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Rafael Fonseca MD, Mayo Clinic

The Treatment of Ultra High risk MM

Scottsdale, Arizona

Rochester, Minnesota

Jacksonville, Florida

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Disclosures

- **Consulting: AMGEN, Genzyme, BMS, Otsuka, Celgene, Medtronic, Lilly**
- **Speakers Bureaus: None**
- **Research: Cylene, Proteolix**
- **Patent for FISH based prognostication in MM**
  - **About $1500 per year**

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Improved Survival in MM

Greek Myeloma Study Group (GMSG)

Thalidomide available in Greece: 1/1/2000

Group A vs. Group B: 2 (0.2%) vs. 167 (32%) given novel drugs up-front

End-point	Group A N=859	Group B N=517	*P* Value
***≥ PR** to first-line therapy*	56%	67%	< .001
Median Overall Survival	36 months	48 months	< .001
≤ 70 years of age	39 months	74 months	<.001
> 70 years	26 months	33 months	.273

Group B pts treated with novel agents upfront

4-Year Survival: ISS Stage I 85%

ISS Stage II 61%

ISS Stage III 26%

Kastritis et al Leukemia. 2009;23(6):1152-7

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Key questions

- How to integrate this information for treatment selection
- Can we tell all patients “myeloma is becoming a chronic disease”?
- What about “novel” agents?

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Statement in Publications

- *"Now that we have identified a higher risk subset of patients they are candidates for more intensive therapies or clinical trials"*

- **Detection OK (maybe so, so)**
- **Treatment not!**

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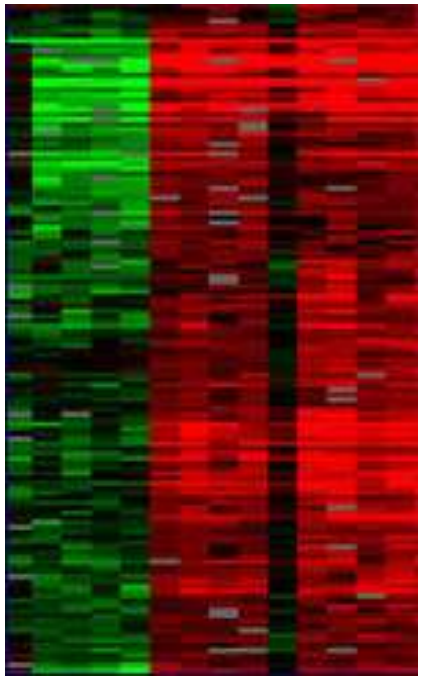
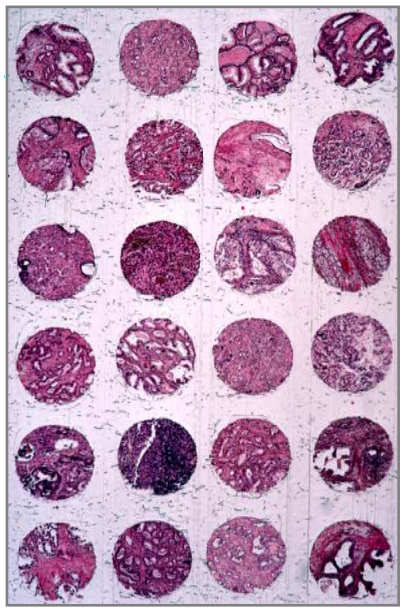
Genetics and Oncology





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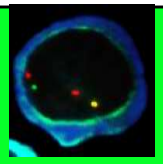
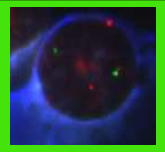
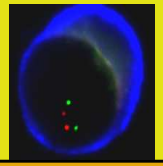
Classification of MM

	Ploidy	Prognosis	H	□	Morph	CD20	*ras*	-13	Bone DKK1	CCND
t(11;14) *(CCND3)*	NH	Good	G	κ		+++	++	-/+	++	D1 D3
t(14;16) (other *MAF*)	NH	Poor	A	λ		-	-	++	+/-	D2
t(4;14)	NH/h	Poor	A	λ		-	-	+++	+/-	D2
Other IgH	H/NH	Poor	?	?		-	-/+	?	+	?
Hyper	H	Good	G	κ		-	++	+/-	++	D1>D2

