CENTRE HOSPITALIER
UNIVERSITAIRE DE NANTES

Prospective Evaluation of MRI and PET-CT at Diagnosis and before Maintenance Therapy in Symptomatic Patients with Multiple Myeloma Included in the IFM/DFCI 2009 Trial

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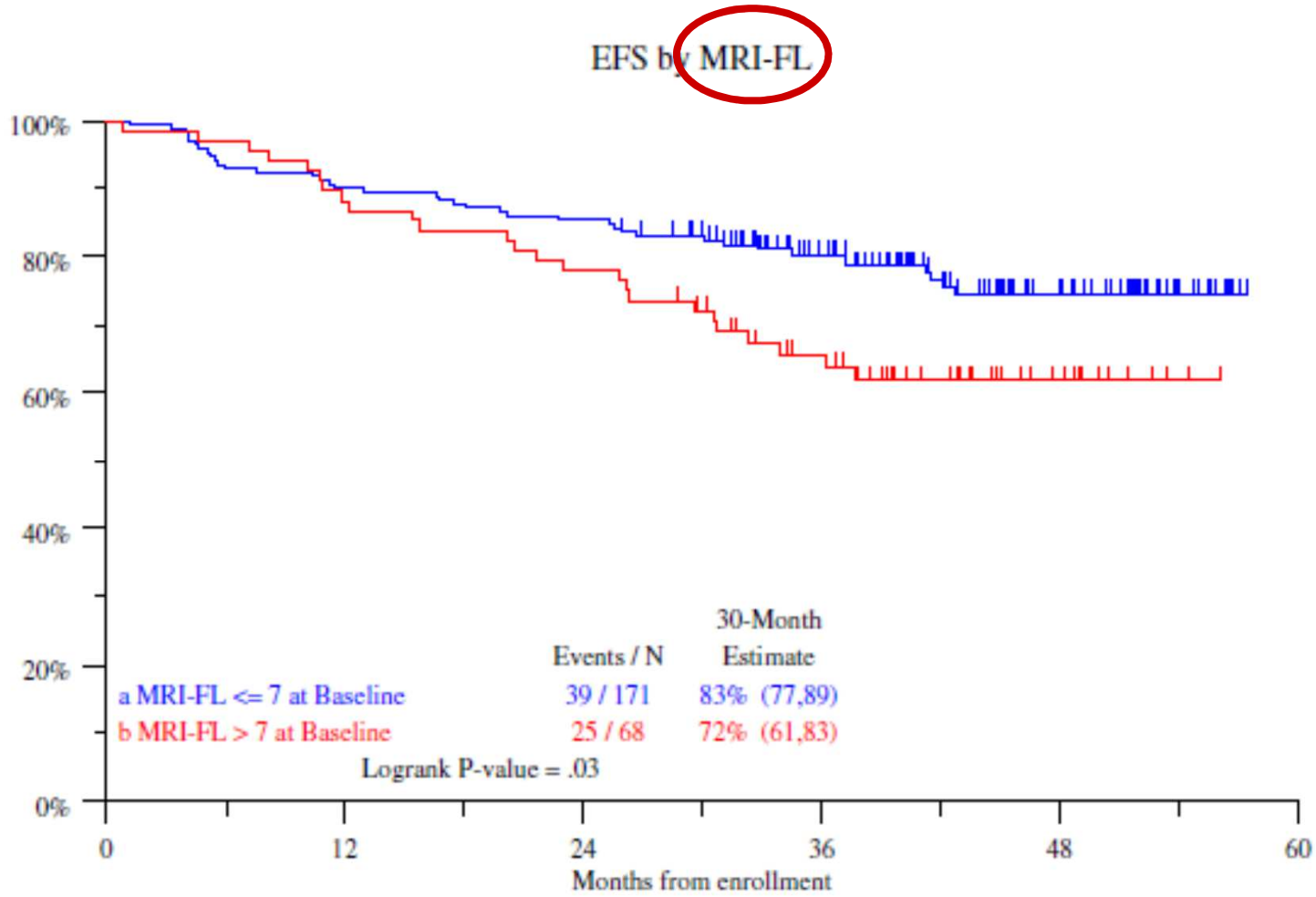
Rationale

MRI and PET-CT are important imaging techniques to detect bone lesions in multiple myeloma at diagnosis

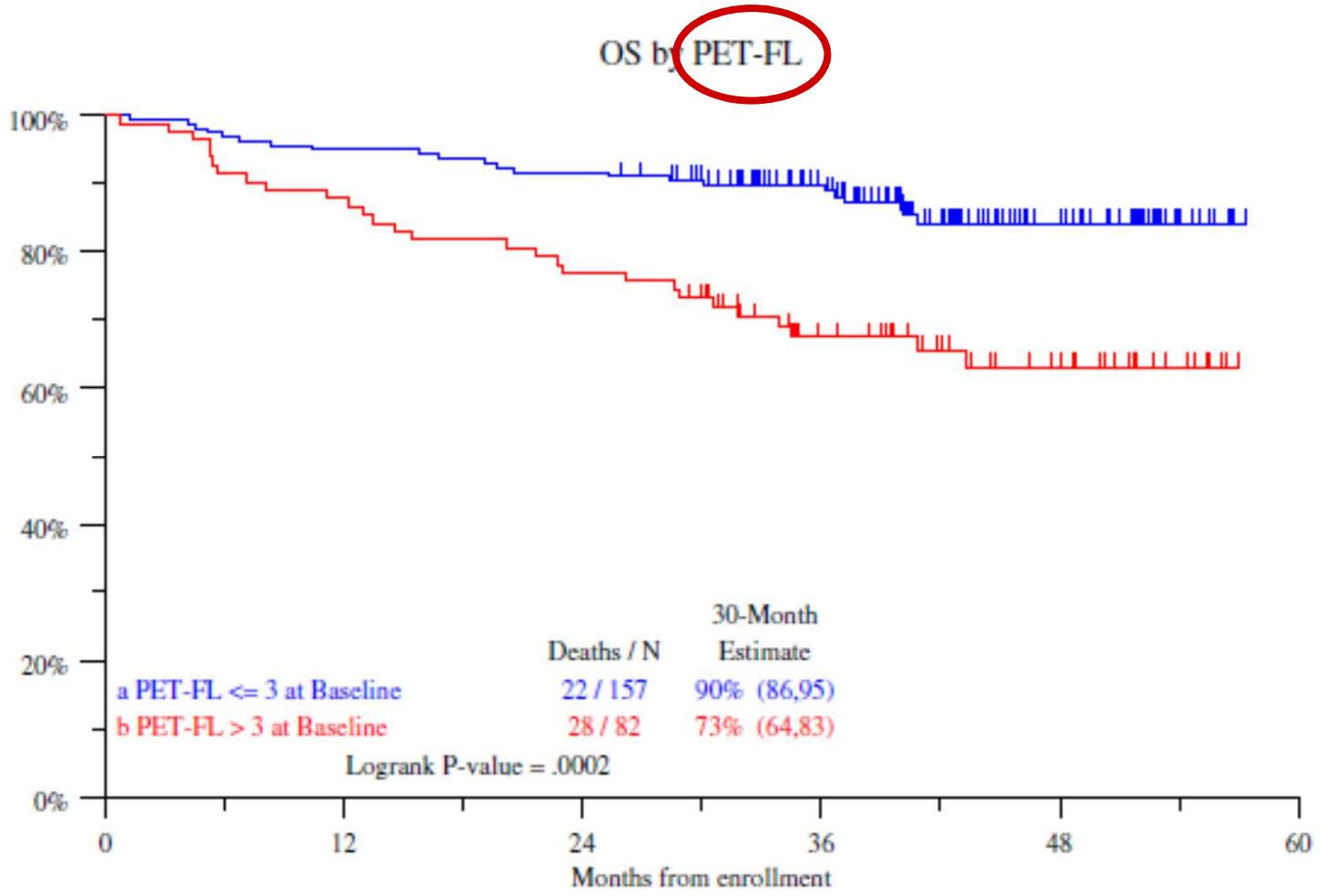
Both MRI and PET-CT have been described to have pronostic value for PFS and/or OS (at diagnosis, during follow-up)

