

A Phase III Study to Determine the Efficacy and Safety of Lenalidomide in Combination with Melphalan and Prednisone Followed by Lenalidomide (MPR-R) in Patients ≥ 65 Years with Newly Diagnosed Multiple Myeloma (NDMM)

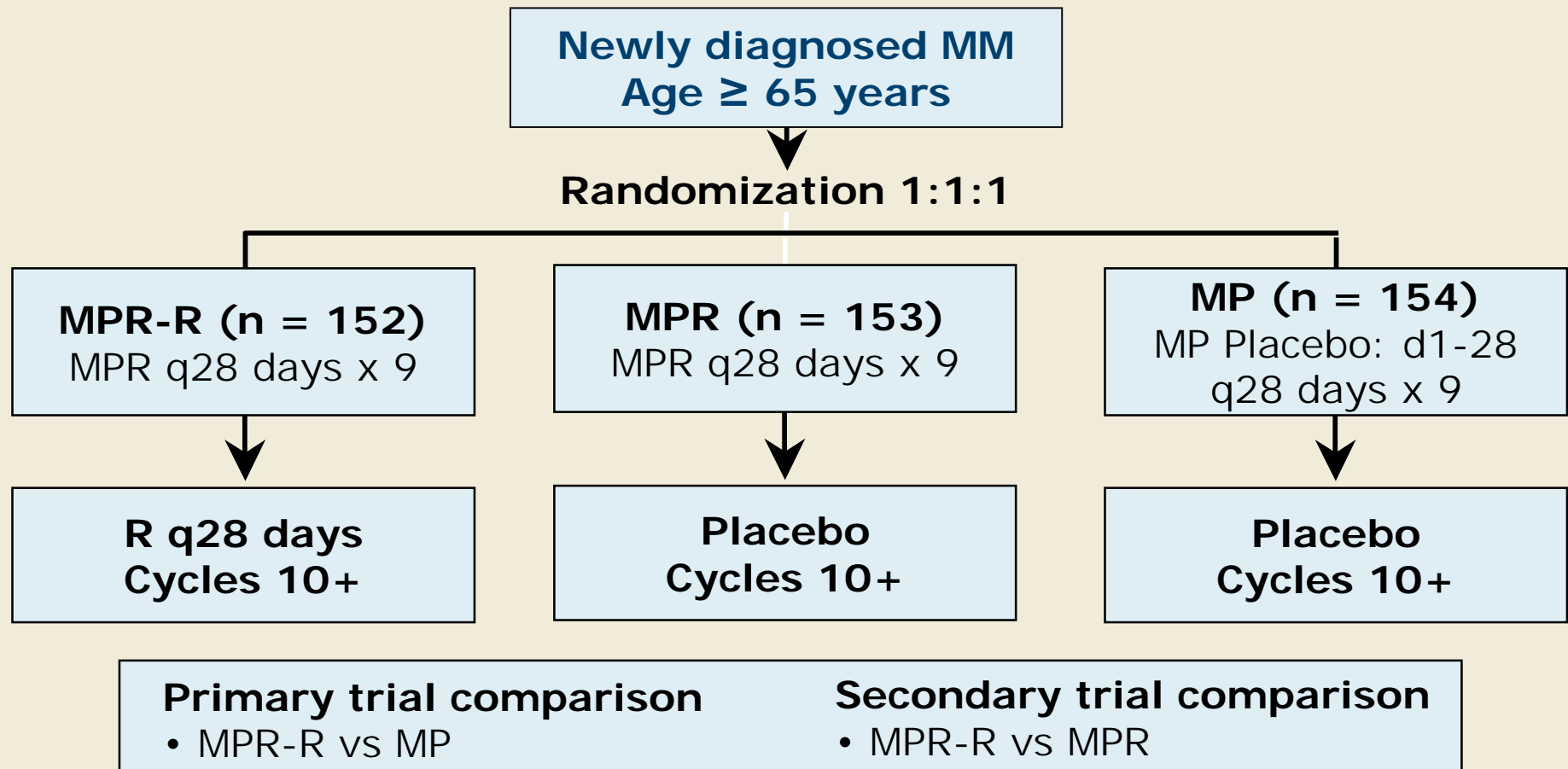
Palumbo A et al.

Proc ASH 2009; Abstract 613.

Introduction

- Prolonged lenalidomide therapy has been shown to improve overall survival in patients with relapsed/refractory multiple myeloma (ASH 2008; Abstract 3702).
- Phase I/II study has demonstrated that MPR is an effective therapy with manageable toxicity for patients with NDMM (*Clin Lymphoma Myeloma* 2009; 9: 145).
- **Current study objective:**
 - Compare the efficacy and safety of MPR with or without lenalidomide maintenance with that of MP alone in patients with NDMM.

Phase III, Multicenter, Randomized Trial of MPR in Elderly Patients with NDMM



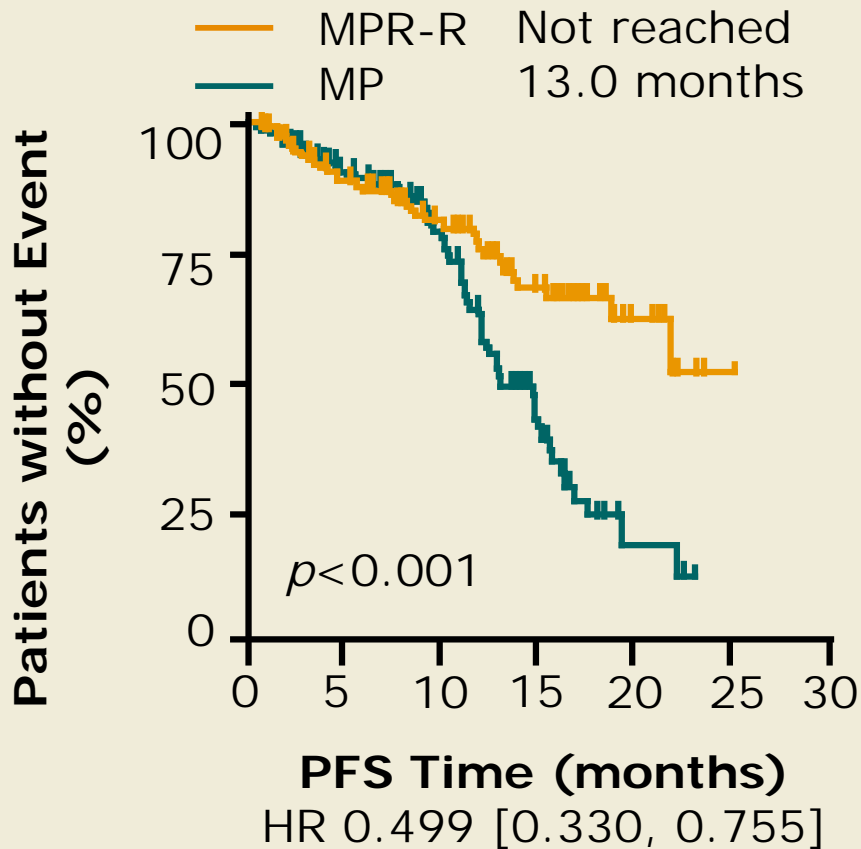
Clinical Response

| Best overall response* | MPR-R (n = 152) | MPR (n = 153) | MP (n = 154) | p-value MPR-R vs MP |
|-------------------------------|--------------------|------------------|-----------------|---------------------------|
| Overall response rate | 77% | 67% | 48% | <0.001 |
| Complete response | 18% | 13% | 5% | <0.001 |
| ≥Very good partial response | 32% | 33% | 11% | <0.001 |
| Partial response | 45% | 34% | 37% | — |
| Progressive disease | 0% | 1% | 0% | — |
| Median time to first response | 1.9 mo | 1.9 mo | 2.8 mo | <0.001 |

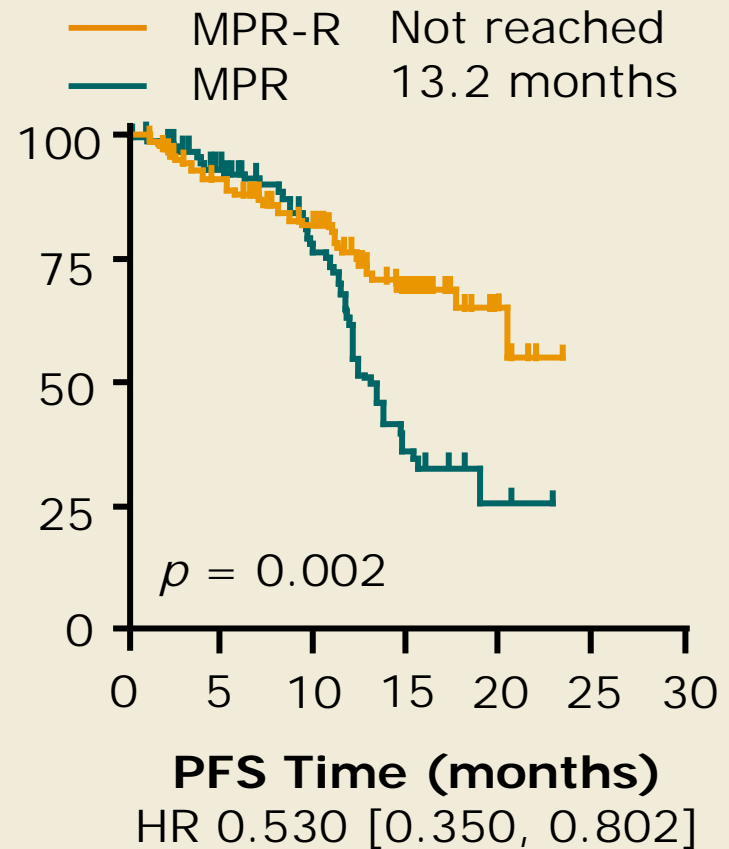
* Measured by EBMT criteria

Median Progression-Free Survival (PFS)

Primary Analysis MPR-R vs MP



Secondary Analysis MPR-R vs MPR



With permission from Palumbo A et al. *Proc ASH* 2009; Abstract 613.