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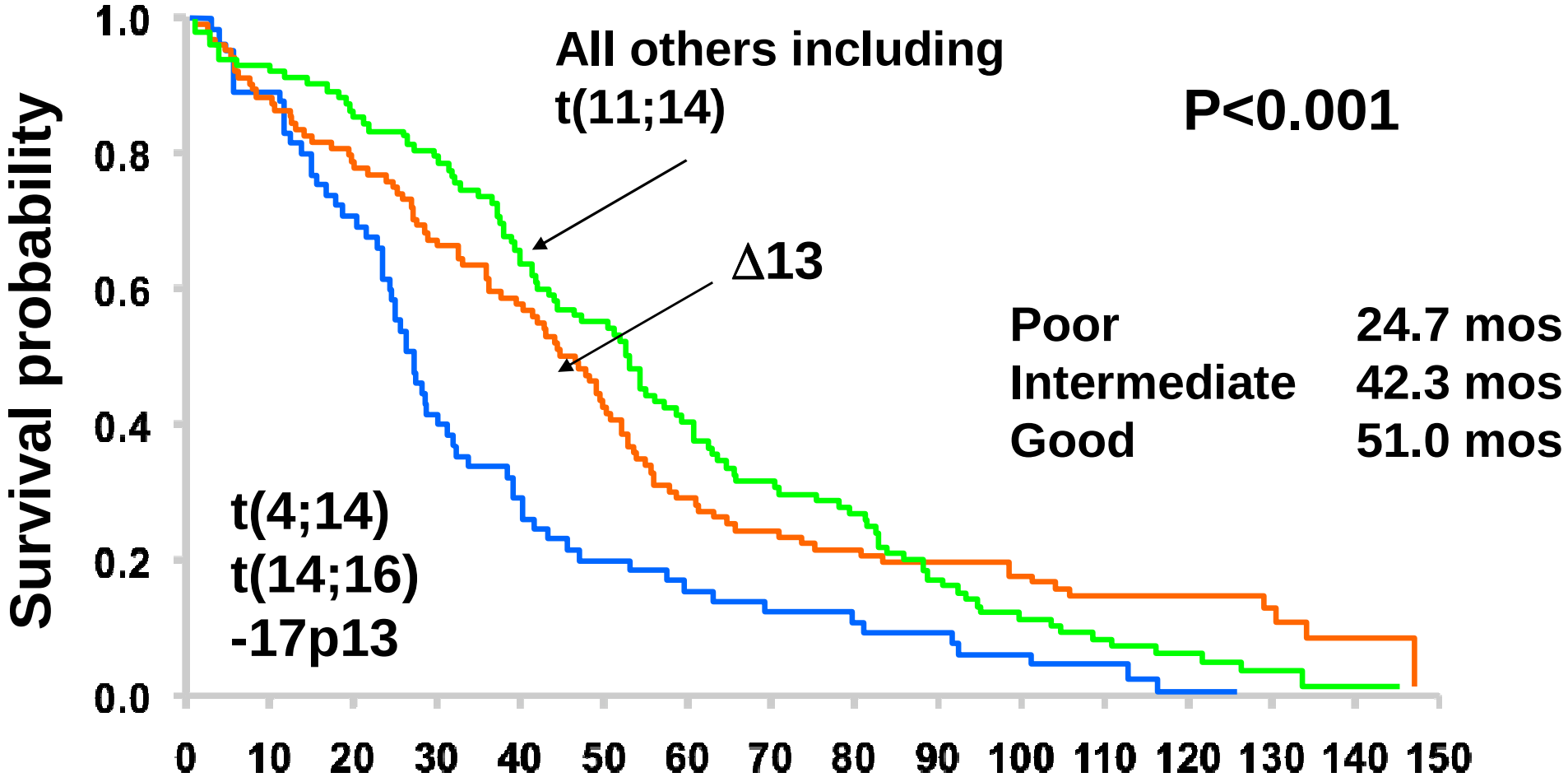
Molecular Prognostic Model



Fonseca et al Blood 101:4569, 2003

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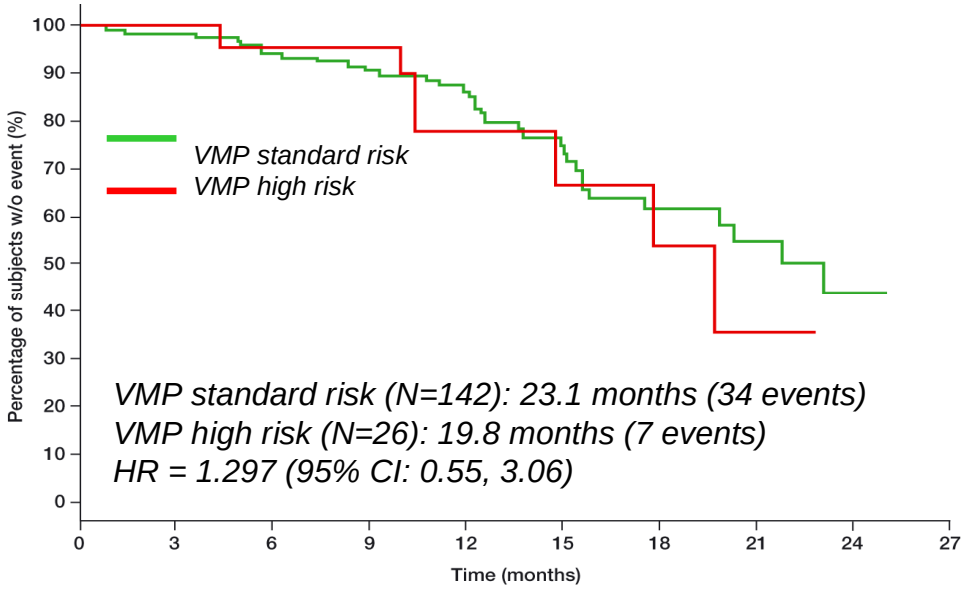
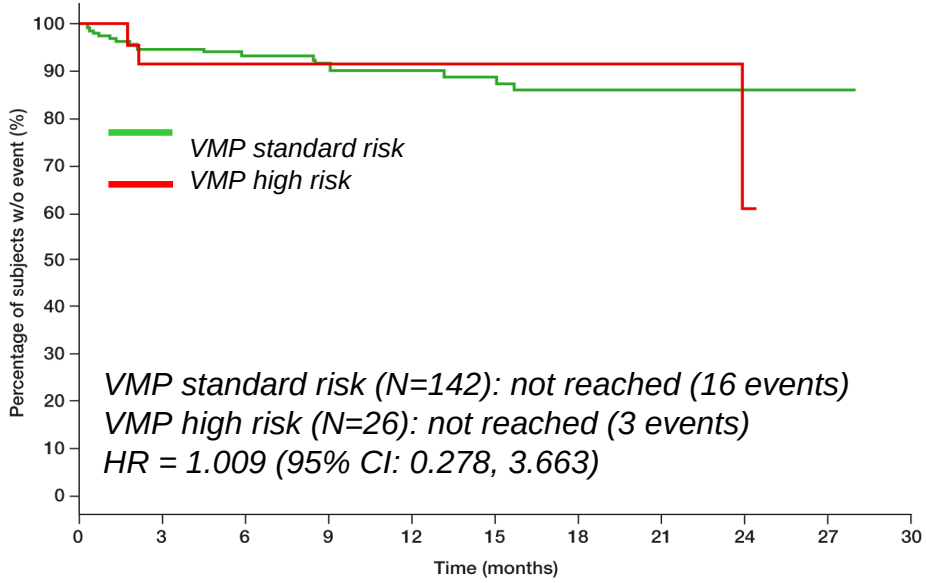
VMP and High Risk Disease

