

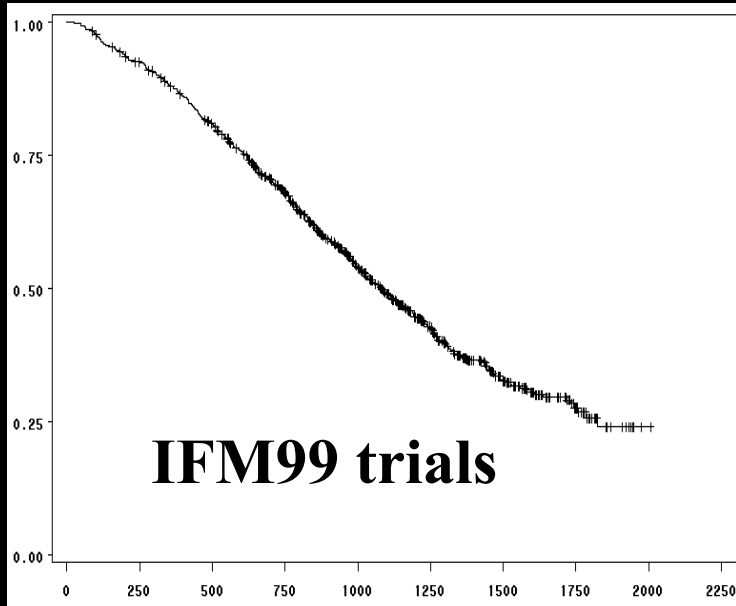
# **New Prognostic Factors & Staging Systems in Myeloma**

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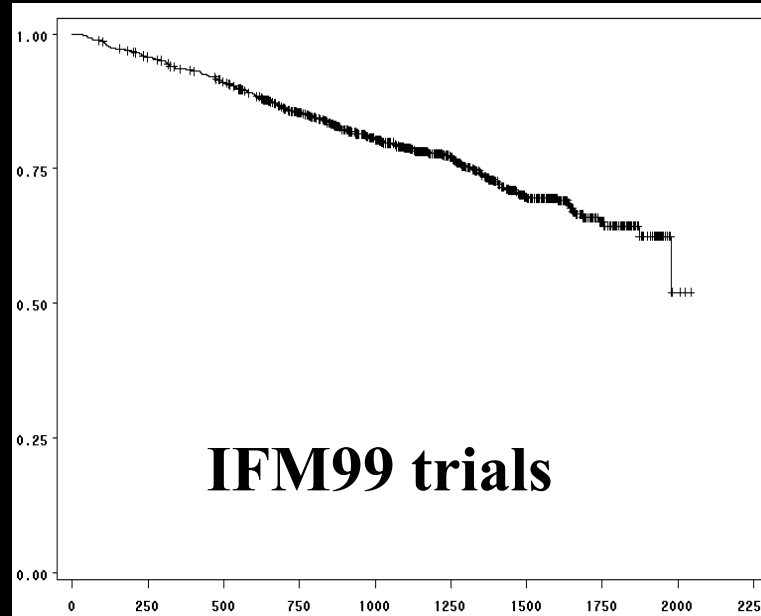
# Why prognostic staging in myeloma?

Because of a wide heterogeneity in survival:  
from a few weeks or months to more than 10 years