Conclusions

- Continuous lenalidomide is superior to regimens of limited duration in patients ≥ 65 years with NDMM.
- MPR-R resulted in an approximately 50% reduced risk of progression compared to MP.
- MPR-R had a tolerable safety profile (data not shown).
 - No Grade 3/4 peripheral neuropathy
 - Grade 4 neutropenia: 36%
- MPR-R is a potential new standard treatment option for elderly patients with NDMM.

Faculty Comments

DR RICHARDSON: This Phase III study demonstrated the efficacy and safety of lenalidomide both as part of induction therapy in combination with MP and as maintenance therapy.

Melphalan/prednisone/lenalidomide (MPR) followed by lenalidomide causes superior responses and a substantially reduced risk of disease progression over time in comparison to MP alone.

The safety profile is manageable, with only a few patients developing neuropathy of any kind and an overall low discontinuation rate of 16 percent, even with a 36 percent rate of Grade IV neutropenia.

Faculty Comments (Continued)

DR JAGANNATH: Even though higher numbers of responses occur with MPR without R maintenance therapy compared to MP, the progression-free survival curves are absolutely superimposable.

However, PFS is significantly superior when MPR is followed by R maintenance compared to MP. Clearly lenalidomide maintenance after melphalan/prednisone seems to be the key.

**A Prospective, Multicenter,
Randomized Trial of Bortezomib/
Melphalan/Prednisone (VMP) versus
Bortezomib/Thalidomide/Prednisone
(VTP) as Induction Therapy Followed
by Maintenance Treatment with VT
versus VP in Elderly Untreated
Patients with Multiple Myeloma
Older than 65 Years**

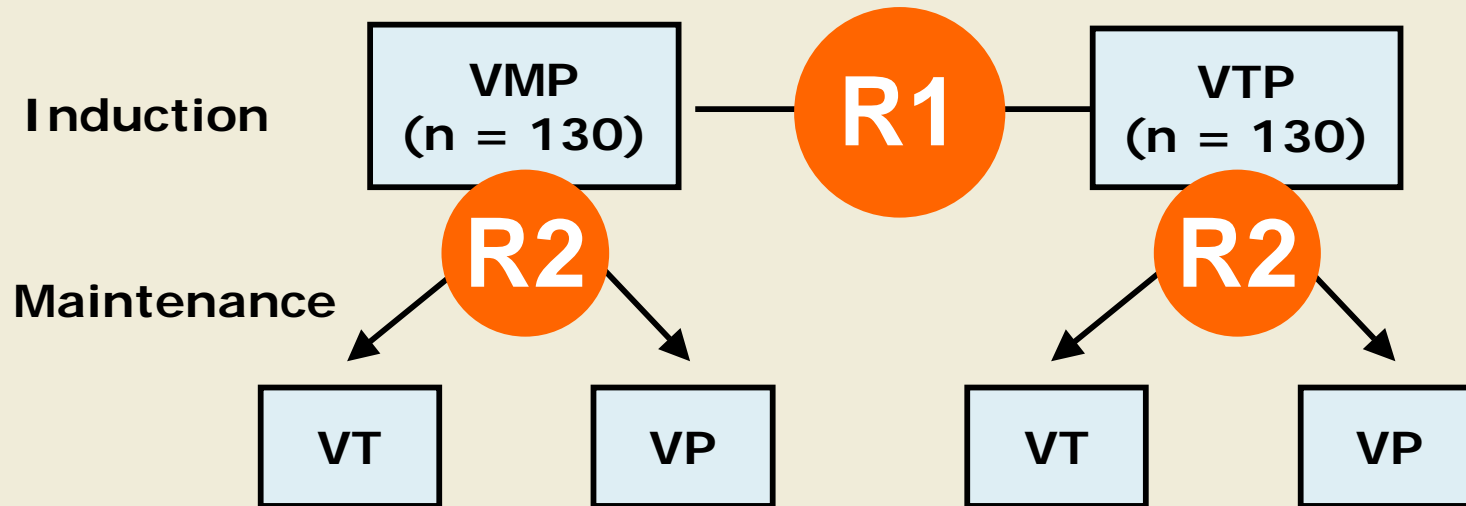
Mateos MV et al.

Proc ASH 2009; Abstract 3.

Introduction

- VMP is tolerable and effective in elderly patients.
 - 89% > PR; 32% CR (*Blood* 2006;108:2165)
 - Median PFS = 25 months (*Haematologica* 2008;93:560)
 - Overall survival = 50 months
 - 17% GIII-IV peripheral neuropathy
- **Current study objectives:**
 - Compare the efficacy (ORR and CR rate) of VMP vs VTP when used as induction therapy
 - Assess if maintenance therapy (VT vs VP) can improve response rates with a favorable toxicity profile
 - Increase CR by 15% (from 20-35% to 35-40%)

Induction with VMP versus VTP Followed by Maintenance with VT versus VP for Untreated MM in Patients > 65 Years



Bortezomib (V): Induction phase, 1.3 mg/m² twice weekly during a 6-week first cycle, then weekly during subsequent cycles; maintenance phase, 1.3 mg/m² twice weekly days 1, 4, 8 and 11 every 3 months

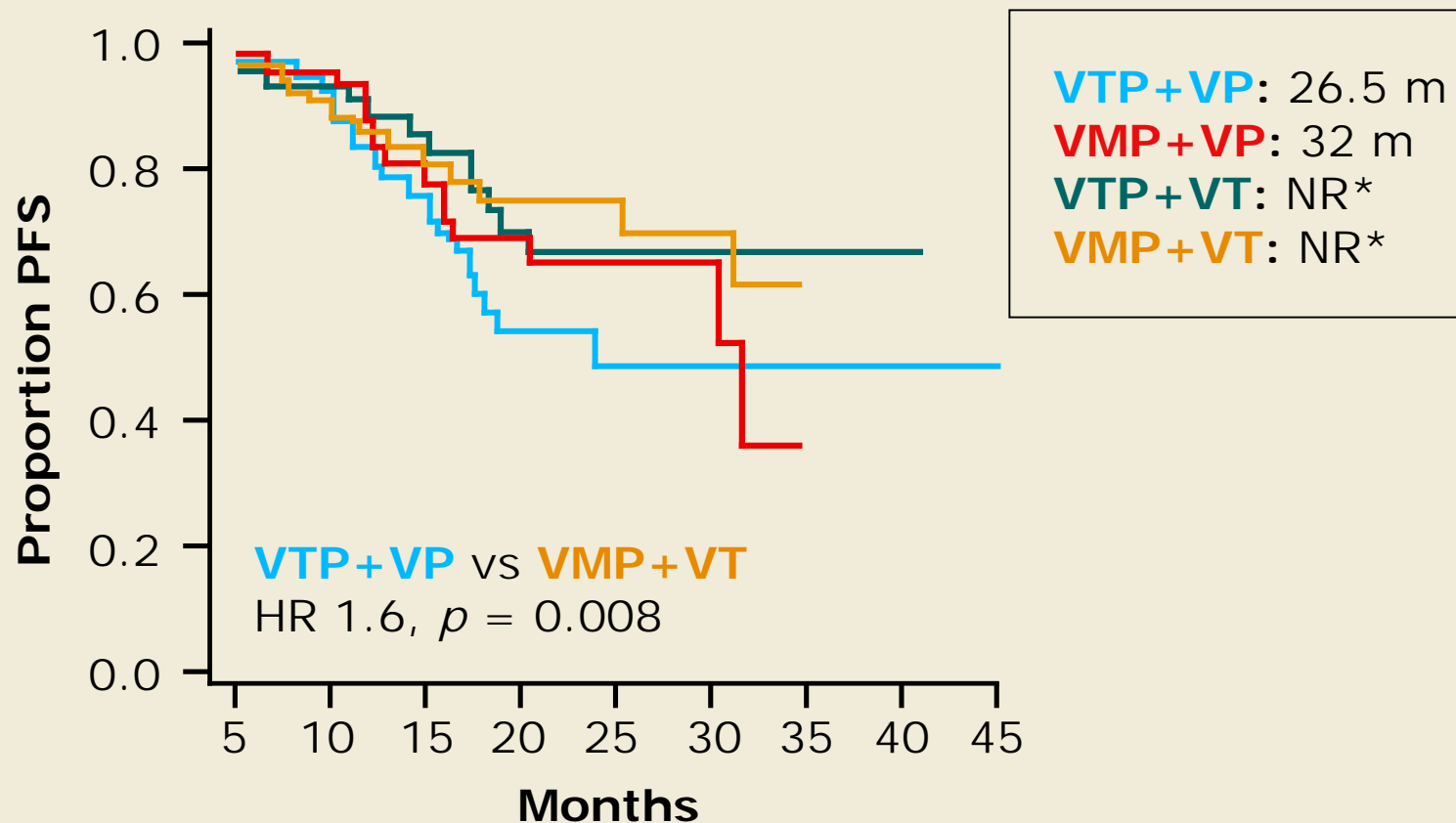
Induction: Response and Toxicity Profile

| Response Rate (EBMT criteria) | VMP | VTP |
|--------------------------------------|-----|-----|
| ORR | 80% | 81% |
| CR immunofixation (CRIF)-negative | 20% | 27% |
| CRIF-positive | 12% | 10% |
| PR | 48% | 46% |
| Select Adverse Events (\geq G3-4) | VMP | VTP |
| Infections | 7% | <1% |
| Peripheral neuropathy | 5% | 9% |
| Cardiologic events | 0% | 8% |

