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# EMORY WINSHIP CANCER INSTITUTE

A Cancer Center Designated by  
the National Cancer Institute

## Initial Therapy

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# Disclosures

<b>Advisory Committee</b>	Bristol-Myers Squibb Company, Celgene Corporation, GlaxoSmithKline, Janssen Biotech Inc, Merck, Novartis, Onyx Pharmaceuticals, an Amgen subsidiary, Takeda Oncology
<b>Consulting Agreements</b>	Bristol-Myers Squibb Company, Celgene Corporation, GlaxoSmithKline, Janssen Biotech Inc, Merck, Onyx Pharmaceuticals, an Amgen subsidiary, Takeda Oncology

# Case presentation 1: Dr Chen

**57-year-old woman with hepatitis C (successfully treated with peg-interferon and ribavirin)**



- Mental status change and weakness
  - Pancytopenia (Hgb 4.7), total protein 10.7, albumin 2.0 and hypercalcemia (zoledronic acid)
  - SPEP: IgG lambda monoclonal gammopathy, M-spike 2.2, beta-2 microglobulin 5.9
  - Diagnosis: Stage III MM; Cytogenetics: Normal; FISH: Del(17p)
- Surgical stabilization → C-spine RT

## Case presentation 2: Dr Nadeem

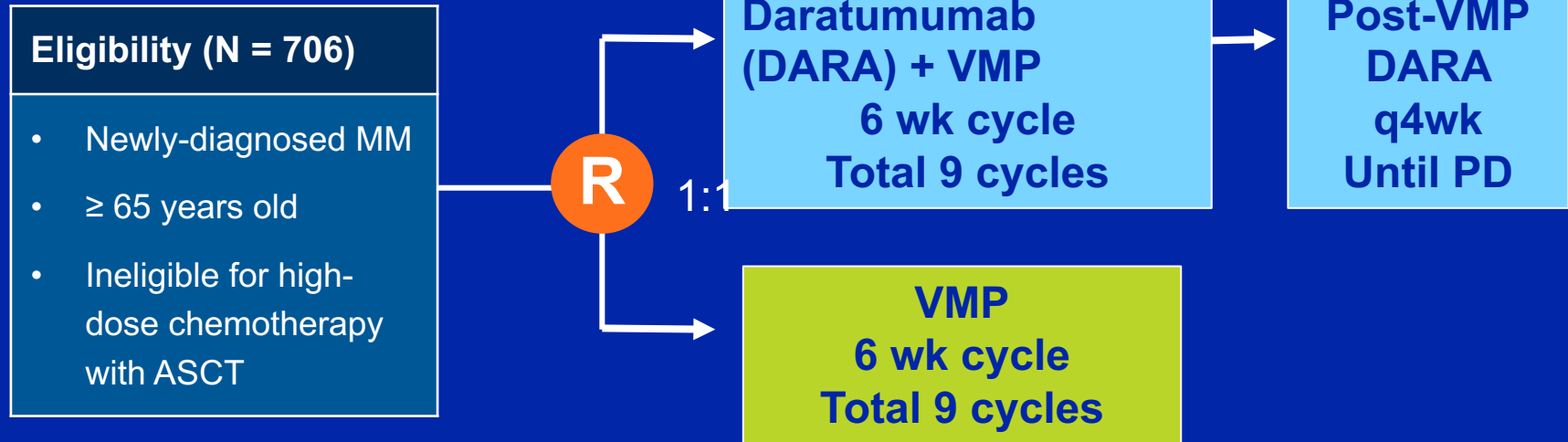
### 82-year-old woman (PS = 2) with comorbidities including diabetes and hypertension

- 2017: Diagnosed with ISS Stage II, IgG kappa multiple myeloma
- Cytogenetics: t(11;14)
- Feb 2017: RVD-lite (weekly bortezomib, lenalidomide 15 mg, dexamethasone 20 mg on a 35-day cycle) x 8 cycles
  - VGPR; no tolerability issues
- Currently receiving lenalidomide maintenance



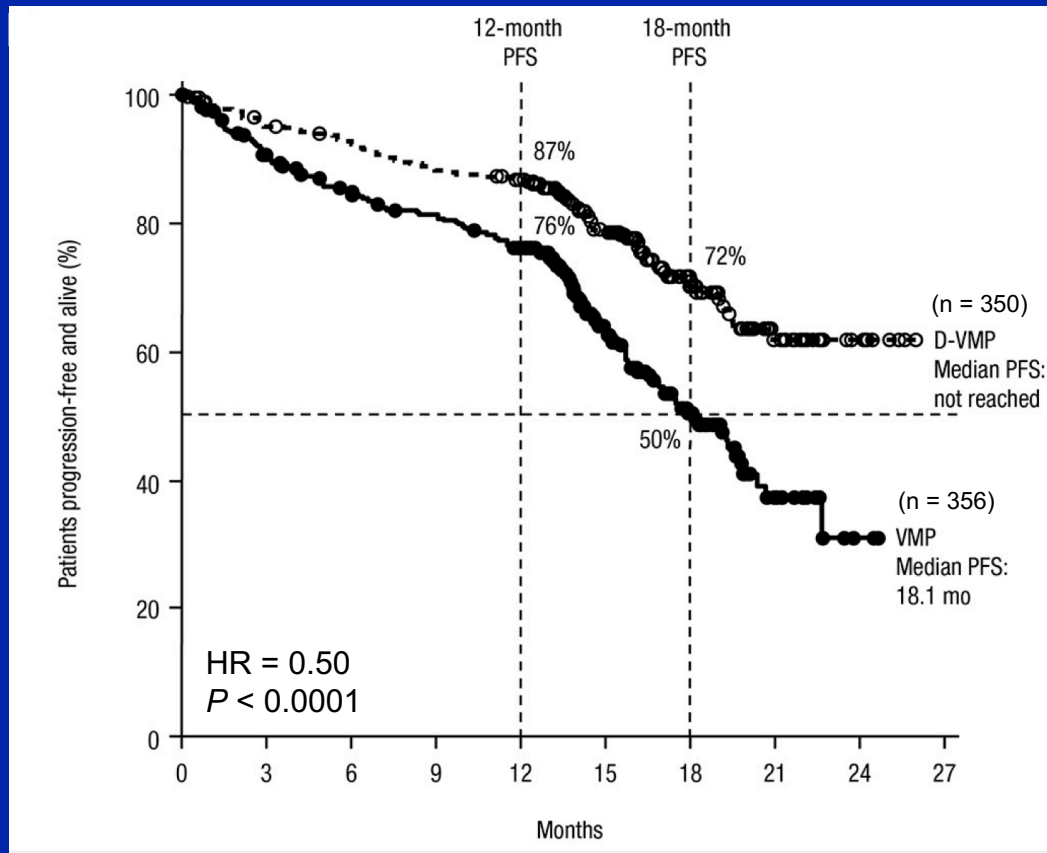
# ALCYONE: Phase III Trial of Daratumumab with Bortezomib/Melphalan/Prednisone in Newly Diagnosed MM