AT DIAGNOSIS



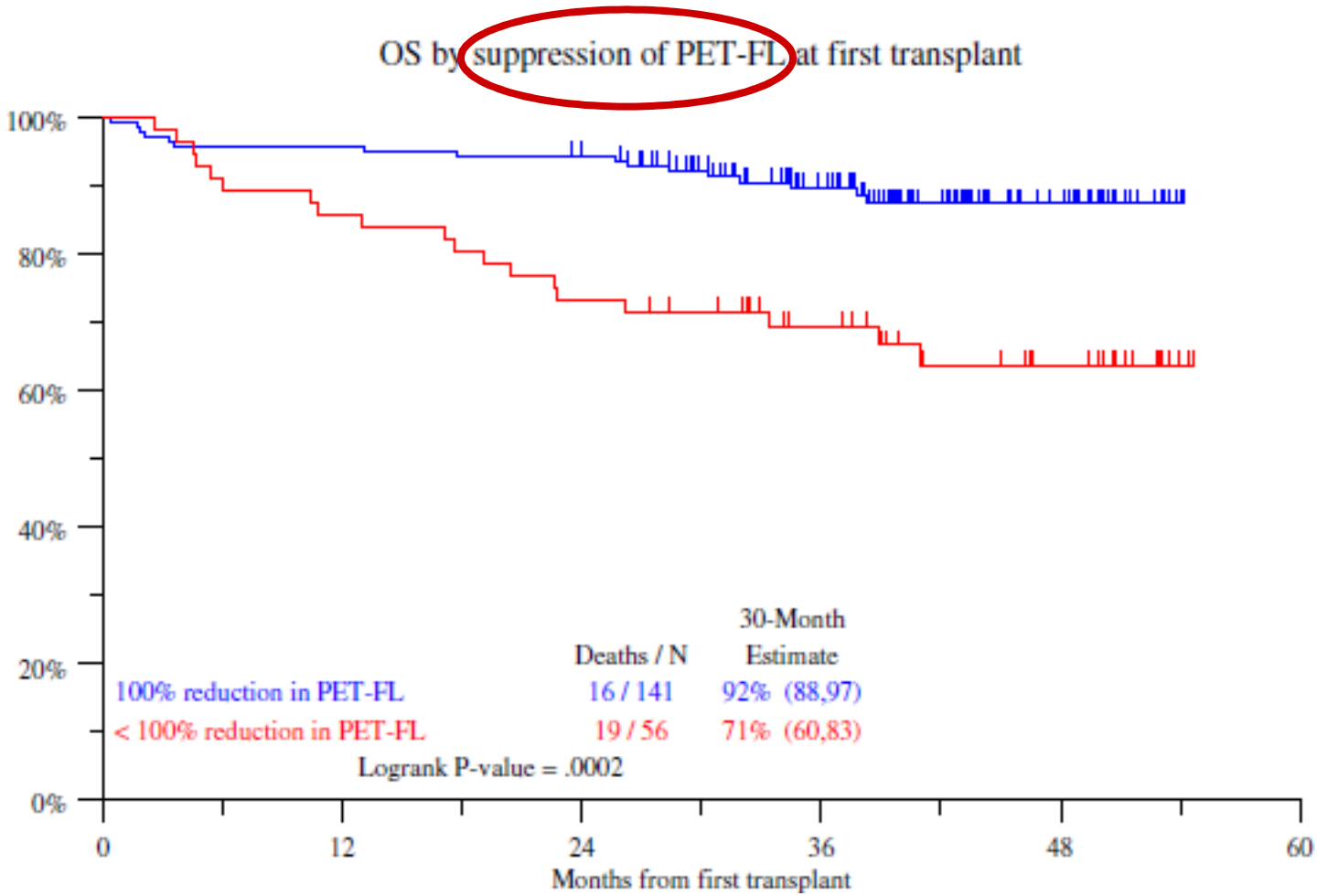
Bartel et al. Blood 2009;114:2068-2076

AT DIAGNOSIS



Bartel et al. Blood 2009;114:2068-2076

FOLLOW-UP / DYNAMIC



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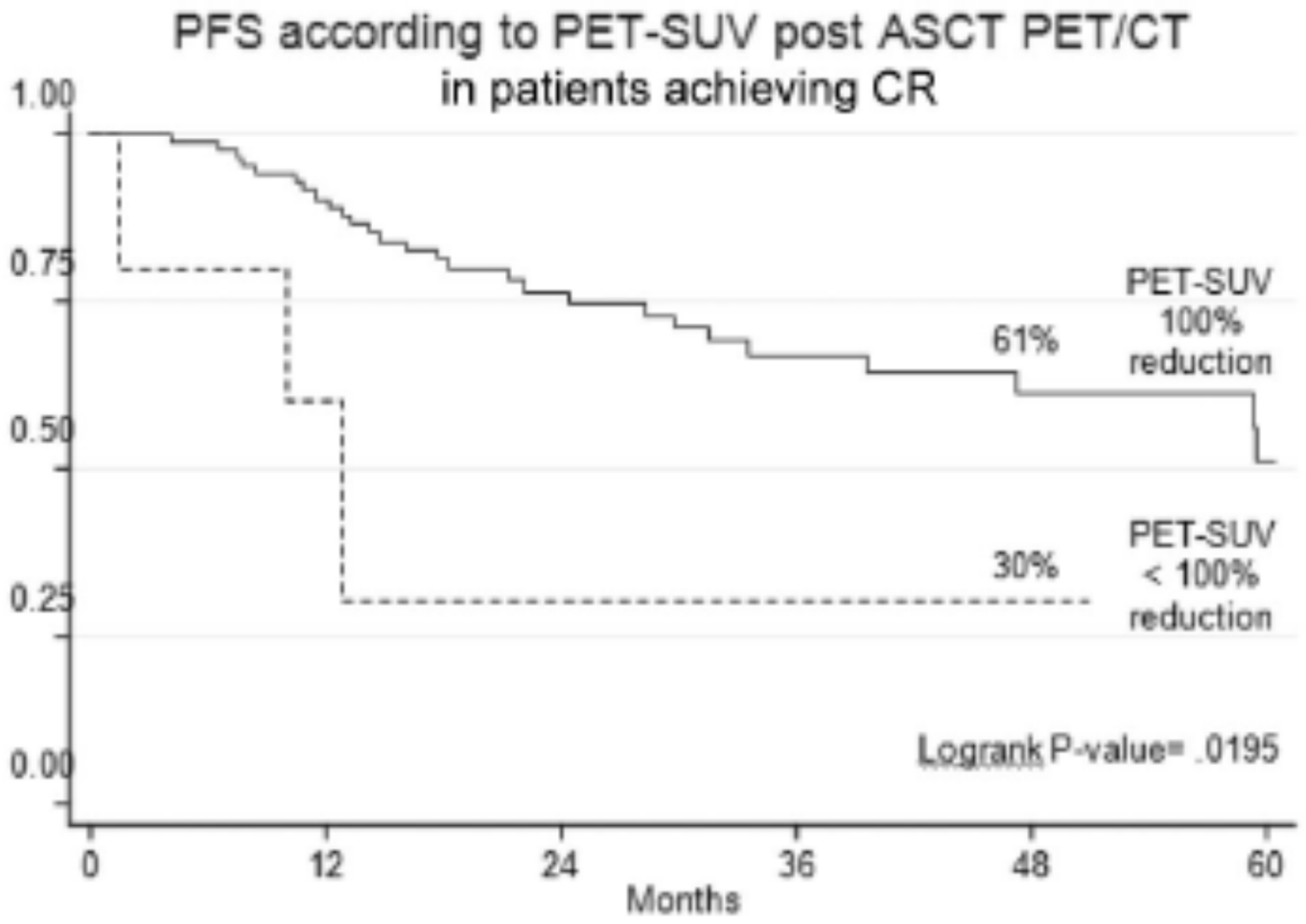
FOLLOW-UP / DYNAMIC



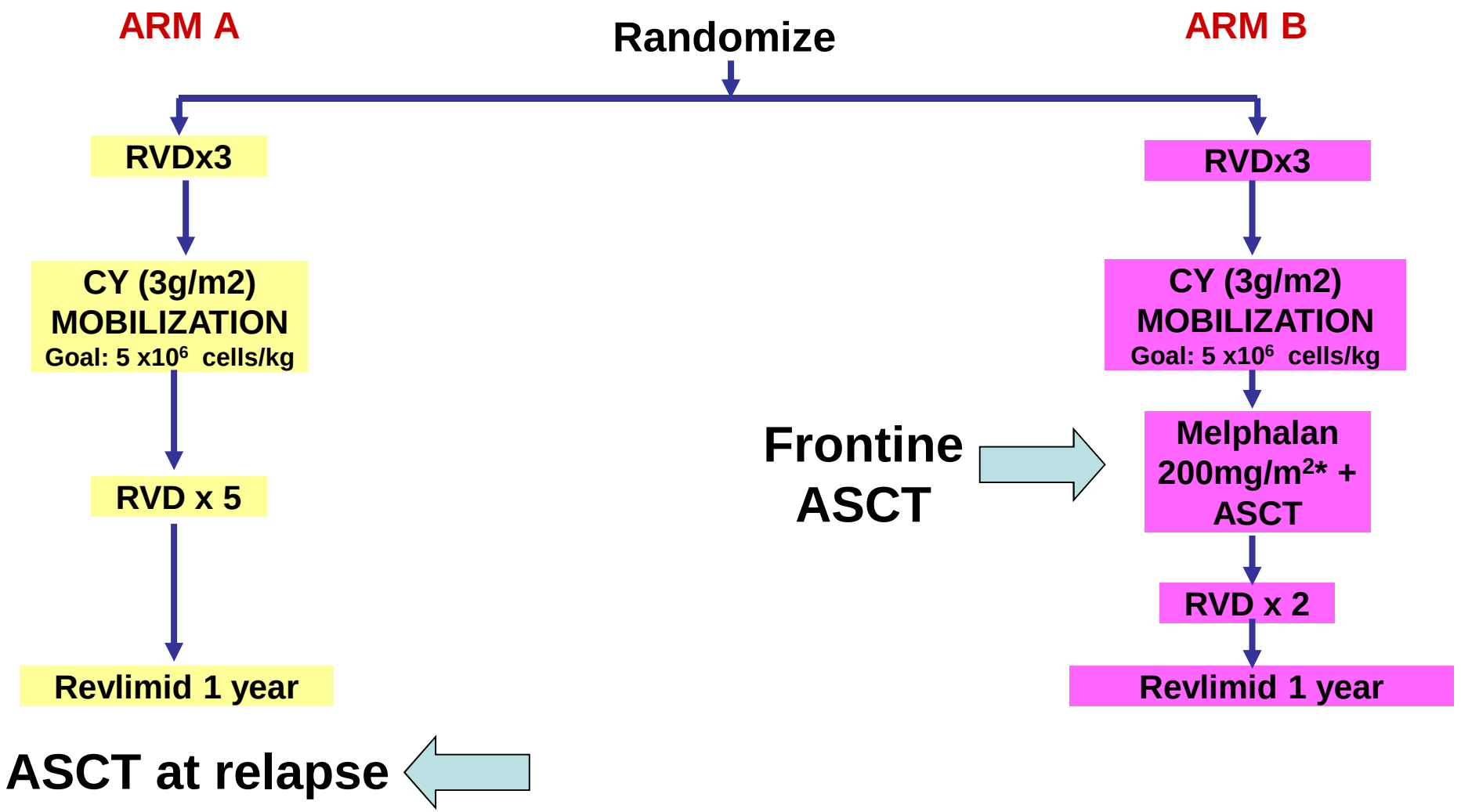
Zamagni et al, Blood 2011;118:5989-5995

Few trials have compared prospectively

MRI and PET-CT

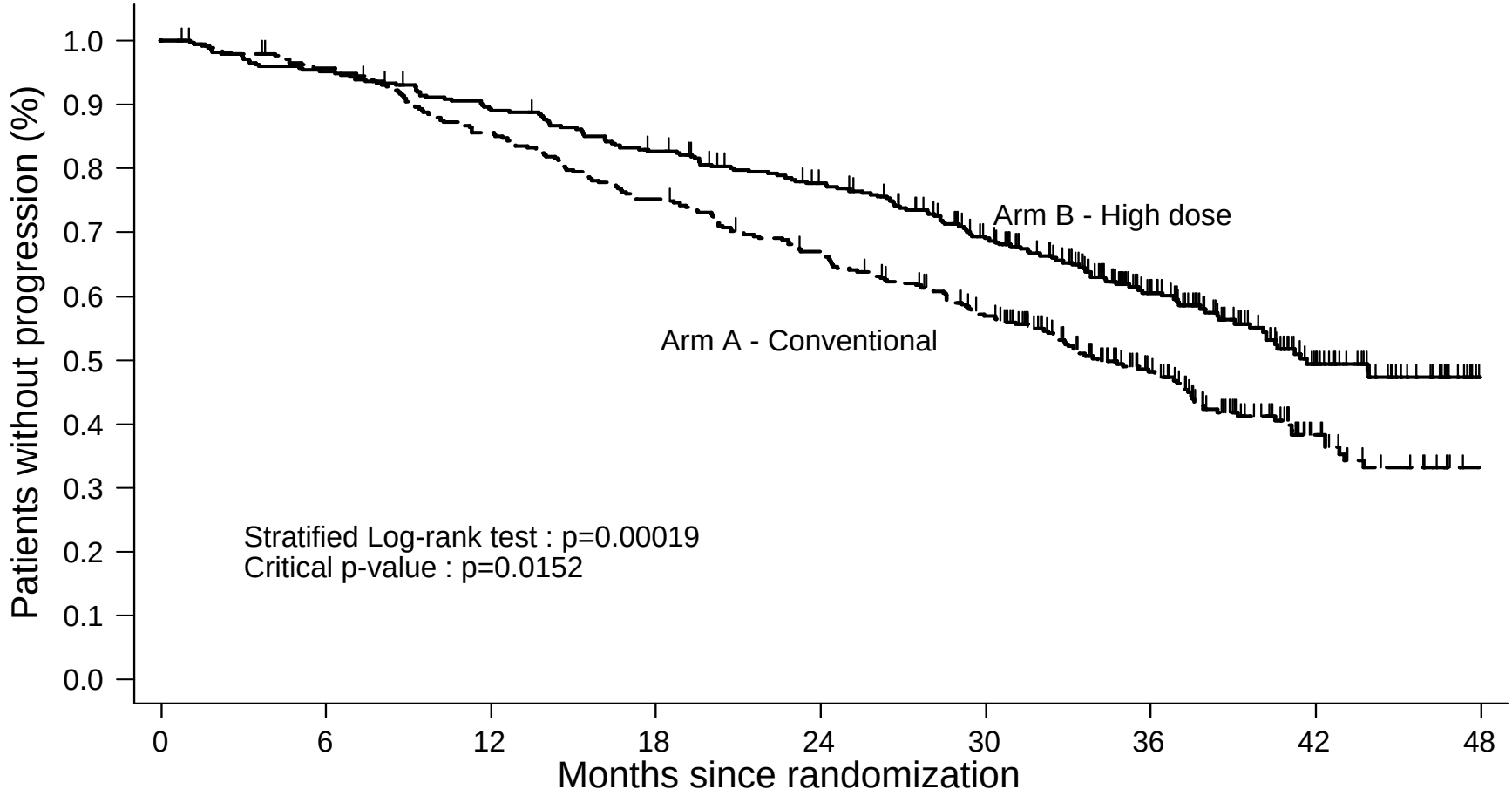
in the setting of **recent** frontline intensive therapy programs

IFM/DFCI 2009 Study
Newly Diagnosed MM Pts (SCT candidates)