Maintenance: Response and Toxicity Profile

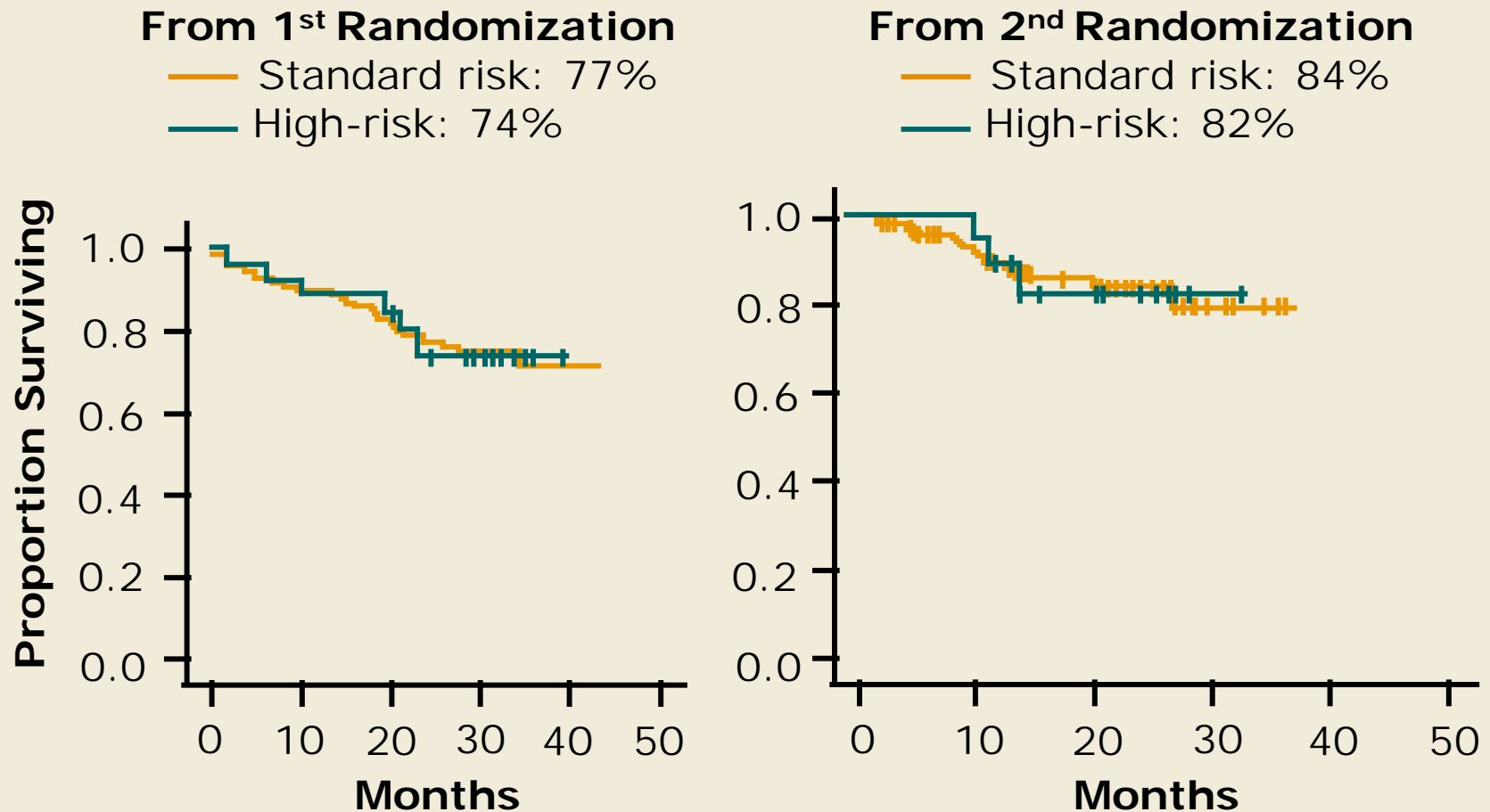
| Response Rate (EBMT criteria) | VT (n = 91) | VP (n = 87) |
|--------------------------------------|-------------|-------------|
| CR/nCR | 59% | 55% |
| CRIF-negative | 44% | 39% |
| CRIF-positive | 15% | 16% |
| PR | 39% | 44% |
| Select Adverse Events (\geq G3-4) | VT (n = 91) | VP (n = 87) |
| Peripheral neuropathy | 5% | 2% |
| Cardiologic events | 2% | 1% |

Median PFS by Induction-Maintenance Treatment Cohorts (n = 178)



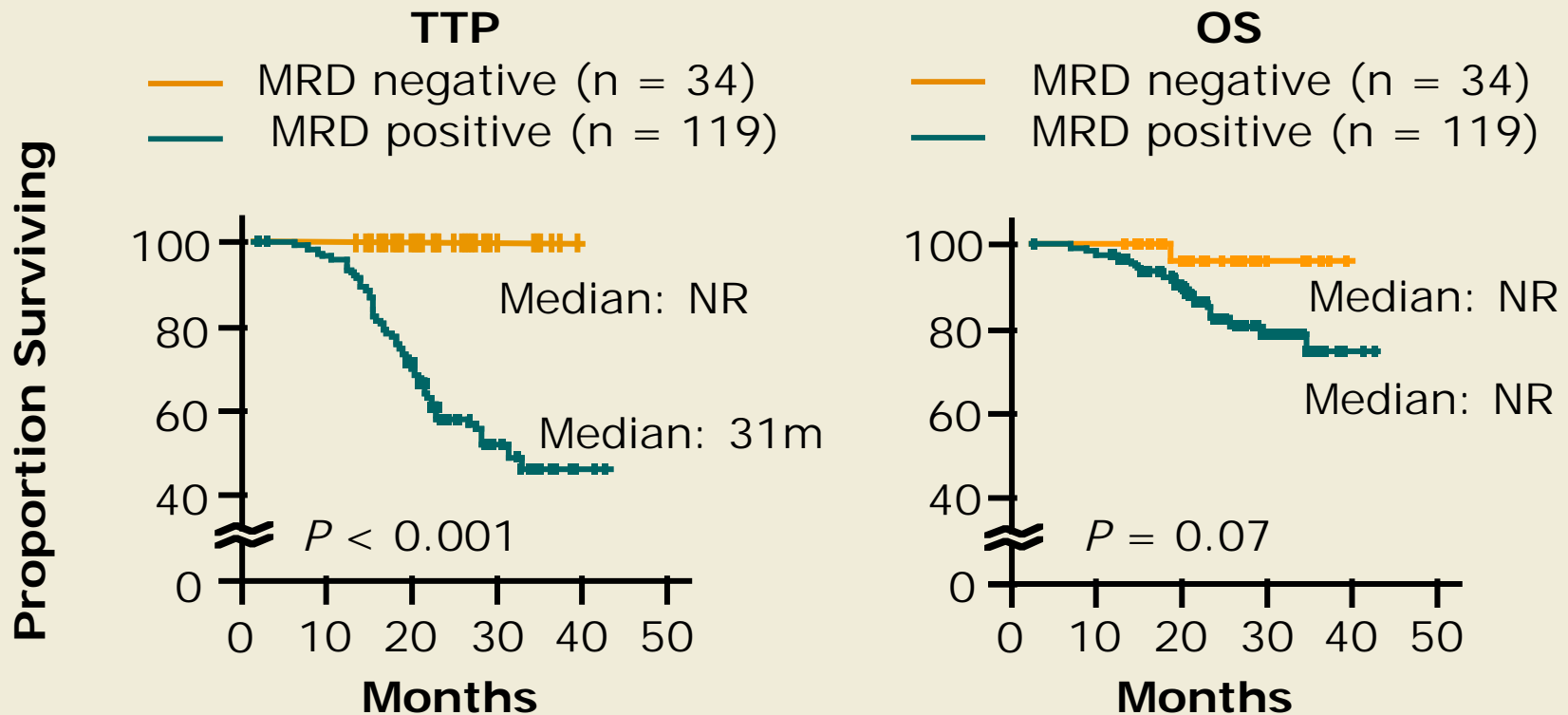
* NR = not reached

Two-Year Overall Survival According to Cytogenetic Risk Profile (VMP or VTP Followed by VT or VP)



With permission from Mateos MV et al. *Proc ASH* 2009; Abstract 3.

