Bortezomib as consolidation after high-dose melphalan and autologous stem cell transplantation in multiple myeloma:

a Nordic Myeloma Study Group (NMSG) randomized trial

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Disclosures

Honoraria: Celgene and Janssen

Study grant: Johnson & Johnson

Objectives

Primary:

Progression free survival

Secondary:

Response
Overall survival
Toxicity
Quality of life

Study design

Open randomized multicenter study

Initial therapy optional (no bortezomib)

Inclusion from stem cell infusion up to 3 months after ASCT

Randomization 3 months post ASCT

Stratification for age (<60 or 60+ years) and single/double ASCT

Bortezomib therapy

Initiated 3 months post ASCT

Standard dose 1.3 mg/m^2

Two initial conventional cycles (day 1, 4, 8 and 11), followed by four cycles of weekly injections for 3 weeks plus 1 week rest

In total, 20 injections over a period of 21 weeks

No doses were postponed, instead dose reduction to zero

No corticosteroids were added

Patient material

403 included from 2006 until April 2009

4 excluded -
- 2 non-secreting myeloma
- 2 not fullfilling diagnostic criteria

399

29 not randomised -
- 17 withdrawn consent
- 4 neuropathy
- 4 progressive disease
- 2 logistic reasons
- 1 death
- 1 infection

370

188 Bortezomib

182 Control

Toxicity

Hematological:

Neutropenia

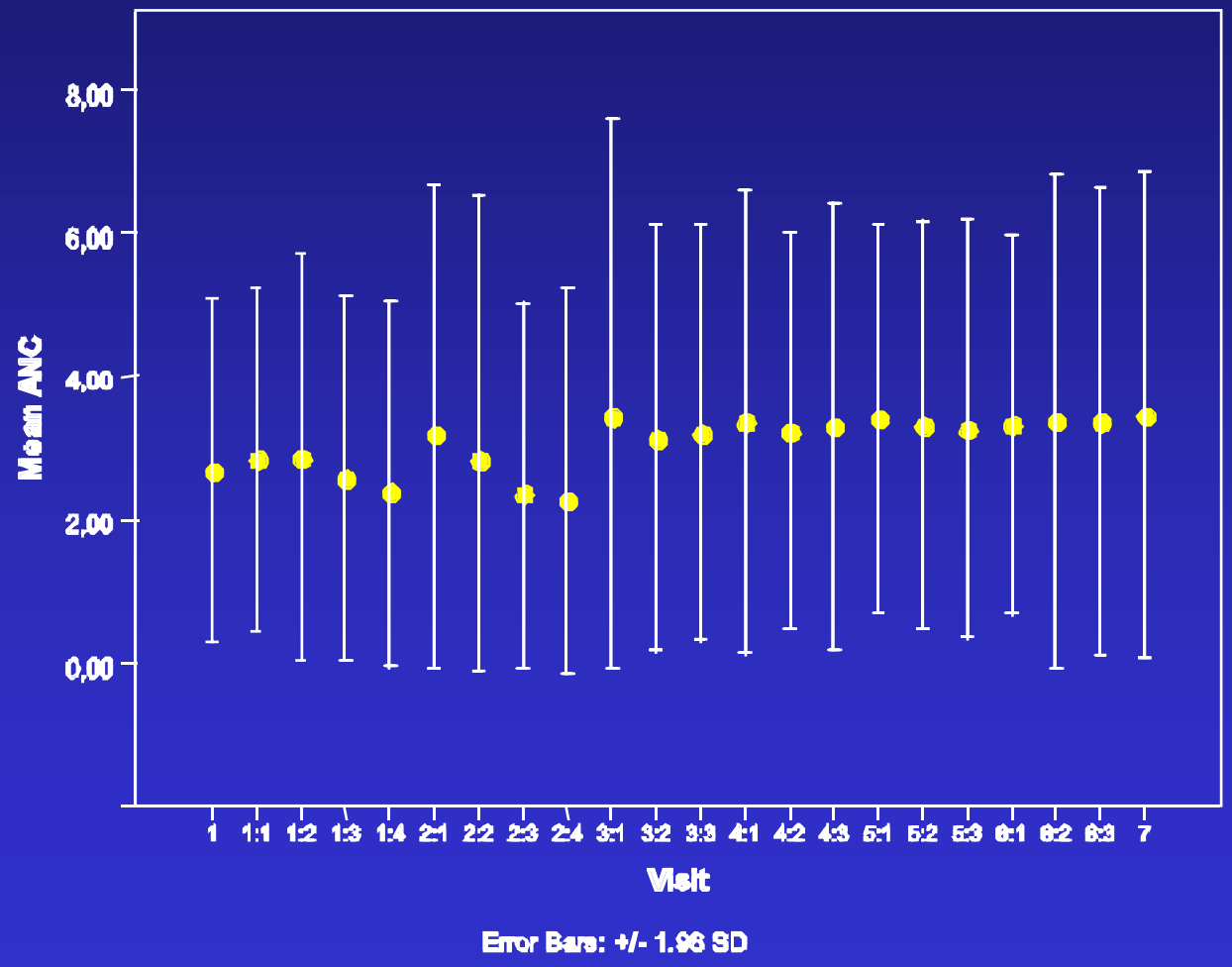
Thrombocytopenia

Neurological:

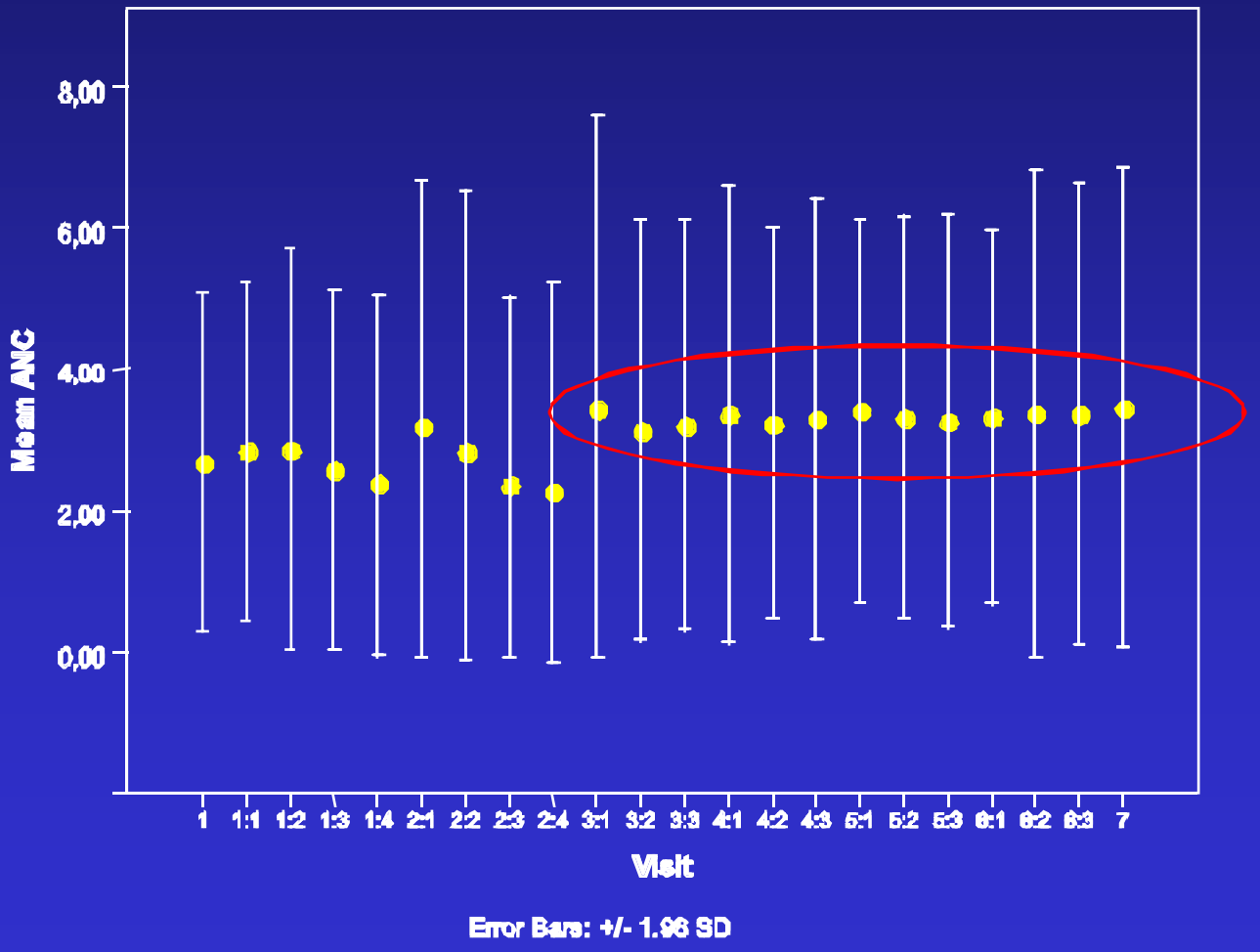
Neuropathic pain

Peripheral sensory neuropathy

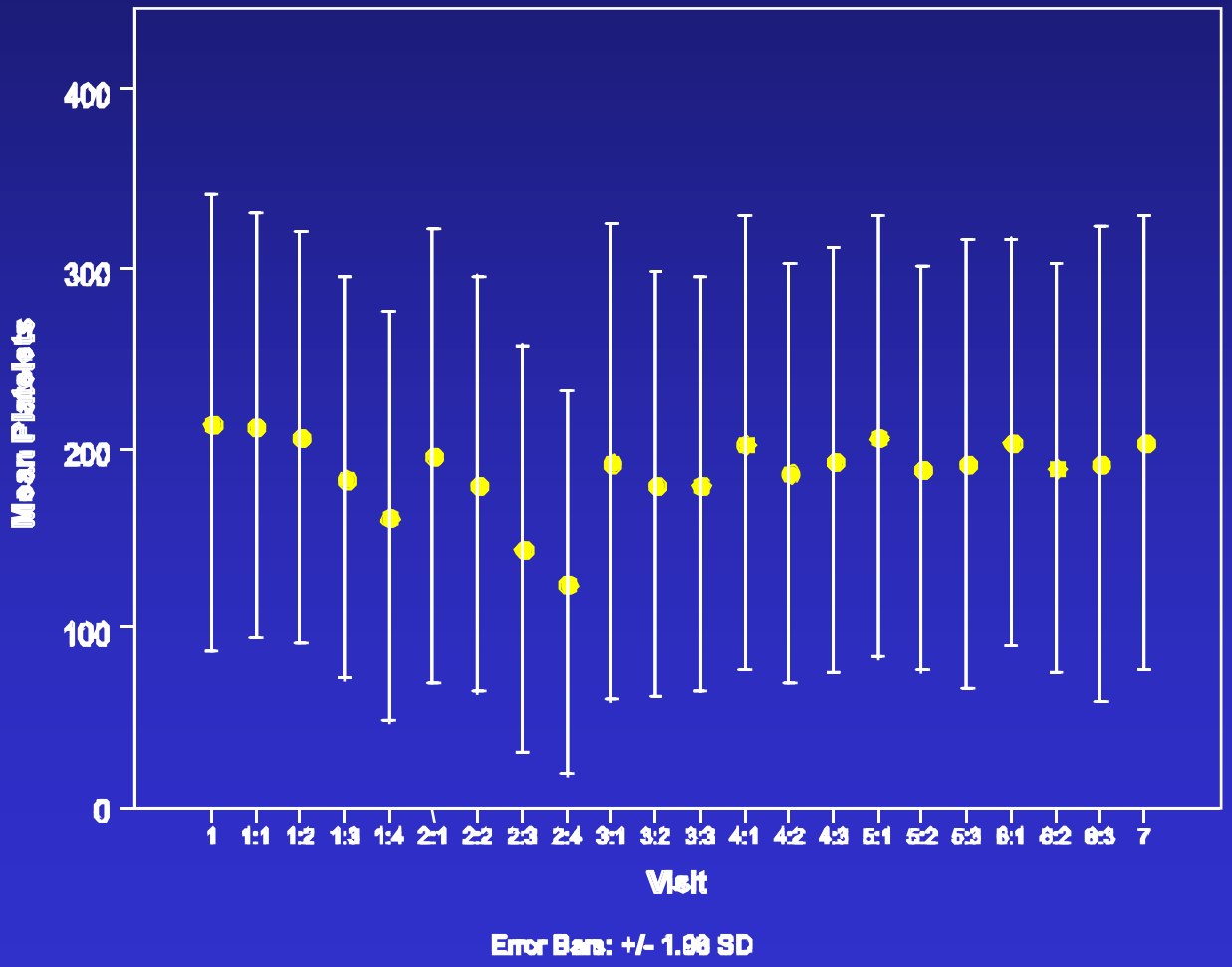
Mean neutrophil count



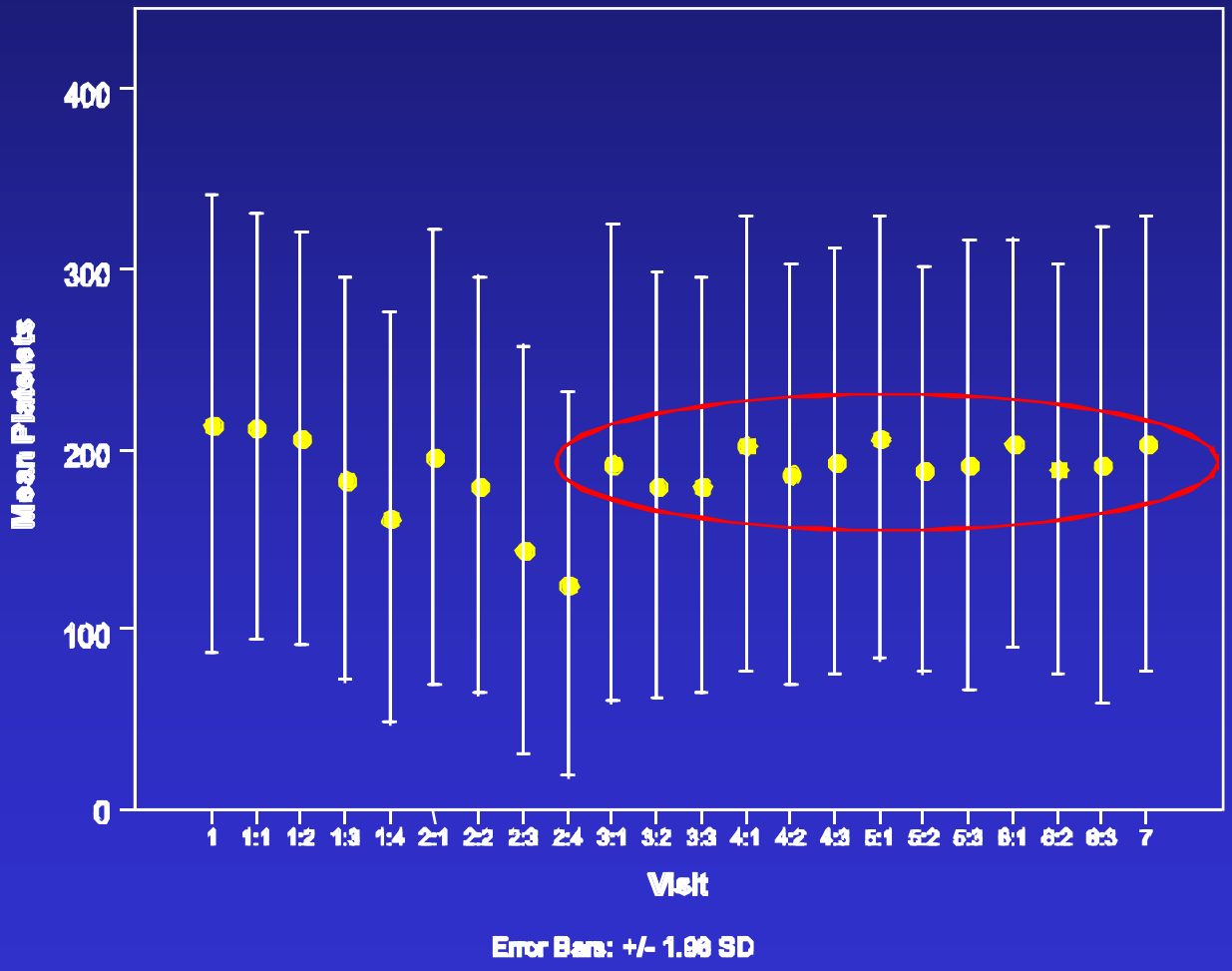
Mean neutrophil count



