
**Thalidomide/Dexamethasone (TD) vs.
Velcade/Thalidomide/Dexamethasone (VTD) vs.
VBMCP/VBAD/Velcade as Induction Regimens prior to
Autologous Stem Cell Transplantation (ASCT) in Younger
Patients with Multiple Myeloma (MM): First Results of a
Prospective Phase III PETHEMA/GEM Trial.**

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Background

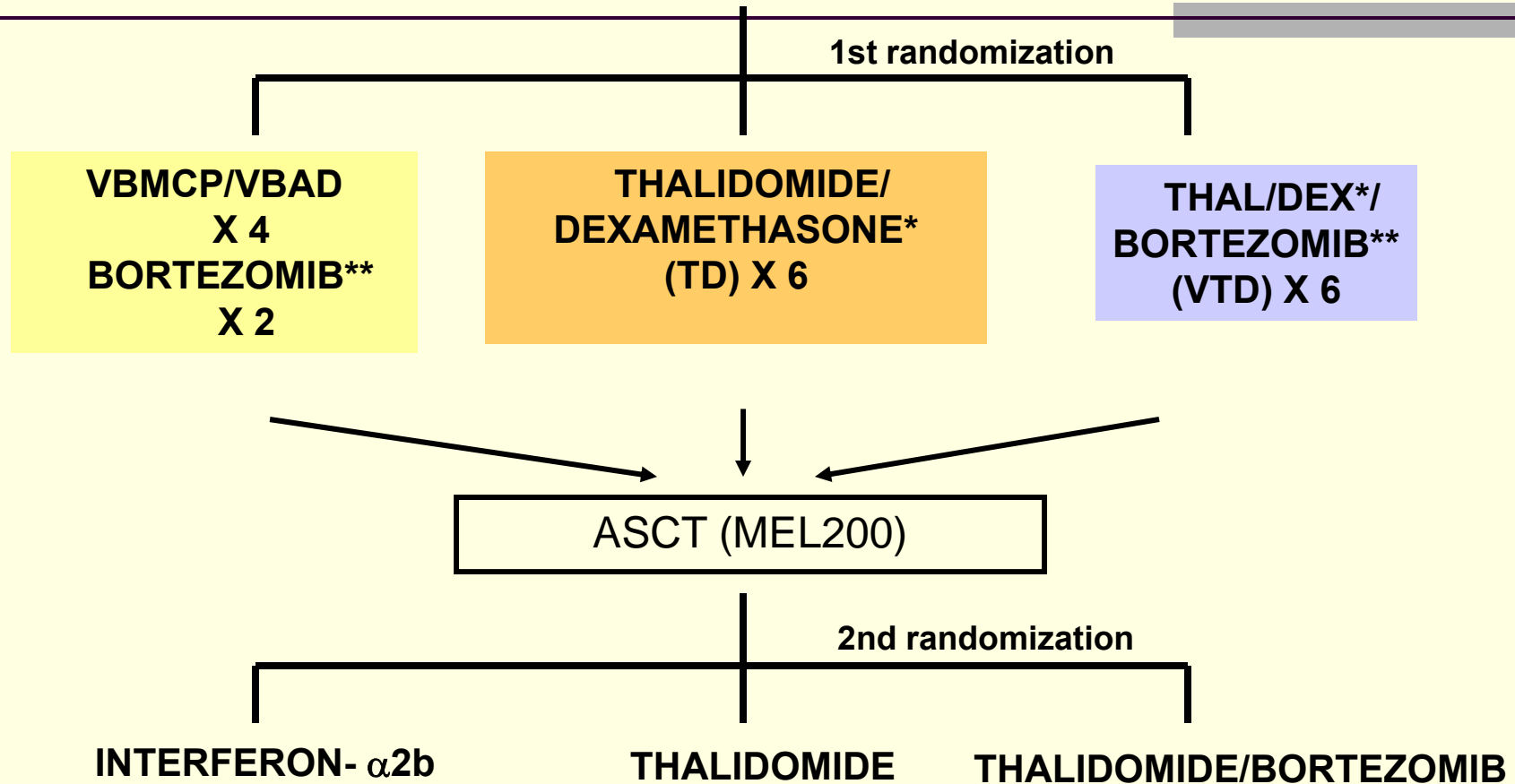
- Autologous stem cell transplantation (ASCT) has become the standard of care in the up-front therapy of younger patients with multiple myeloma.
- The achievement of a complete remission (CR) post-ASCT is the crucial step for long-lasting response and prolonged survival.
- The degree of tumor reduction achieved with the induction pre-transplantation therapy is the key factor for the post-transplant CR rate.

