

New IMWG Response Criteria

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Scottsdale, Arizona

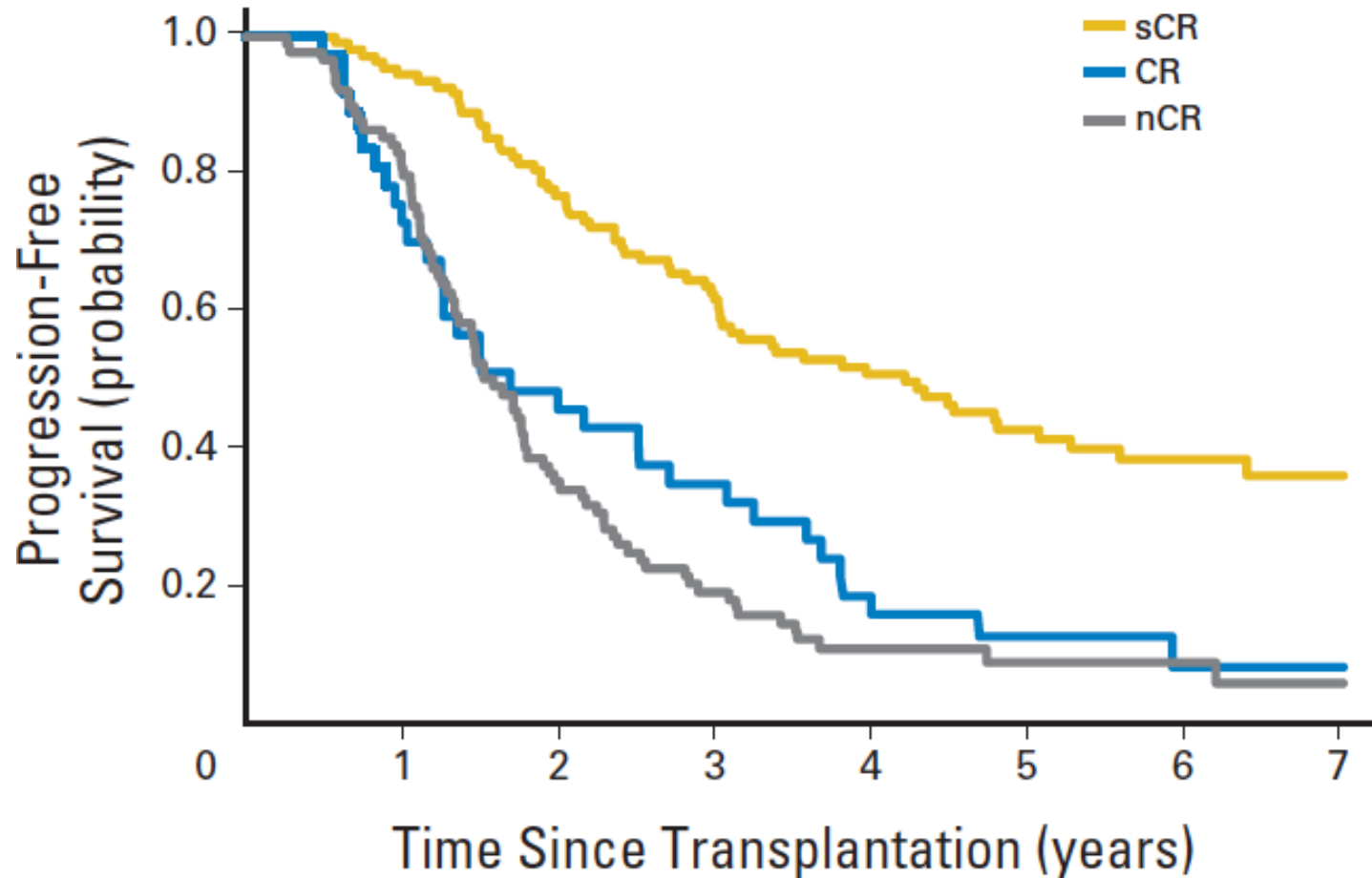


Rochester, Minnesota