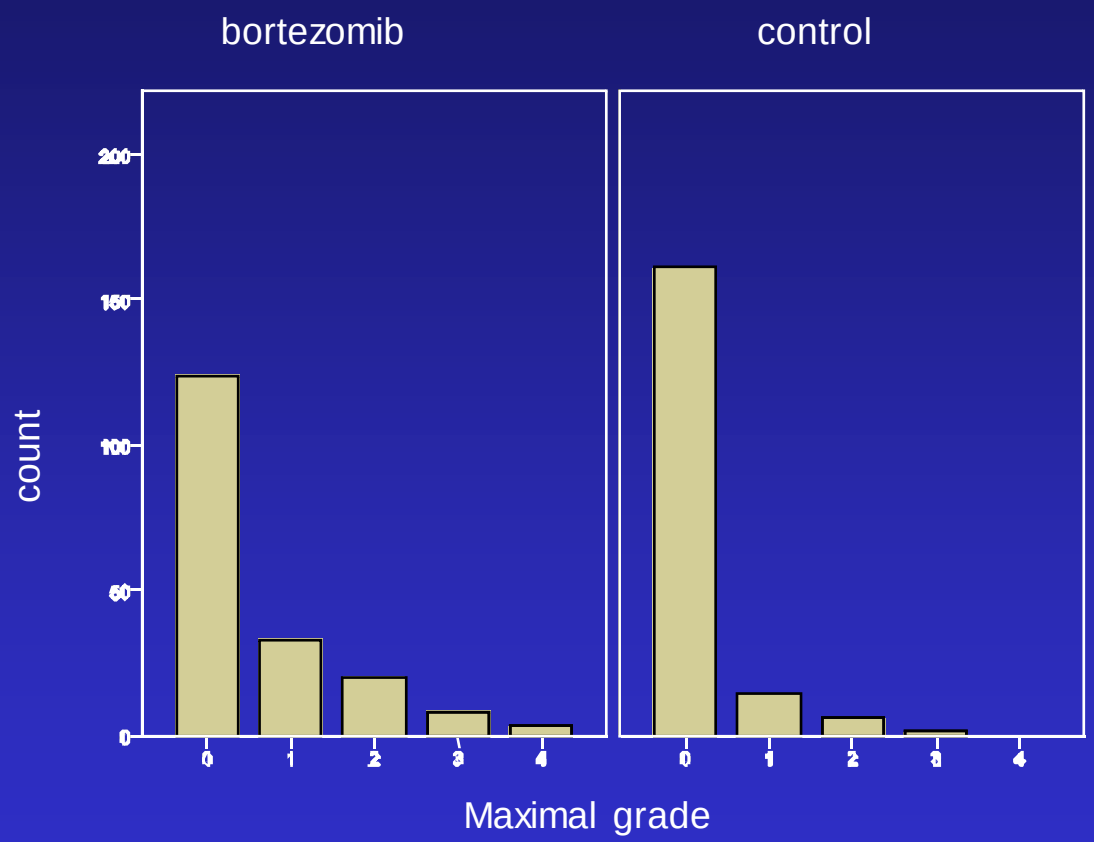
Mean platelet count



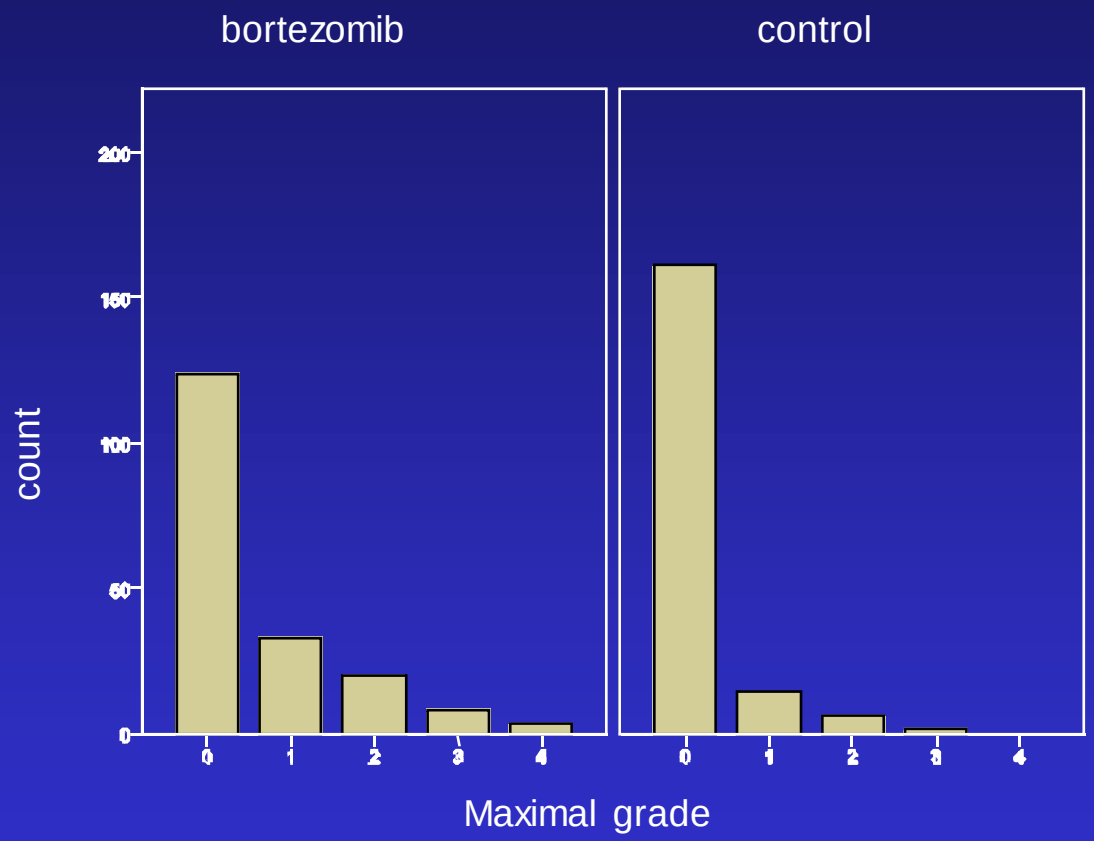
Mean platelet count



Neuropathic pain

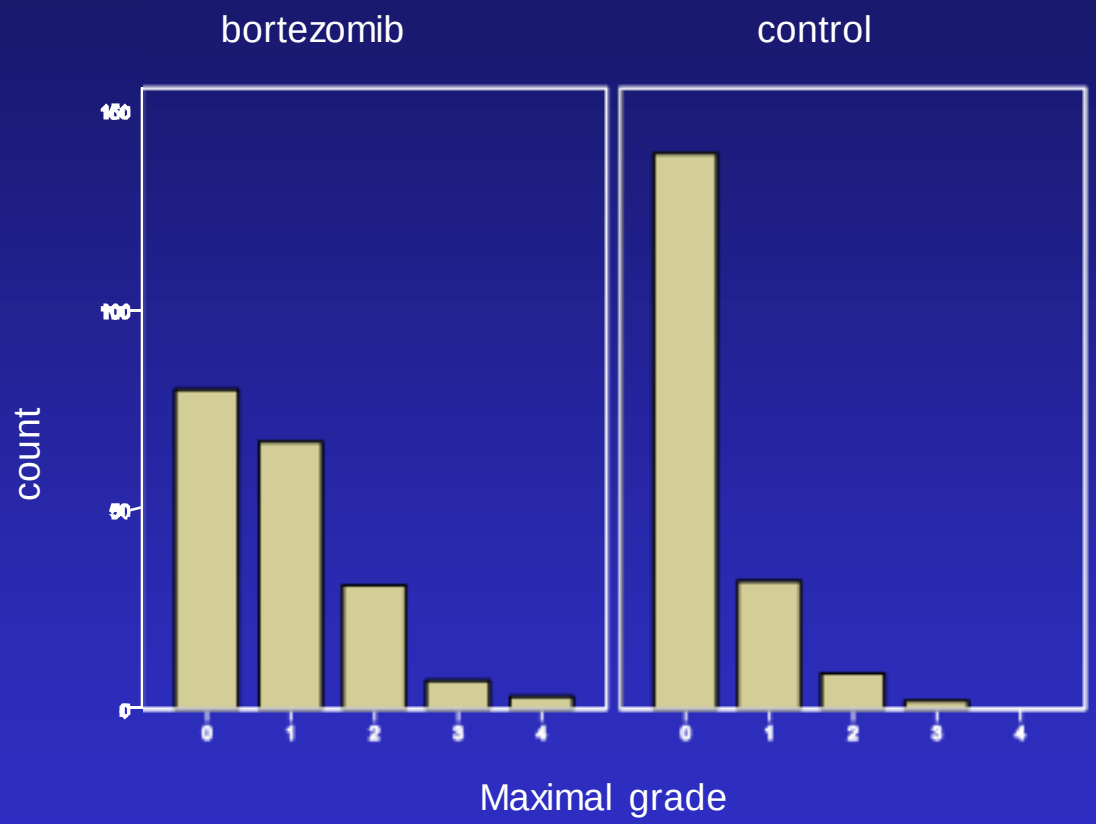