Aim

- To investigate the efficacy and safety of three pre-transplant induction regimens:
 - VBMCP/VBAD + bortezomib
 - Thalidomide/dexamethasone (TD)
 - Bortezomib/thalidomide/dexamethasone (VTD)

GEM05MENOS65

De “novo” symptomatic MM <65 yrs



*Thalidomide: 200 mg/day; Dexamethasone: 40 mg on days 1-4, 9-12

**Bortezomib: 1.3 mg/m² on days 1,4,8, and 11

TD and VTD at 4 week-interval

End-points

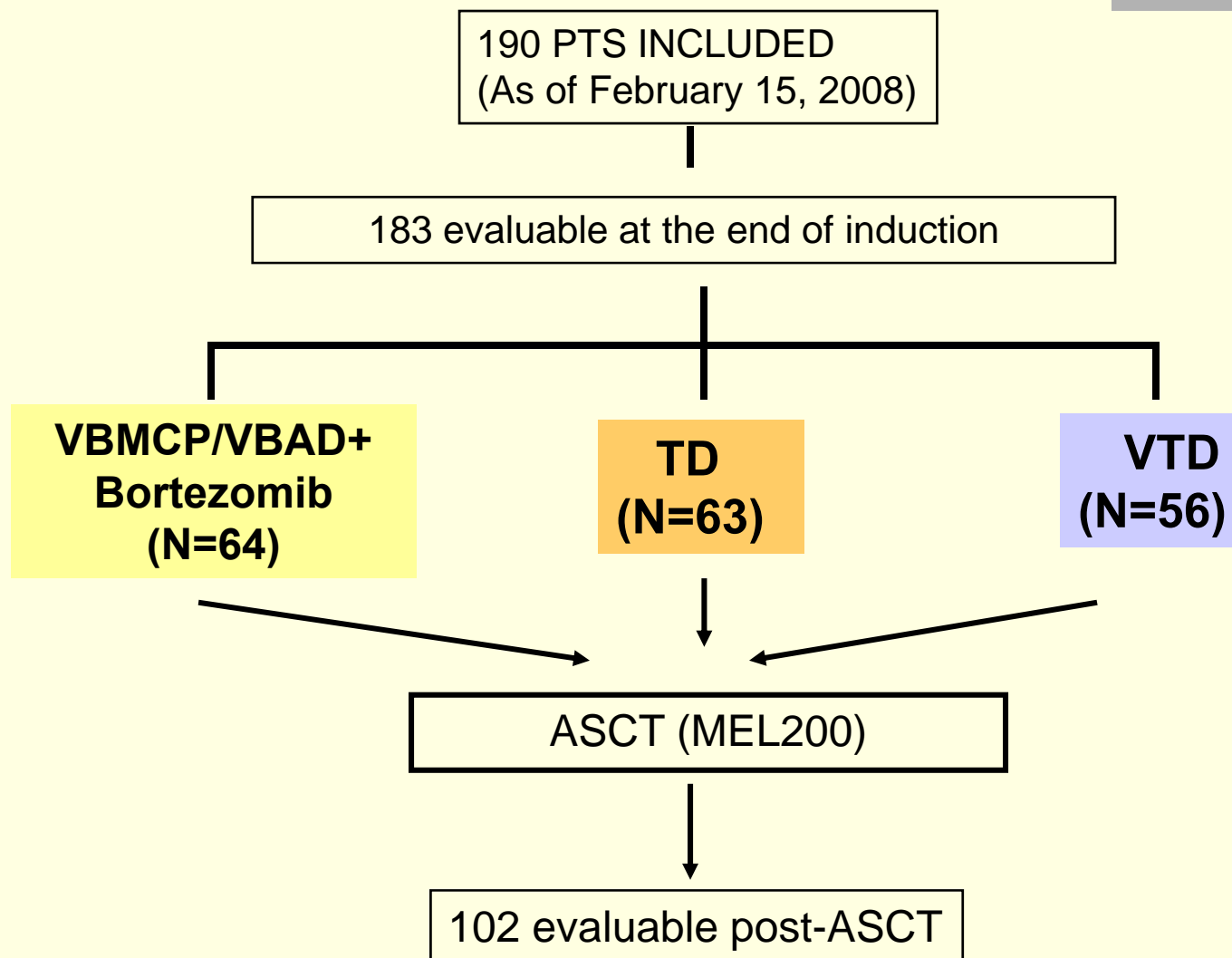
- Primary
 - Response rate
- Secondary
 - Time to progression
 - Overall survival
 - Safety