Survival According to MRD* After Induction Therapy (VMP or VTP Followed by VT or VP)



* Minimal residual disease (MRD) assessed by immunophenotyping in bone marrow

Conclusions

- Weekly bortezomib dosing resulted in less peripheral neuropathy compared to rates seen with historical biweekly administration.
- Maintenance therapy increased the CR rate with an acceptable toxicity profile.
- Progression-free survival with induction VMP followed by maintenance VT is significantly superior to VPT-TP.
- The bortezomib-based combinations appeared to overcome the poor prognosis of high-risk cytogenetics.
- Alkylating agents remain effective drugs for elderly patients with previously untreated multiple myeloma.

Faculty Comments

DR RICHARDSON: Response rates are impressive and similar with either of the three-drug induction regimens. VMP causes more myelosuppression and bortezomib/thalidomide/prednisone (VTP) is associated with cardiac events and slightly more neuropathy.

A critical aspect of this study is maintenance therapy with VT or VP. VT has a marginally worse adverse event profile, but PFS results strongly favor VT maintenance.

Faculty Comments (Continued)

DR ORLOWSKI: Bortezomib was administered weekly after the first cycle in the induction phase, and this led to less neuropathy in both arms despite maintaining efficacy. A significant improvement in PFS occurs with VT relative to VP maintenance.

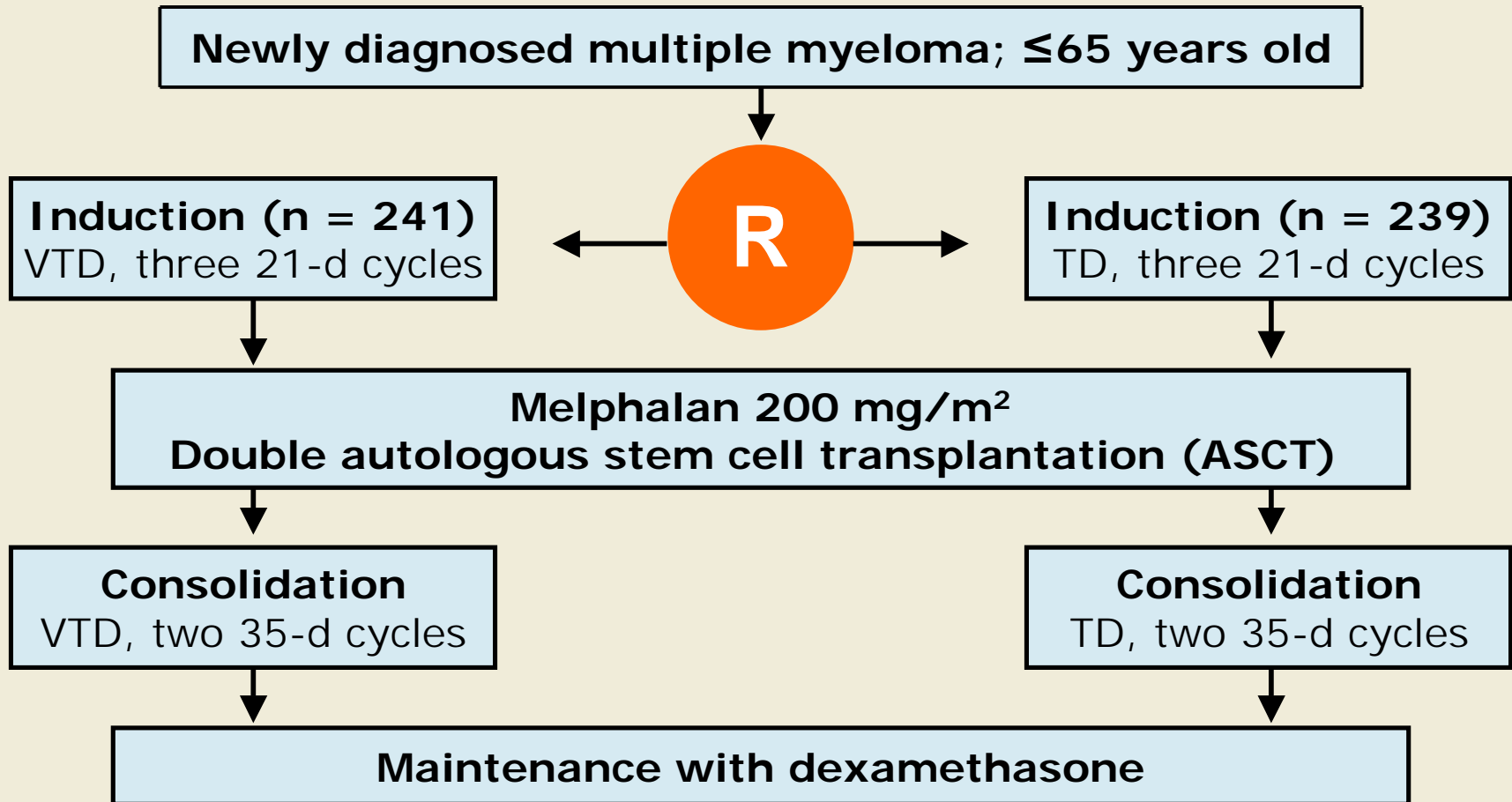
There is also a suggestion that patients who started out with VMP and then received VT maintenance therapy had the best PFS. PFS was also better for patients with no minimal residual disease (MRD) in follow-up, and this is the first time that the correlation between no MRD and positive long-term outcome has been described in myeloma.

A Phase III Study of Double Autotransplantation Incorporating Bortezomib-Thalidomide-Dexamethasone (VTD) or Thalidomide-Dexamethasone (TD) for Multiple Myeloma: Superior Clinical Outcomes with VTD Compared to TD

Cavo M et al.

Proc ASH 2009; Abstract 351.

Trial Schema



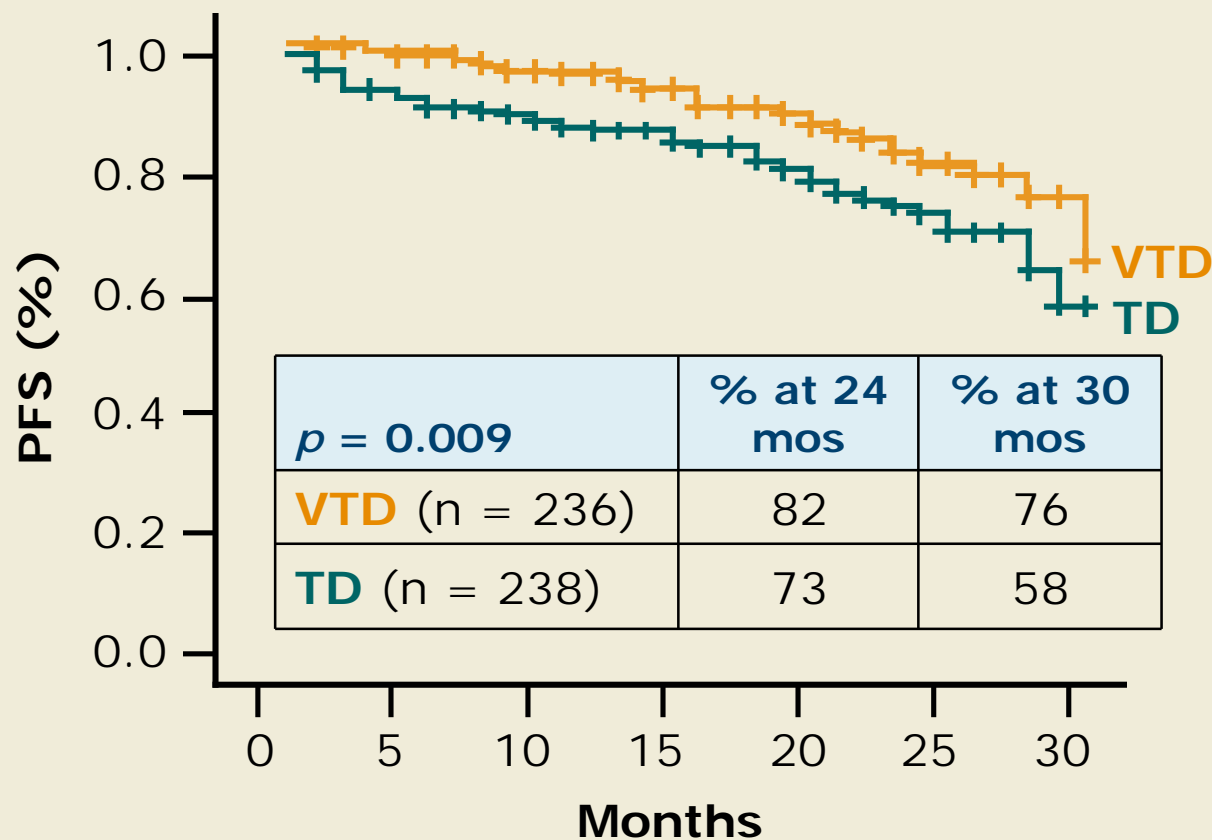
Response to Induction Therapy Intent-to-Treat Analysis*

| | VTD (n = 241) | TD (n = 239) | p-value |
|----------|------------------|-----------------|---------|
| CR | 57% | 31% | 0.0001 |
| CR + nCR | 70% | 51% | <0.0001 |
| ≥VGPR | 88% | 72% | <0.0001 |
| ≥PR | 95% | 89% | 0.01 |

CR, complete response; nCR, near complete response; VGPR, very good partial response; PR, partial response.