## Where are we starting from?



**EFS**



**OS**



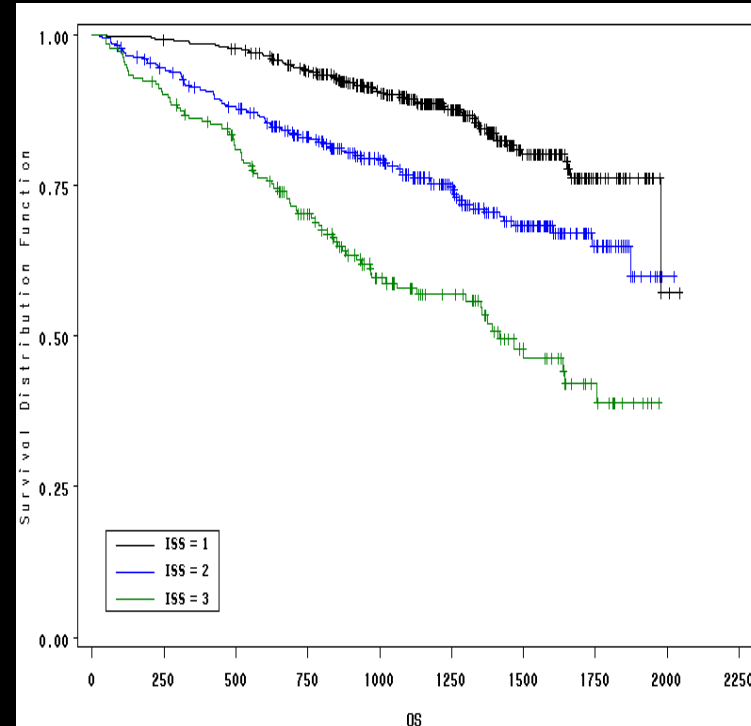
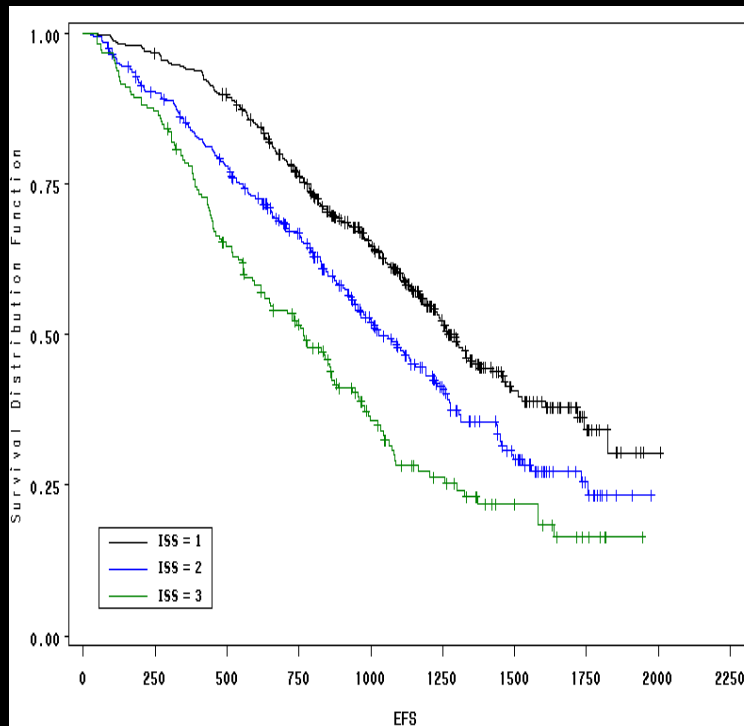
# Individual prognostic parameters

- $\uparrow$   $\beta$ 2-microglobulin
- $\downarrow$  albumin
- $\uparrow$  CRP
- $\uparrow$  LDH
- $\downarrow$  Hb
- $\downarrow$  platelets

# The International Staging System (ISS)

More than 10,000 pts throughout the world

Stage 1 : albumin  $\geq 35$   
 $\beta 2m < 3,5$       Stage 2 : neither 1, nor 3      Stage 3 :  $\beta 2m \geq 5,5$