Neuropathic pain

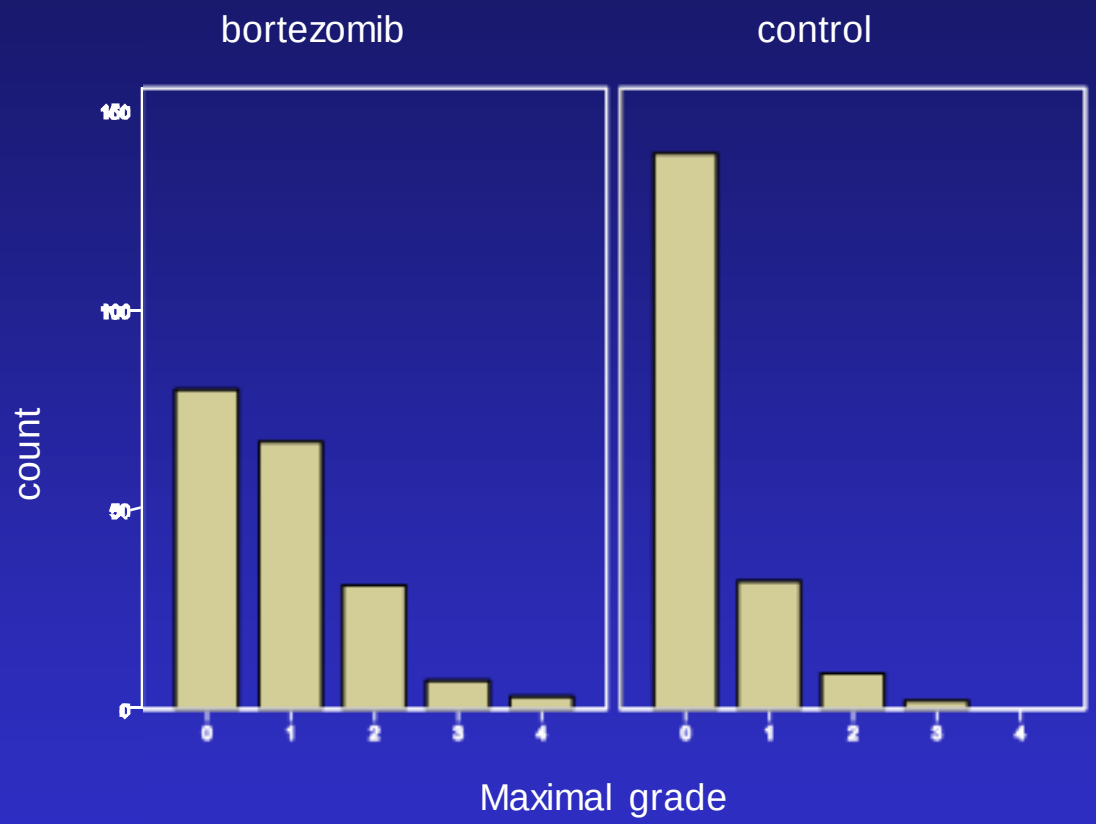


CTC ≥ III bortezomib 6 %
control 0.5 %

Peripheral sensory neuropathy



Peripheral sensory neuropathy

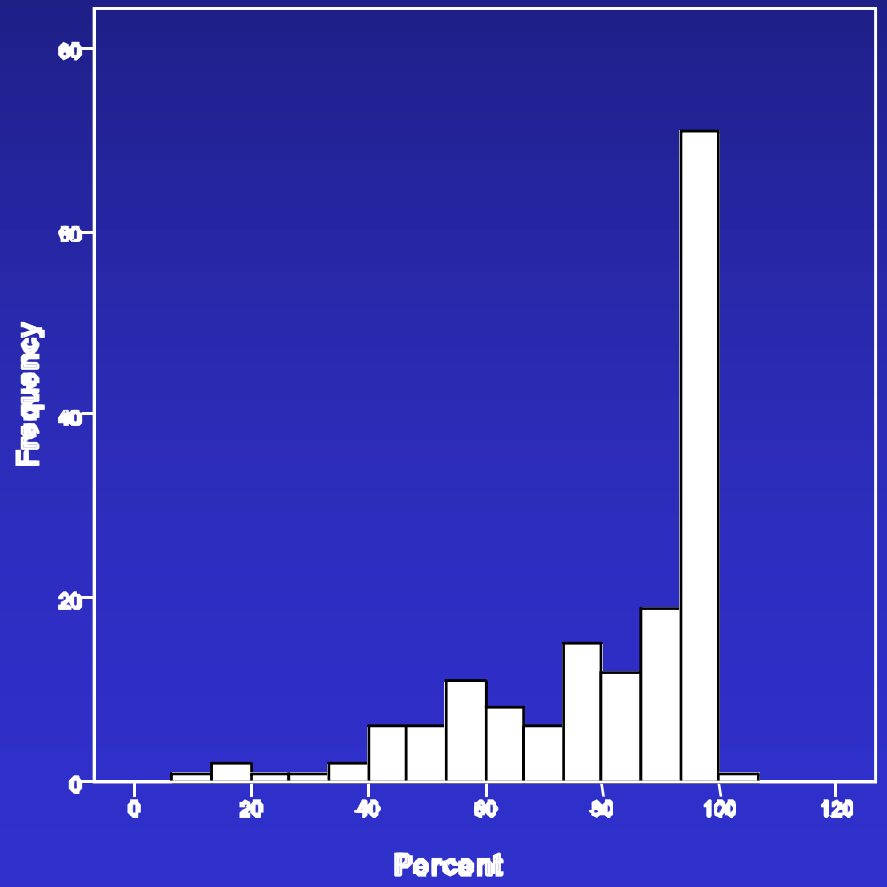


CTC ≥ III bortezomib 5 %
control 2 %

Feasibility

Feasibility

Actually given total dose in relation to planned total dose



Median = 90 %
Mean = 82 %

Response

Bortezomib		
	After ASCT	Best reported
CR/nCR	20 %	45 %
≥ VGPR	39 %	71 %

Control		
	After ASCT	Best reported
CR/nCR	21 %	35 %
≥ VGPR	39 %	57 %

Response

Bortezomib		
	After ASCT	Best reported
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≥ VGPR	39 %	71 %