IFM 2009: PFS, 700 patients

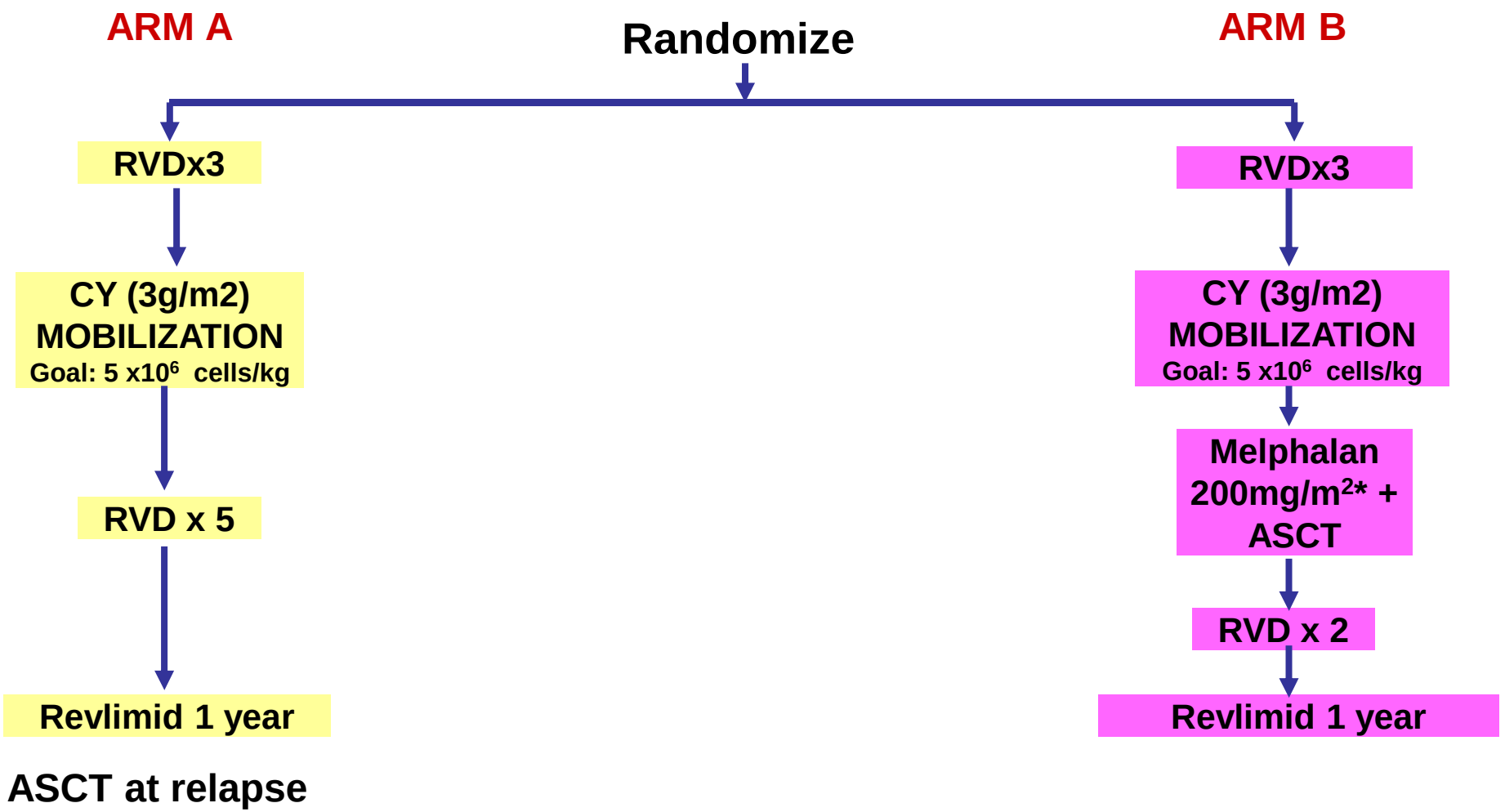
Attal et al. ASH 2015



N at risk (events)

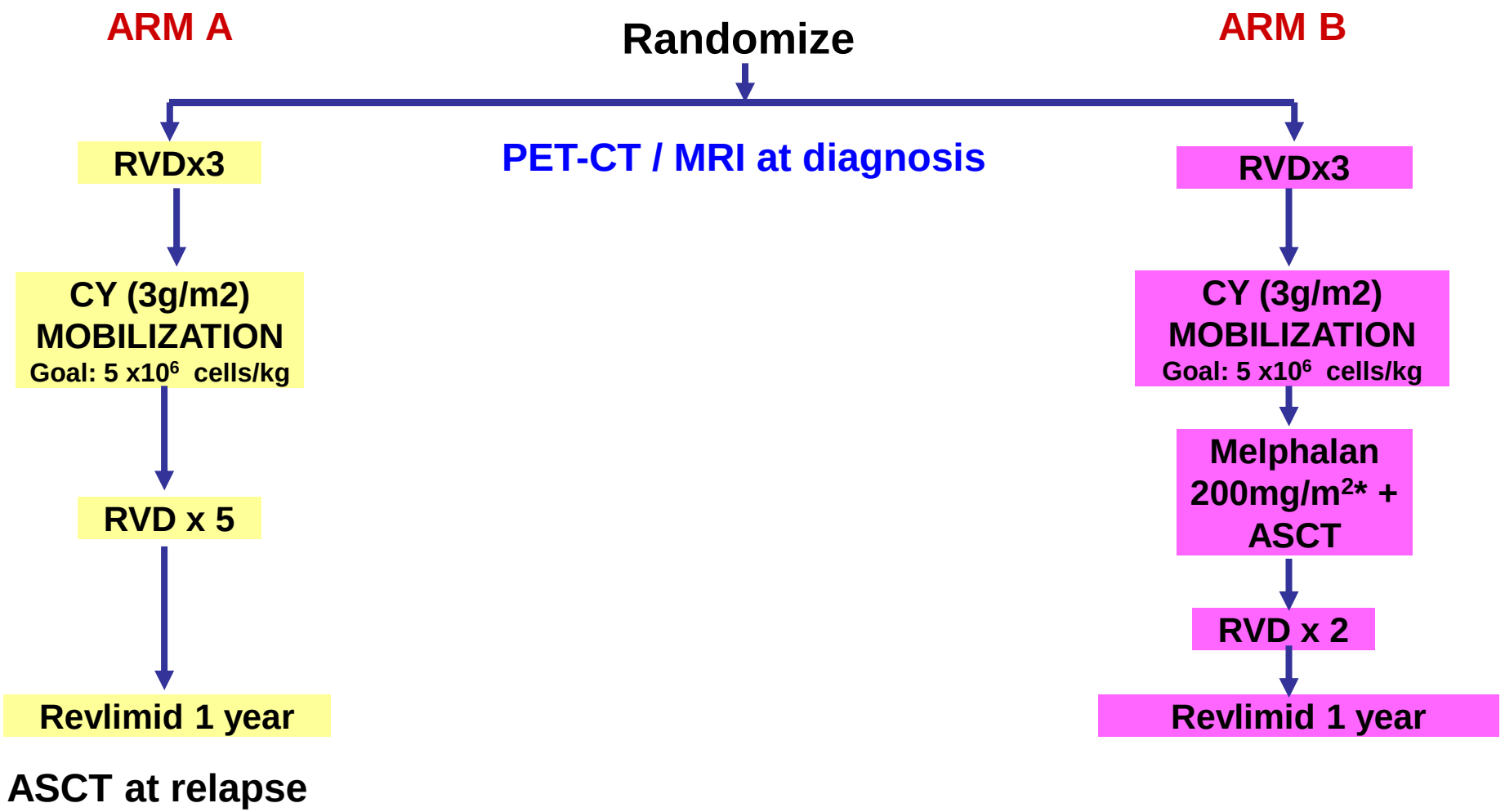
Conventional	350	(15)	332	(35)	296	(36)	260	(28)	228	(34)	185	(24)	108	(18)	41	(5)	18
High Dose	350	(17)	332	(21)	309	(22)	285	(17)	259	(28)	212	(23)	128	(18)	59	(2)	13