NCT02195479



VMP = bortezomib/melphalan/prednisone

# ALCYONE: Primary Endpoint PFS



# Updated IMWG Criteria for Diagnosis of Multiple Myeloma

## MGUS

- M-protein < 3 g/dL
- Clonal plasma cells in BM < 10%
- No myeloma defining events

## Smoldering Myeloma

- M-protein  $\geq$  3 g/dL (serum) or  $\geq$  500 mg/24 hrs (urine)
- Clonal plasma cells in BM  $\geq$  10% - 60%
- No myeloma defining events

## Multiple Myeloma

- Underlying plasma cell proliferative disorder
- AND**
- 1 or more myeloma defining events including either:
    - ✓  $\geq$  1 **CRAB** feature(s)
- OR**
- ✓  $\geq$  1 **Biomarker Driven**

**C:** Calcium elevation ( $>$  11 mg/dL or  $>$  1 mg/dL higher than ULN)

**R:** Renal insufficiency (creatinine clearance  $<$  40 mL/min or serum creatinine  $>$  2 mg/dL)

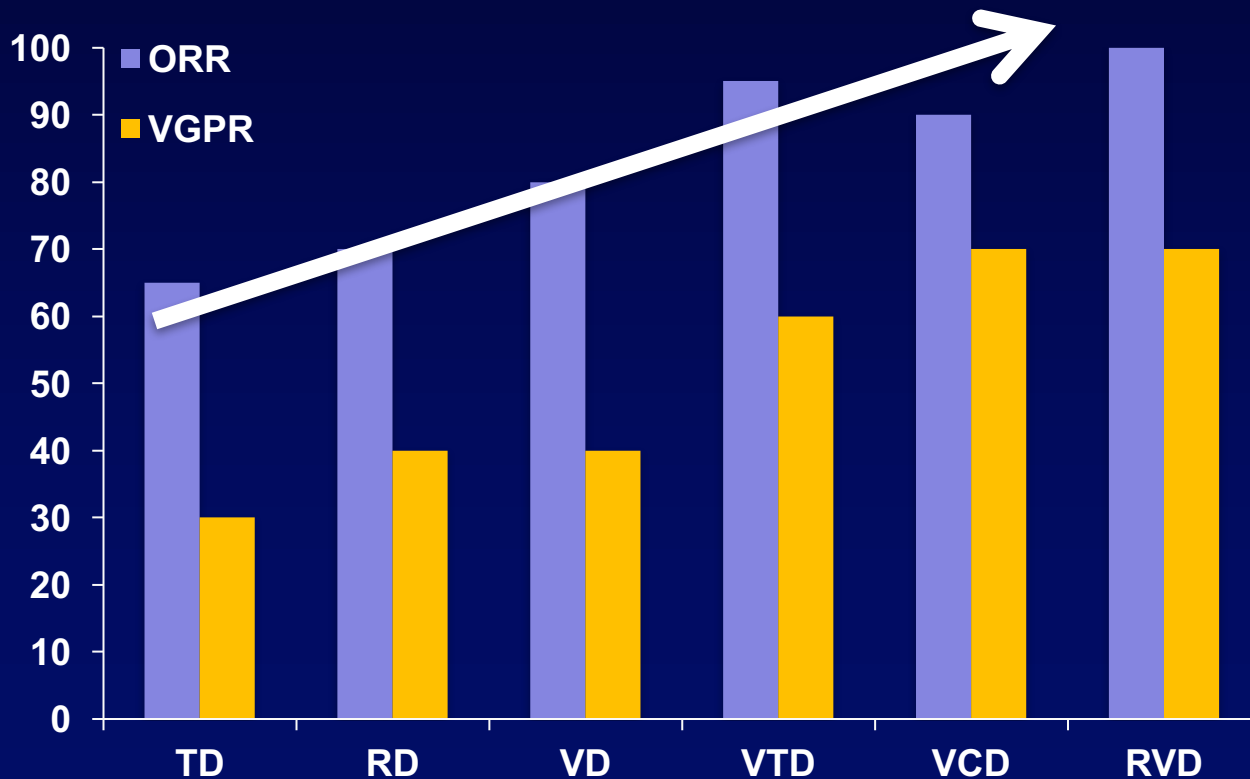
**A:** Anemia (Hb  $<$  10 g/dL or 2 g/dL  $<$  normal)