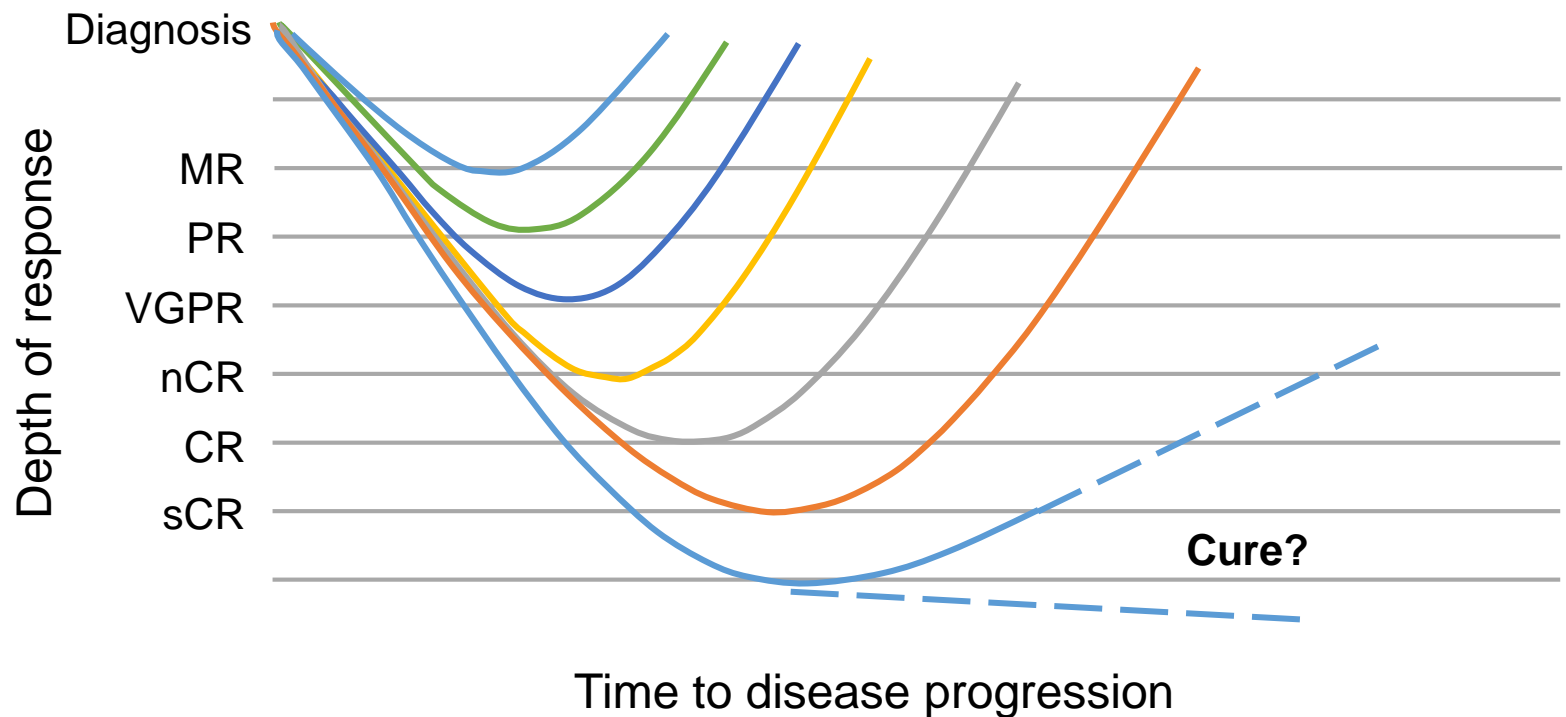


Jacksonville, Florida

Limitations of current criteria

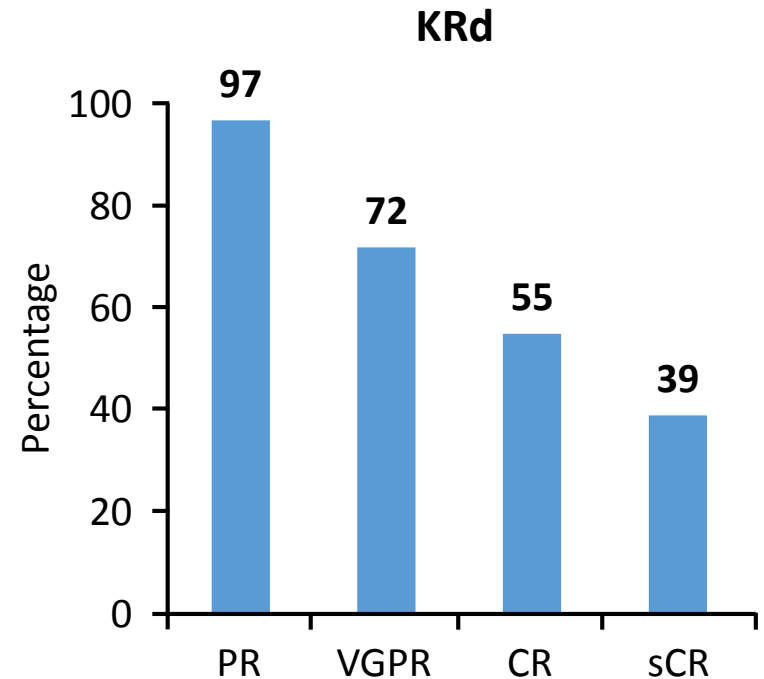
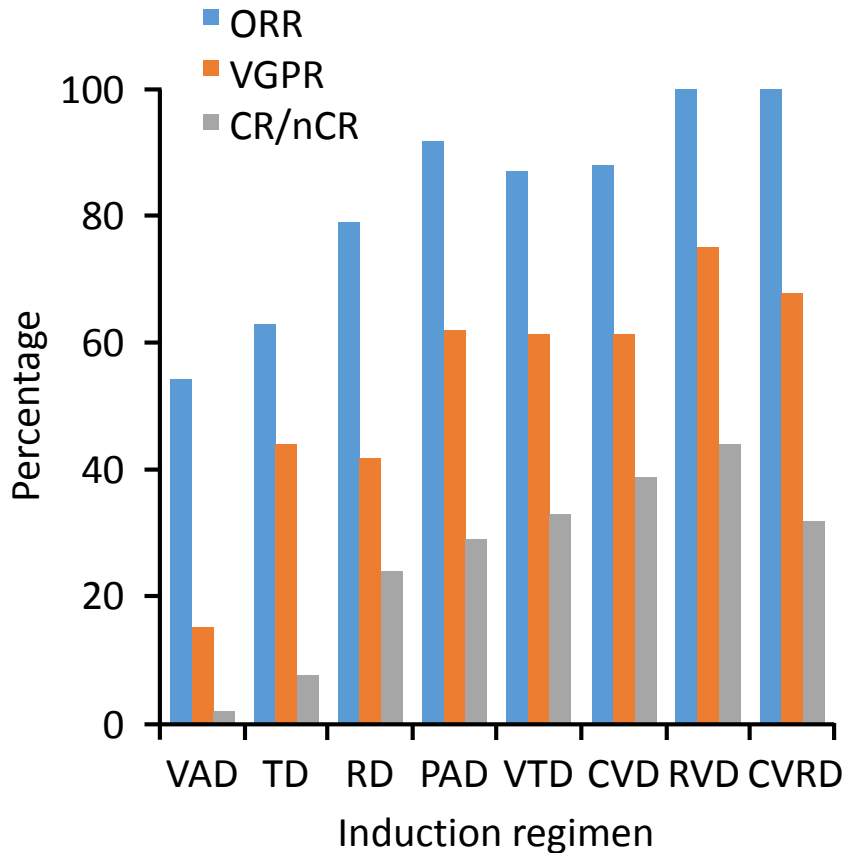


