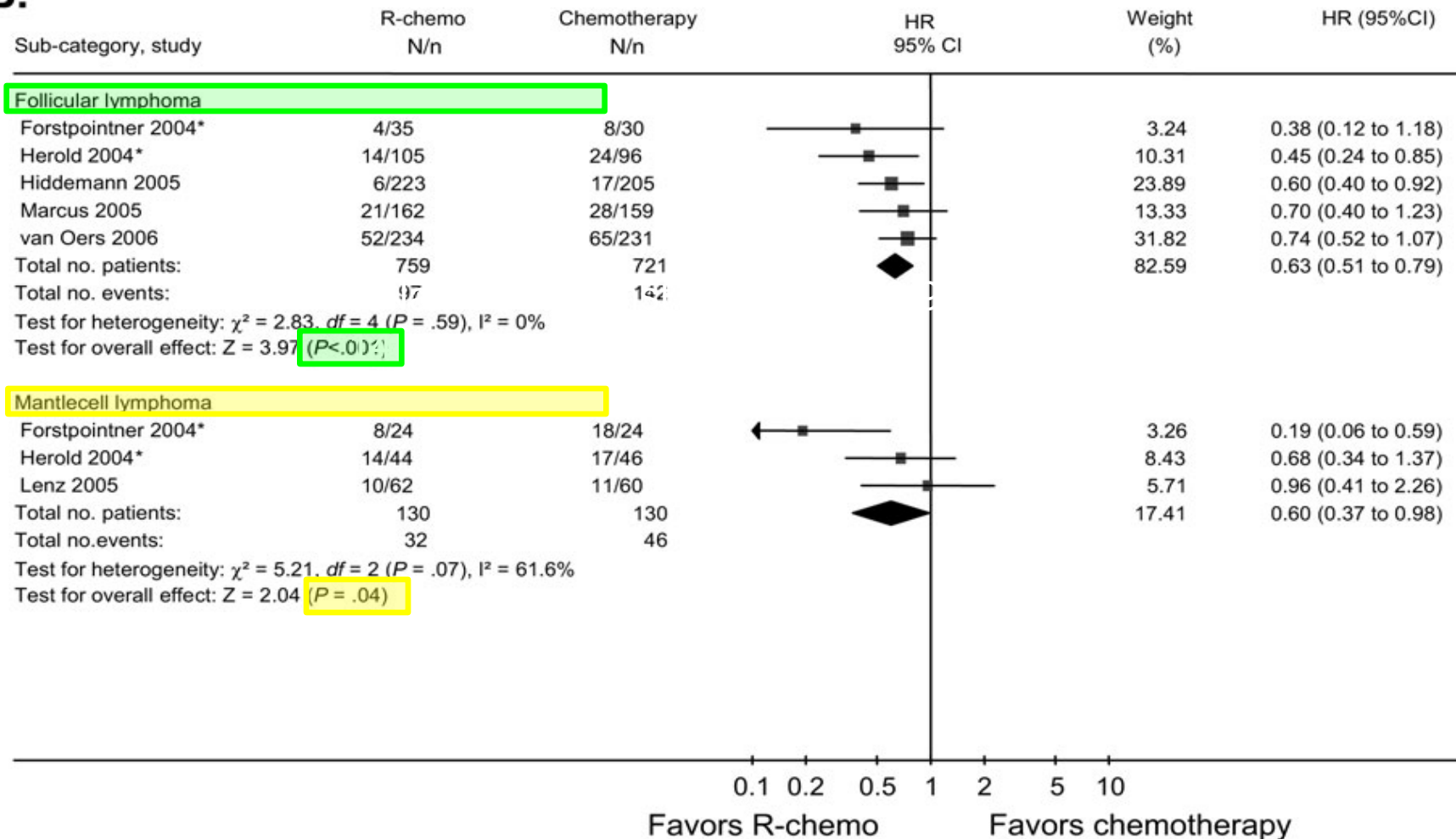
Regimen	RR (%)	EFS (mos)	2y OS (%)
CVP	60-84	10-20	45-65
CHOP	75-88	7-21	60-76
MCP	63-73	13-15	85
R-CHOP	94-96	17-20	76
R-MCP	71	18	-

CR rates w/o R: 10-40%

CR rates w R: 30-50%

Rituximab + Chemo Meta-analysis (Overall Survival)

B.

