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

- 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?

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**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...

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→ del 1p32 ?

8-10% of patients

→ 1q gain ?

35% of patients

Hebraud et al. Leukemia 2014

Avet-Loiseau et al. JCO 2012
The final model retains 6 independent variables:

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

Score $\leq 0$ : Good prognosis
Score $> 0$ & $\leq 1$ : Intermediate prognosis
Score $> 1$ : Poor prognosis

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