Best M-protein Response, n (%)	Total (N=165)	High Risk (N=26)	Std Risk (N=139)
CR (IF-)	32%	35%	32%
≥PR	82%	81%	82%

TTP

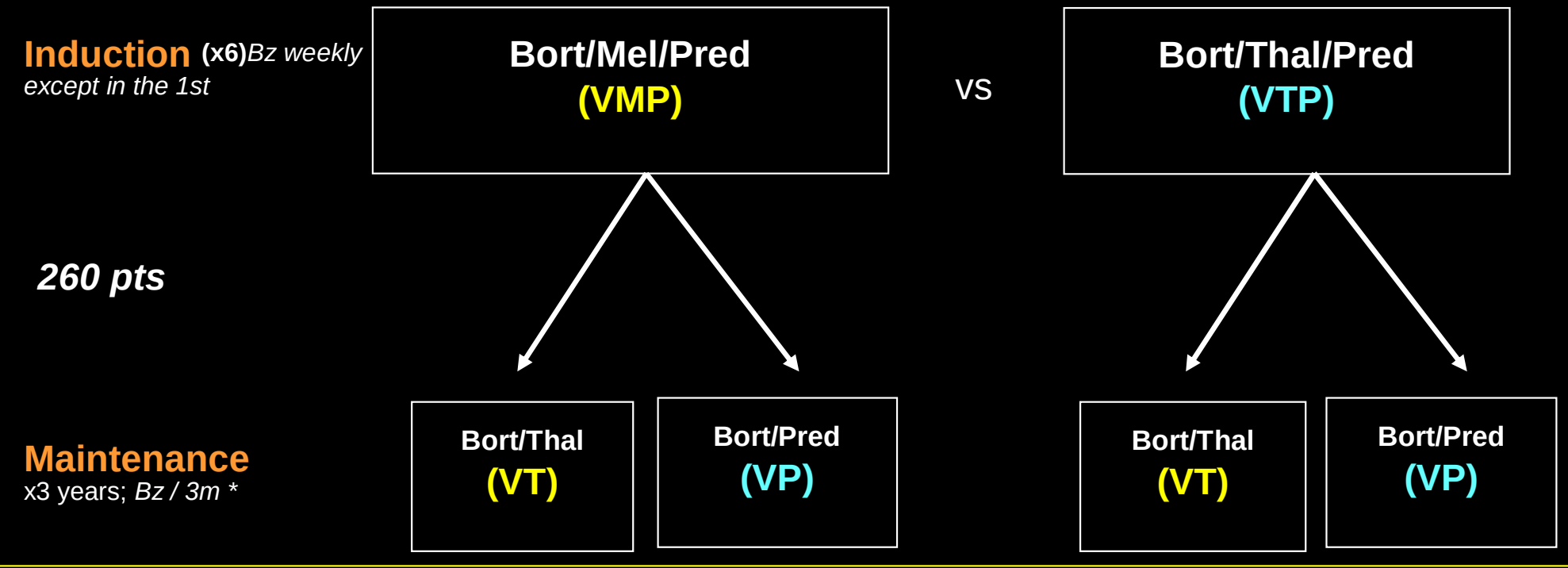


OS



San Miguel et al NEJM 2008, 359:906

Study design and aim



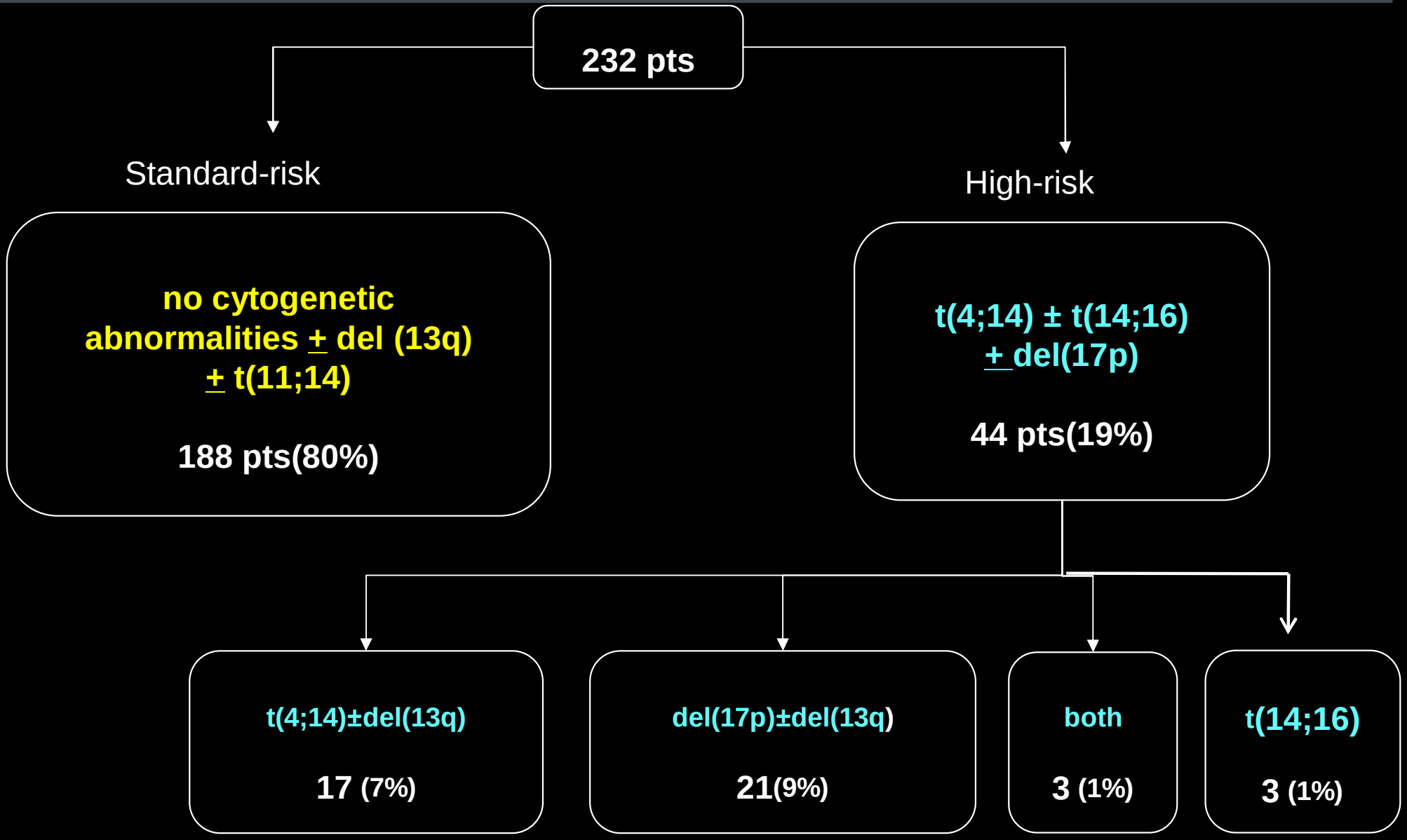
ORR (CR) rate ……..80%[1] (42%[2])

TTP/PFS ……35 m/31m; OS (at 3 y)…….70%