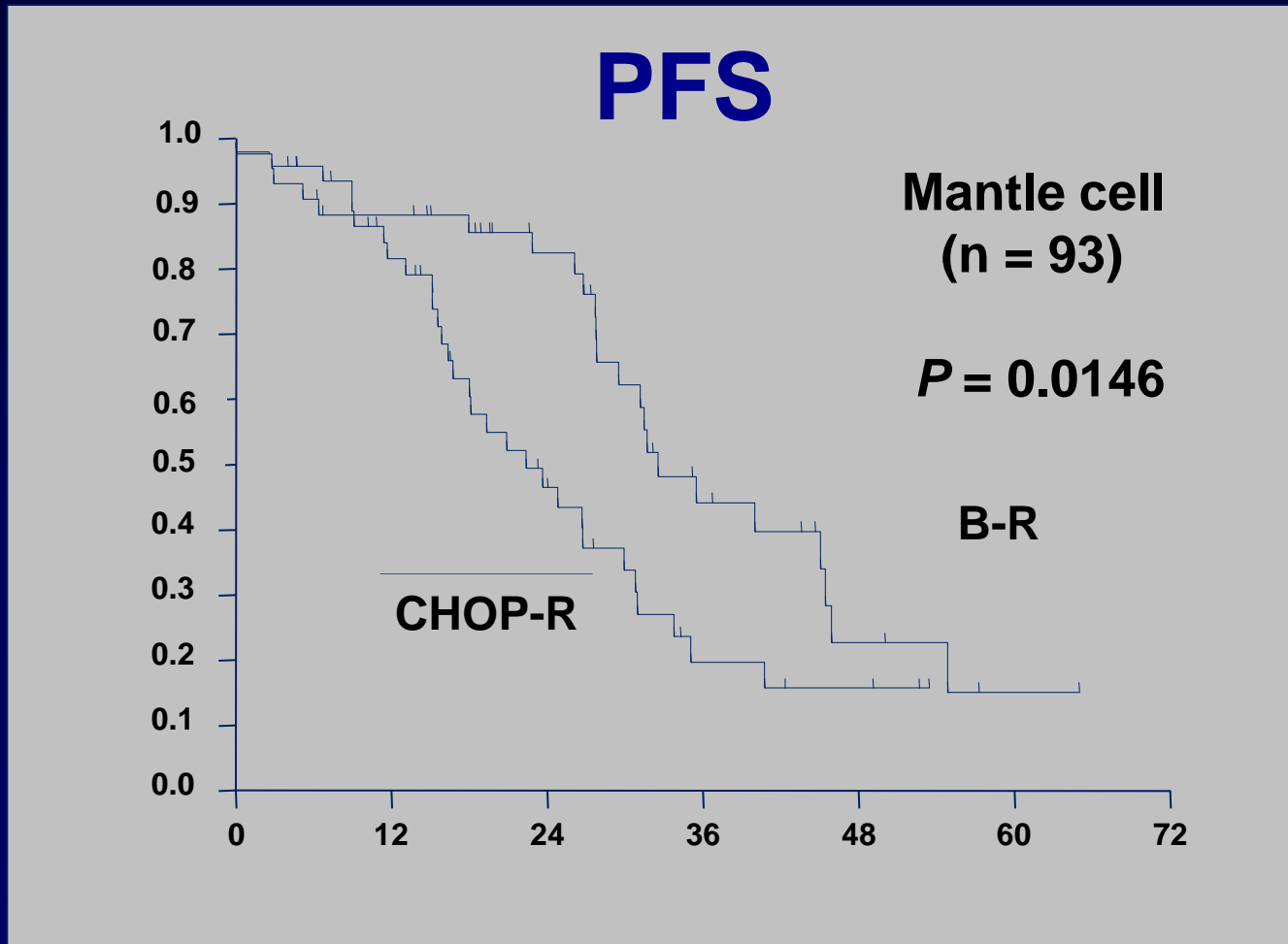


Bendamustine + Rituximab In Relapsed MCL

	N	RR	CR	EFS
Rummel 2005¹	16	75%	50%	18m
Robinson 2008²	12	92%	42%	19m

¹Rummel MJ, et al. *J Clin Oncol*. 2005;23(15):3383-3389. ²Robinson KS, et al. *J Clin Oncol*. 2008;26(27):4473-4479.