IMAJEM (NCT01309334), 134 patients

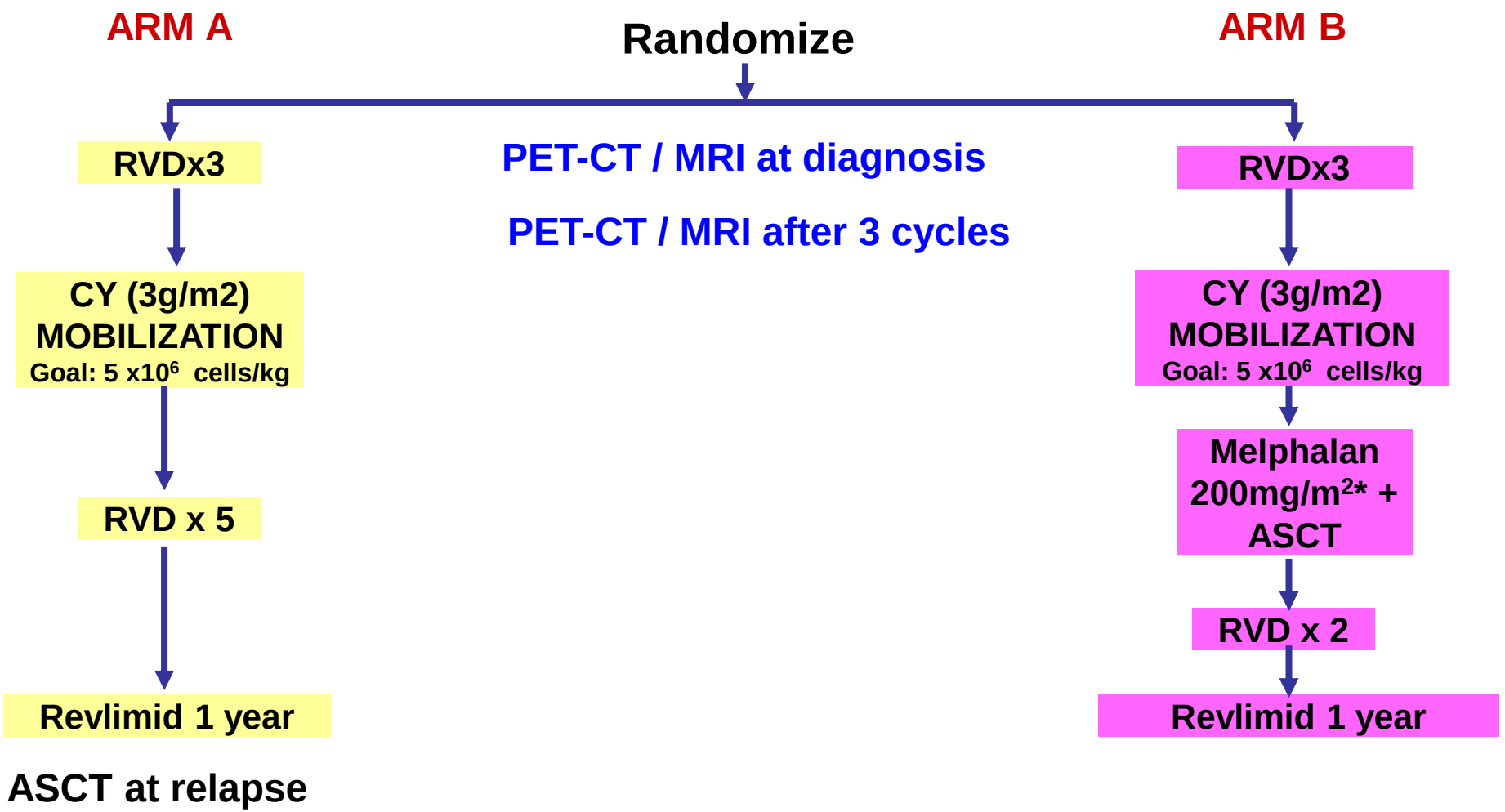


ASCT at relapse

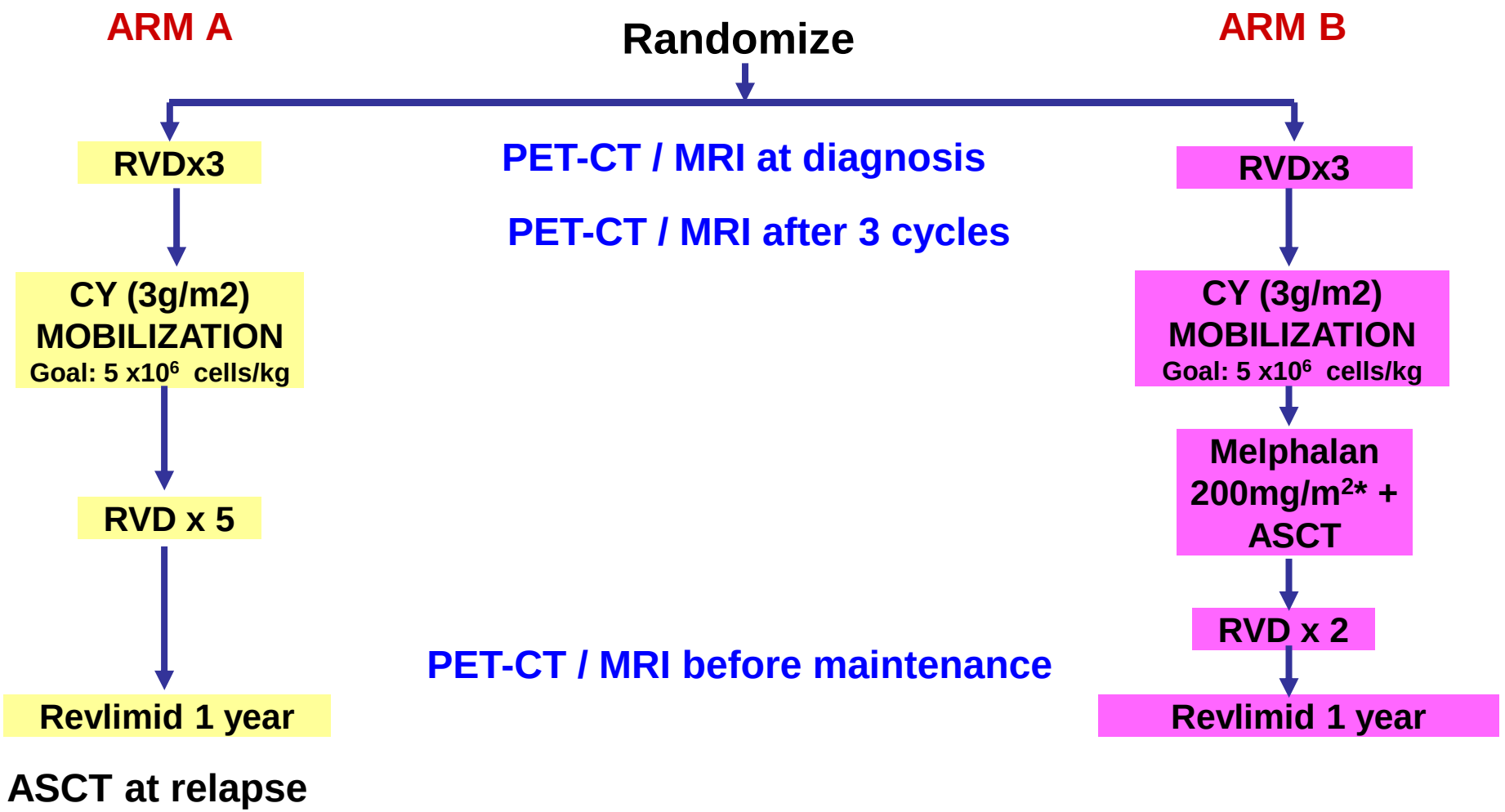
IMAJEM (NCT01309334), 134 patients



IMAJEM (NCT01309334), 134 patients



IMAJEM (NCT01309334), 134 patients



Primary end-point : DIAGNOSIS / STAGING

Compare MRI (spine and pelvis) vs PET-CT
regarding the **number of bone lesions at diagnosis**

Secondary end-points : PROGNOSTIC IMPACT

- Evaluate prognostic impact of PET-CT vs MRI
after 3 cycles of induction therapy with RVD
(PFS / OS → PET negativity / MRI negativity)

- Evaluate prognostic impact of PET-CT vs MRI
before maintenance
(PFS / OS → PET negativity / MRI negativity)

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All 134 x 3 MRI and 134 x 3 PET-CT were centrally reviewed by 2 x 2 experts, blinded to treatment arm
(2 radiologists / 2 nuclear medicine physicians)

Patients characteristics

	n = 134
Median age (range)	59 (37-65)
Male / female	83 / 51(62% / 38%)
ISS1	41 (31%)
ISS2	74 (55%)
ISS3	19 (14%)
Median Calcium mM/L (range)	2.28 (2.04-2.95)
Median LDH UI (range)	211 (71-843)
Median Hb g/dL (range)	10.9 (8-14.6)
Median creatinine µM/L (range)	78 (39-162)
t(4;14) yes/no	6 / 129
del17p	5 / 129
Arm A, n (%)	71 (53%)
Arm B, n (%)	63 (47%)

Primary end-point : DIAGNOSIS / STAGING

Compare MRI (spine and pelvis) vs PET-CT regarding the **number of bone lesions at diagnosis**

- At diagnosis,

MRI was positive in 127/134 (94.7%),

and PET-CT in 122/134 (91%) patients,

(McNemar test = 0.94, p-value = 0.33).

- MRI of the spine and pelvis and whole-body PET-CT are **equally** effective to detect bone involvement in symptomatic patients at diagnosis.

- **MRI patterns of marrow involvement were the following:**
  - normal in 7 cases (5%)
  - focal lesions (FL) in 46 cases (34%);
  - homogeneous diffuse infiltration in 41 cases (31%)
  - combined diffuse infiltration and FL in 35 cases (26%)
  - variegated or "salt-and-pepper" pattern with inhomogeneous bone marrow in 5 cases (4%)

- **PET-CT patterns were the following:**
  - normal in 12 cases (9%);
  - FL in 44 cases (33%);
  - diffuse infiltration in 12 cases (9%);
  - combined diffuse infiltration and FL in 66 cases (49%)
  - extramedullary disease in 10 cases (7.5%).

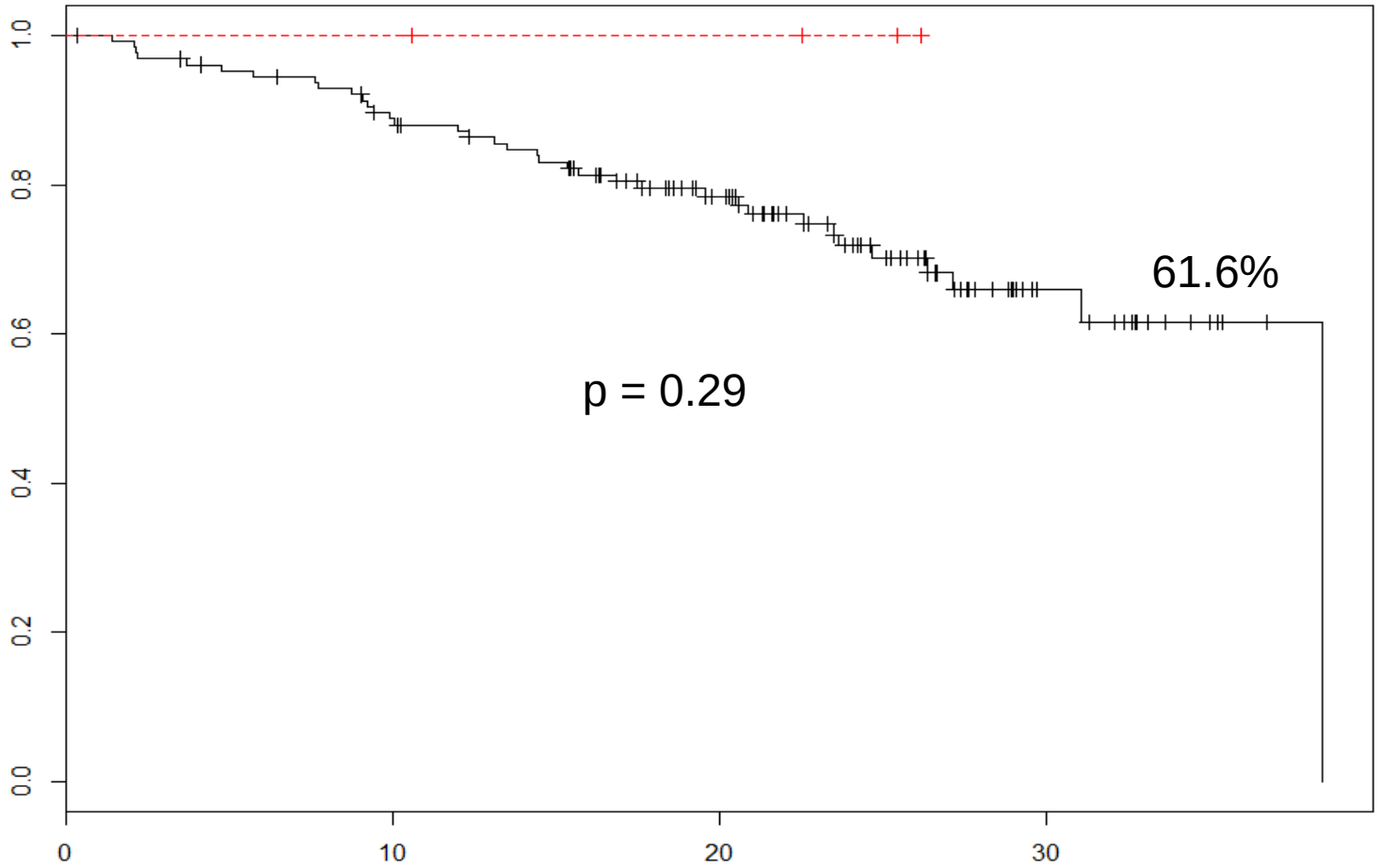
- The median number of FL assessed by PET-CT was 3 (0 to >10), with a median SUVmax of 4.1 (range 1.5-28.4).