Response depth and outcome



CR, complete response; MR, minor response;
MRD, minimal residual disease; nCR, near complete response;
PR, partial response; sCR, stringent complete response;
VGPR, very good partial response

Therapy and depth of response



CR, complete response; CVD, cyclophosphamide, bortezomib, and dexamethasone; CVRD, bortezomib, dexamethasone, cyclophosphamide and lenalidomide; KRd, carfilzomib, lenalidomide and dexamethasone; nCR, near complete response; ORR, overall response rate; PAD, bortezomib, doxorubicin, and dexamethasone; PR, partial response; RD, lenalidomide and dexamethasone; RVD, lenalidomide, bortezomib and dexamethasone; sCR, stringent complete response; TD, thalidomide and dexamethasone; VAD, vincristine, doxorubicin and dexamethasone; VGPR, very good partial response; VTD, bortezomib, thalidomide, and dexamethasone

Transitioning from conventional CR

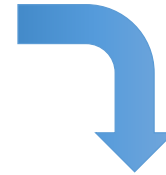
Complete Response (CR)

- Negative serum and urine immunofixation
- <5% PCs in marrow



MRD negative

- Flow negative MRD
- Sequencing negative MRD
- Imaging negative MRD



Stringent Complete Response (sCR)

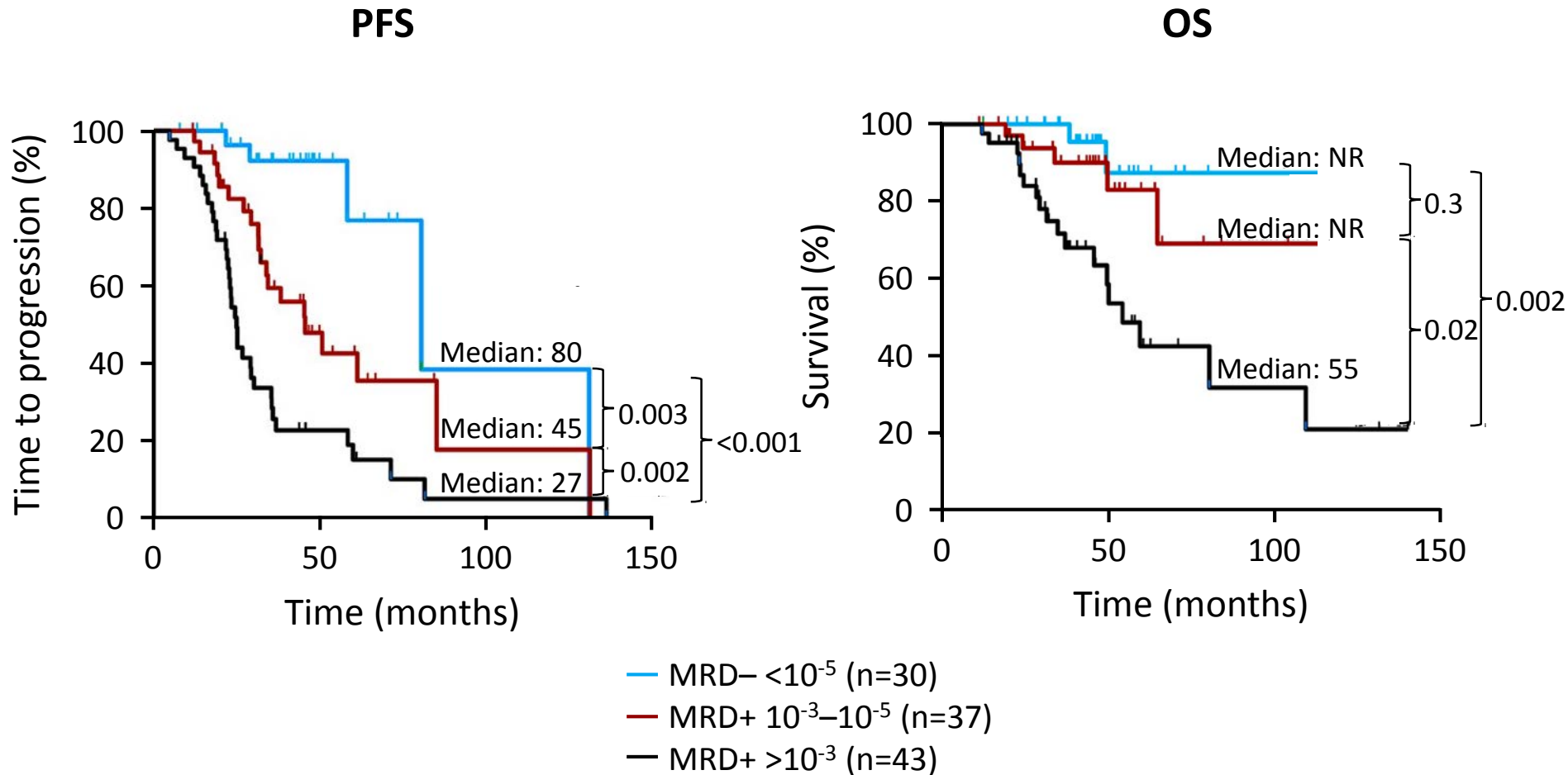
- Normal FLC ratio
- No clonal plasma cells in marrow

How do we define MRD negativity?