1. No differences in RR between VMP &VTP
2. Increase in CR from 23% to 42% withmaintenance without differences between VT/VP
3. No differences in outcome between both induction and maintenance regimens

Mateos *et al*. Lancet Oncology 2010; 10(11): 934-41

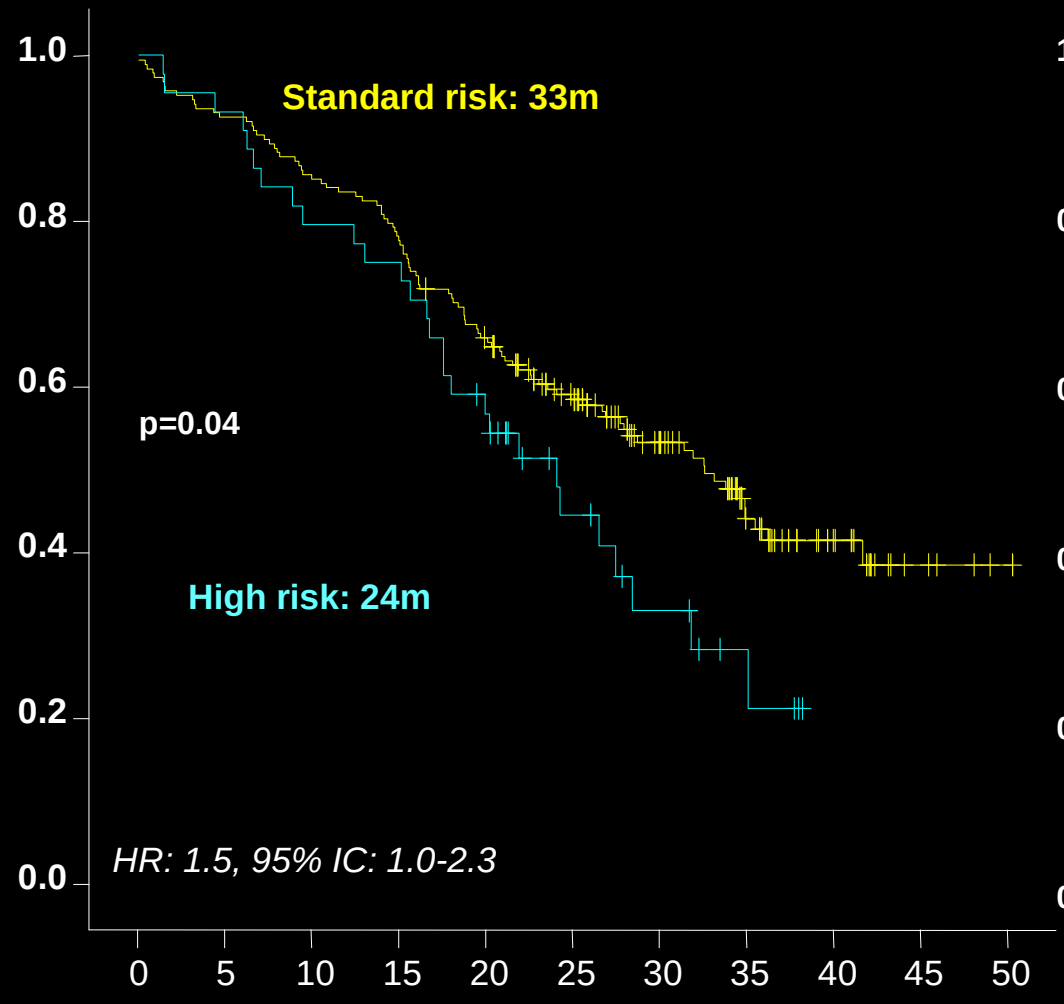
Study population stratified according to cytogenetic abnormalities