**B:** Bone disease ( $\geq$  1 lytic lesions on skeletal radiography, CT, or PET-CT)

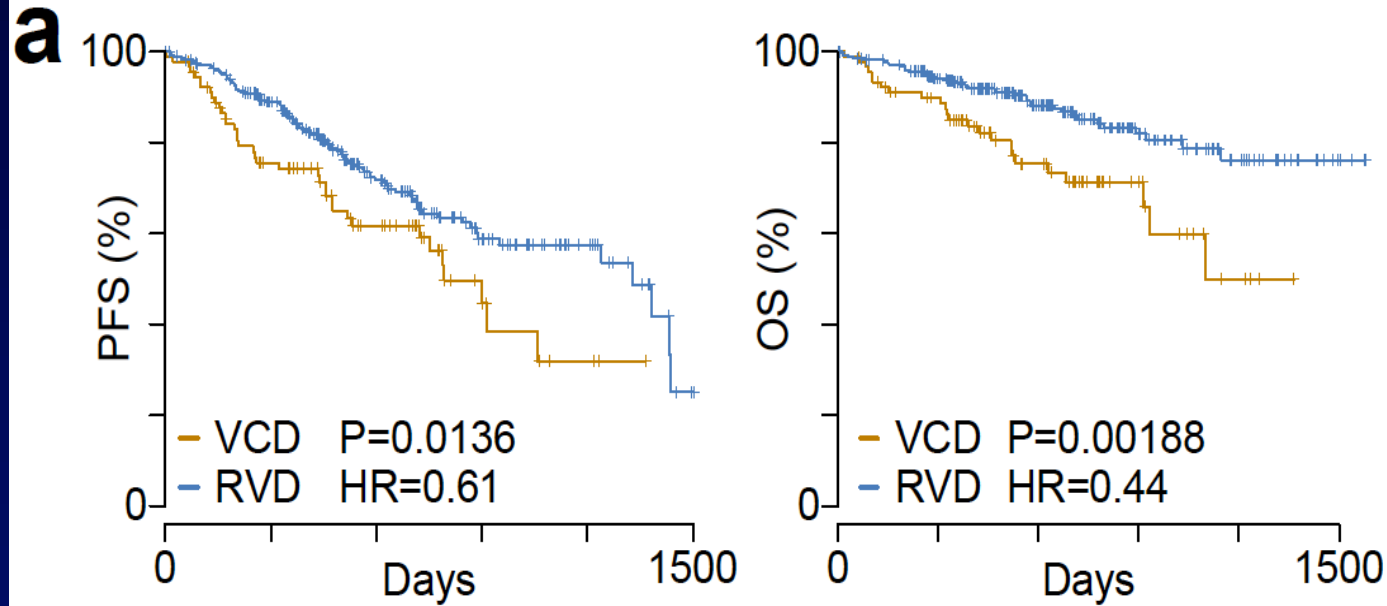
**Biomarker driven (1)** Sixty-percent ( $\geq$ 60%) clonal PCs by BM; **(2)** Serum free Light chain ratio involved:uninvolved  $\geq$ 100; **(3)** >1 focal lesion detected by MRI



