How should we define standard and high risk MM in 2022?

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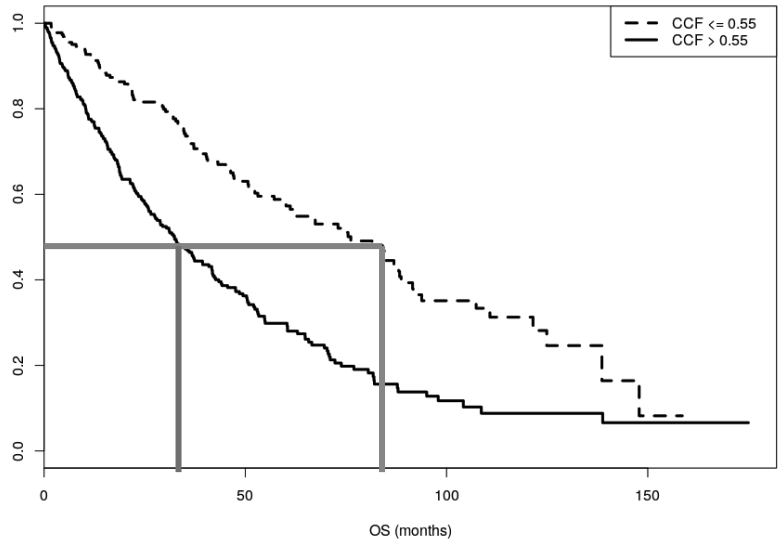
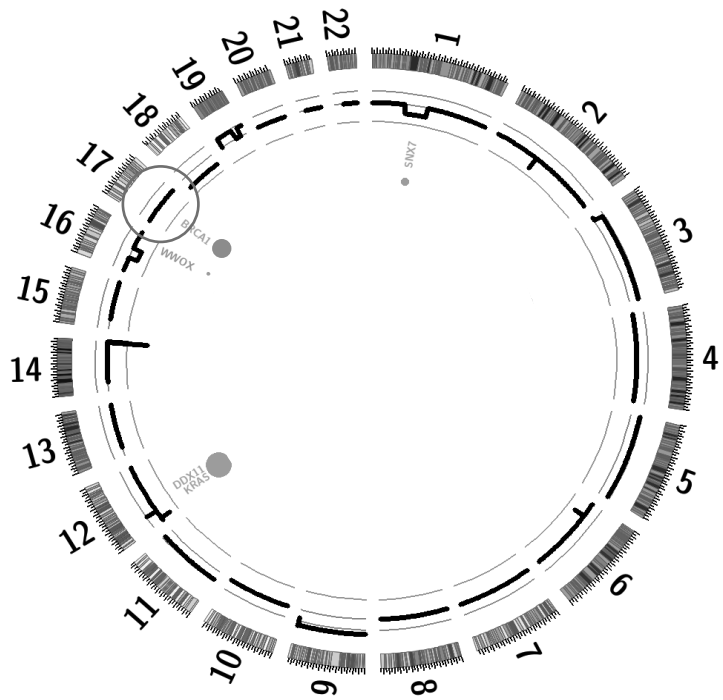
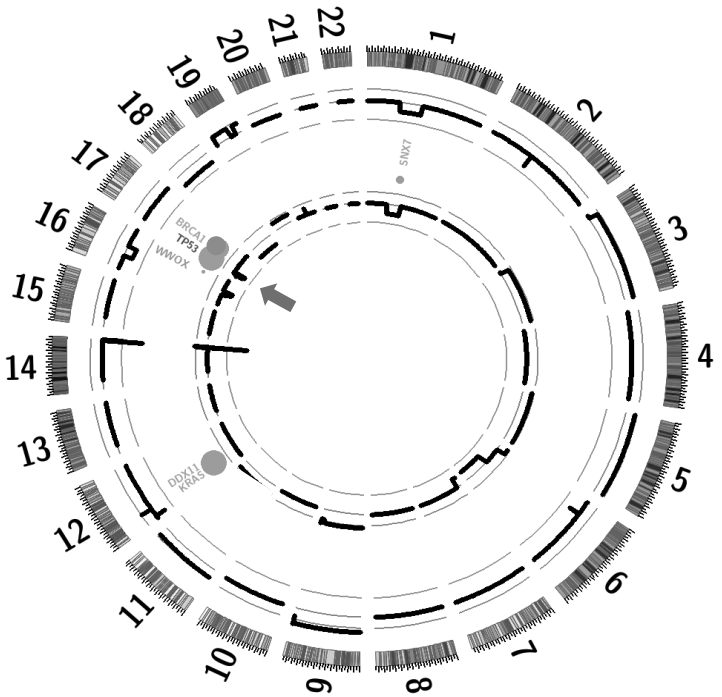
Mainly based on genetic abnormalities
IMWG: del(17p), t(4;14) or t(14;16)