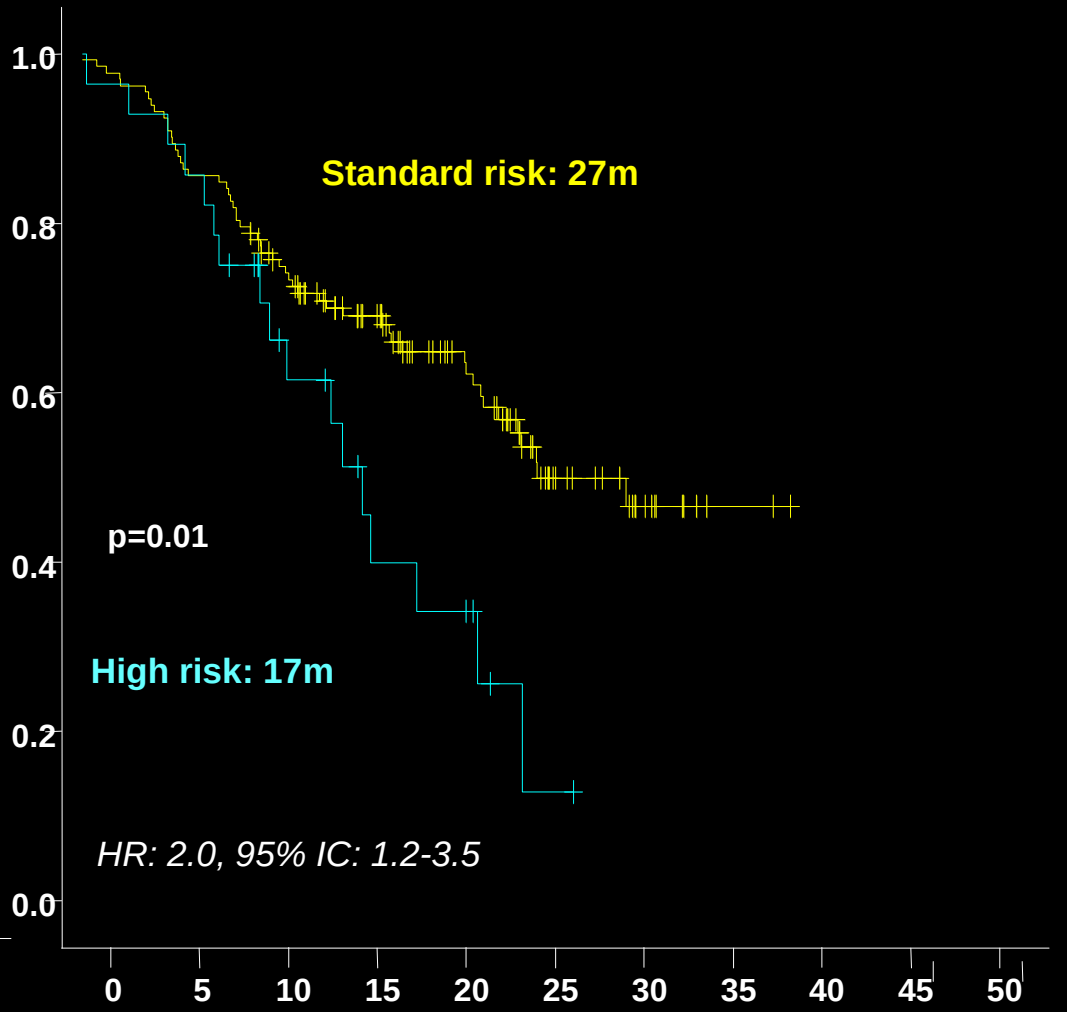
Outcome according to cytogenetic abnormalities from 1st/2nd randomization