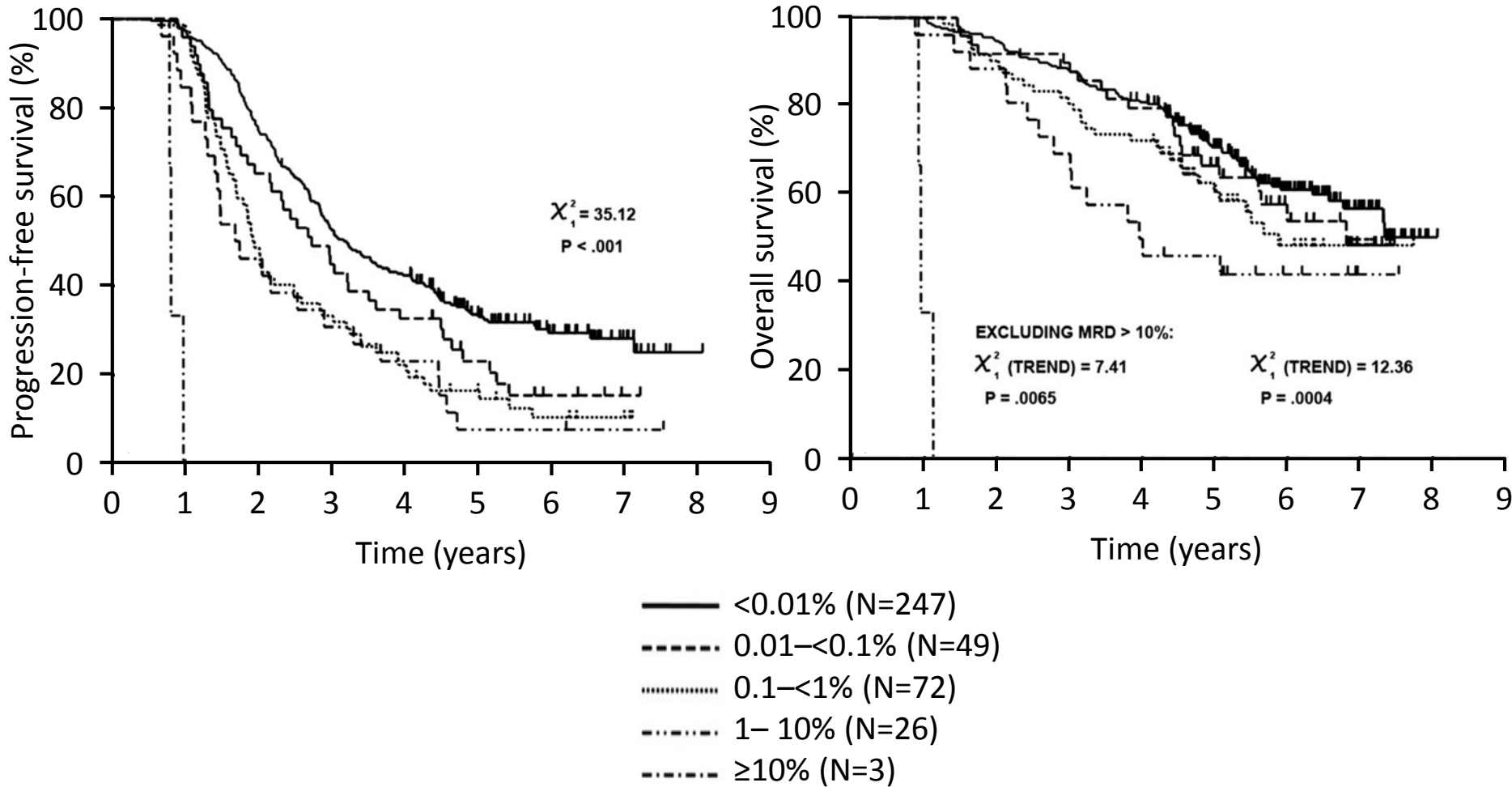
The tools:

- Flow cytometry
- NextGen sequencing
- Imaging

Depth of response and outcome

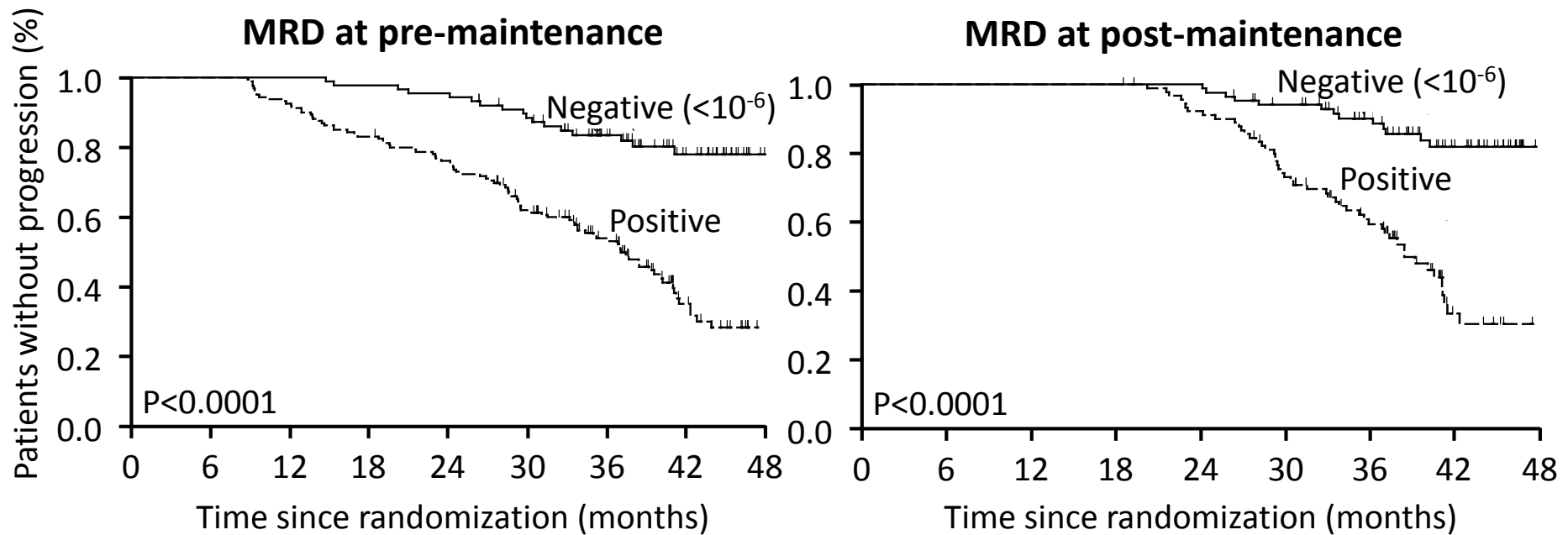


Deeper response... better outcome



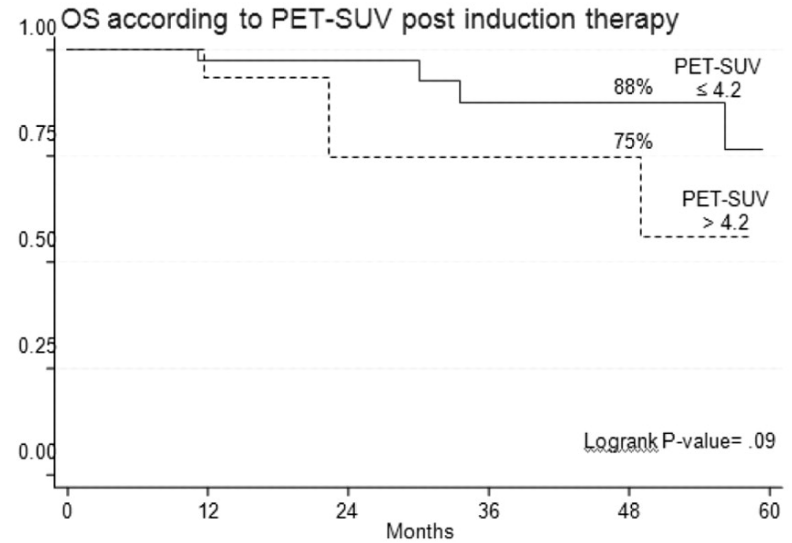
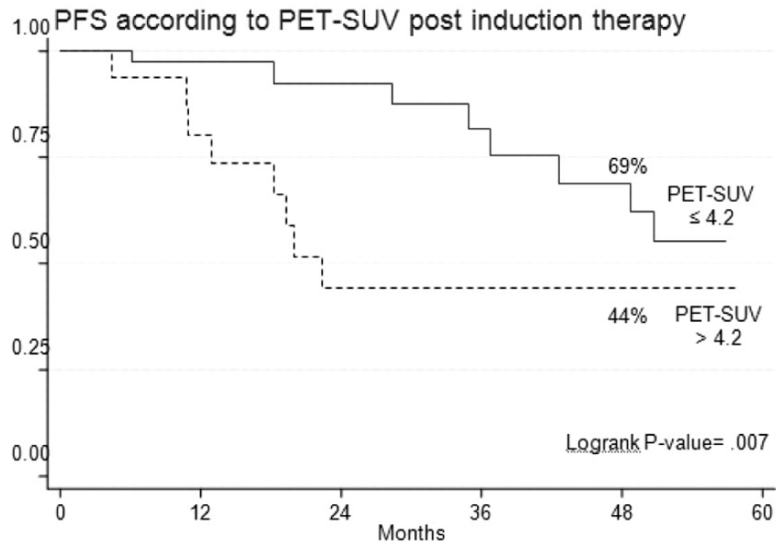
MRD after novel combinations

VRD induction → VRD or HDT consolidation → VRD consolidation →
Len maintenance for 1 year



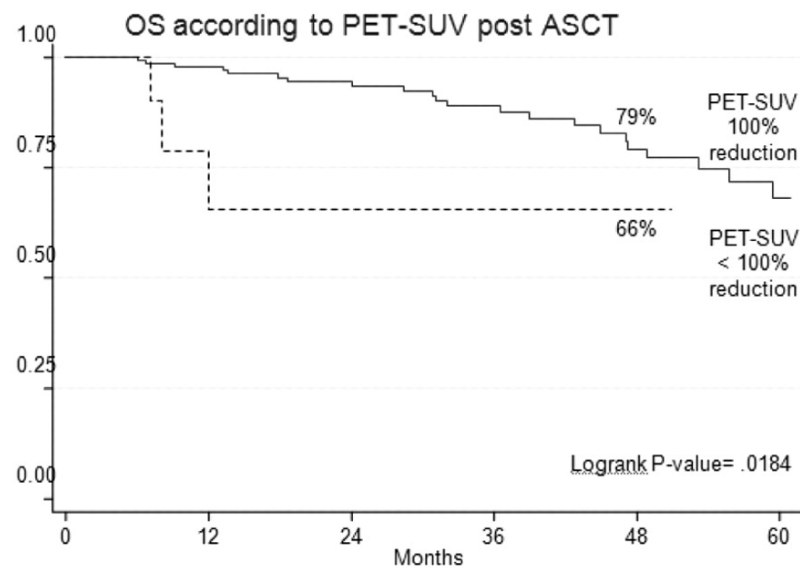
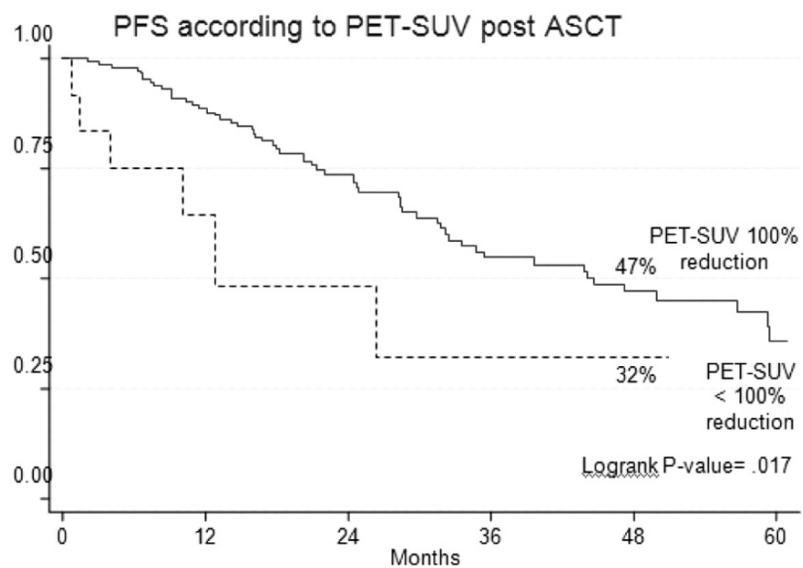
Role of imaging