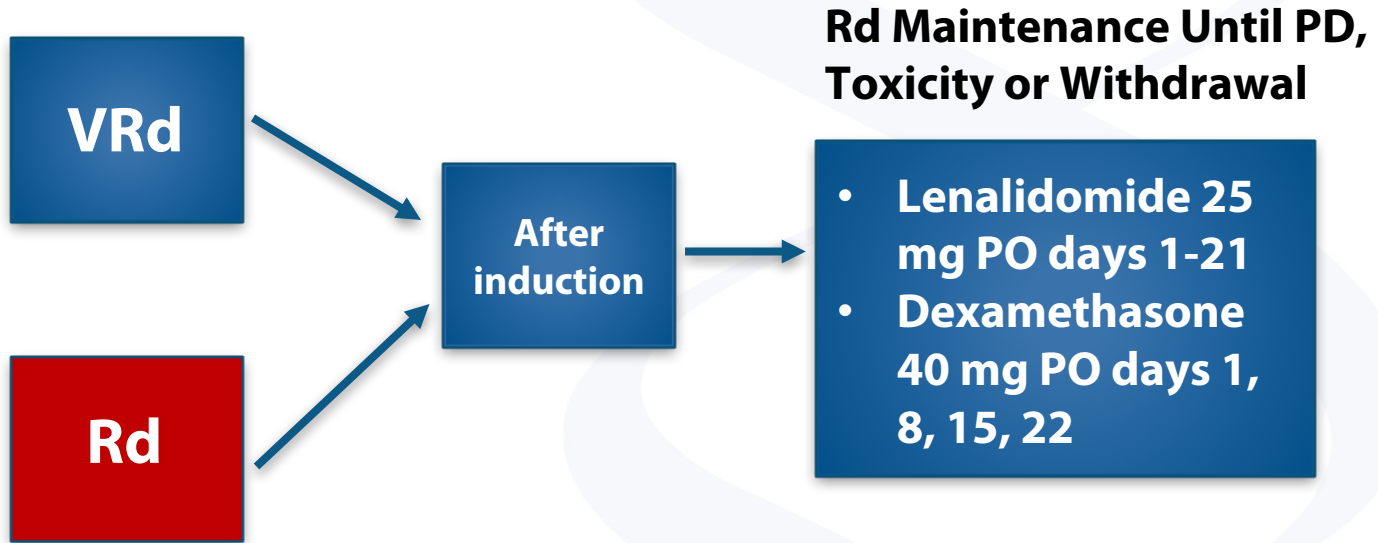
# Three Drugs Are Better Than Two



# RVD is better than VCD

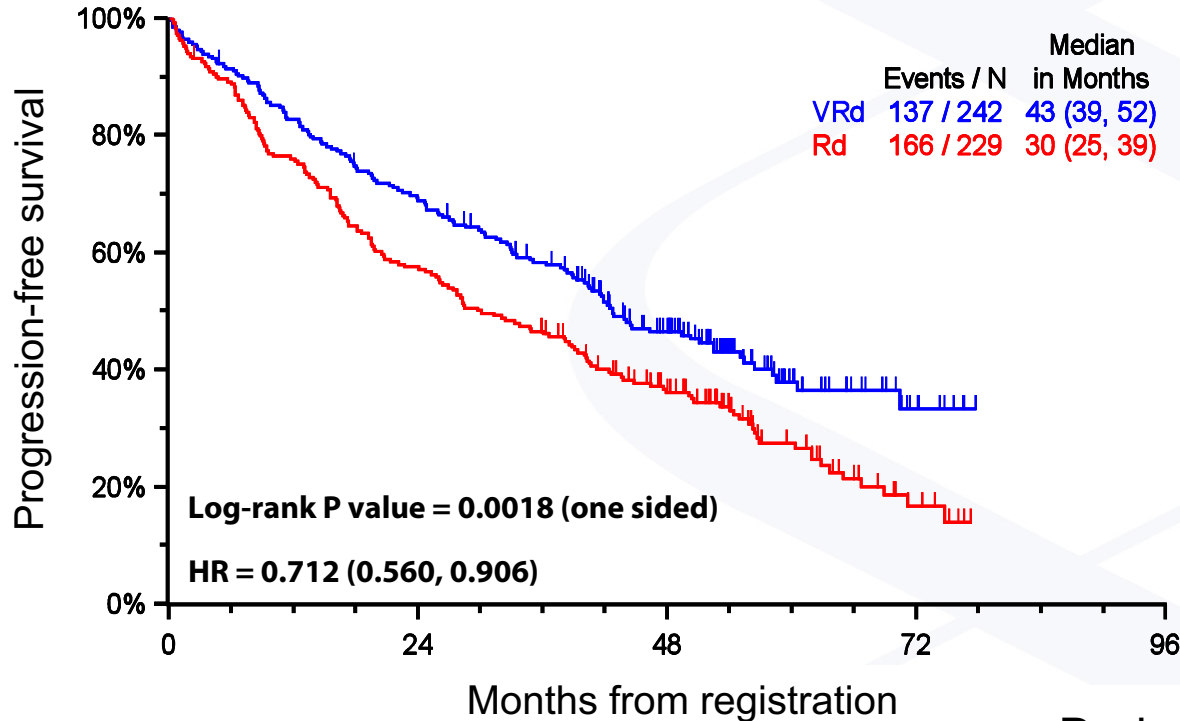


# SWOG-S0777 Study Design (continued)



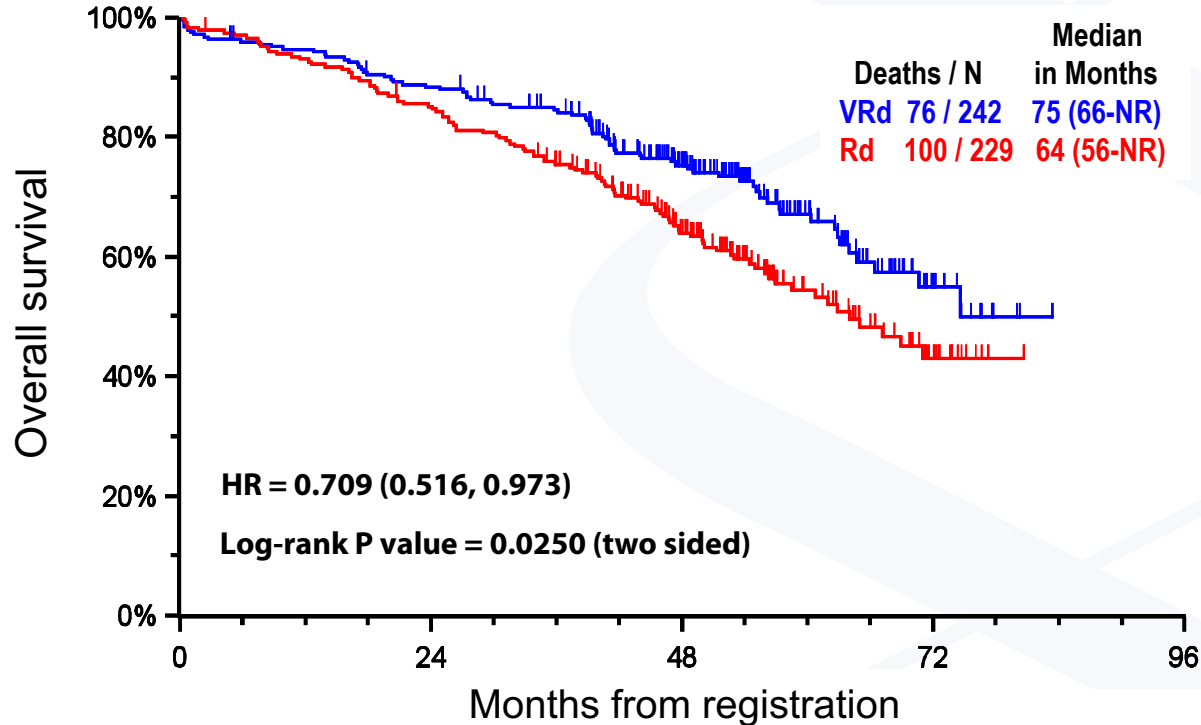
- All patients received aspirin 325 mg/day
- VRd patients received HSV prophylaxis