Median follow-up: 32 m

PFS from 1st randomization

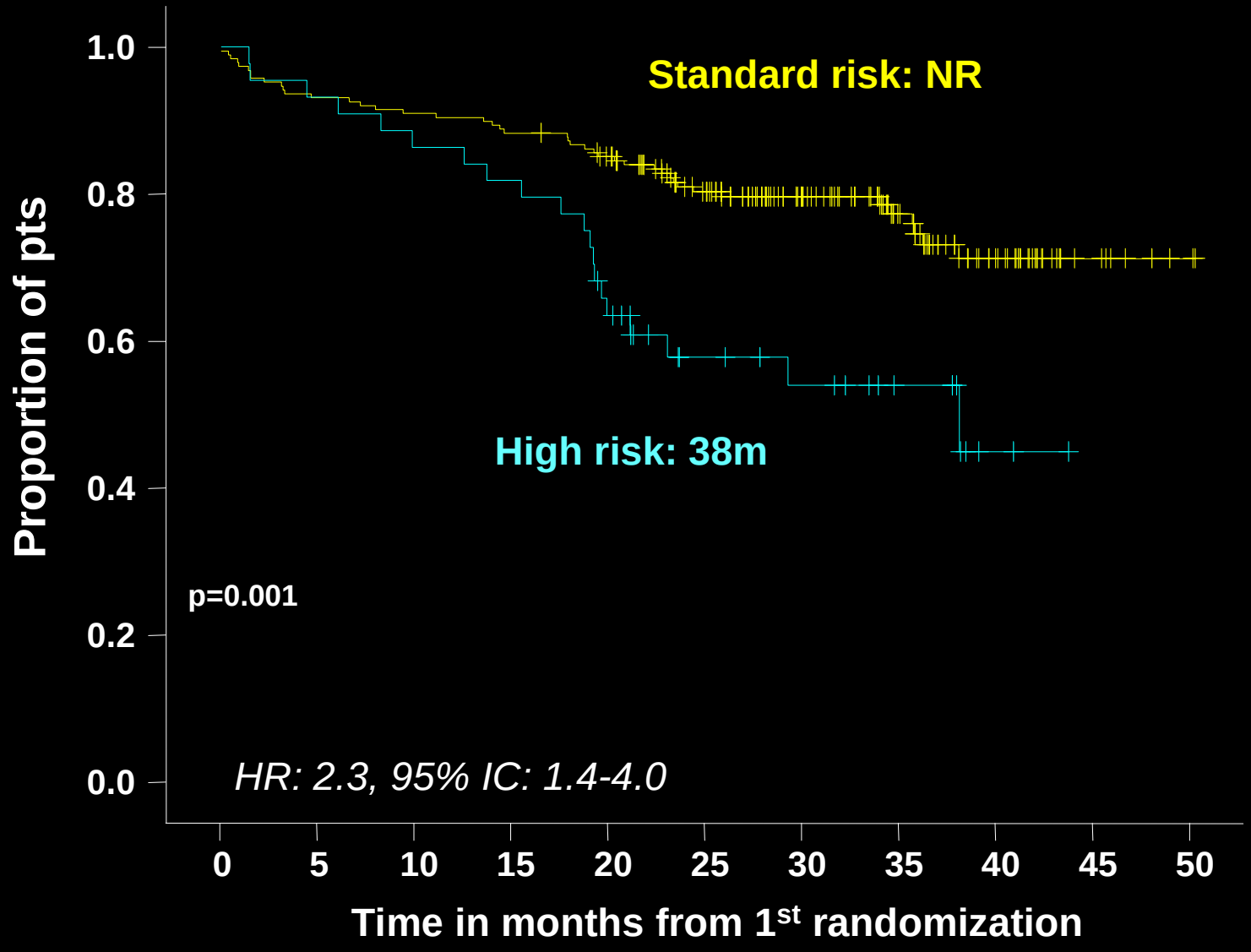


PFS from 2nd randomization



Time in months

Overall survival according to cytogenetic abnormalities



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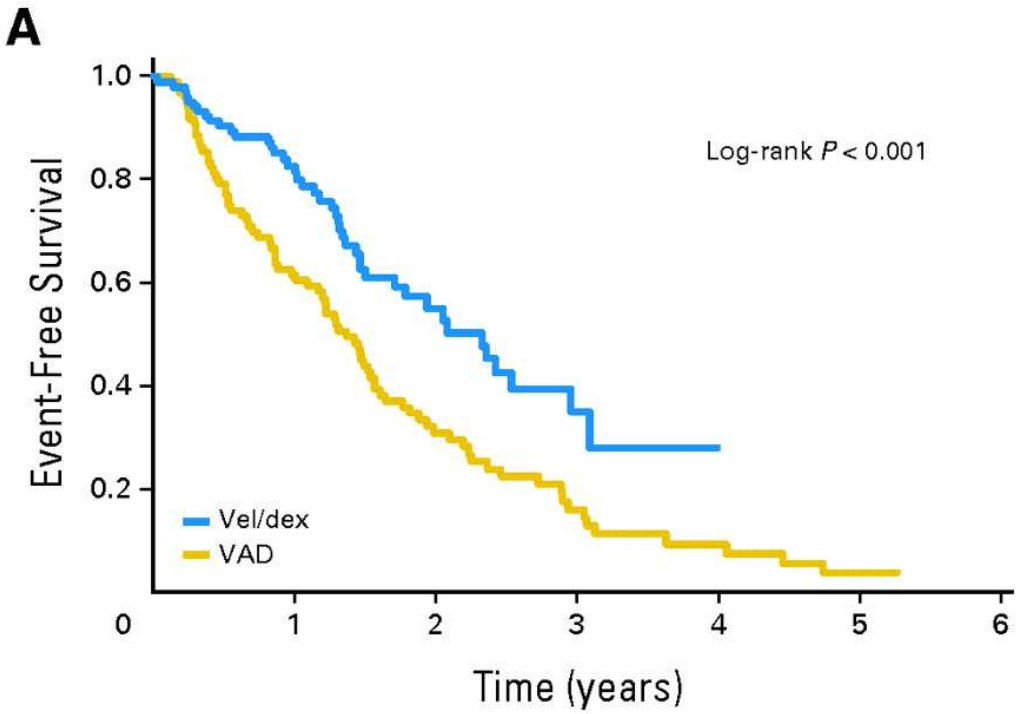
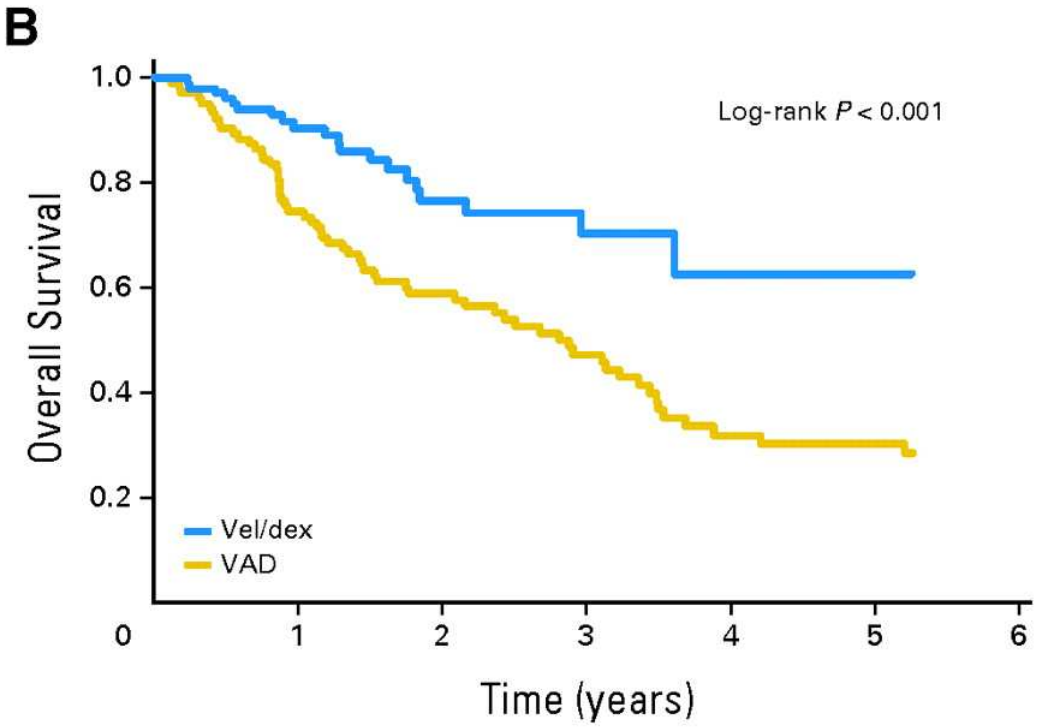
EFS and OS; t(4;14) VD (n = 106) vs VAD (n = 98)