Post-induction PET



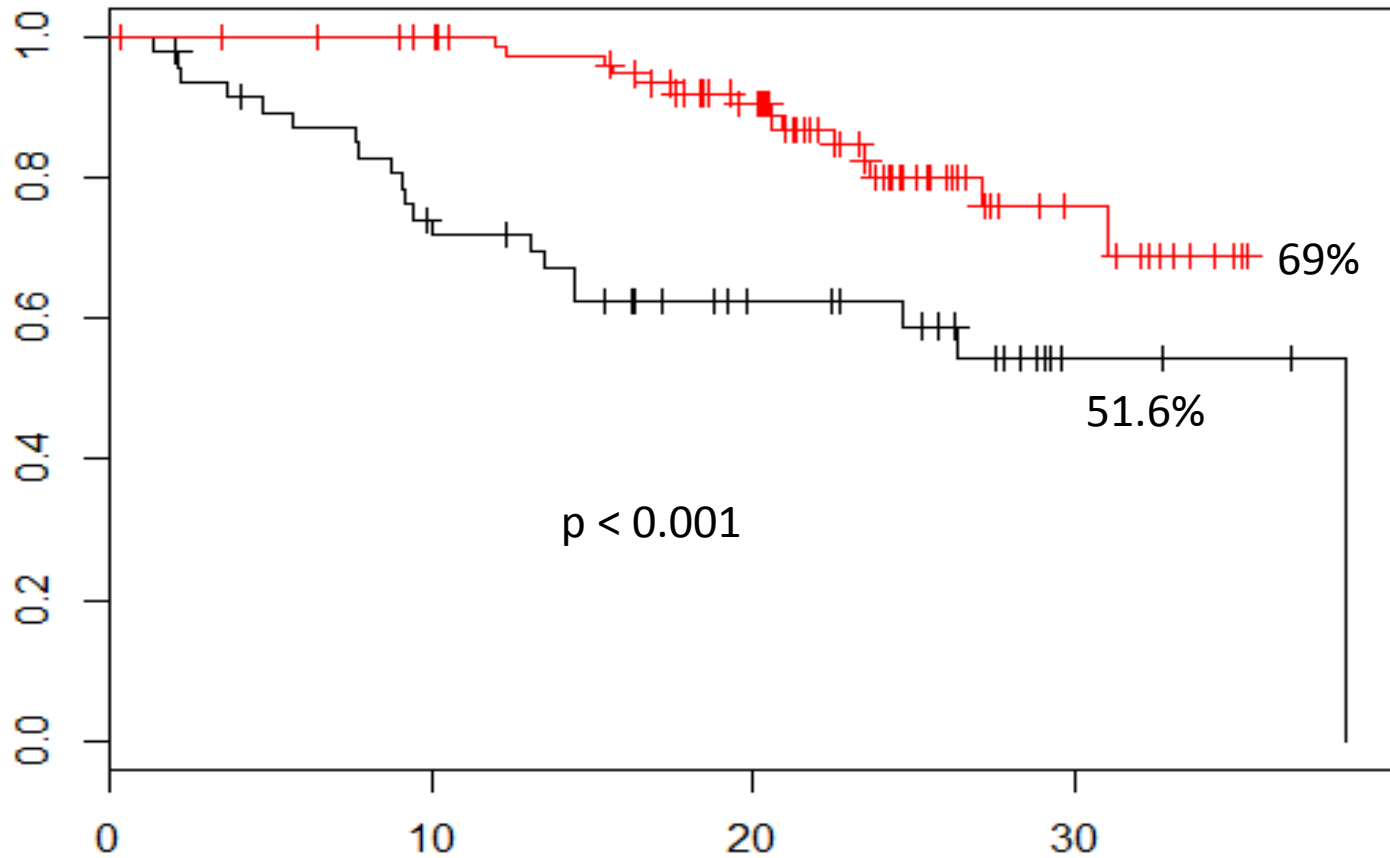
Elena Zamagni et al. Blood 2011;118:5989-5995

