

The use of new genetic tools for prognostication in myeloma: Introduction on risk-adapted strategies

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Current Knowledge

Karyotype : low informativity

Plasma cells = low proliferation

Partial bone marrow involvement

Sample quality

→ Other molecular techniques are mandatory :
FISH, GEP, SNParray

Myeloma Specificities

Partial bone marrow infiltrate

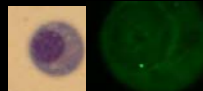
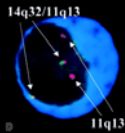
→ 6% plasma cells in laboratory samples

→ For FISH, plasma cell identification is mandatory

Immuno-FISH

Cell sorting/CD138

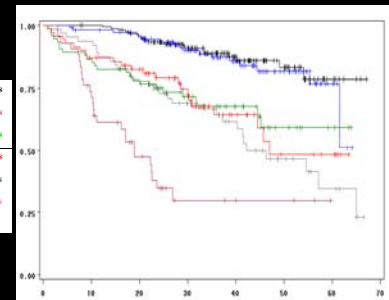
GIEMSA + FISH



FISH + β 2m Model.

Overall survival

No t(4;14), no del(17p), β 2m<4, no del(13)	155 pts
No t(4;14), no del(17p), β 2m<4, del(13)	110 pts
No t(4;14), no del(17p), β 2m<4, no del(13)	74 pts
No t(4;14), no del(17p), β 2m<4, del(13)	69 pts
t(4;14) or del(17p)>60%, β 2m<4	63 pts
t(4;14) or del(17p)>60%, β 2m<4	42 pts



Avet-Loiseau H et al., Blood 2007



How to improve this prognostication ?

Expression profiling (GEP) : tumor RNA analysis

Plasma cells Sorting



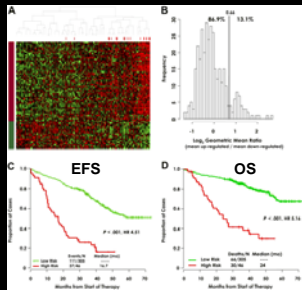
Tumor RNA extraction



Hybridation on Affymetrix chips

GEP : Tumor RNA analysis

Identification of a 70/17-gene set

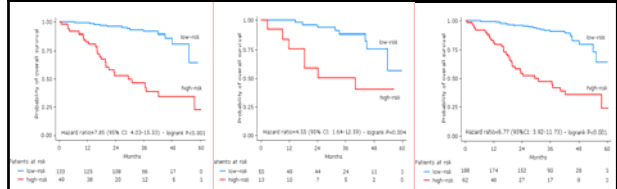


→ Identifies a high-risk population (13%)

Shaughnessy et al., Blood 2007; 109:2276-2284

GEP : Tumor RNA analysis

Identification of a 15-gene set

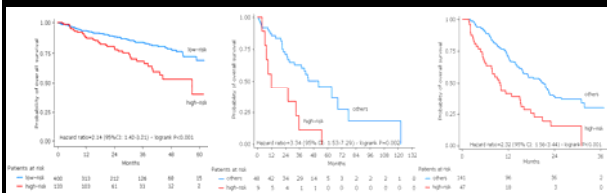


→ Identifies a high-risk population (25%)

Decaux et al., JCO 2008; 26:4798-4805



GEP : Validation



Validation (UAMS data set)

Validation (Mayo Clinic data set)

Validation (Mulligan's data set bortezomib alone)

Decaux et al., JCO 2008; 26:4798-4805

CGH or SNParray : Tumor DNA analysis

Purification plasma cells

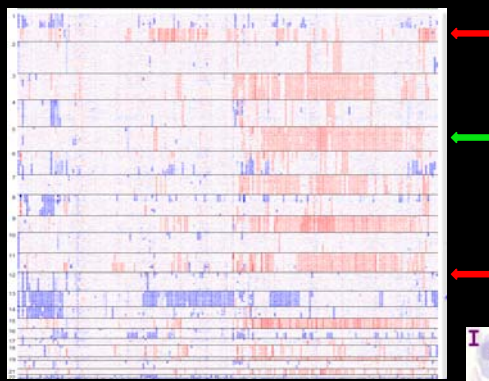


Tumor DNA extraction

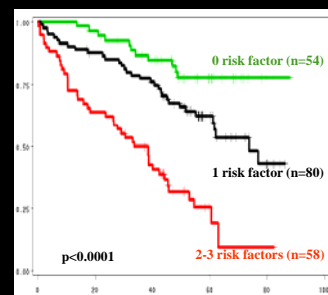


Hybridization on 500.000 SNPs chips

Chromosomal multivariate analyses



Chromosomal multivariate analyses

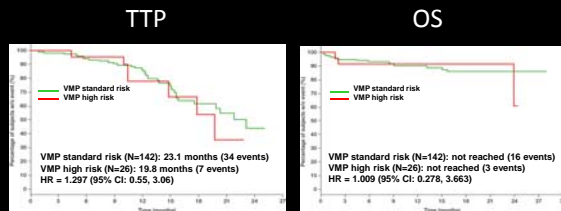


Avet-Loiseau et al., JCO in press



Velcade® overcomes poor-prognosis?

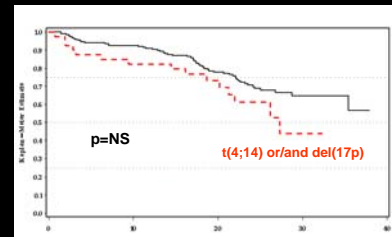
VISTA: MP vs VMP



San Miguel et al., NEJM 2008;359:906-17

Velcade® overcomes poor-prognosis?

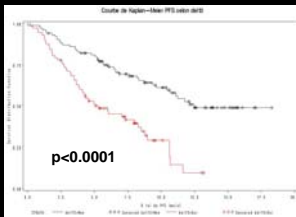
IFM 2005-01: VAD vs Vel/Dex



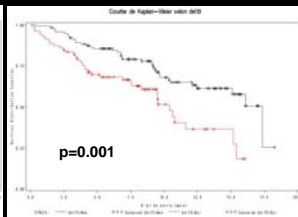
Revlimid®: conflicting data

PAMELA Study : 207 end-stage pts, Rev/Dex

Del(13) PFS



Del(13) OS



MM016 (Reece, Blood online) : 130 pts, Rev/Dex overcomes del(13) & t(4;14), but not del(17p)



Conclusions

Genetic/genomic analyses are required at diagnosis

Whether FISH or GEP or SNParray ?

Ongoing studies correlating genetics and response/PFS

Future : Individualized therapy ?