Avet-Loiseau H et al. JCO 2010;28:4630-4634

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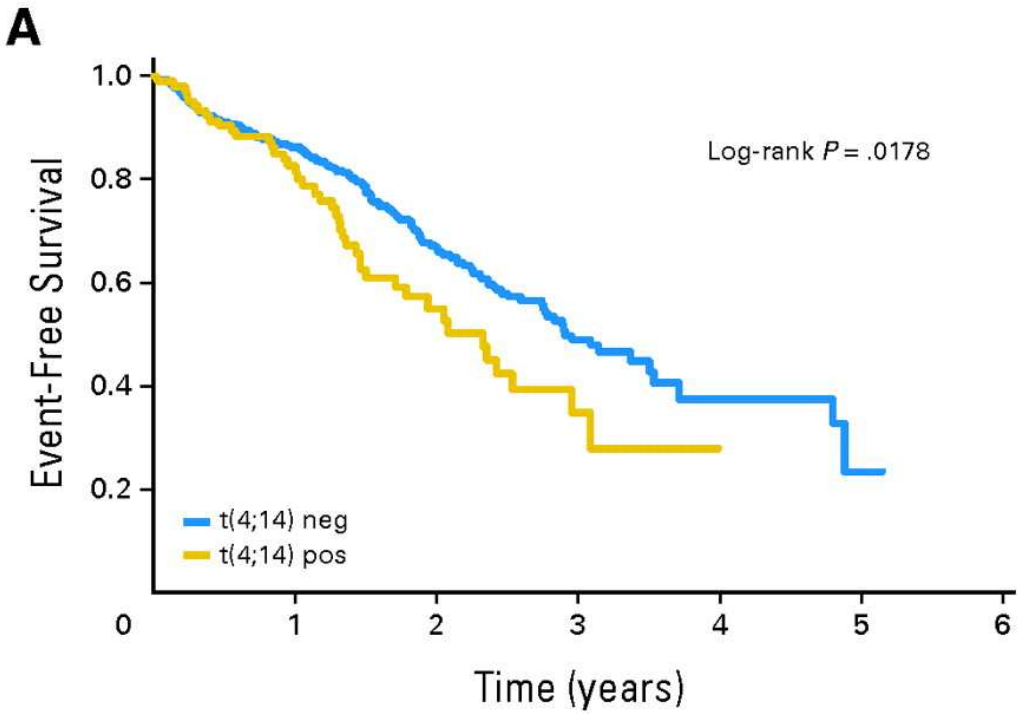
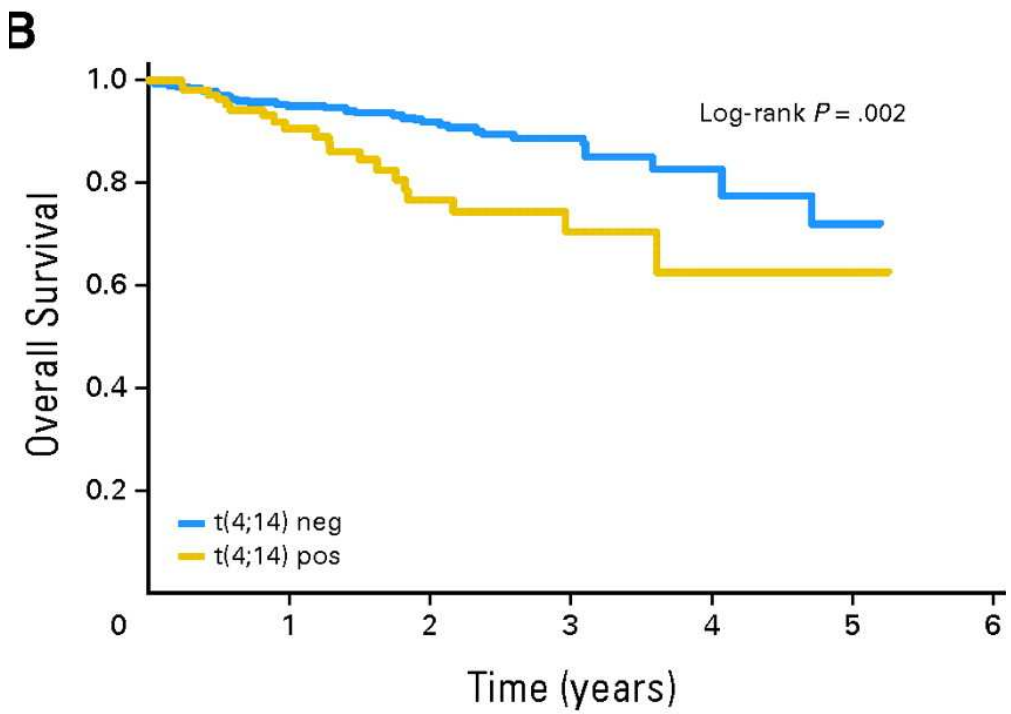
EFS and OS; VD Treated t(4;14) (n = 106) vs not (n = 401)