** Responses were centrally reassessed and defined by EBMT criteria.*

Progression-Free Survival (PFS)



With permission from Cavo M et al. *Proc ASH* 2009; Abstract 351.

PFS in Patients with High-Risk Cytogenetic Profiles*

| | VTD | | TD | |
|-----------------|----------|----------|----------|----------|
| | Positive | Negative | Positive | Negative |
| Events | 22.7% | 12.1% | 36% | 20.3% |
| PFS at 24 mo | 73% | 83% | 53% | 77% |
| PFS at 30 mo | 60% | 67% | 42% | 59% |
| <i>p</i> -value | 0.16 | | 0.02 | |

* Patients with $t(4;14) \pm del(17p)$

Conclusions

- VTD plus double ASCT provided superior short- and long-term outcomes to TD plus double ASCT.
 - The rates of CR + nCR/ \geq VGPR were significantly improved with VTD vs TD.
 - PFS was significantly improved with VTD vs TD.
- The toxicity of VTD as an induction and consolidation therapy was relatively low (data not shown).
- The VTD regimen may be considered as a new standard treatment option for younger ASCT-eligible patients with multiple myeloma.

Faculty Comments

DR GIRALT: This study shows that induction therapy before transplant makes a difference.

Bortezomib/thalidomide/dexamethasone (VTD) improved complete response (CR) rates and PFS. For patients who undergo stem cell transplants, a bortezomib-containing induction therapy should be considered a standard approach.

To date, no study has compared a bortezomib-based induction therapy to a lenalidomide-based induction therapy, so both strategies could be considered appropriate for these patients.

Faculty Comments (Continued)

DR ORLOWSKI: Notice that the induction on the VTD arm consists of three 21-day cycles — about nine weeks of induction therapy — which is substantially shorter than the standard 16 weeks of induction. Despite this limited duration, all efficacy outcomes, including CR and PFS, improved with VTD.

Incorporation of bortezomib also improved outcomes for patients at high risk. Other approaches are likely still needed to further enhance efficacy in the presence of high-risk cytogenetic features, but this is definitely an encouraging improvement in that category also.

Lenalidomide Plus High-Dose Dexamethasone versus Lenalidomide Plus Low-Dose Dexamethasone as Initial Therapy for Newly Diagnosed Multiple Myeloma: An Open-Label Randomised Controlled Trial

Rajkumar SV et al.

Lancet Oncol 2010; 11(1):29-37.

Introduction

- In newly diagnosed multiple myeloma (MM), the response rate with lenalidomide (R) plus high-dose dexamethasone (D) is 91% (*Blood* 2005; 106: 4050).
- **Current study objective:**
 - Assess if R plus low-dose dexamethasone (Rd) can preserve the efficacy of RD but with reduced toxicity
 - Primary study endpoint: Overall response rate (ORR) in first 4 cycles of treatment
 - Survival analysis of patients who received transplant after 4 cycles vs patients who continued Rd beyond 4 cycles

Open-Label Trial of RD versus Rd in MM

Accrual: 445

| Eligibility |
|---|
| Measurable, untreated symptomatic MM or bone marrow plasmacytosis or plasmacytoma |
| Hgb > 70g/L, platelet $\geq 75 \times 10^9$ /L, neutrophil > 1×10^9 /L |



R 25 mg/d + **D** 40 mg/d
d1-4, 9-12, 17-20 q
28 days* (n = 223) x
4 cycles

R 25 mg/d + **d** 40 mg/d
d1, 8, 15, 22 q 28 days*
(n = 222) x 4 cycles

** After 4 cycles, patients may proceed to stem cell transplant (SCT); patients with progression or no response may receive thalidomide + dexamethasone.*

Select Adverse Events (AE) in First Four Months

| AE | RD (n = 223) | Rd (n = 220) | p-value |
|---|-----------------|-----------------|---------|
| ≥Grade III | 52% | 35% | 0.0001 |
| Deaths | 5% | 0.4% | 0.003 |
| Deep vein thrombosis or pulmonary embolism | 26% | 12% | 0.0003 |
| Infections or pneumonia | 16% | 9% | 0.04 |
| Fatigue | 15% | 9% | 0.08 |

Primary Study Results: Overall Response and Survival

| | RD (n = 214) | Rd (n = 208) | p-value |
|---|--------------------------|--------------------------|---------|
| ORR (complete plus partial) at 4 cycles | 79% | 68% | 0.008 |
| 1-year overall survival (OS)* < 65 years old ≥ 65 years old 2-year OS* | 87% 91% 83% 75% | 96% 98% 94% 87% | 0.0002 |
| Successful stem cell mobilization (n = 167) | 163 (98%) | | |

** Not a protocol-specified endpoint; study stopped at 12.5 months follow-up because of higher OS with Rd. Patients on RD crossed over to Rd.*

Survival Outcome with Post-Induction SCT, No SCT or Continued Primary Therapy*

| Three-year overall survival | RD | Rd | p-value |
|---|-----|-----|--------------|
| No SCT after 4 cycles of primary therapy (n = 54, 39) | 55% | 55% | 0.631 |
| SCT after 4 cycles of primary therapy (n = 50, 40) | 92% | 92% | 0.528 |
| Primary therapy beyond 4 cycles (n = 108, 140) | 79% | 79% | Not reported |

** At four months, 183 of 431 patients alive discontinued from study +/- subsequent SCT and 248 continued primary therapy in the absence of SCT.*

Conclusions

- Primary analysis of induction RD vs Rd
 - ORR RD vs Rd: 79% vs 69% (absolute difference within prespecified margin of noninferiority)
 - Lower toxicity and treatment-related mortality with Rd (0.5% vs 5.0%)
 - Greater 2-year OS with Rd (87% vs 75%)
- Impact of SCT and continued primary therapy on outcome
 - Lenalidomide plus dexamethasone may be a good option for pretransplant induction therapy (3-year OS: 92%)
 - Continued primary therapy (>4 cycles) with Rd seems effective and tolerable as a front-line regimen for myeloma, particularly in the elderly

Faculty Comments

DR GIRALT: Survival was significantly better on the lenalidomide/low-dose dexamethasone (Rd) arm despite a lower response rate.

Rd is an excellent option for transplant-eligible patients as the three-year survival rate with Rd followed by transplant is approximately 92 percent.

This is also a good induction regimen for transplant-ineligible patients as it is well tolerated and resulted in a three-year survival rate of 55 percent for patients who did not undergo transplant.

Faculty Comments (Continued)

DR JAGANNATH: The difference in the two arms is the intensity of dexamethasone. Lenalidomide/high-dose dexamethasone (RD) caused significant side effects, especially thrombosis and infections, and thus caused increased mortality, especially among older patients.

However, I believe RD should still be used, especially during the first cycle, for some patients — such as those with renal impairment or hypercalcemia, who need a rapid tumor response. Appropriate prophylaxis for infection and deep vein thrombosis should be administered.

Lenalidomide Plus Dexamethasone versus Thalidomide Plus Dexamethasone in Newly Diagnosed Multiple Myeloma: A Comparative Analysis of 411 Patients

Gay F et al.

Blood 2010;115(7):1343-50.

Introduction

- Lenalidomide and thalidomide are each active in combination with dexamethasone for the treatment of multiple myeloma (MM).
 - Lenalidomide is more potent in preclinical assays than thalidomide, but causes more hematologic side effects (*Blood* 2002; 100: 3063; *NEJM* 2007; 357: 2123).
- No randomized trial of thalidomide/dexamethasone (Thal/Dex) versus lenalidomide/dexamethasone (Len/Dex) has been reported or is ongoing/planned.
- **Current study objective:**
 - Compare the efficacy and toxicity of Len/Dex or Thal/Dex as initial therapy for MM using a retrospective analysis.