Control		
	After ASCT	Best reported
CR/nCR	21 %	35 %
≥ VGPR	39 %	57 %

$P<0.05$

Improvement of response

- Bortezomib: 68 patients

  51 from PR to ≥ VGPR

  17 from VGPR to ≥ nCR

- Control 42 patients

  32 from PR to ≥ VGPR

  10 from VGPR to ≥ nCR

Improvement of response

- Bortezomib: 68 patients

  51 from PR to ≥ VGPR

  17 from VGPR to ≥ nCR

$P<0.05$

- Control 42 patients

  32 from PR to ≥ VGPR

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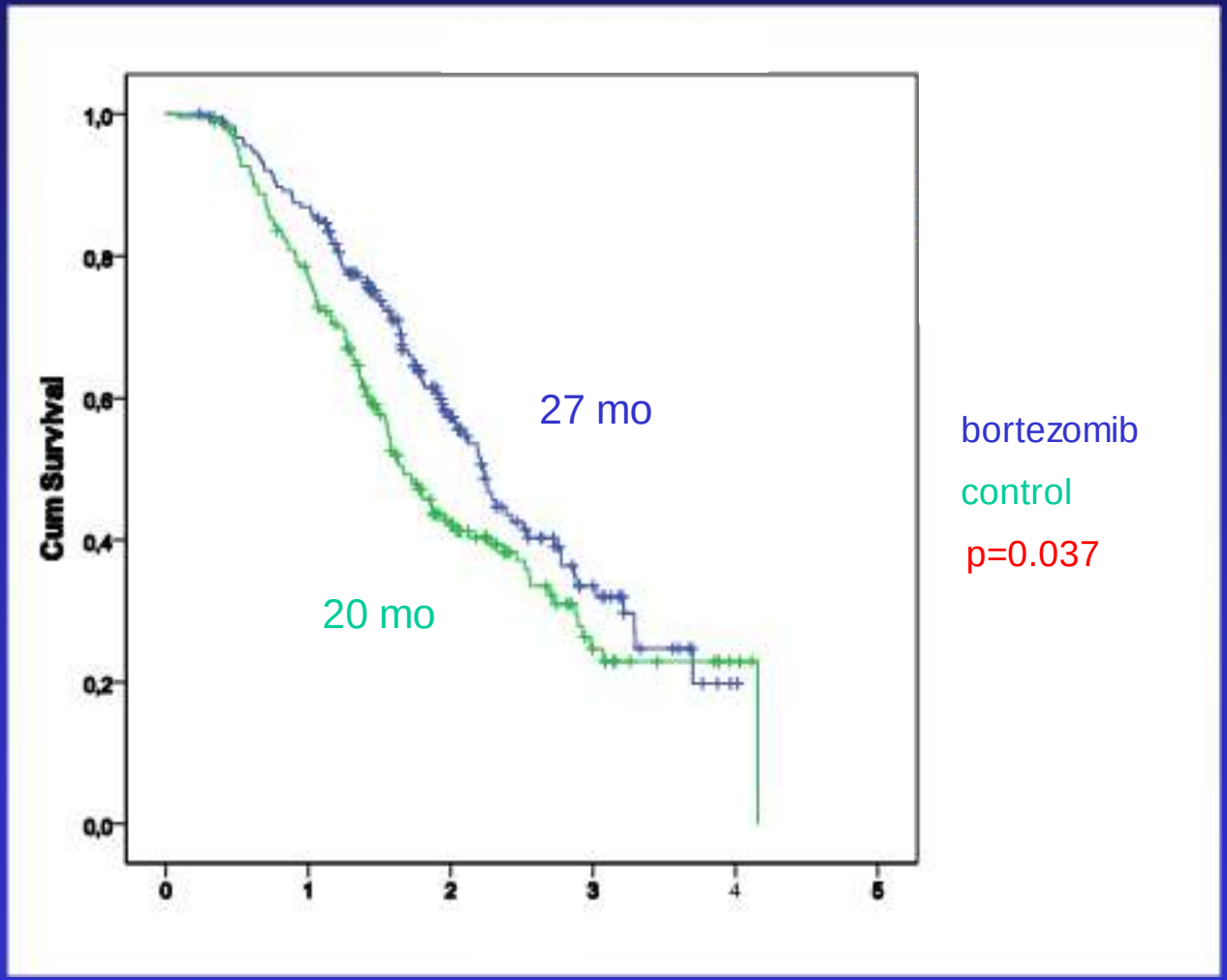
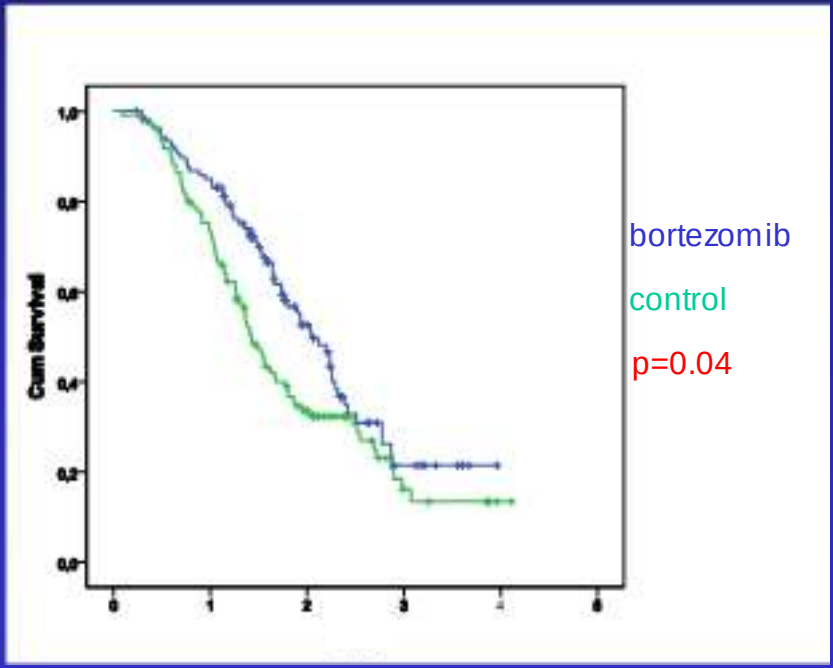
Progression free survival