# Progression-Free Survival By Assigned Treatment Arm



Durie et al, Lancet 2016

# Overall Survival By Assigned Treatment Arm

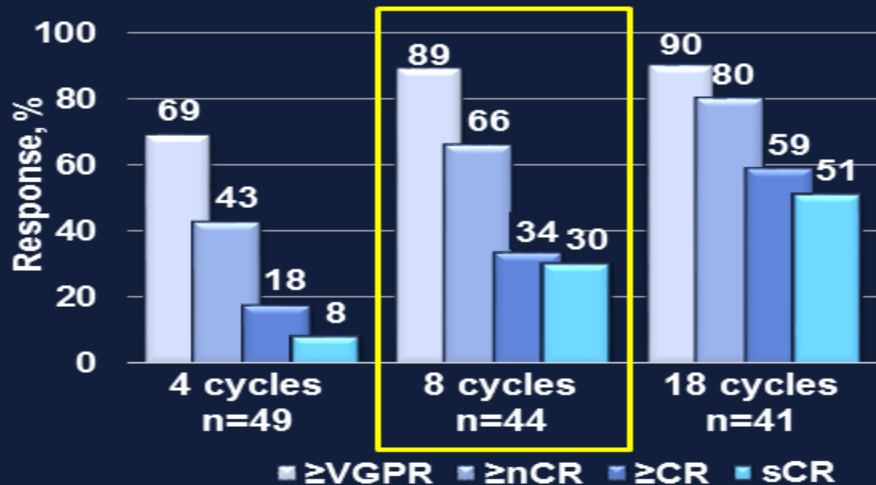


NR = not reached

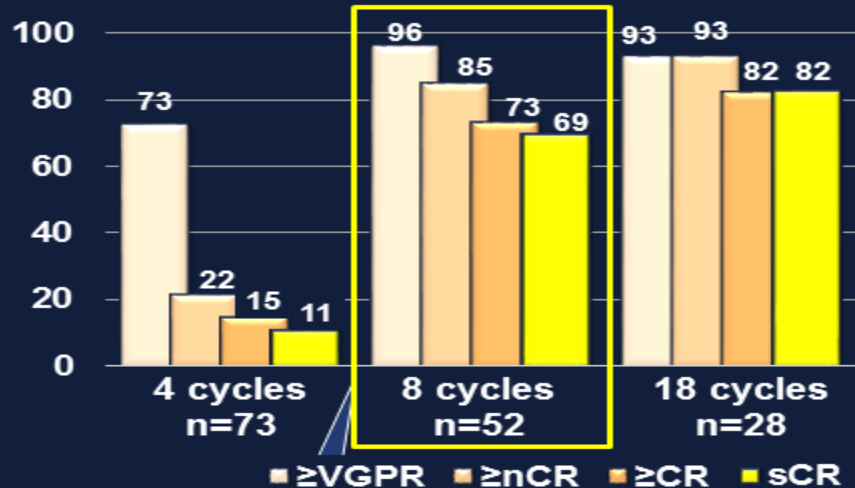
Durie et al, Lancet 2016

# KRD for Newly Diagnosed Myeloma

## KRd w/o ASCT



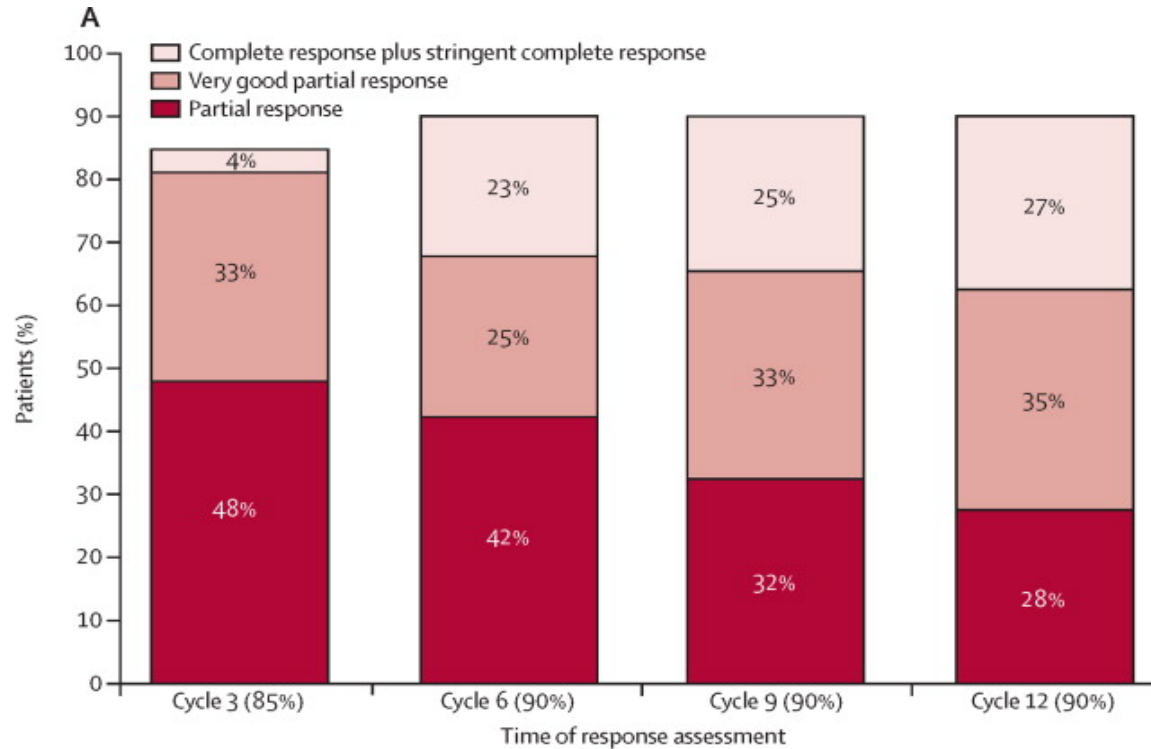
## KRd + ASCT



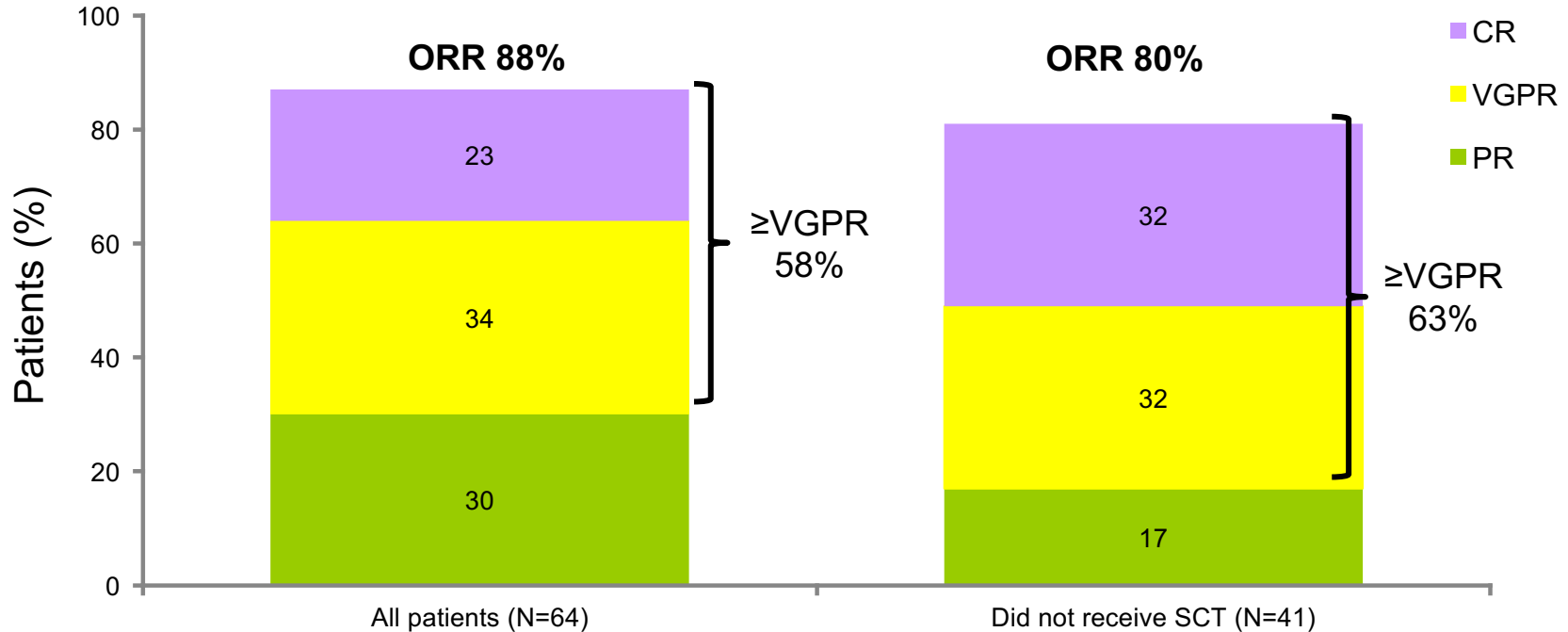
Response after ASCT (n=64)