Secondary end-point : PROGNOSTIC IMPACT

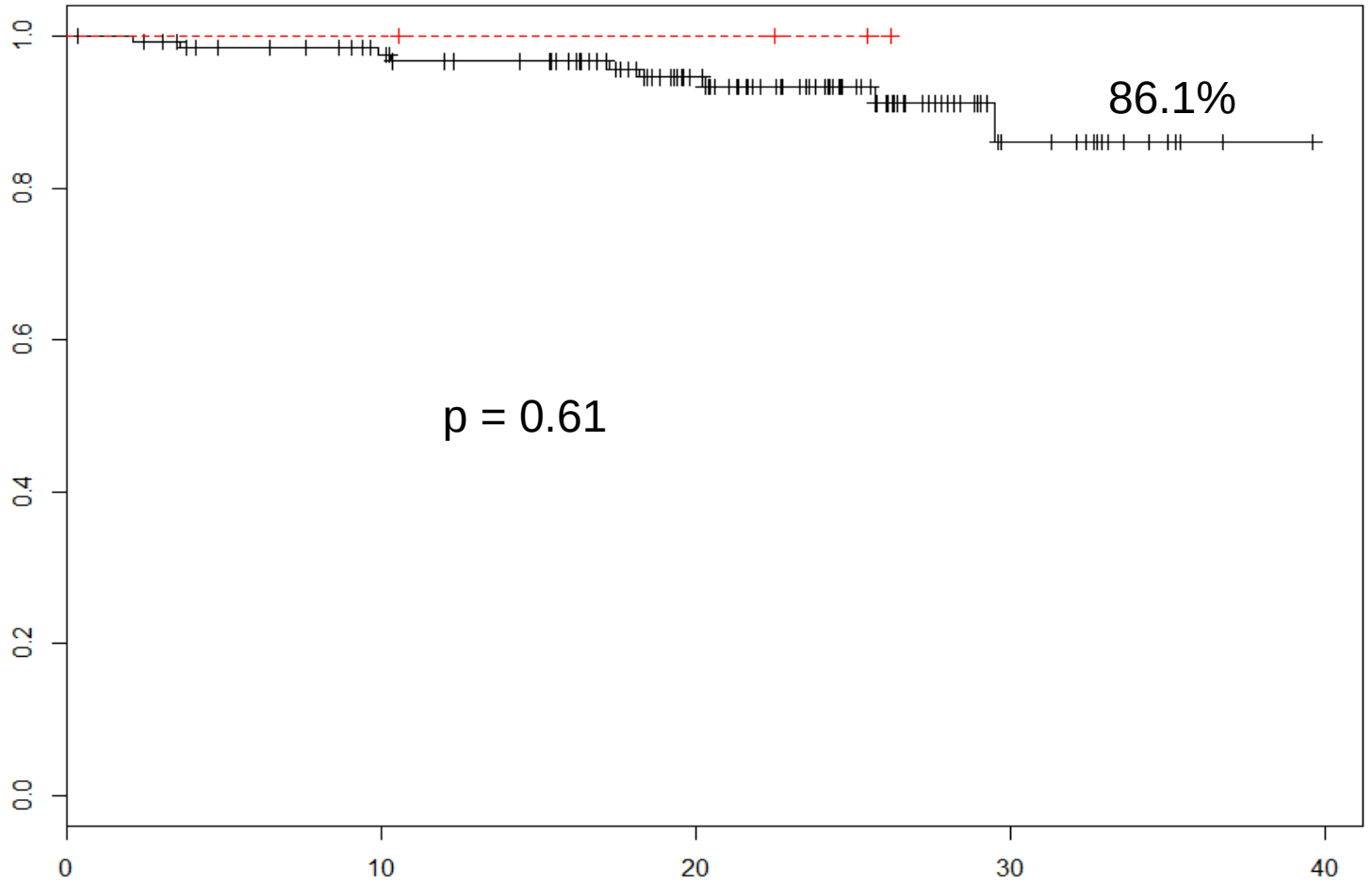
PET-CT vs MRI

after 3 cycles of induction therapy with RVD

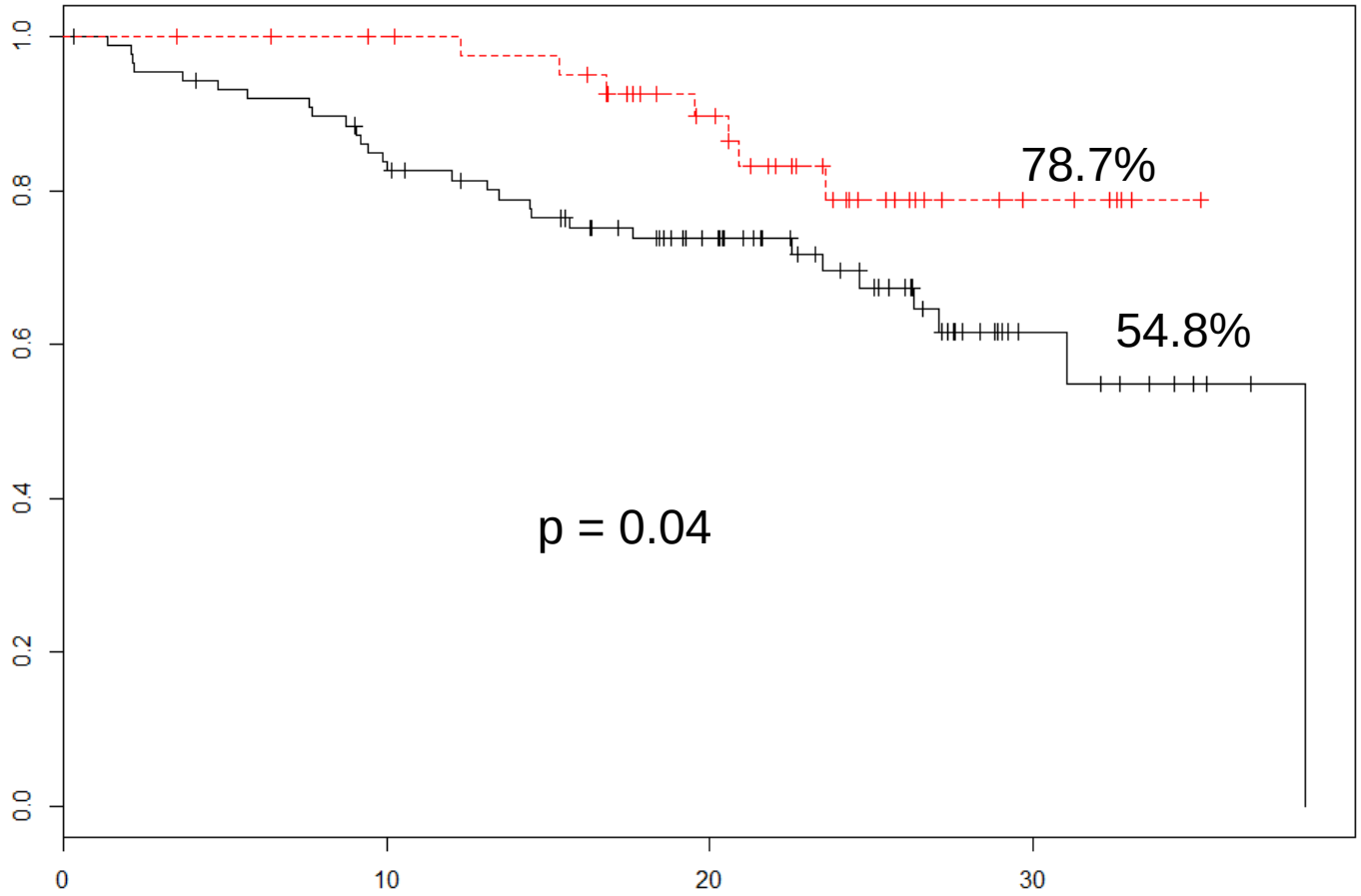
MRI normalisation following 3 cycles of RVD
Impact on PFS (3% normalised)



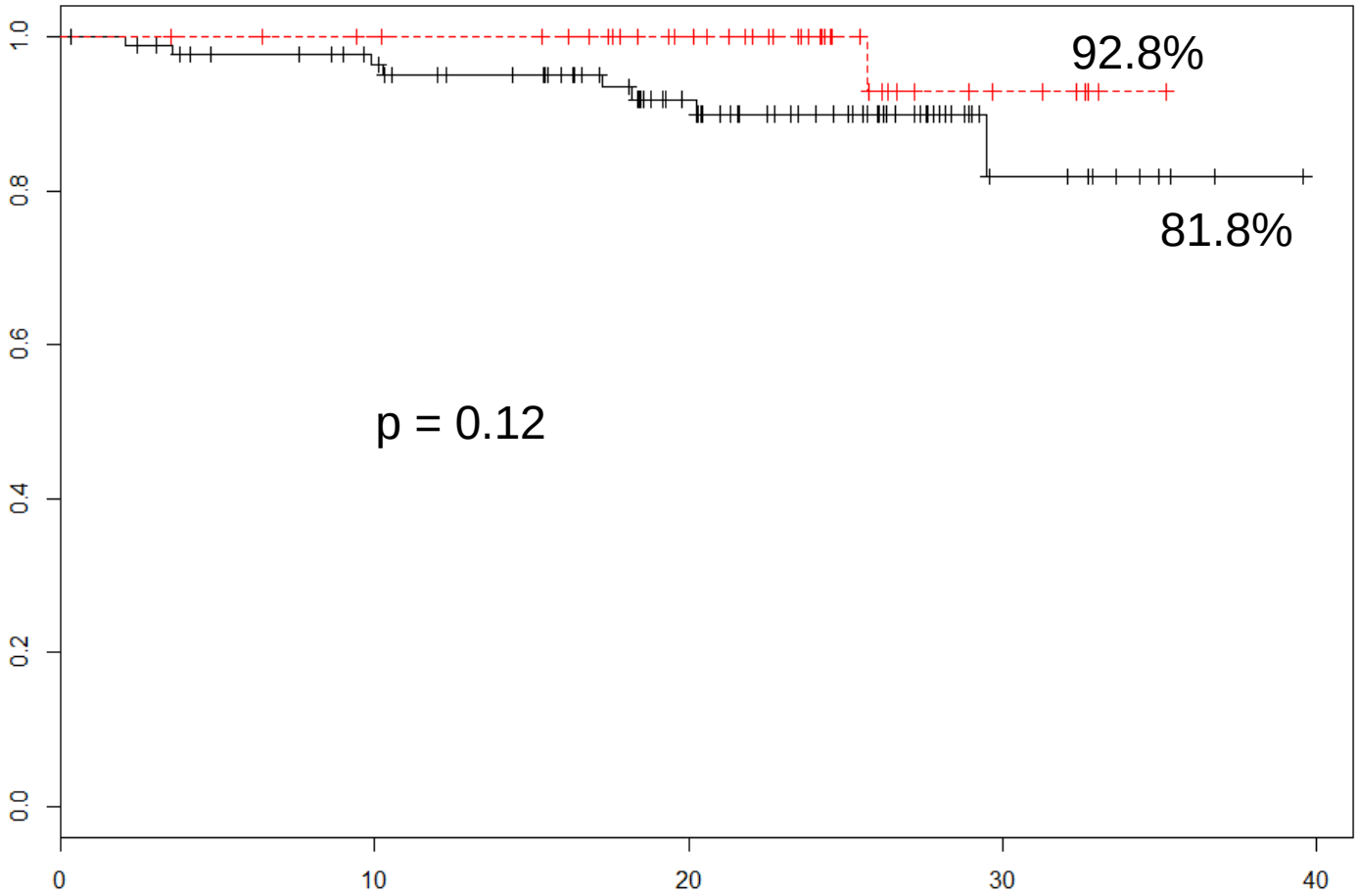
MRI normalisation following 3 cycles of RVD
Impact on OS (3% normalised)



PET-CT normalisation following 3 cycles of RVD
Impact on PFS (32% normalised)



PET-CT normalisation following 3 cycles of RVD
Impact on OS (32% normalised)