Methods

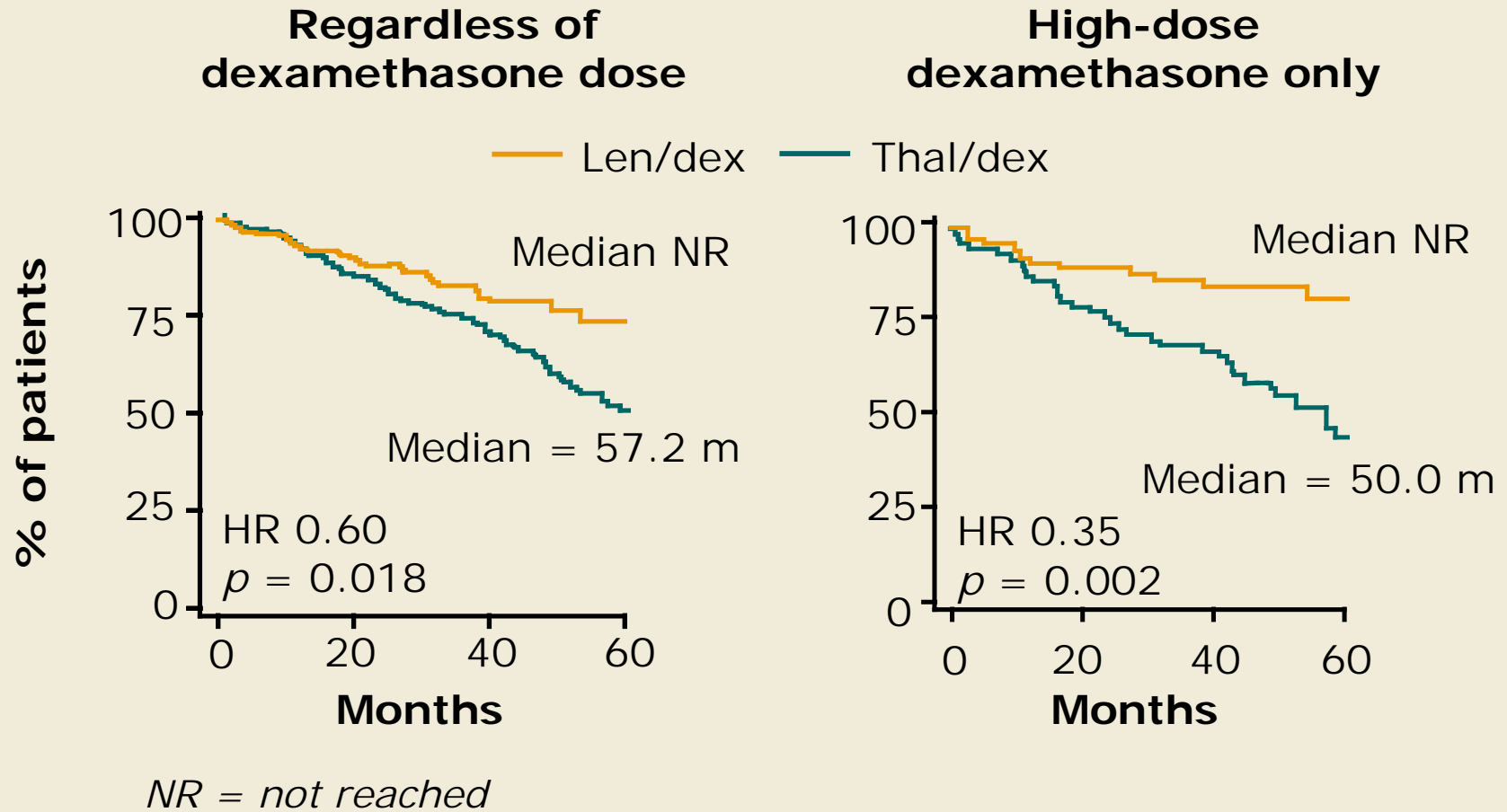
- Case-control retrospective study conducted using data from 411 consecutive patients from the Mayo Clinic with newly diagnosed MM.
 - Patients treated with Thal/Dex: 183 (110 received SCT)
 - Patients treated with Len/Dex: 228 (111 received SCT)
- All patients were administered either:
 - High-dose dexamethasone (40 mg orally, twice weekly)
 - Low-dose dexamethasone (40 mg orally, weekly)
- Risk stratification of patients:
 - High risk: del 17p, t(4;14), t(14;16) by FISH or loss of chromosome 13 by metaphase cytogenetics
 - Standard risk: Patients without any of the above

Efficacy Outcomes

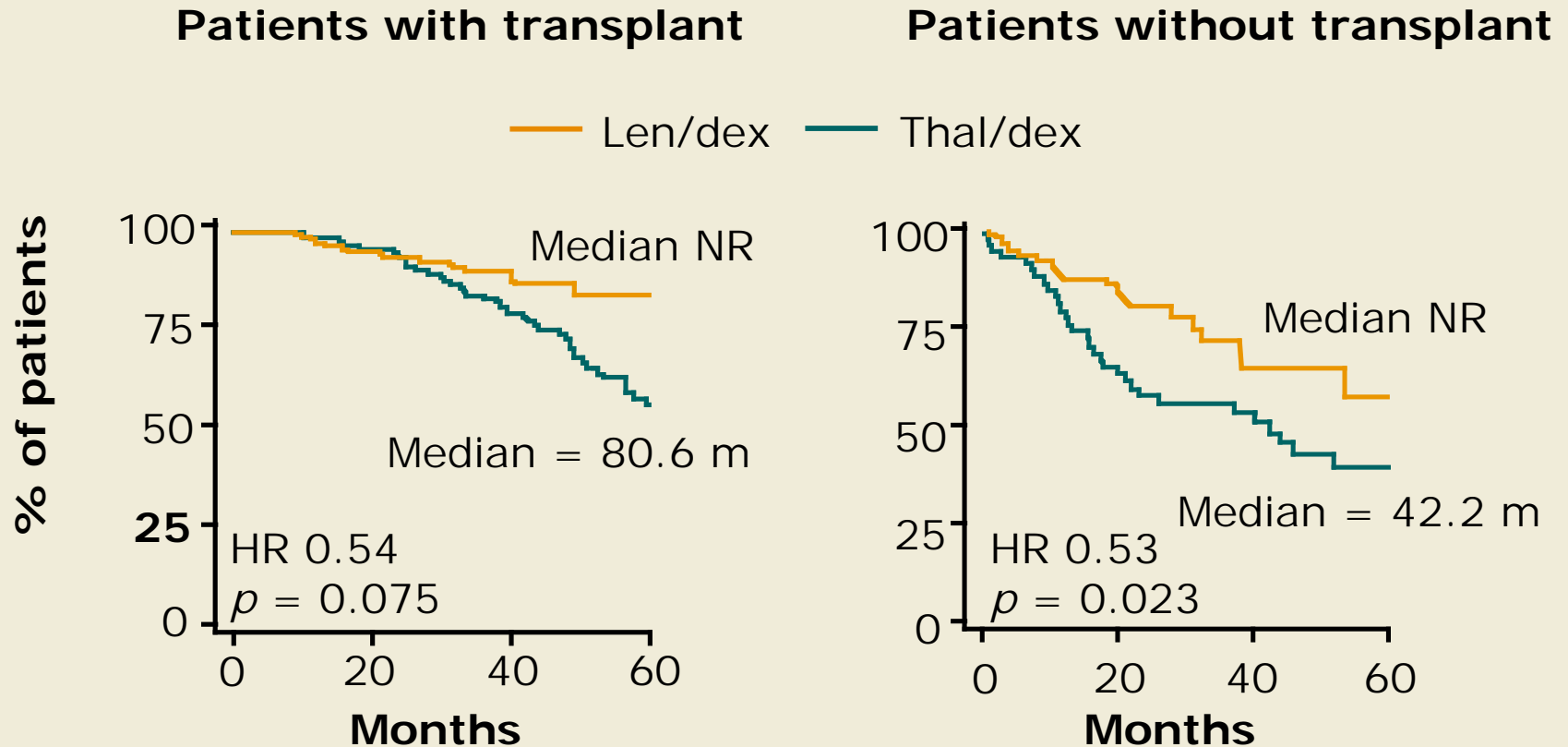
| Efficacy | Thal/Dex (n = 183) | Len/Dex (n = 228) | p-value |
|----------------------------|-----------------------|----------------------|---------|
| CR | 3.3% | 13.6% | <0.001 |
| ≥VGPR | 12.0% | 34.2% | <0.001 |
| ≥PR | 61.2% | 80.3% | <0.001 |
| Median time to progression | 17.2 mo | 27.4 mo | 0.019 |
| Progression-free survival | 17.1 mo | 26.7 mo | 0.036 |

*CR = complete response; VGPR = very good partial response;
PR = partial response*

Median Overall Survival with Len/Dex versus Thal/Dex



Overall Survival with Respect To Transplantation Status



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Gay F et al. *Blood* 2010;115(7):1343-50.

Grade 3 and 4 Adverse Events

| Adverse event | Thal/Dex (n = 183) | Len/Dex (n = 228) | p-value |
|------------------------|-----------------------|----------------------|---------|
| Anemia | 0% | 4.4% | 0.003 |
| Thrombocytopenia | 0% | 4.8% | 0.002 |
| Neutropenia | 0.6% | 14.0% | <0.001 |
| Peripheral neuropathy | 10.4% | 0.9% | <0.001 |
| Constipation | 4.9% | 0% | 0.001 |
| Diarrhea | 0% | 3.5% | 0.01 |
| Venous thromboembolism | 15.3% | 9.2% | 0.058 |
| Infections | 8.2% | 13.1% | 0.109 |

Summary

- Len/Dex appears superior to Thal/Dex in all efficacy outcomes including overall survival.
- Outcomes remain superior with Len/Dex after adjusting for the dose of dexamethasone and for transplantation status.
- Differences in the adverse events with the two regimens are consistent with what has been previously reported.
 - Hematological side effects were more common with lenalidomide; peripheral neuropathy was more common with thalidomide.
- Randomized trials are required for confirmation of these results.