Bendamustine: At Least as Good as CHOP



Watch and Wait in MCL

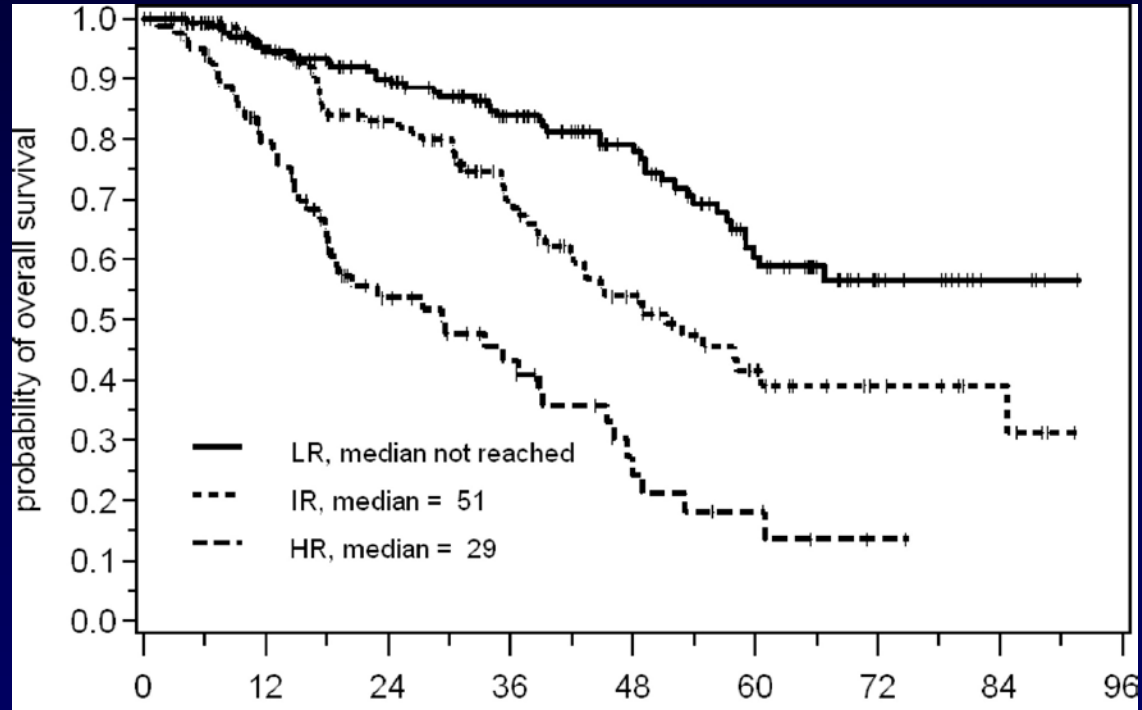
- **Not all MCLs have an aggressive course from the beginning**
- **In centers observing asymptomatic MCL (1/3 of cases), the median time to treatment is 1 year**
- **These cases do not show a worse survival**

Clinical Prognostic Factors: MIPI

N = 455

Adverse factors:

- Age
- ECOG PS
- LDH
- Extranodal sites

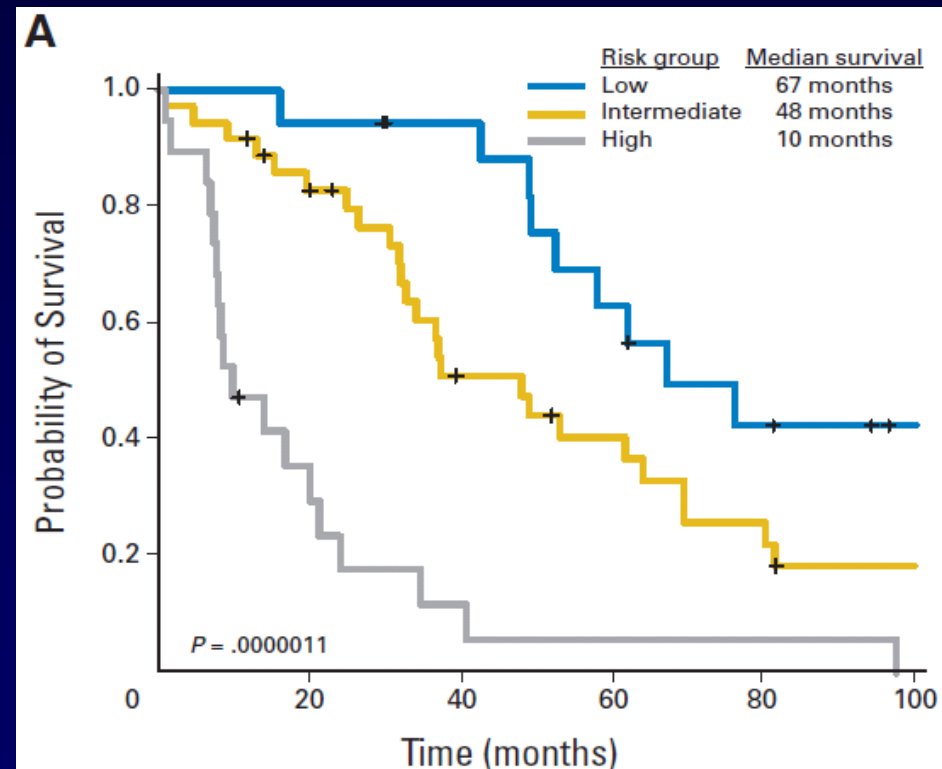


Score calculated with a rather complex formula

Prognostic Factors: 5 Gene Model

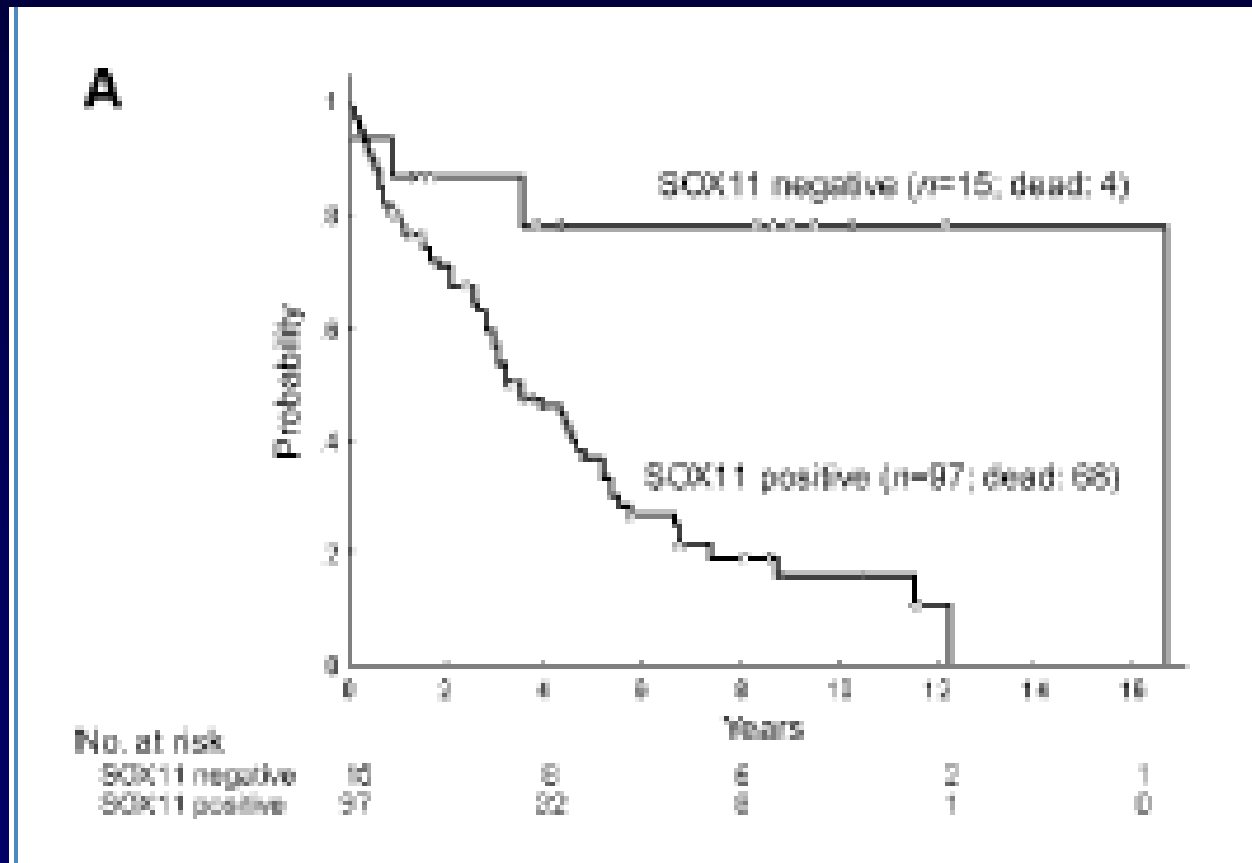
Factors predicting a poor prognosis

- Ki-67 proliferation index
- Blastoid (or pleomorphic) morphology
- GEP proliferation signature
- 5-gene q-RT-PCR model



Prognostic Factors: GEP

Expression of SOX11 predicts a poor prognosis



How I Treat Advanced MCL

Young (< 65y) and fit	Elderly (>65y) and fit	Unfit
R-Hyper CVAD / R-HDMTX -HD AraC x 4-6 ↓ BEAM + PBSCT	R-Benda or R-CHOP x6	R-CLB for 3-6 months (ev. W + W)