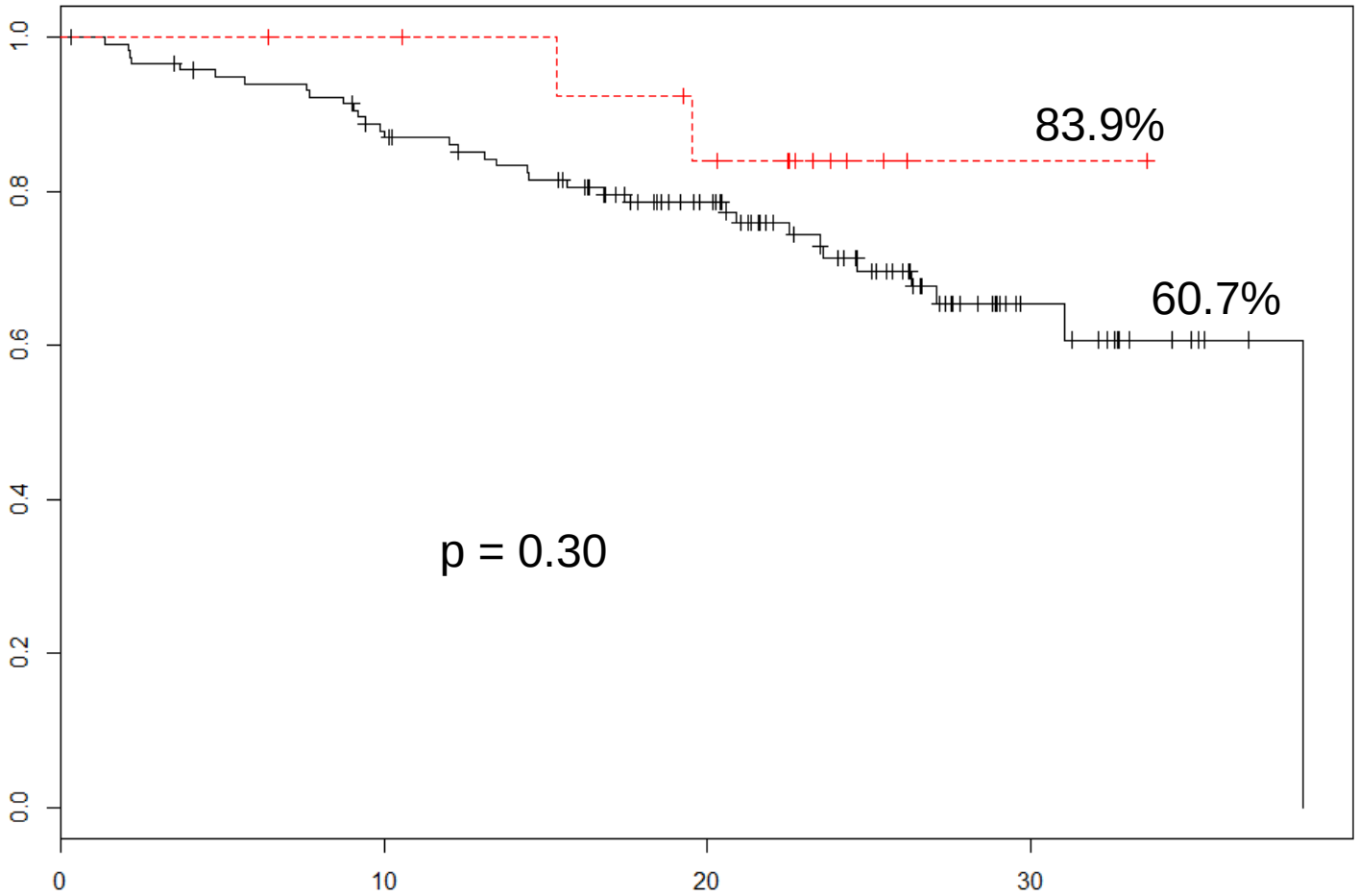


Secondary end-point : PROGNOSTIC IMPACT

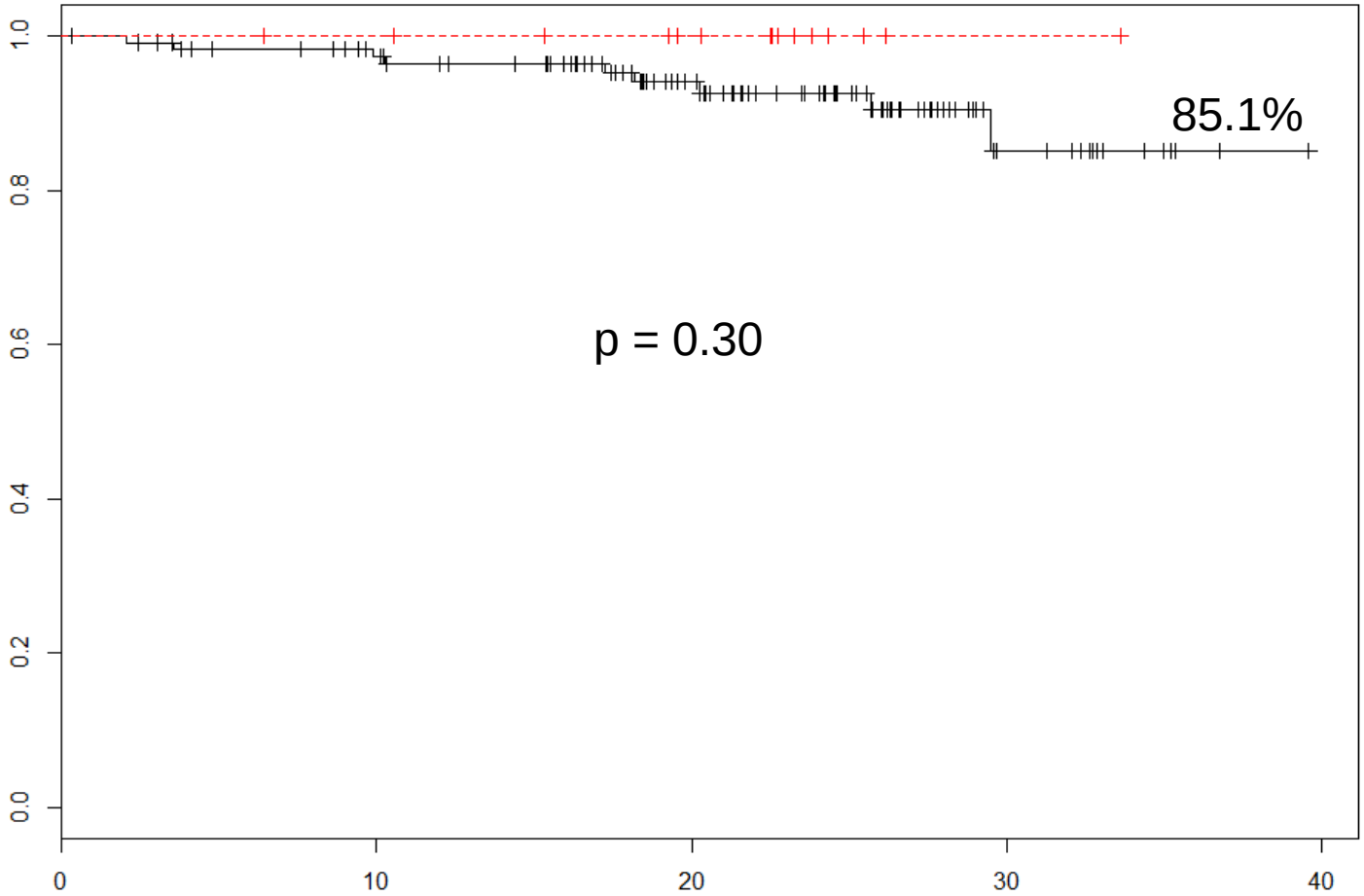
PET-CT vs MRI

before maintenance

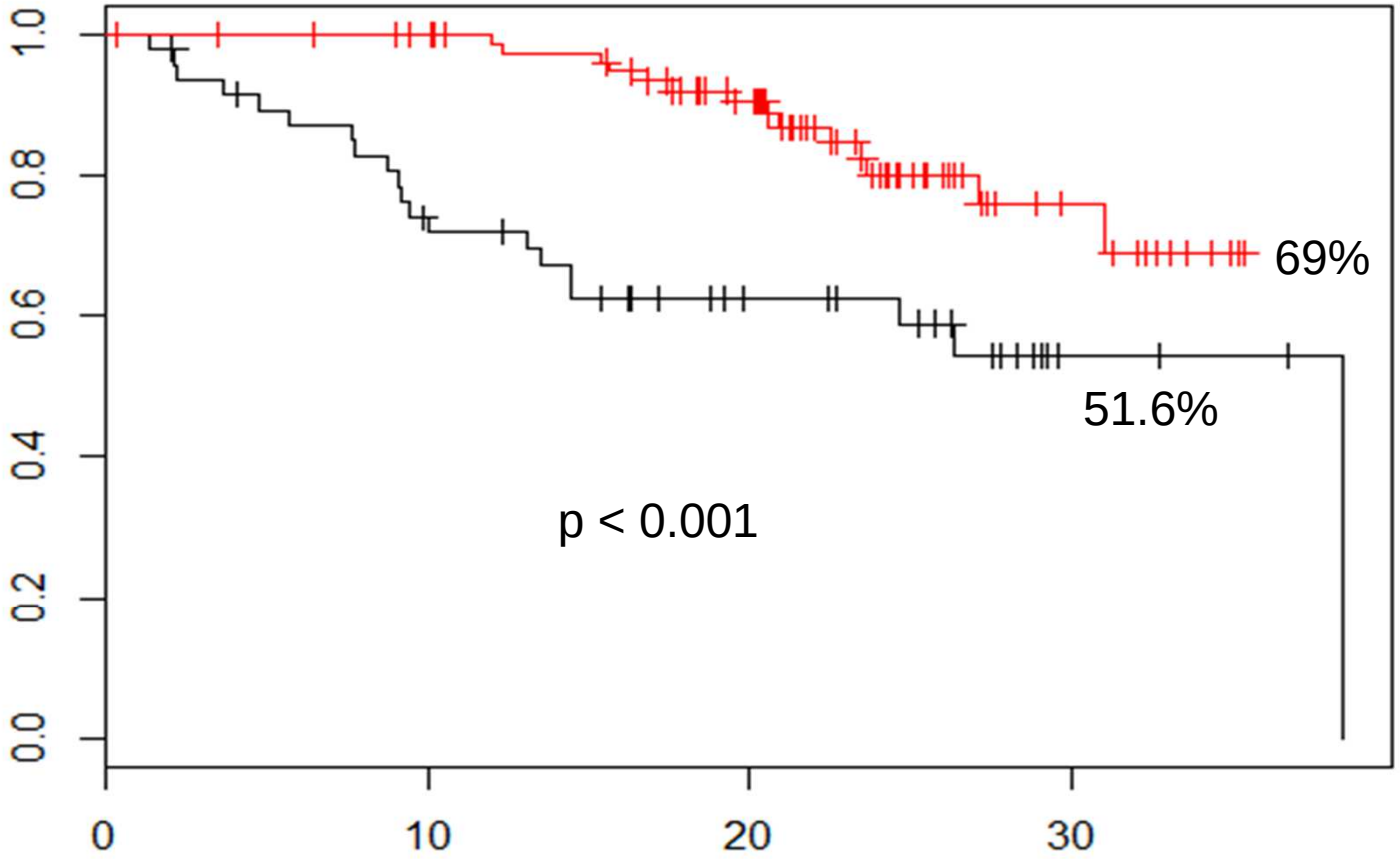
MRI normalisation before maintenance
Impact on PFS (11% normalised)



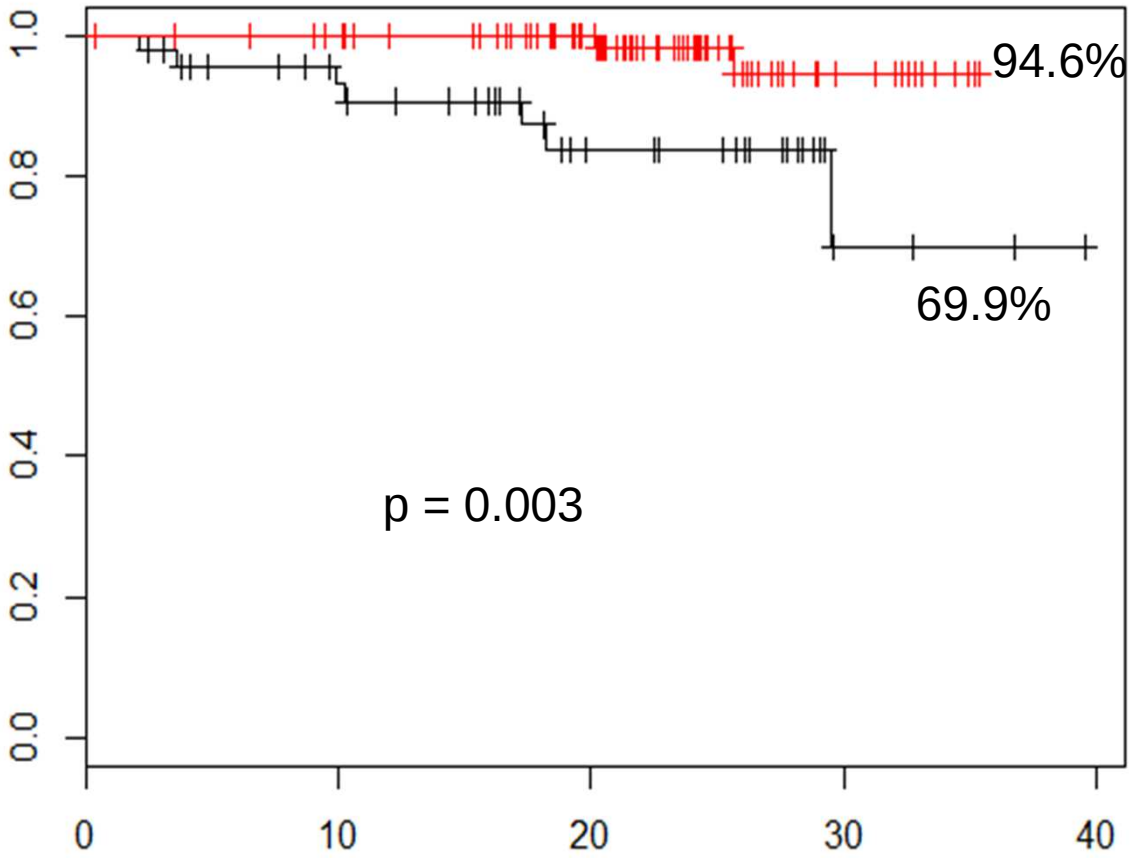
MRI normalisation before maintenance
Impact on OS (11% normalised)