Faculty Comments

DR GIRALT: The results of this retrospective analysis support the hypothesis that induction therapy with lenalidomide/dexamethasone (len/dex) is superior to that of thalidomide/dexamethasone (thal/dex).

The higher complete and overall response rates recorded with len/dex were statistically significant and clinically relevant.

A survival benefit was observed with len/dex as induction versus thal/dex irrespective of transplant status or whether high- or low-dose dexamethasone was administered.

Faculty Comments (Continued)

In the absence of randomized clinical trials and recognizing the caveats of a retrospective study, I cannot say definitively that patients should receive induction therapy with len/dex over thal/dex.

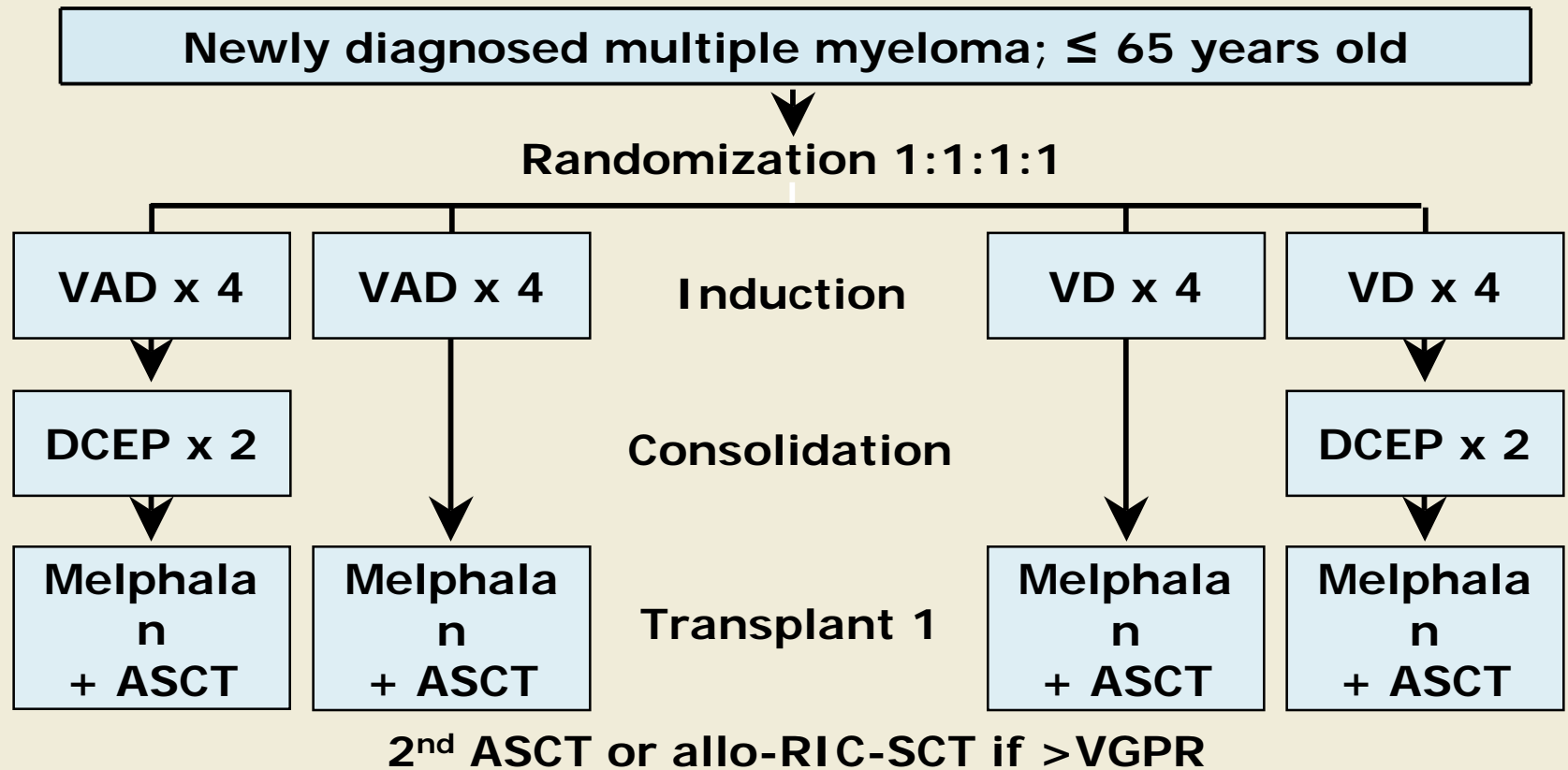
However, in my practice I have begun to offer this as a potential induction therapy for those patients with low-risk disease, those considered to be transplant ineligible or those with preexisting neuropathy.

High Complete and Very Good Partial Response Rates with Bortezomib-Dexamethasone as Induction Prior to ASCT in Newly Diagnosed Patients with High-Risk Myeloma: Results of the IFM2005-01 Phase 3 Trial

Harousseau J-L et al.

Proc ASH 2009; Abstract 353.

Trial Schema



VAD = vincristine/doxorubicin/dexamethasone

VD = bortezomib/dexamethasone

Clinical Response (\geq VGPR)

| | VAD (n = 218) | VD (n = 223) | p-value |
|-----------------|------------------|-----------------|---------|
| After induction | 16% | 39% | <0.0001 |
| After ASCT 1 | 37% | 54% | 0.0003 |
| After ASCT 2 | 47% | 68% | <0.0001 |

A higher response rate was achieved in patients on the VD arm receiving induction therapy despite:

- A slightly higher proportion of patients with poor-risk cytogenetics*
- A smaller proportion of patients having received a second ASCT*

Progression-Free Survival (PFS)

Median Follow-Up 32 Months

| Patient Group | VAD | VD | <i>p</i> -value |
|---|-------|---------|-----------------|
| All patients (n = 242, 240) | 30 mo | 36 mo | 0.057 |
| Patients with ISS Stage II-III (n = 136, 133) | 23 mo | 33 mo | 0.006 |
| Patients with poor cytogenetics* (n = 29, 40) | 24 mo | 33.5 mo | 0.113 |

** Patients with poor cytogenetics were defined as having t(4;14) and/or del(17p).*

Impact of Post-Induction VGPR or Better on PFS

| Patient Group | ≥VGPR | <VGPR | p-value |
|---|-------------|-------|---------|
| All patients (n = 117, 324) | 41 mo | 30 mo | <0.0001 |
| Patients with ISS Stage II-III (n = 65, 204) | Not reached | 23 mo | <0.0001 |
| Patients with poor cytogenetics* (n = 21, 48) | 37 mo | 24 mo | 0.0036 |

* Patients with poor cytogenetics were defined as having $t(4;14) \pm del(17p)$.

Conclusions

- Pre-ASCT induction therapy with VD versus VAD resulted in:
 - Longer PFS, irrespective of cytogenetic risk profile
 - Higher rates of complete response and VGPR
- Achieving at least VGPR after induction therapy appears to be a major prognostic factor for improved PFS, especially in patients with high-risk multiple myeloma.

Faculty Comments

DR RICHARDSON: The high rate of responses with bortezomib/dexamethasone (VD) versus vincristine/doxorubicin/dexamethasone (VAD) prior to transplant translated into a longer progression-free survival (PFS), suggesting that the quality of response with induction therapy before transplant really matters. This applied to patients with early-stage and advanced-stage disease in addition to those with adverse cytogenetic features.

Interestingly, achieving at least a very good partial response after induction is an important prognostic factor, especially for patients with ISS Stage II/III disease or those with adverse cytogenetic features.

Faculty Comments (Continued)

DR ORLOWSKI: An important observation is that improvement in PFS occurred with VD in comparison to VAD despite a shorter duration of induction and the fact that a lesser proportion of patients in the bortezomib group received a second transplant.

Additionally, VD overcame the negative outcome predicted by ISS staging and poor-risk cytogenetic features like t(4;14) and/or del 17p.