Del(17p): importance of the clonal fraction

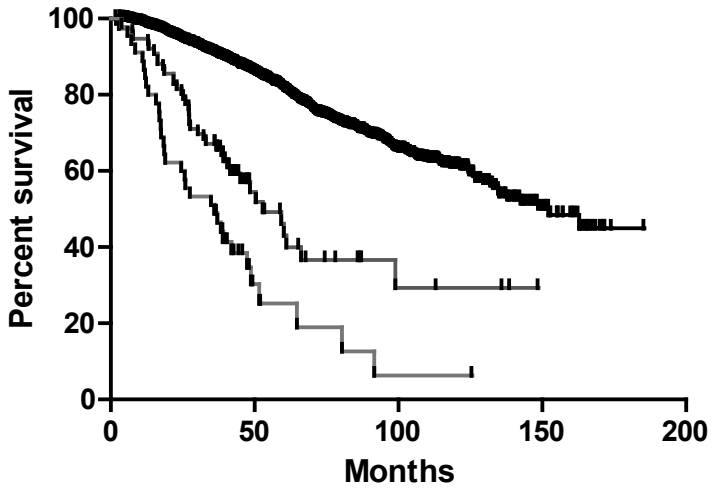


Not only at diagnosis





Double hit > del17p > Standard Risk

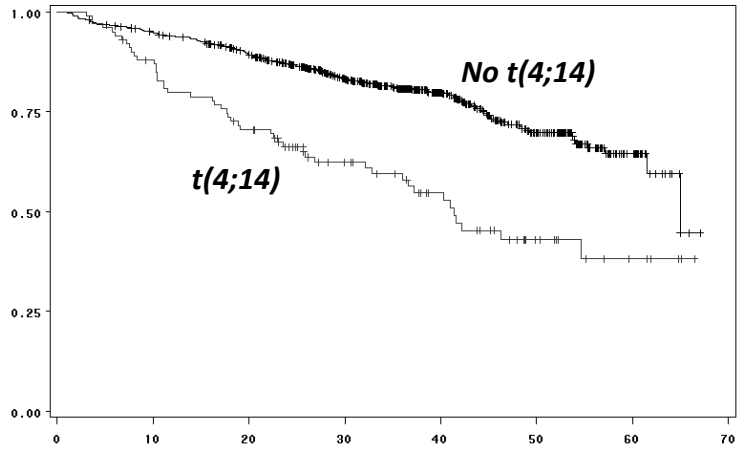


	Event/N	Median survival (mo)
no del(17p)	601/2505	152,2
del(17p)/TP53wt	39/76	52,8
del(17p)/TP53mut	33/45	36

Log-rank p-value < .0001

t(4;14)

12-15% of patients



Probably a very heterogeneous entity
Some HR, others SR →Breakpoints location?

Avet-Loiseau H et al, Blood 2007

t(14;16)

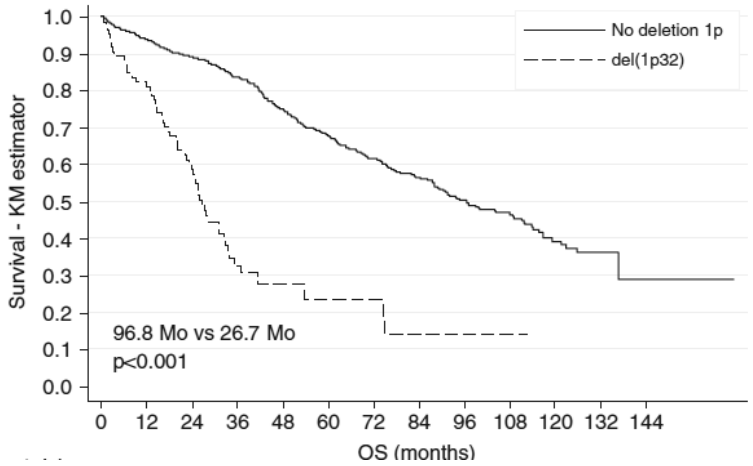
Early event
Rare entity (3.5%)
Really independent prognostic value ?

- **Not in the IFM studies (retrospective, IFM/DFCI 2009)**
- **Retrospective study at ASH 2018 on 213 patients (largest series)**
  median OS=88 months…

Avet-Loiseau H et al., Blood 2008; Artur Jurczyszyn et al., ASH 2018; Goldman-Mazur et al. Am J Hematol 2020

→ del 1p32 ?