# Cytogenetics in Myeloma

**Cytogenetics =  
the most powerful prognostic factor in acute leukemias**

**In myeloma: low informativity (low proliferation, low infiltrate)**

**→ chromosomal abn 100% of pts / karyotypes abnormal =20-30%**



**Interphase FISH**

**But requires plasma cell recognition  
(cIg-FISH, sorting, or combination morphology/iFISH)**

# Cytogenetics in Myeloma

**Del(13)** (965 pts) = **48%**

**t(11;14)** (760 pts) = **21%**

**t(4;14)** (727 pts) = **14%**

**Hyperdiploidie** (658 pts) = **40%**

**c-myc** (576 pts) = **13%**

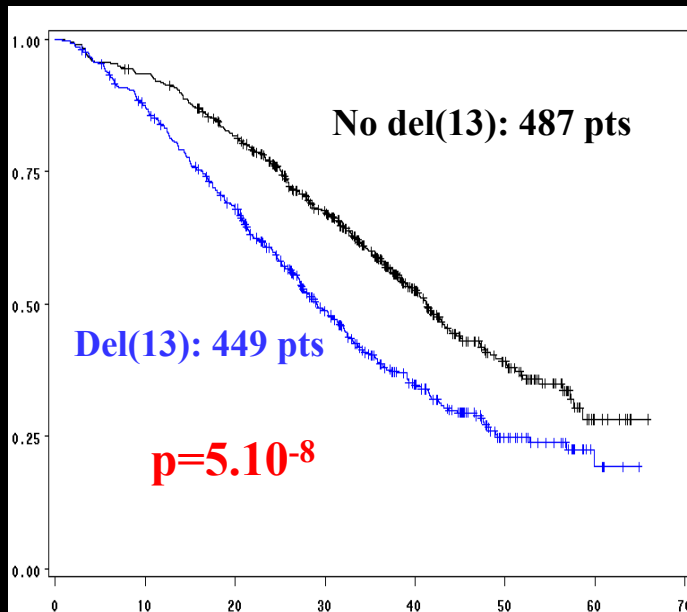
**Del(17p)** (526 pts) = **11%**

**Gains 1q** (365 pts) = **35%**

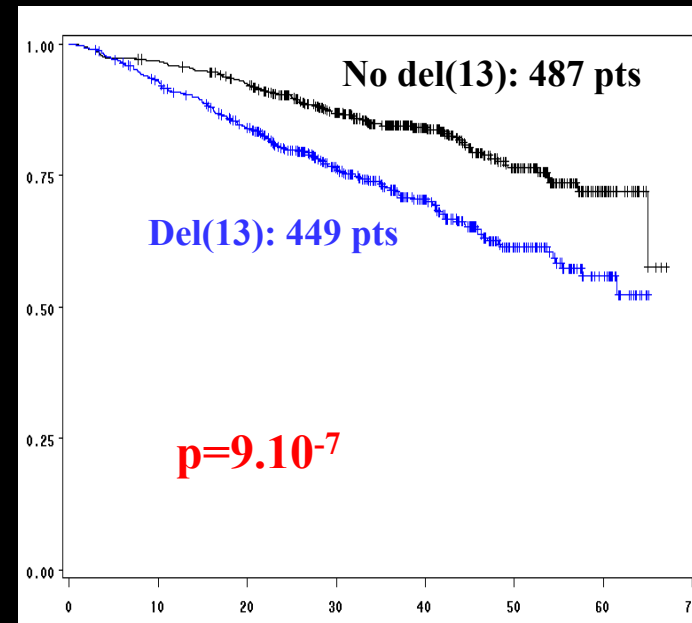


# Cytogenetics for Prognostication in Myeloma

## Chromosome 13 abnormalities = del(13)



**EFS**

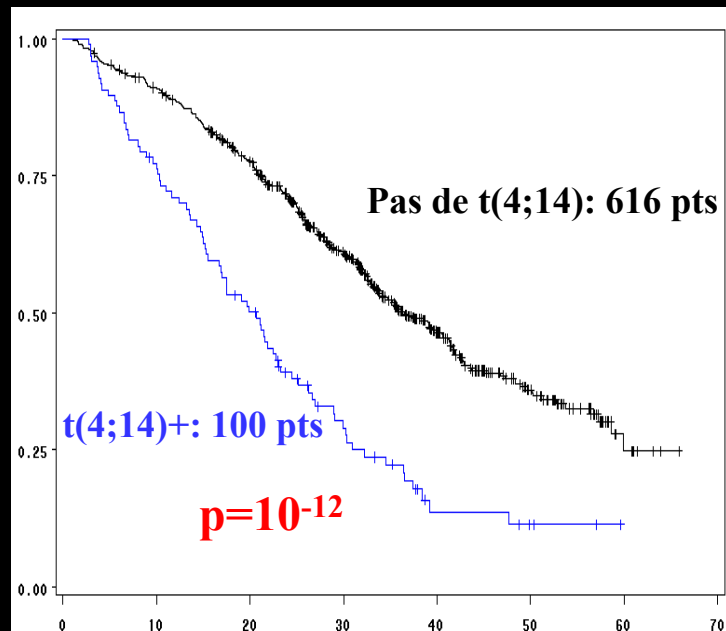


**OS**

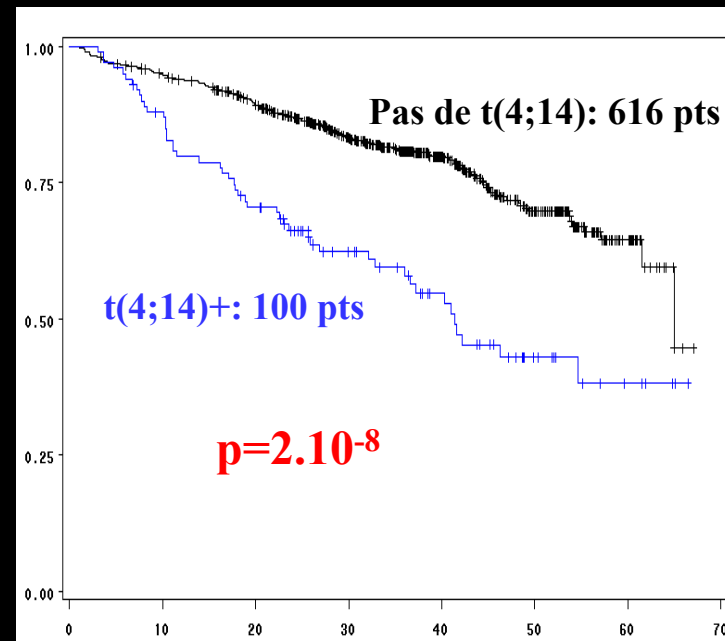