Bortezomib Plus Melphalan and Prednisone Compared with Melphalan and Prednisone in Previously Untreated Multiple Myeloma: Updated Follow-Up and Impact of Subsequent Therapy in the Phase III VISTA Trial

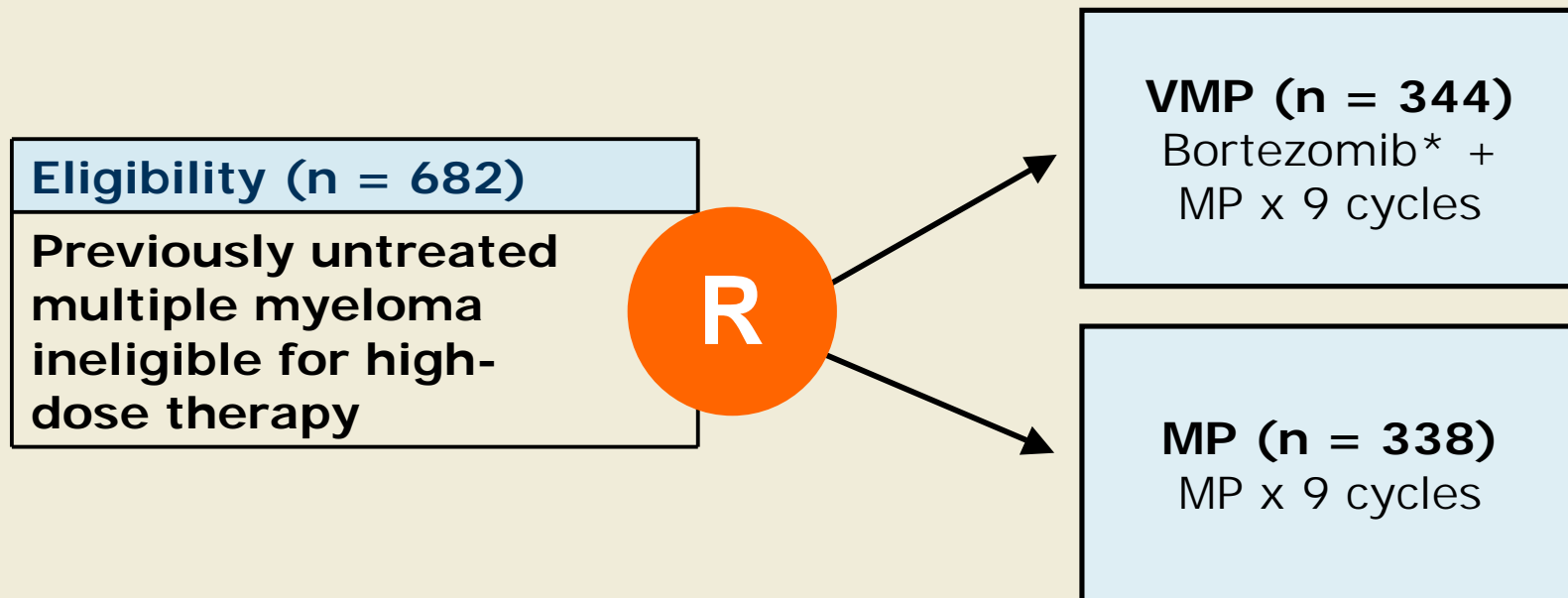
Mateos M-V et al.

J Clin Oncol 2010; 28(13):2259-66.

Introduction

- Overall survival has been shown to be improved with VMP compared with MP in previously untreated patients with multiple myeloma (MM) ineligible for transplant (*NEJM* 2008; 359: 906).
- Rescue therapies may affect overall survival in longer follow-up.
- **Current study objective:**
 - Examine updated survival analysis of bortezomib (V) with melphalan/prednisone (MP) versus MP alone in patients with untreated MM ineligible for high-dose therapy

VISTA Trial Schema

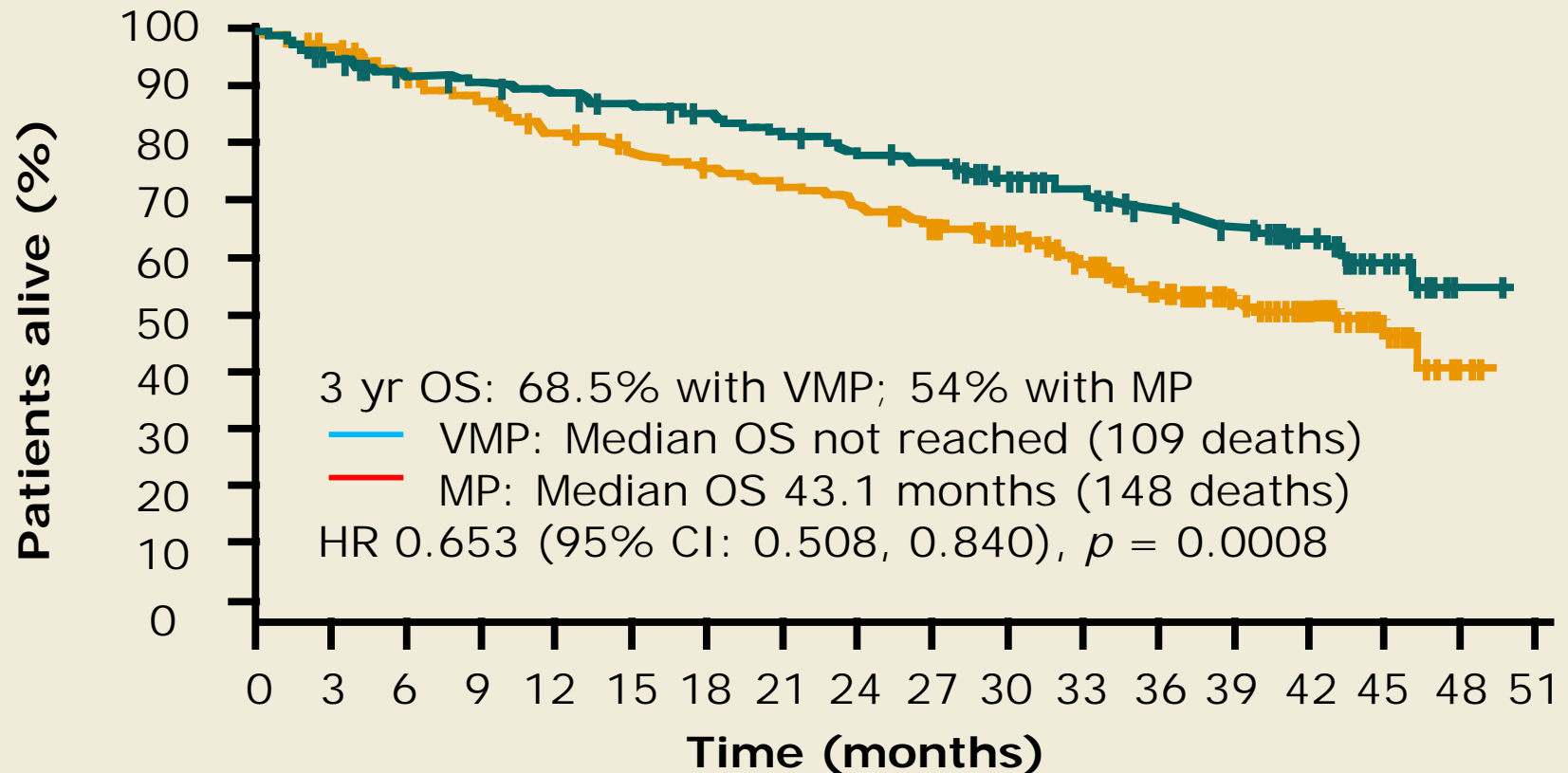


** Bortezomib administered on standard twice-weekly schedule during cycles 1-4. Bortezomib administered on weekly schedule during cycles 5-9.*

Subsequent Therapy

- 52% of patients on VMP and 69% on MP have received subsequent therapy.
- Among patients who received subsequent therapy, 24% on VMP arm and 50% on MP arm received bortezomib.
- Median time to next treatment (TTNT) and treatment free interval (TFI) were significantly longer with VMP.
 - 43% and 18% of VMP and MP patients, respectively, had TFI \geq 2 years

Updated Survival Benefit with VMP (Median Follow-Up 36.7 Months)



With permission, originally published by the American Society of Clinical Oncology.
Mateos M-V et al. *J Clin Oncol* 2010;28(13):2259-66.

Subset Analyses

- Among those patients who received subsequent therapy, the survival benefit with VMP over MP was retained.
- A trend of improved survival from start of subsequent therapy was observed (HR 0.815, $p = 0.21$) in all patients who received subsequent therapy.
- In the VMP subgroup, OS was better among patients aged < 75 vs ≥ 75 years (HR 1.664, $p = 0.011$).
- No statistically significant difference in overall survival among patients treated with VMP was apparent when results were analyzed by baseline renal function or cytogenetic risk profile.

Conclusions

- Updated analysis confirms that VMP results in significantly improved survival compared to MP.
- Survival benefit is seen both overall and also in patients who had received subsequent therapy.
- VMP results in significantly longer TTNT and TFI.
- Salvage therapies are similarly effective following VMP and MP, suggesting that bortezomib use as initial therapy does not induce more resistant relapse.

Faculty Comments

DR RICHARDSON: This updated analysis after more than three years of follow-up confirms that bortezomib/melphalan/prednisone (VMP) improves overall survival compared to MP, and the survival benefit is also evident among patients who received subsequent therapy. This emphasizes the fact that initial treatment matters.

The other important conclusion is that salvage therapies are similarly effective after VMP or MP and that front-line bortezomib does not induce a more resistant relapse.

Faculty Comments (Continued)

DR ORLOWSKI: The median overall survival for patients who received MP is 43.1 months and has not yet been reached for those who received VMP. Three-year overall survival is 54 percent with MP and 68.5 percent for VMP.

Additionally, VMP improves the treatment-free interval and extends the time to next treatment.

Also, the addition of bortezomib appears to be partially overcoming the adverse outcomes from high-risk cytogenetics and renal impairment.