PET-CT normalisation before maintenance
Impact on PFS (62% normalised)



PET-CT normalisation before maintenance
Impact on OS (62% normalised)



Univariate analysis for PFS / 134 patients

Variables tested:

Gender, age, Ca, creatinine, ISS, response after 3 cycles of induction, response pre-maintenance, cytogenetics, MRI after 3 cycles, PET-CT after 3 cycles, MRI pre-maintenance, PET-CT pre-maintenance

- **PET-CT after 3 cycles, p = 0.04**
- **PET-CT pre-maintenance, p < 0.001**
- **Response after 3 cycles (≥ VGPR), p = 0.04**

Univariate analysis for OS / 134 patients

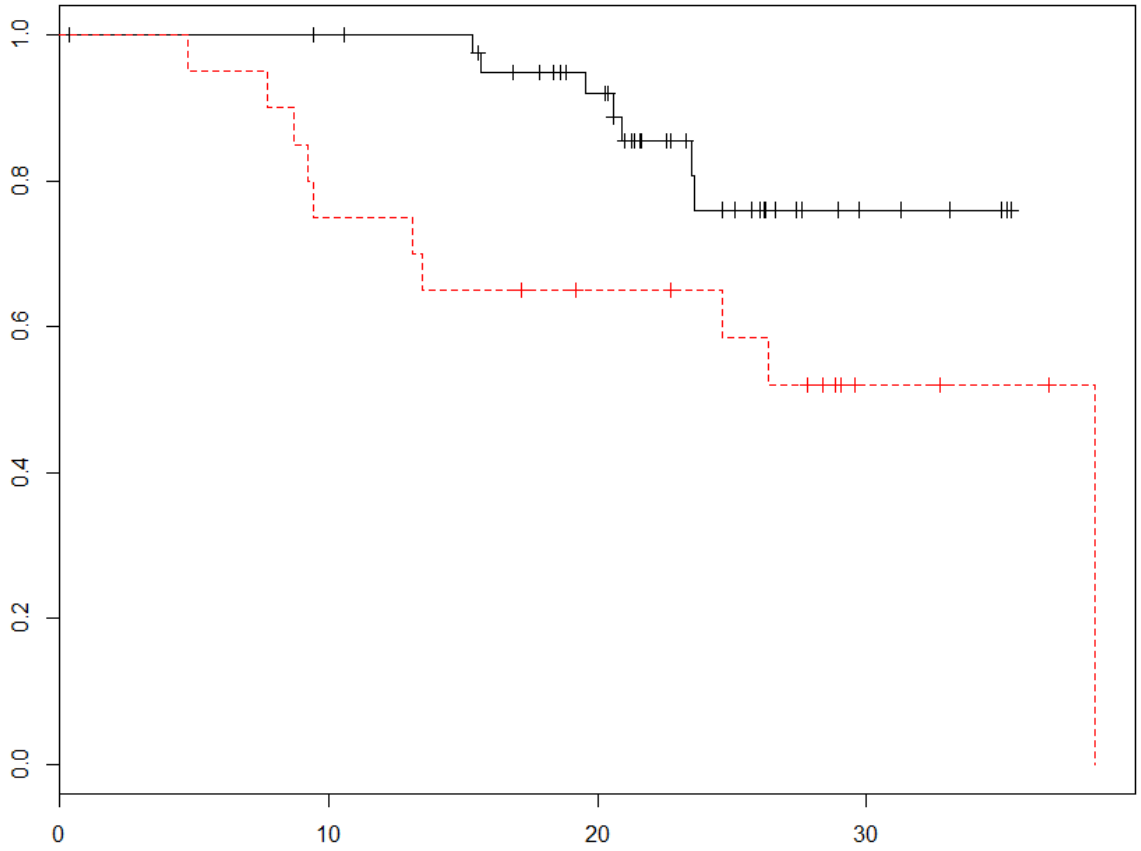
Variables tested:

Gender, age, Ca, creatinine, ISS, response after 3 cycles of induction, response pre-maintenance, cytogenetics, MRI after 3 cycles, PET-CT after 3 cycles, MRI pre-maintenance, PET-CT pre-maintenance

- PET-CT pre-maintenance, p = 0.003

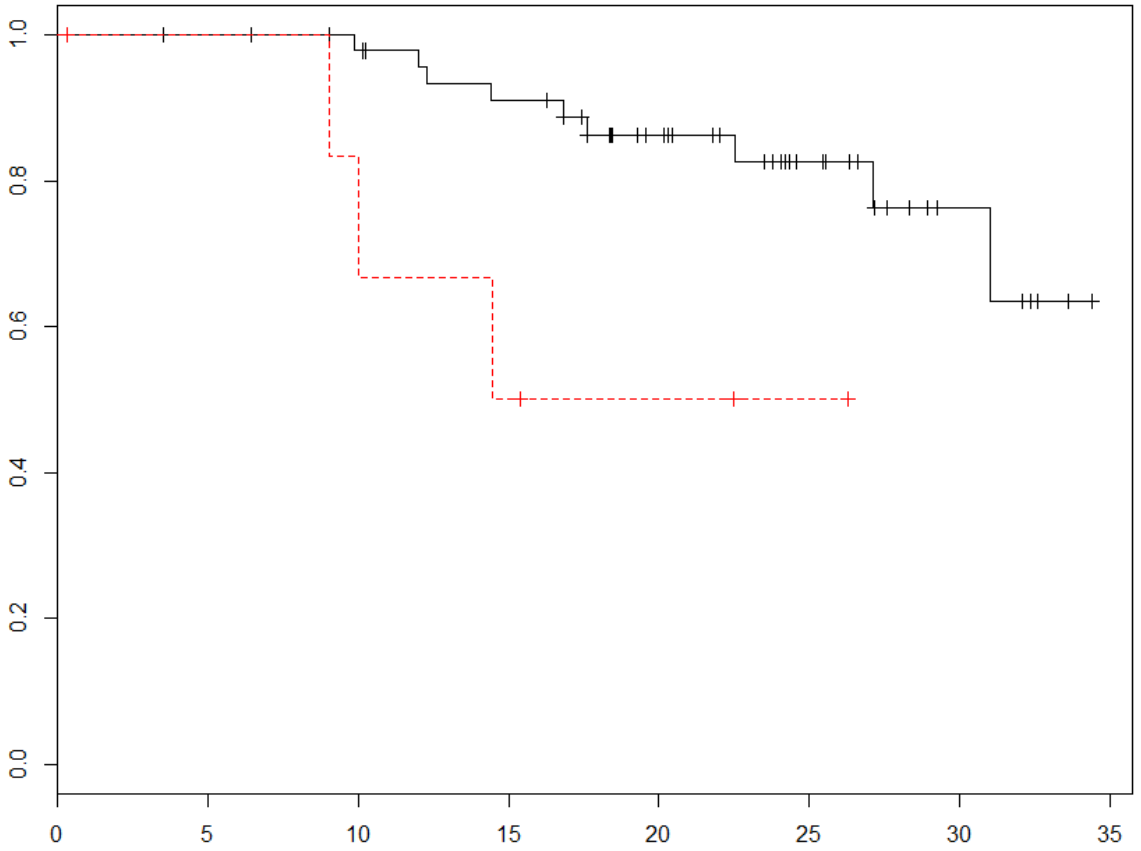
PET-CT pre-maintenance is a prognostic factor for PFS in Arm A: RVD x 8 cycles

Adjusted on other prognostic factors p = 0.009
Univariate log-rank, p = 0.027



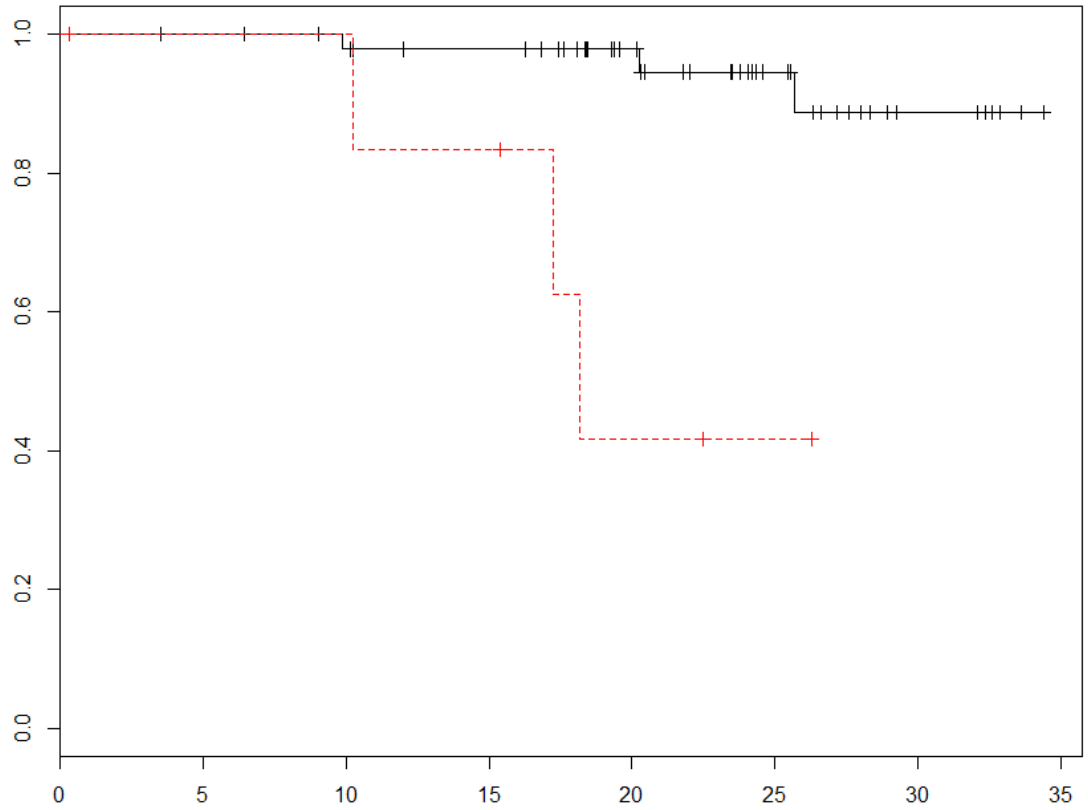
PET-CT pre-maintenance is a prognostic factor for PFS in Arm B: frontline ASCT