# Cytogenetics for Prognostication in Myeloma

**Translocation  $t(4;14)(p16;q32)$  : 14% of the pts**



**EFS**

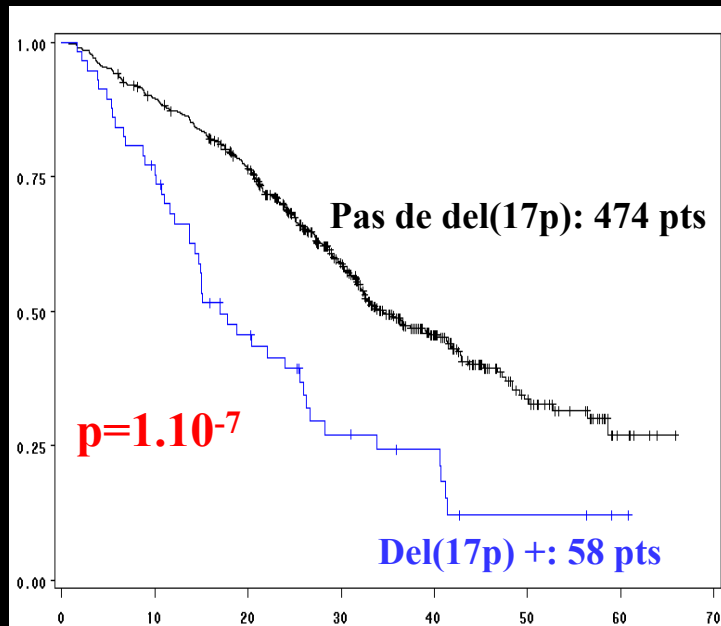


**OS**

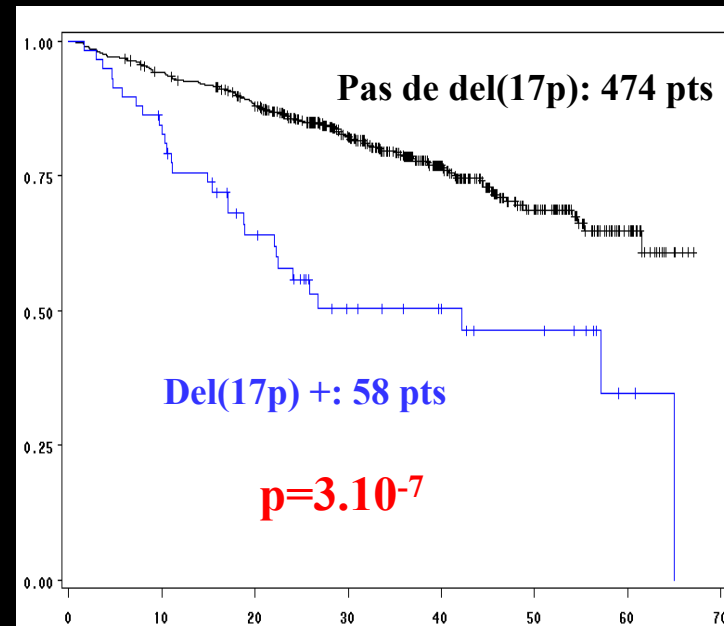


# Cytogenetics for Prognostication in Myeloma

## Deletion 17p: 10% of the pts



**EFS**



**OS**



# Cytogenetics for Prognostication in Myeloma

## Correlations between cytogenetic markers

84% of the pts with t(4;14) display del(13)

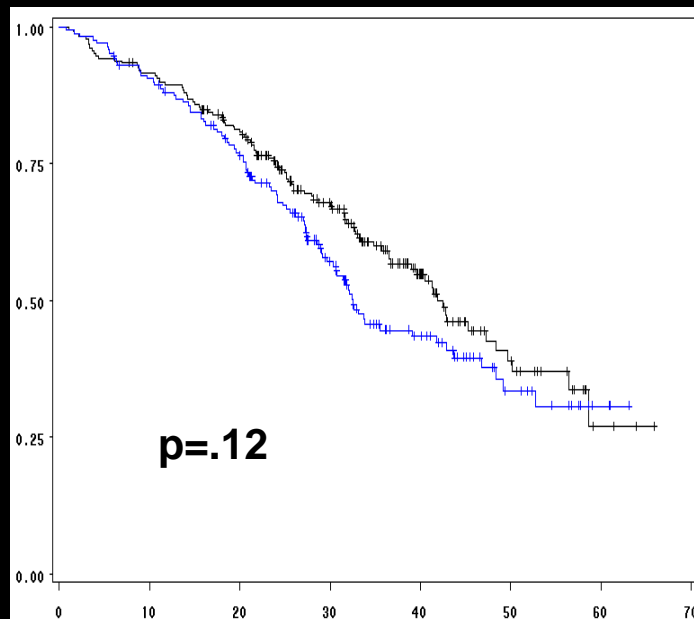
77% of the pts with del(17p) display del(13)