Post ASCT PET

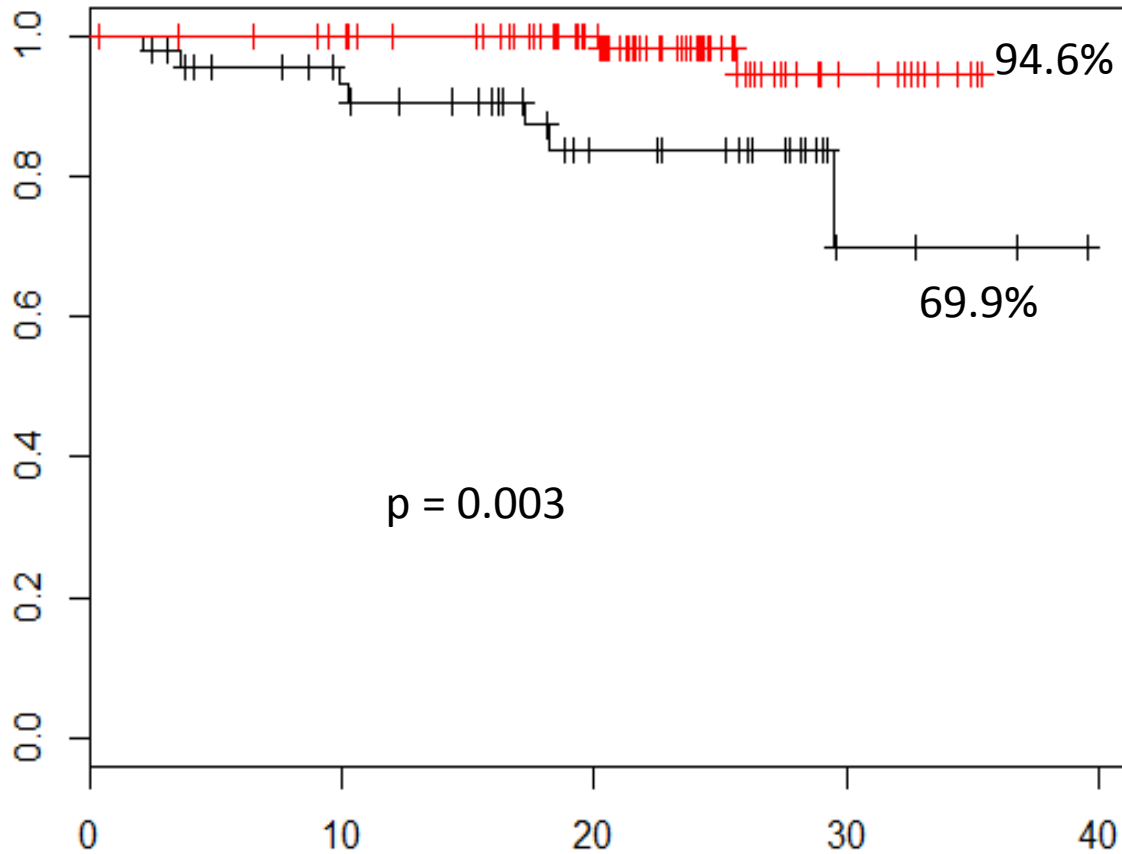


Elena Zamagni et al. *Blood* 2011;118:5989-5995

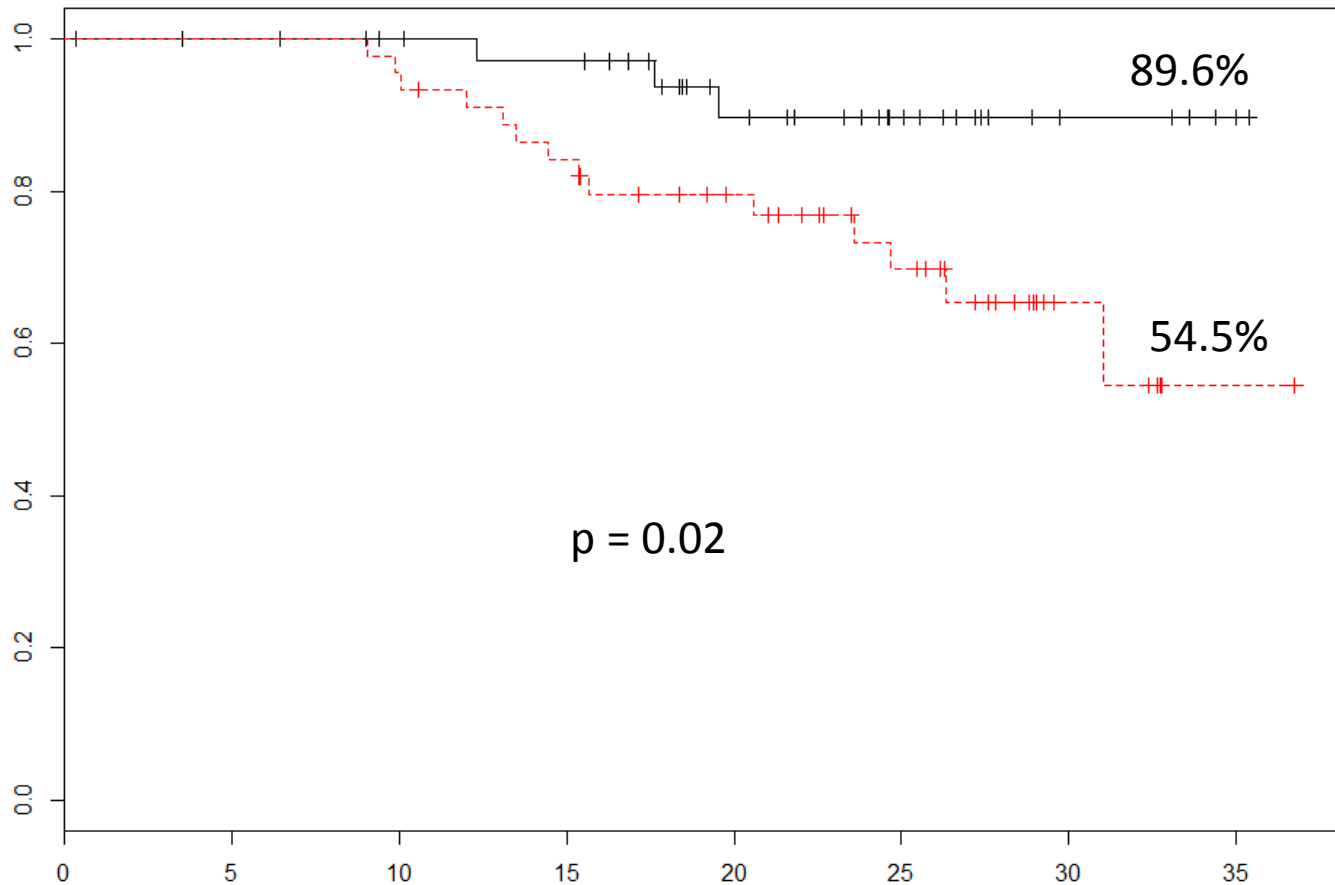
PET-CT normalisation Pre-maintenance: PFS