Response Category	Percentage
≥VGPR	92%
≥nCR	45%
≥CR	27%
sCR	20%

# IRD Response Rates

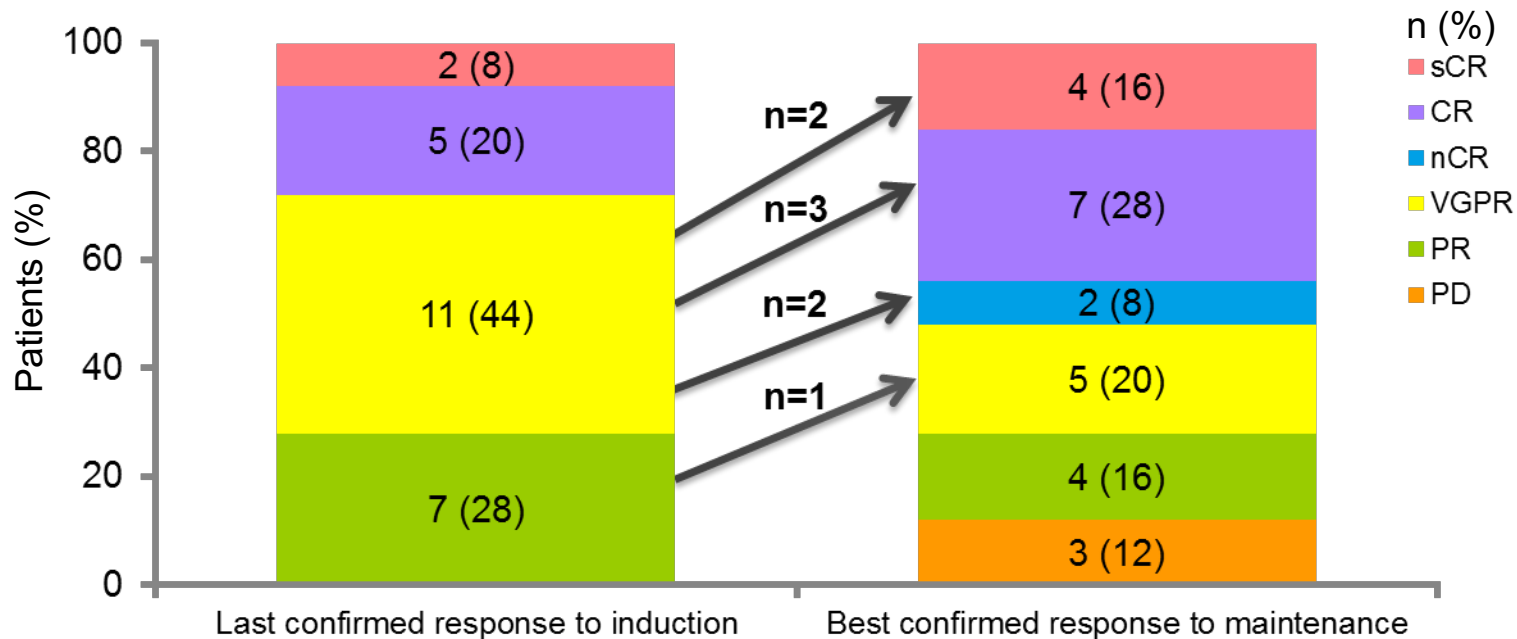


# Best response IRD with I maintenance (response-evaluable population)





# Deepening responses in patients receiving ixazomib maintenance (N=25)

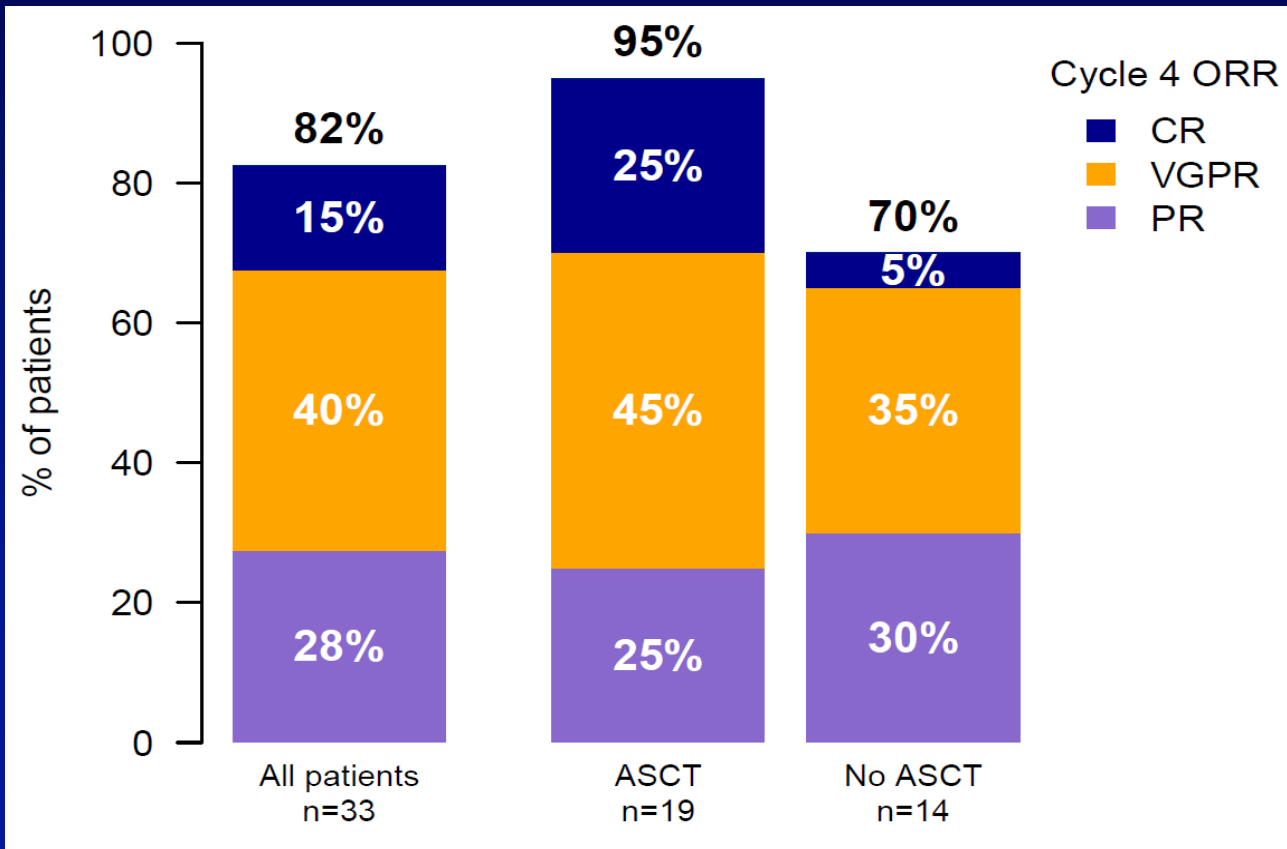


- ▶ 8 (32%) patients improved their response during maintenance
  - 2 VGPR to sCR, 3 VGPR to CR, 2 VGPR to nCR and 1 PR to VGPR