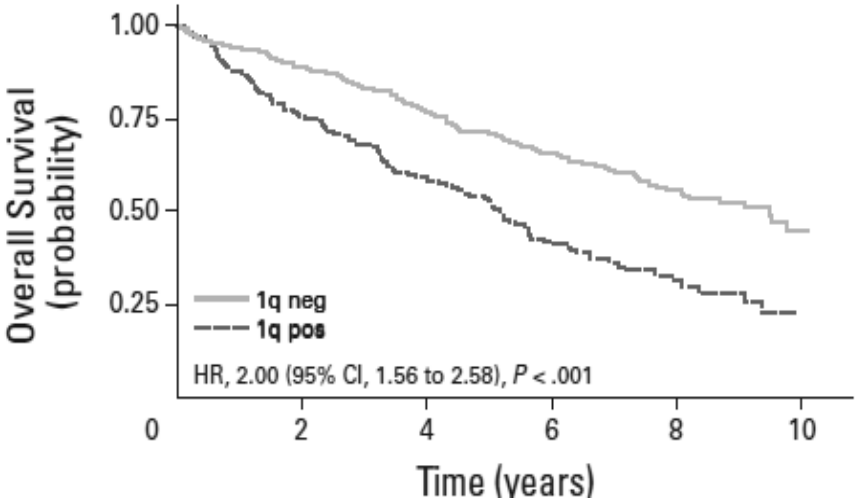
8-10% of patients



Hebraud et al. Leukemia 2014

→ 1q gain ?

35% of patients



Avet-Loiseau et al. JCO 2012

The IFM prognostic model

The final model retains 6 independent variables :

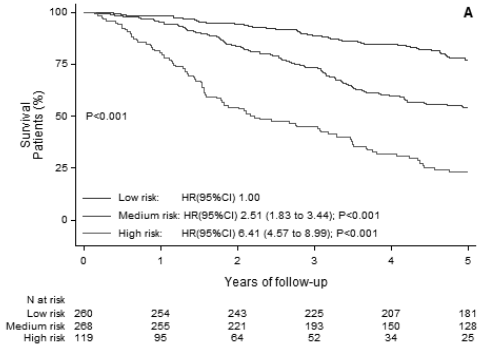
- Trisomy 5 → -0.3
- Trisomy 21 → 0.3
- t(4;14) → 0.4
- 1q gain → 0.5
- del(1p32) → 0.8
- del(17p) → 1.2

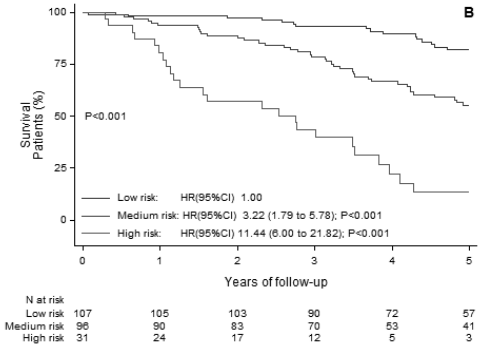
specific coefficient =
weighted prognostic value

Score ≤ 0 : Good prognosis
Score > 0 & ≤ 1 : Intermediate prognosis
Score > 1 : Poor prognosis

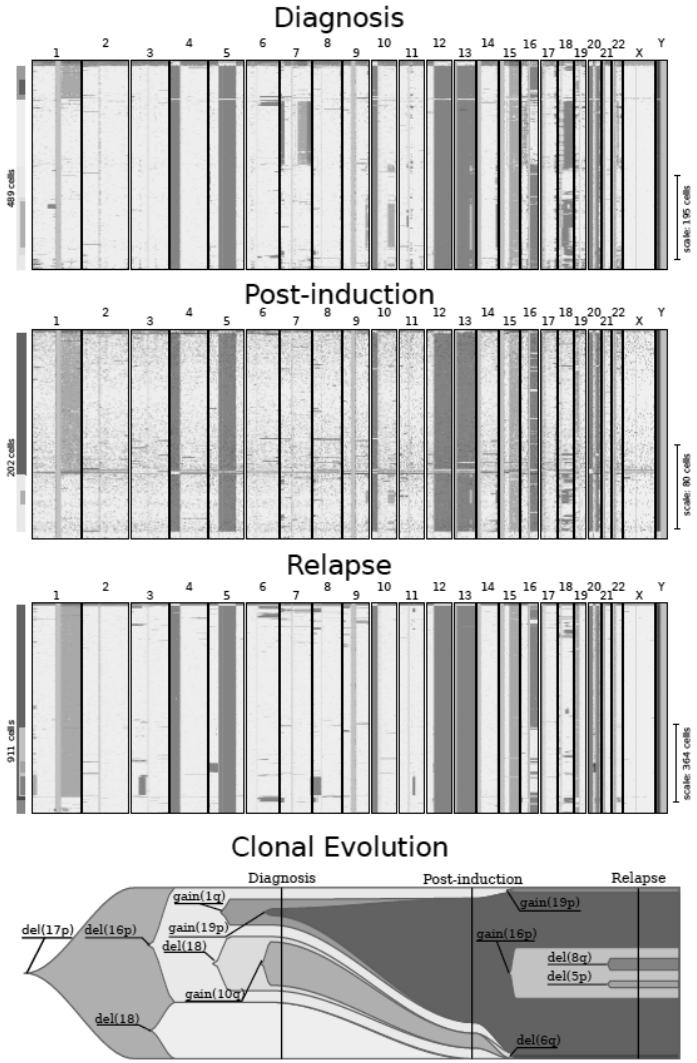
del17p
trisomy 21
t(4;14) del1p32
trisomy 5
gain1q