**What is the respective prognostic value of each abnormality?**

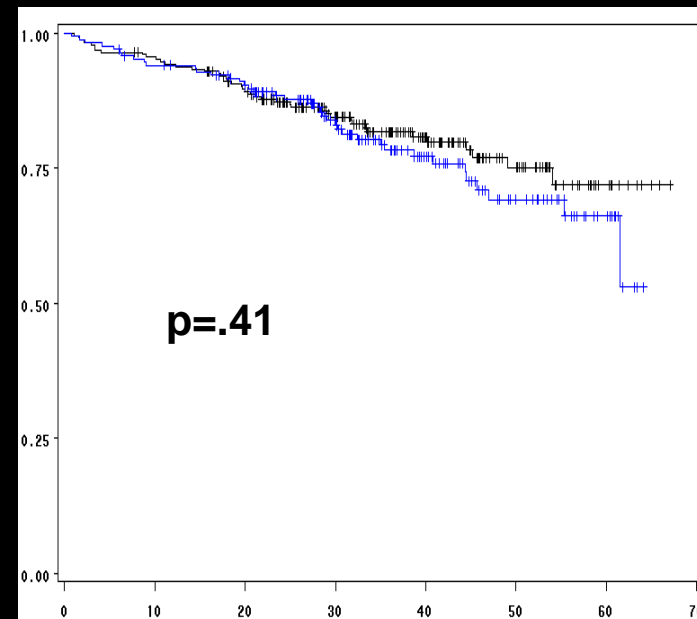
- 2 approaches:
- prognostic impact of del(13) in absence of t(4;14) and del(17p)
  - multivariate analysis

# Cytogenetics for Prognostication in Myeloma

## Prognostic impact of del(13) in pts lacking both t(4;14) and del(13)



**EFS**



**OS**



# Cytogenetics for Prognostication in Myeloma

**Multivariate analysis: del(13), t(4;14), del(17p), 1q gains,  $\beta 2m > 3/4$   
Hb < 10, albumin < 30 or 35, platelets < 130**

## **Independent prognostic parameters**

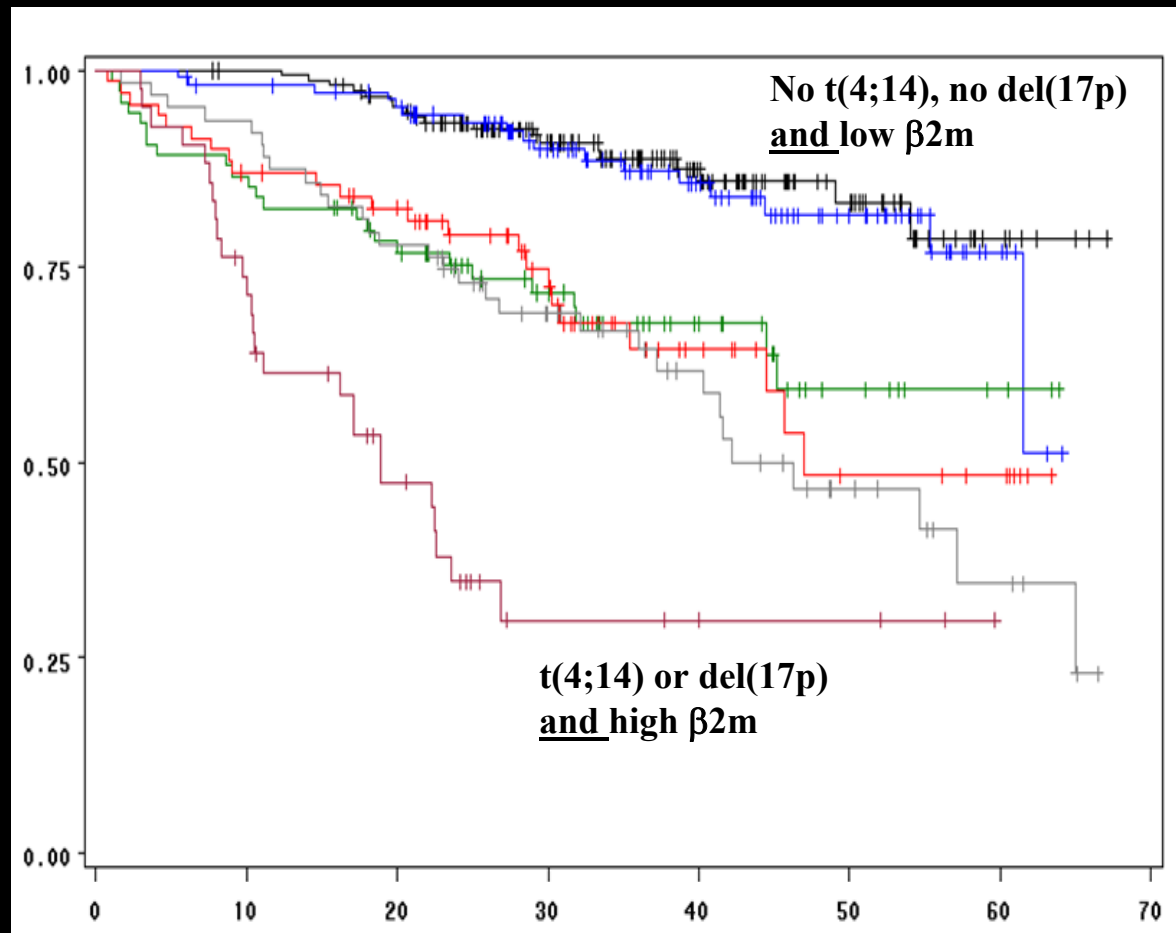
**EFS:** del(17p)  
t(4;14)  
 $\beta 2m > 3$  or 4  
Hb < 10 g/dl