# Minimal residual disease (MRD) evaluation (response-evaluable population)

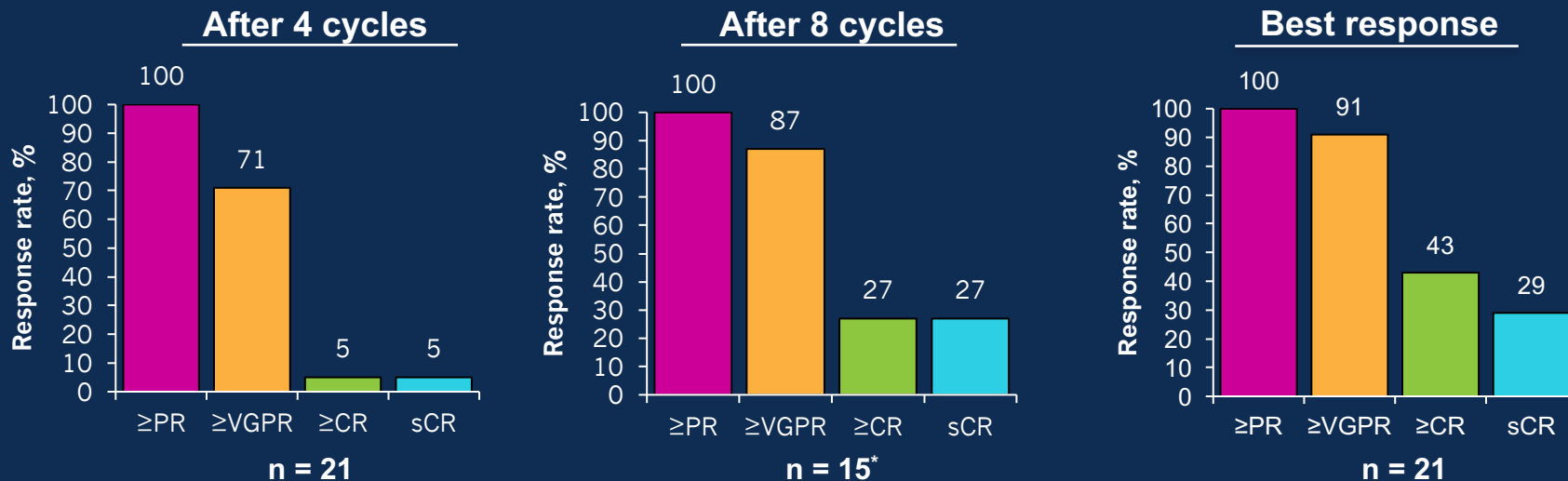
<b>Patients</b>	<b>All patients (N=64)</b>	<b>Did not receive SCT (N=41)</b>
MRD evaluation, n (%)	16 (25)	10 (24)
Best response of sCR/CR, n	9	7
Achieved MRD-negative status, n (% of patients with sCR/CR)	8 (89)	6 (86)

# Response After 4 Cycles Elo-RVD



# KRD + Dara Response Rate

- Median number of treatment cycles: 11.5 (range, 1.0-13.0)



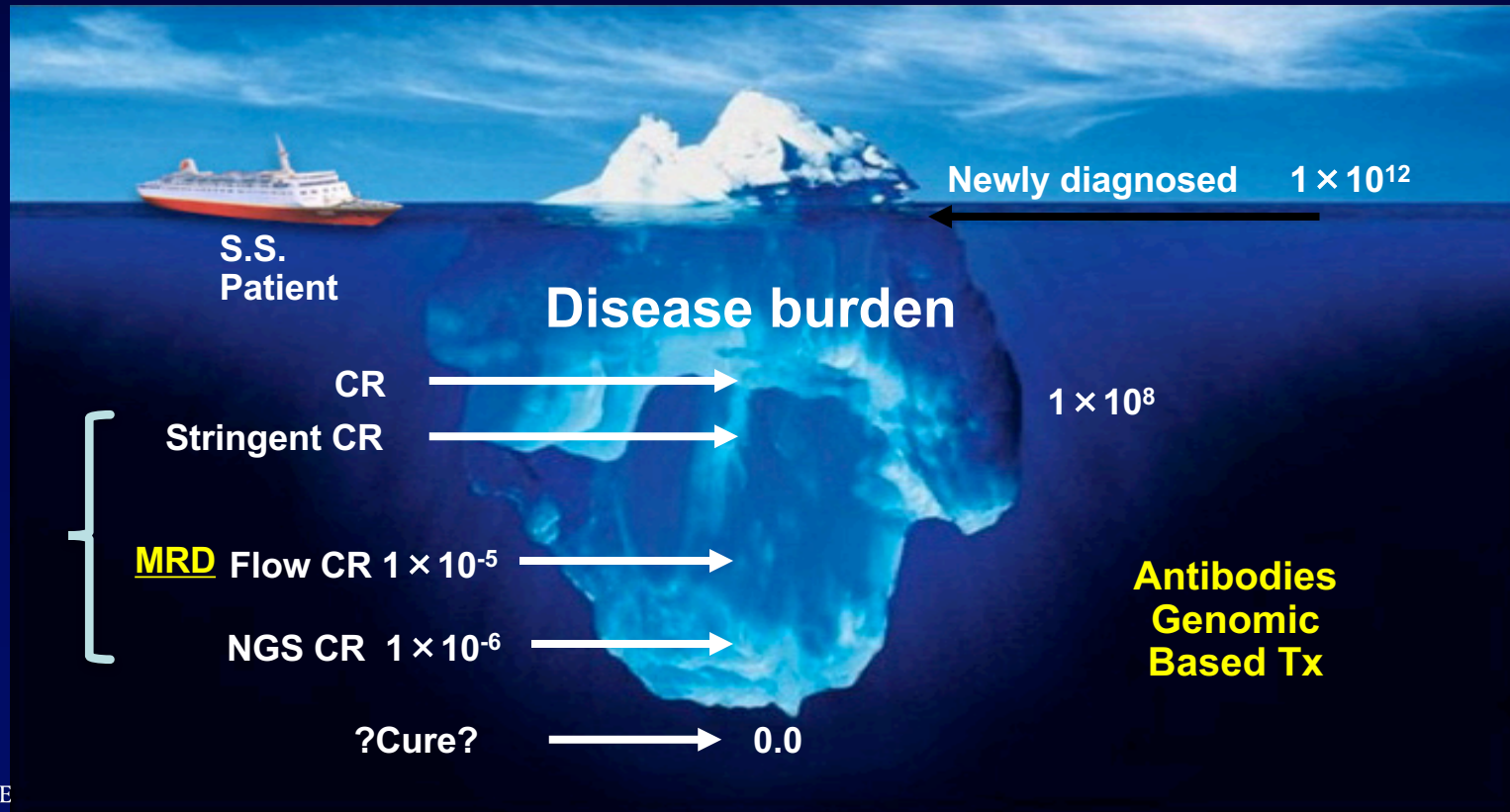
**Depth of response improved with duration of treatment**