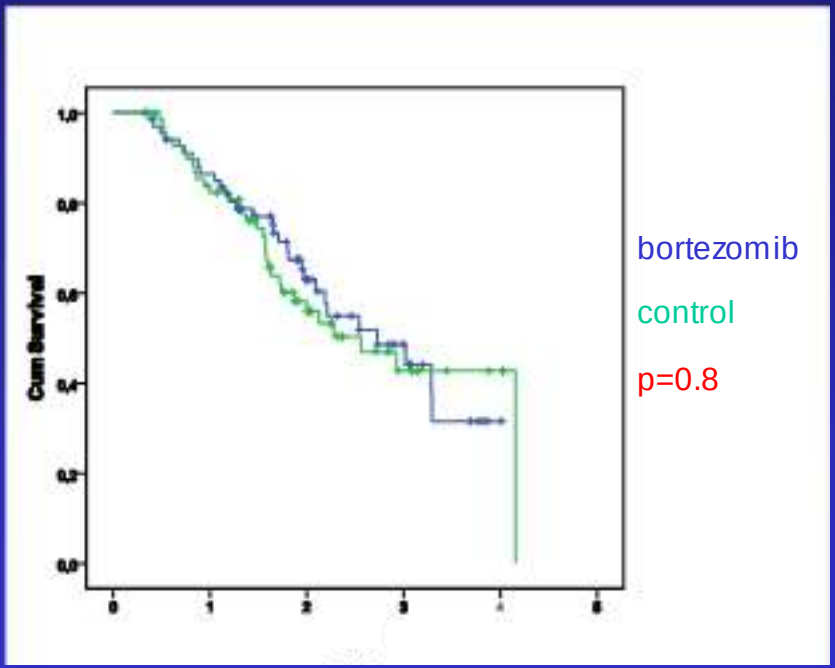


Progression free survival

< VGPR after ASCT



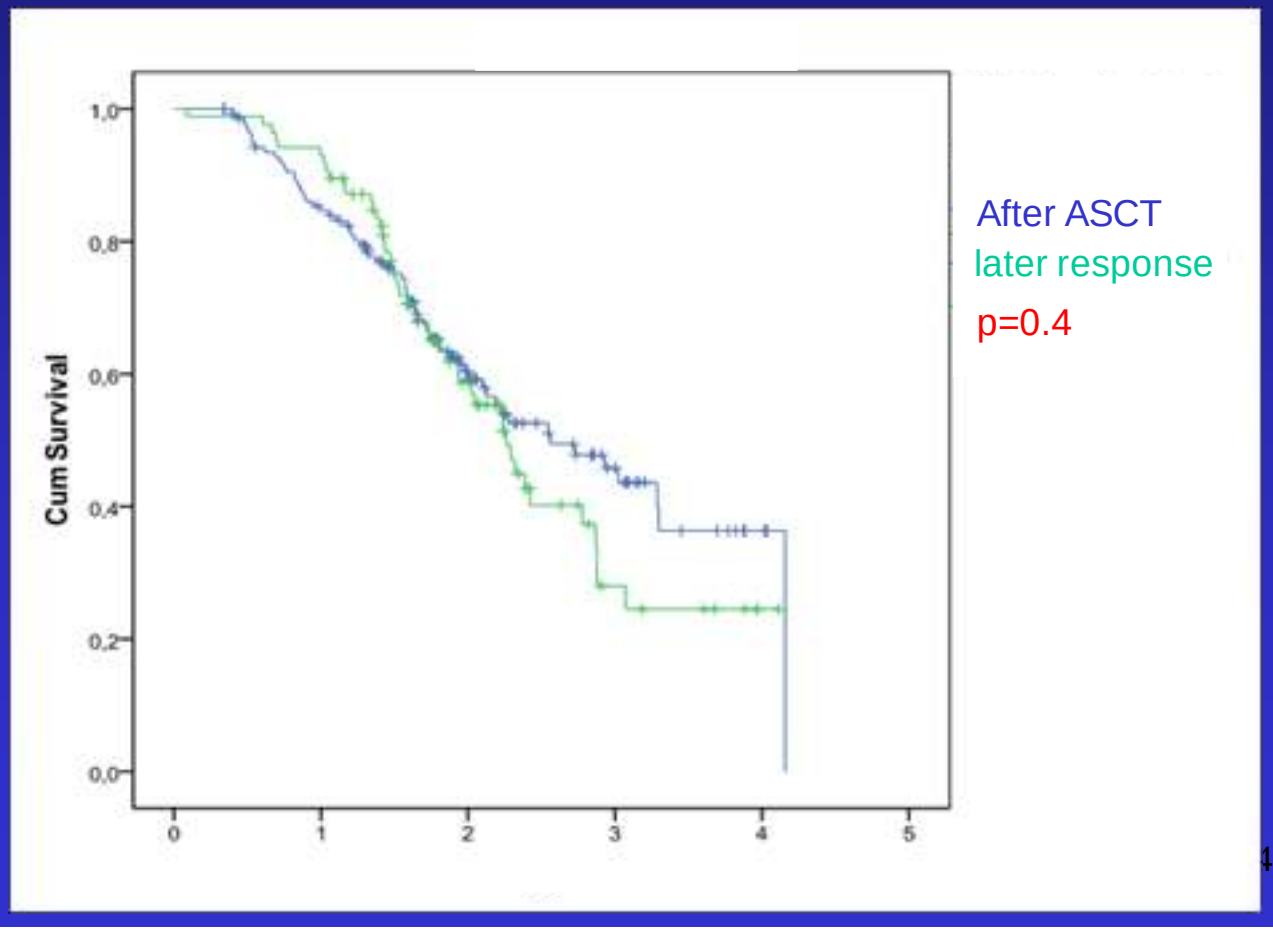
≥ VGPR after ASCT



Progression free survival

All patients

≥ VGPR directly after ASCT vs later



Overall survival

No significant difference in OS after a median follow up of 27 months.

Estimated OS at this time point is approximately 87 % for both groups.

Conclusions I

Consolidation with single drug bortezomib after ASCT:

is feasible

toxicity is manageable

improves degree of response

improves progression free survival

Conclusions II

The results support the hypothesis that a response ≥ VGPR is important in order to achieve a PFS prolongation

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