**OS:** del(17p)  
t(4;14)  
 $\beta 2m > 3$  or 4



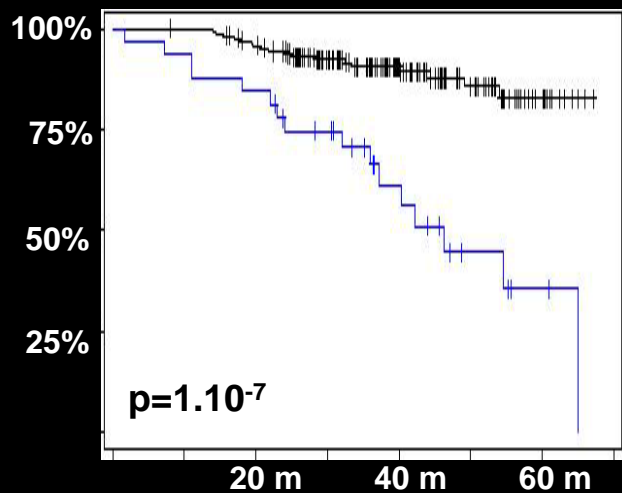
# Novel Prognostic Staging System

## Combination of the ISS and Cytogenetics

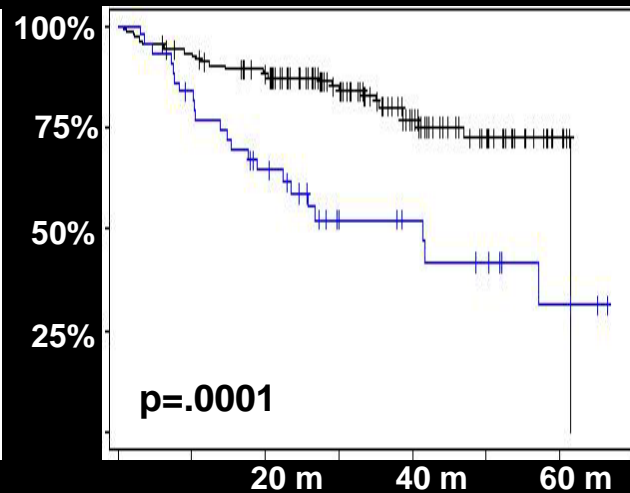


# Novel Prognostic Staging System

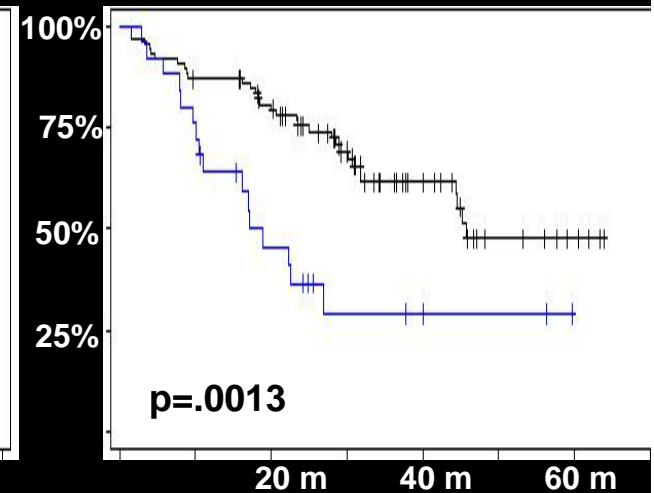
## Improvement of the ISS



ISS 1: Overall Survival



ISS 2: Overall Survival



ISS 3: Overall Survival

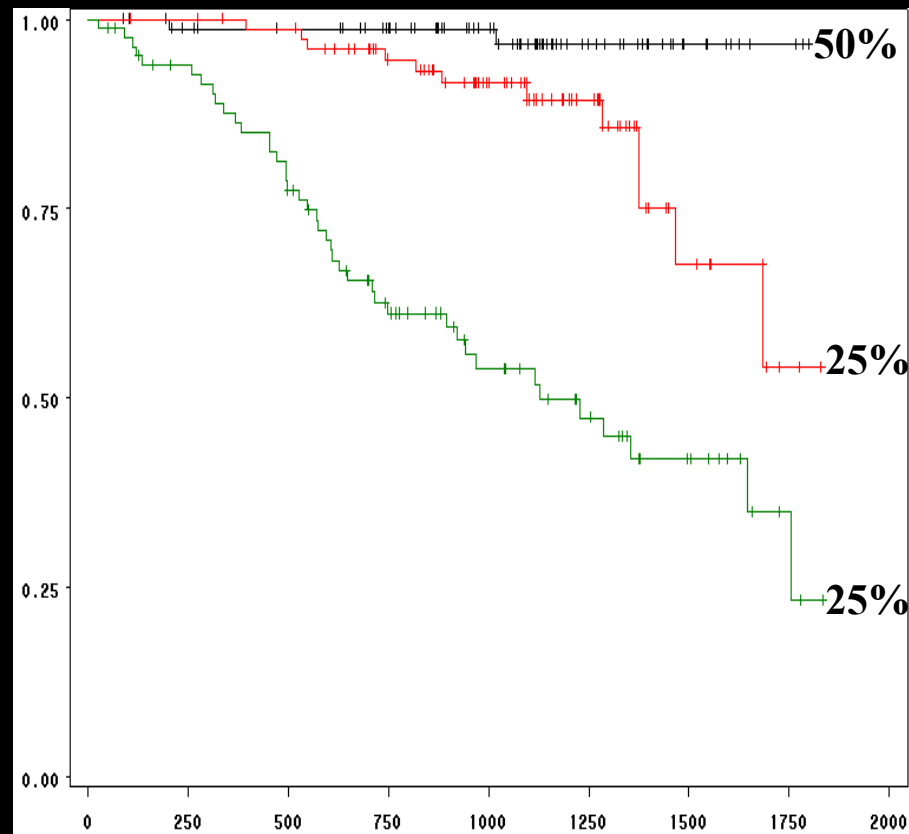


# Prognostication in the future

Possibly based on the microarray technology

Model using Gene Expression Profiling

250 pts  $\leq$  65 years  
Double ABMT  
Model with 15 genes  
(submitted)



# Conclusion

**Prognostic evaluation important at diagnosis**

**Based on ISS and a few chromosomal markers**

**Requires a standardization**

**Mandatory for prospective clinical trials**

**Highly recommended for every patient**

**Question: will novel therapies modify these prognostic factors?**