\*5 patients who proceeded to ASCT before C8 and 1 patient who discontinued due to PD at C7 were excluded.

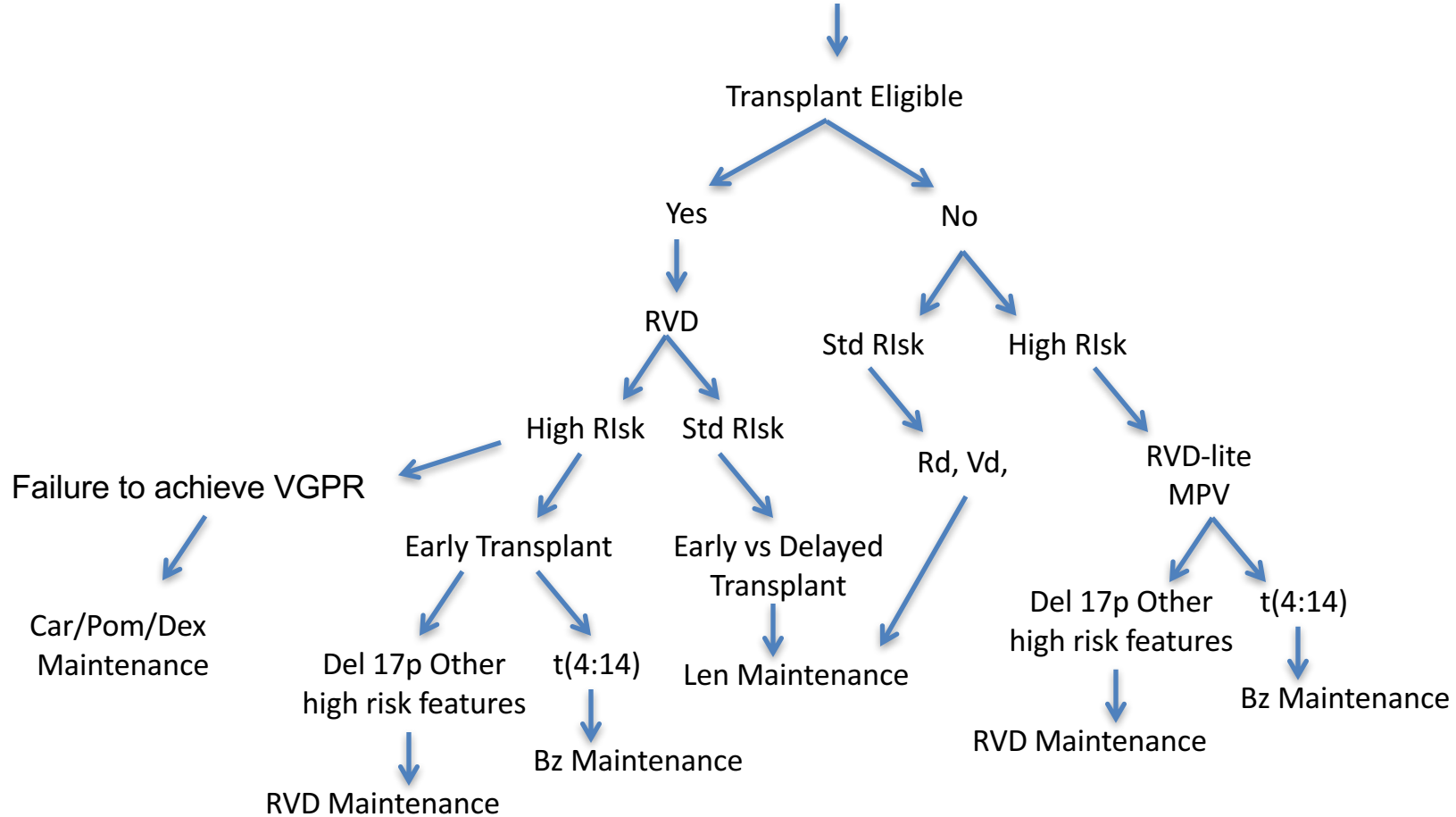
PR, partial response; CR, complete response.

<sup>a</sup>Response-evaluable population. <sup>b</sup>Response rate ( $\geq$ PR) evaluated by IMWG criteria; M-protein measurements by central lab assessment.

# Combinations can Achieve Better Depth and Duration of Response



# Suggested Approach for Newly Diagnosed MM



# Survival outcomes in newly diagnosed myeloma patients with RVD induction among all patients

(at a median follow up of 66 months)