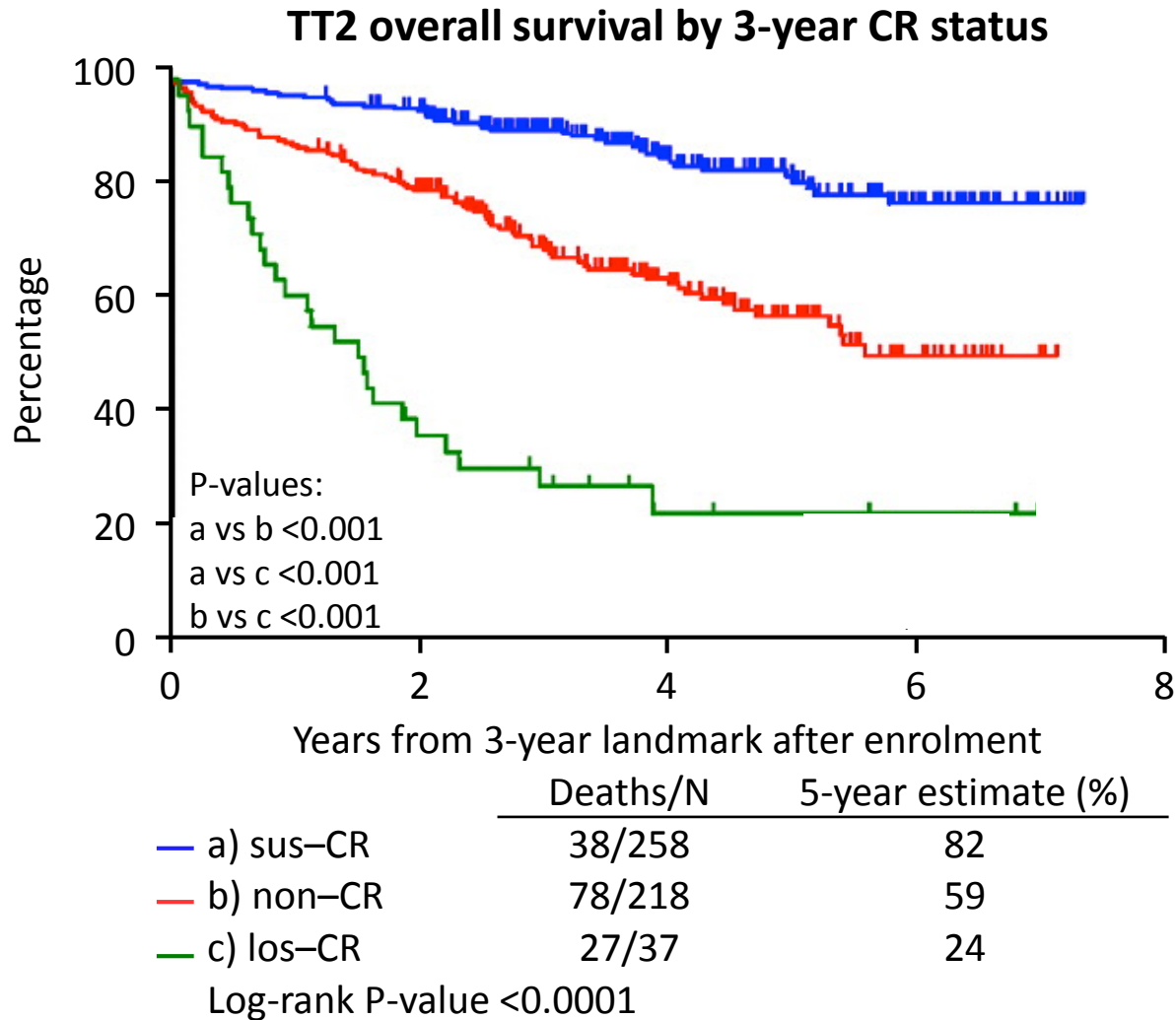
PET-CT normalisation Pre-maintenance: OS



PET and Flow negative: PFS



Durability of response



Revised IMWG response criteria

Response subcategory		Response criteria
IMWG MRD negativity criteria (Requires complete response as originally defined)	Sustained MRD-negative	MRD –ve in the marrow (next-generation flow cytometry [NGFC] and/or next-generation sequencing [NGS]) and by imaging as defined below, confirmed one year apart. Subsequent evaluations can be used to further specify the duration of negativity
	Flow MRD-negative	Absence of phenotypically aberrant clonal plasma cells by NGFC on bone marrow aspirates using the EuroFlow standard operation procedure for MRD detection in MM (or validated equivalent method) with a minimum sensitivity of 1 in 10 ⁵ nucleated cells or higher
	Sequencing MRD-negative	Absence of clonal plasma cells by NGS on bone marrow aspirates in which presence of a clone is defined as less than two identical sequencing reads obtained after DNA sequencing of bone marrow aspirates using the Lymphosight® platform (or validated equivalent method) with a minimum sensitivity of 1 in 10 ⁵ nucleated cells or higher
	Imaging + MRD-negative	MRD negative as defined by NGF or NGS PLUS Disappearance of every area of increased tracer uptake found at baseline or a preceding PET/CT or decrease to < mediastinal blood pool SUV or decrease to less than that of surrounding normal tissue

Endpoints

Endpoint	Definition
TTP	Duration from start of treatment to disease progression, with deaths from causes other than progression censored.
PFS	Duration from start of the treatment to disease progression or death (regardless of cause of death), whichever comes first.
EFS	The definition for EFS depends on how “event” is defined. In many studies, the definition of EFS used is the same as PFS. EFS may include additional “events” that are considered to be of importance besides death and progression, including serious drug toxicity.
DFS	Duration from the start of MRD negativity to the time of reappearance of MRD. DFS applies only to patients in MRD negative state.
DOR	Duration from first observation of PR to the time of disease progression, with deaths from causes other than progression censored.* Duration of MRD, CR and PR should each be reported as appropriate.

Questions