Adjusted on other prognostic factors p = 0.01
Univariate log-rank, p = 0.01



PET-CT pre-maintenance is a prognostic factor for OS in Arm B: frontline ASCT

Adjusted on other prognostic factors p = 0.008
Univariate log-rank, p < 0.001



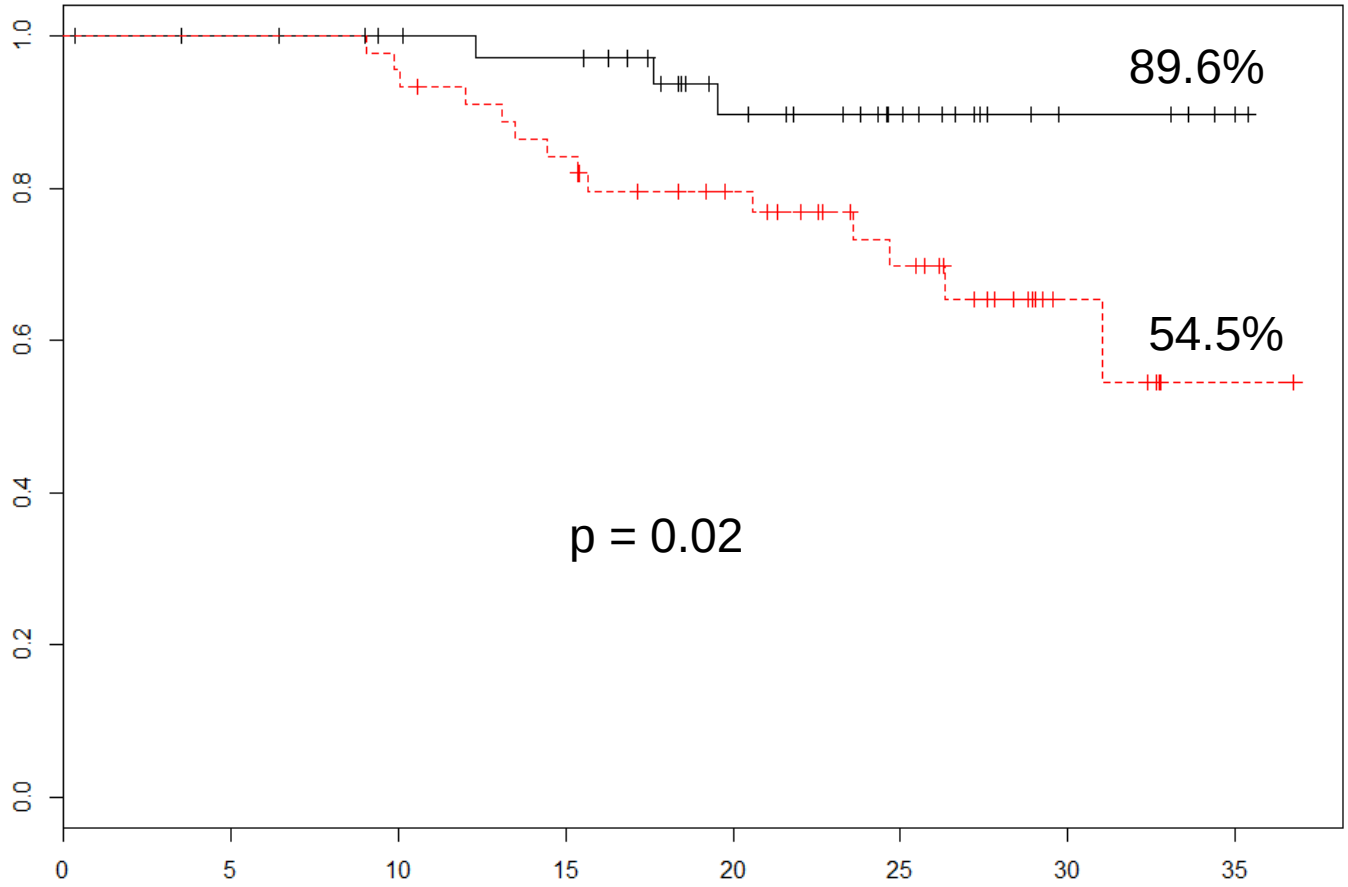
86 / 134 patients had also MRD evaluation pre-maintenance by CMF*

	PET-CT pos	PET-CT neg
MRD pos	11	20
MRD neg	14	41

Fisher exact test: p = 0.33
McNemmar test: p = 0.39

*** Avet-Loiseau et al. ASH 2015**

PFS for patients with negative PET-CT and negative MRD by flow (47.7% of patients) pre-maintenance vs others



Conclusions

- PET-CT and MRI are equally effective to detect bone involvement in symptomatic patients at diagnosis.

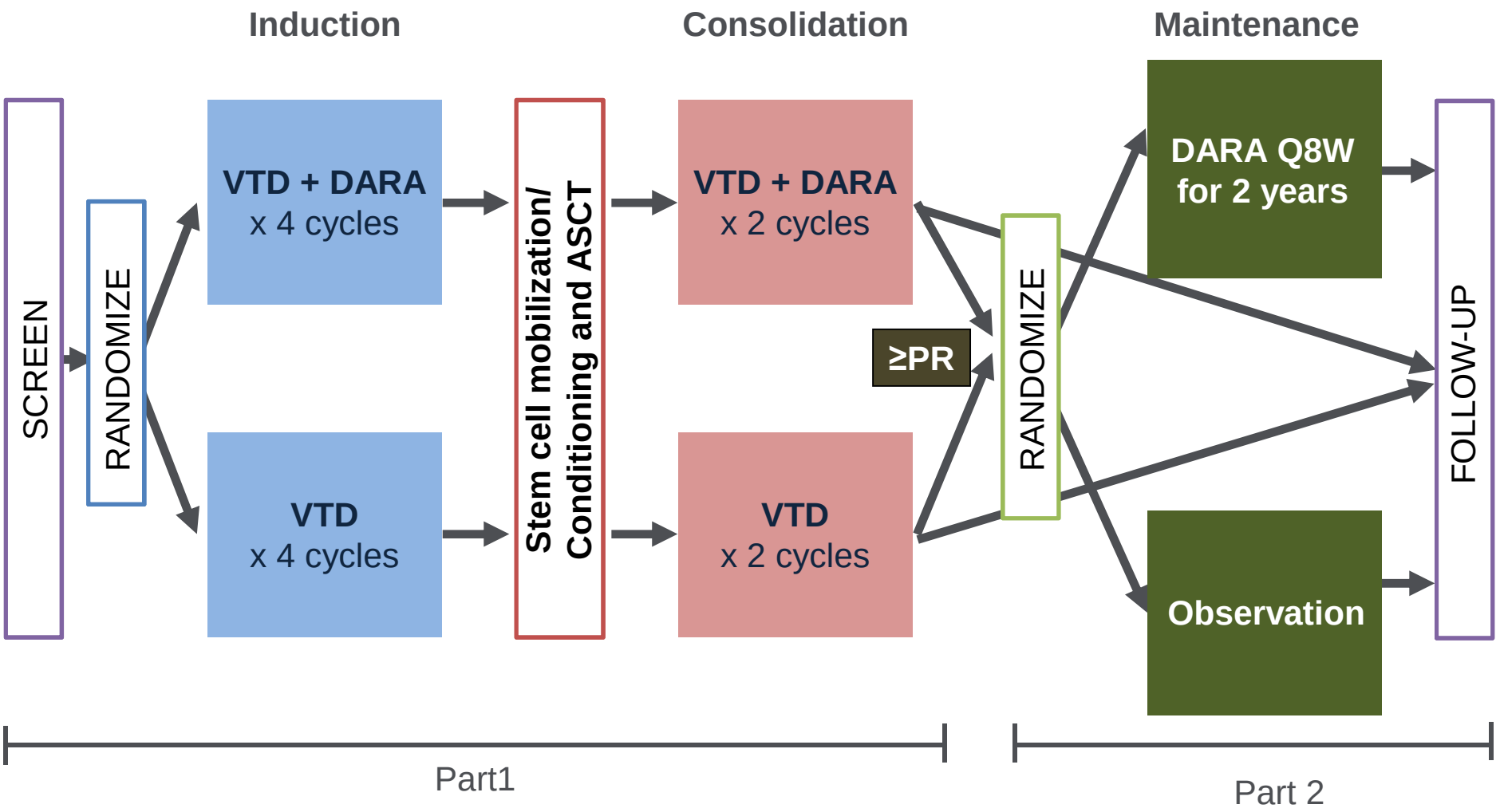
- MRI is not a good imaging method during follow-up

- PET-CT after 3 cycles of RVD and pre-maintenance is a powerful prognostic marker for PFS

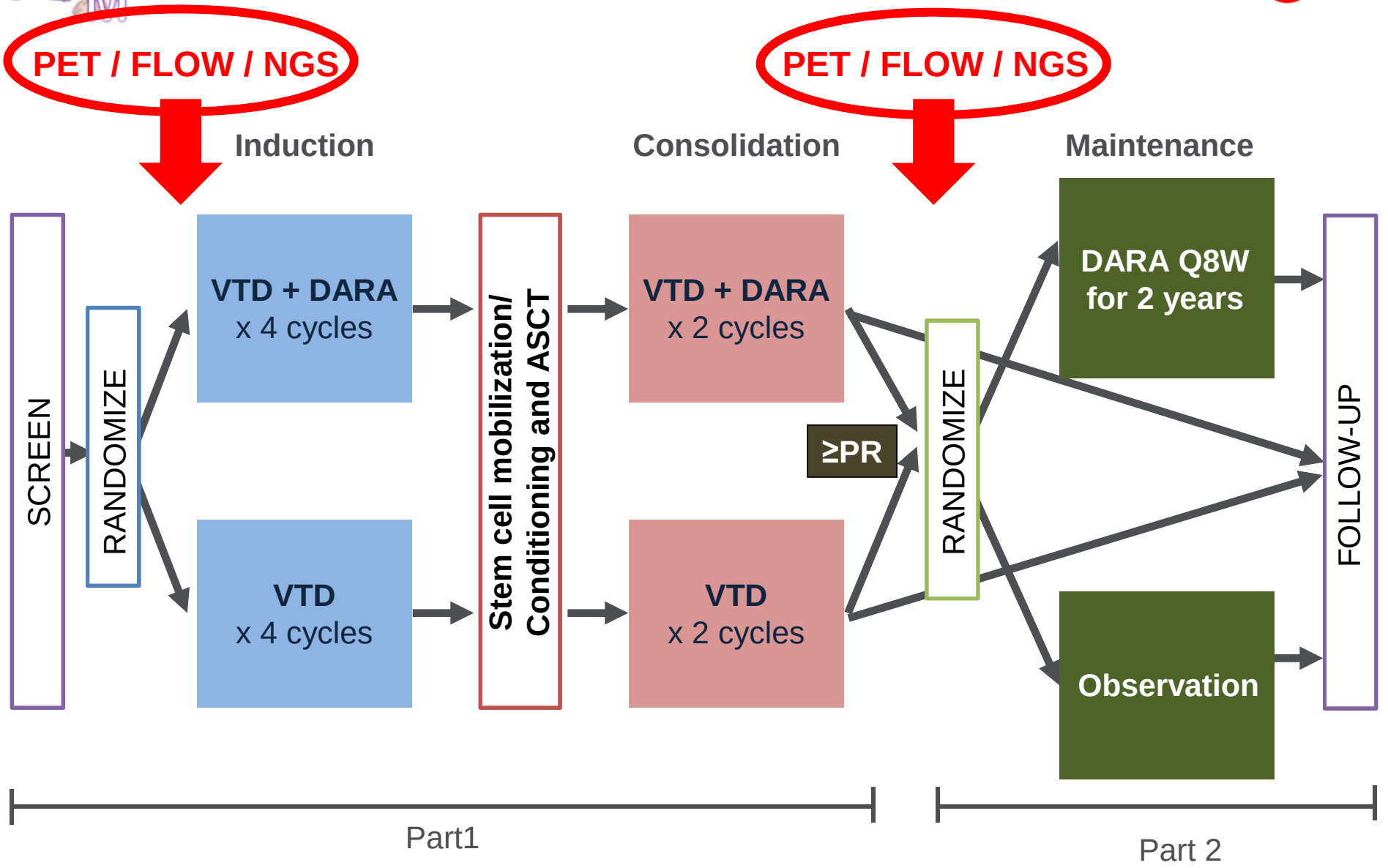
- PET-CT pre-maintenance is a powerful prognostic marker for OS

- PET-CT and CMF are complementary tools to evaluate minimal residual disease

CASSIOPEIA trial



CASSIOPEIA trial



Intergroupe Francophone du Myélome