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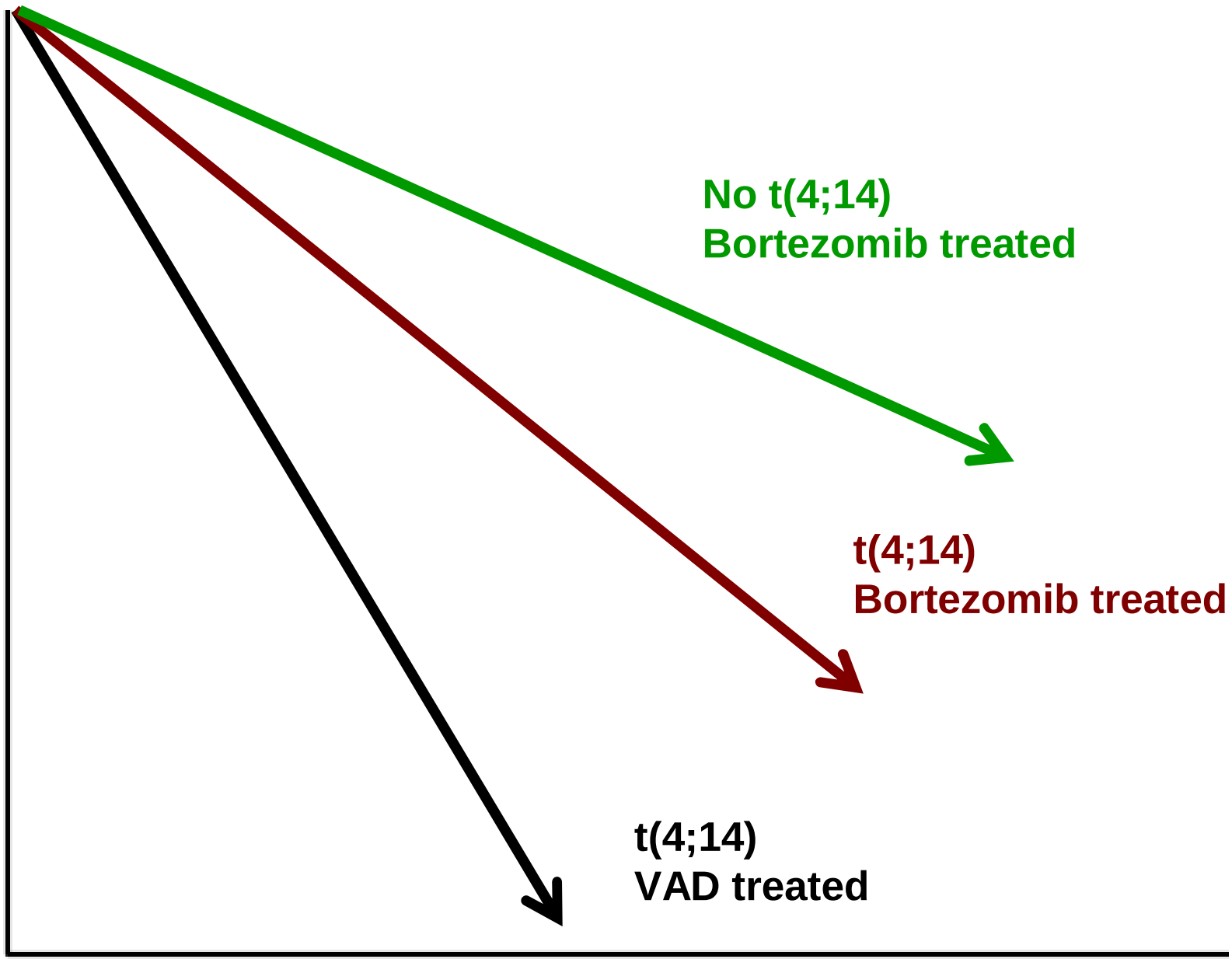

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