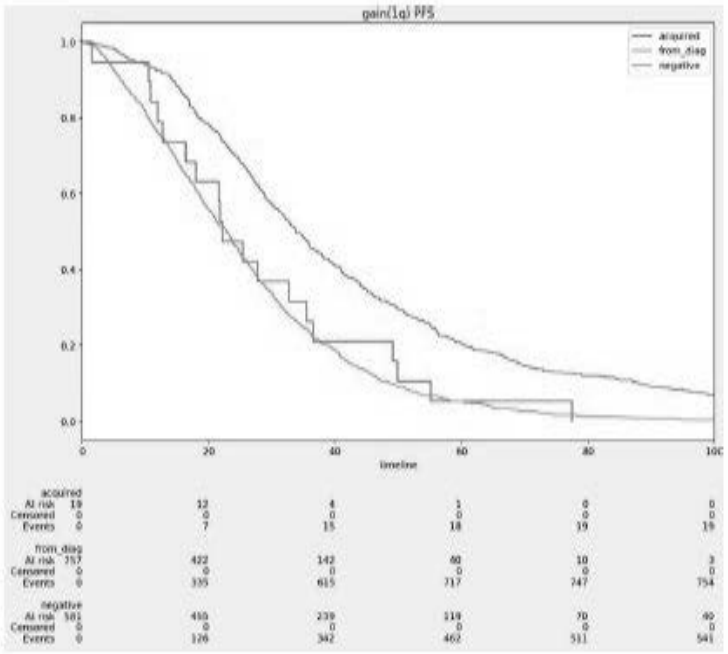
Perrot et al, J Clin Oncol 2019

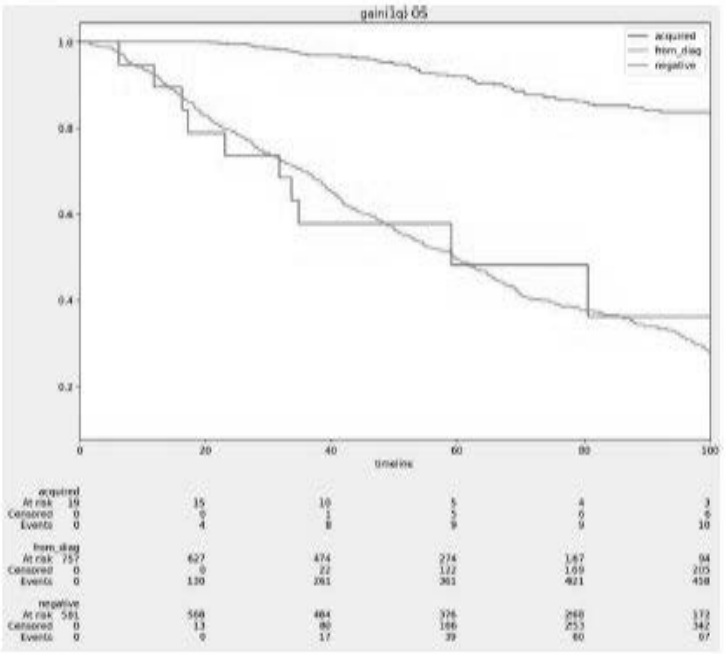




Early clonal selection on single cell analyses







Take home messages

High risk patients: **Del(17p) > 55% plasma cells**
Some t(4;14)
Del(1p32)
Combination of several intermediate risk abnormalities
Some mutations (*TP53*? *DIS3*? *BRAF*?)
Poor responders (MRD)
Early relapses

Standard risk patients: **All the others**