Patients and Methods

- Patients < 65 yrs-old with symptomatic MM
- Response criteria: EBMT (plus near-CR)
- Sample size: 390 patients (130 per arm)
- Statistical methods: chi-square, Kaplan and Meier method, log-rank test.

GEM05MENOS65

De “*novo*” symptomatic MM <65 yrs



Patient Characteristics (I)

	VBMCP/VBAD +Bortezomib (n=64)	TD (n=63)	VTD (n=56)
Age (median)	59	56	57
Gender (M/F)	28/36	29/34	32/24
M-protein type (%)			
IgG	56	59	57
IgA	26	25	27
Light chain	16	13	7
IgD	2	3	7
IgM	-	-	2

Patient Characteristics (II)

	VBMCP/VBAD + Bortezomib (n=64)	TD (n=63)	VTD (n=56)
Hb < 10 g/dL (%)	33	27	23
EMP* (%)	14	21	16
Poor cytogenetics (%): t(4;14); t(14;16), del (17p)	17	17	25

*EMP: extramedullary (soft-tissue) plasmacytomas

Patient Characteristics (III)

	VBMCP/VBAD + Bortezomib (n=64)	TD (n=63)	VTD (n=56)
Durie-Salmon (%)			
I	9	2	5
II	55	58	57
III	36	40	38
ISS (%)			
I	46	37	36
II	35	44	43
III	19	19	21

Results (I)

Response to Induction Therapy

Response	VBMCP/VBAD +Bortezomib (n=64)	TD (n=63)	VTD (n=56)
CR	20%*	6%*	30%*
nCR	8%	6%	11%
PR	44%	54%	39%
MR+NR	14%	15%	9%
PD	14%	19%	11%

*VBMCP/VBAD+bortezomib vs. TD, $p=0.01$

VTD vs. TD, $p=0.0006$

VBMCP/VBAD+bortezomib vs. VTD, $p=NS$

Results (II). Response in patients with extramedullary plasmacytomas

PD in patients with and without EMP: 34% vs 11%, p=0.029

	VBMCP/VBAD + Bortezomib (n=8)	TD (n=12)	VTD (n=9)
CR	25%	8%	33%
nCR	12%	-	-
PR	37%	34%	22%
MR+NR	-	16%	11%
PD	25%	42%	33%

Results (III). Response in patients with poor cytogenetics: t (4;14); t(14;16); del (17p)

	VBMCP/VBAD + Bortezomib (n=11)	TD (n=11)	VTD (n=14)
CR	18%	-	36%
nCR	-	9%	14%
PR	27%	36%	29%
MR+NR	18%	27%	14%
PD	37%	28%	7%

CR: VTD vs. TD, p= 0.03

ORR: VTD vs. VBMCP/VBAD + Bortezomib and TD, p=0.09

Results (IV).

Adverse events / discontinuations

	VBMCP/VBAD + Bortezomib (n=64)	TD (n=63)	VTD (n=56)
AEs (grade 3-4)	29 (45%)	23 (36%)	29 (52%)
Discontinuations due to toxicity	2 (3%)	1(1.5%)	5 (9%)
Deaths during induction	2 (3%)	3 (5%)	0 (0%)

Results (V). Grade ≥ 3 toxicity

	VBMCP/VBAD + Bortezomib (n=64)	TD (n=63)	VTD (n=56)
Neutropenia	15 (23%)	7 (11%)	6 (10%)
Thrombocytopenia	3 (5%)	4 (6%)	8 (14%)
Thrombotic events	3 (5%)	8 (13%)*	1 (1.7%)*
Peripheral neuropathy	0**	1(1.5%)**	9 (16%)**

*p=0.02 **p<0.005

Results (VI). Response post-ASCT

	VBMCP/VBAD + Bortezomib (n=37)	TD (n=32)	VTD (n=33)
CR	43%	34%	49%
nCR	11%	19%	15%
PR	43%	44%	33%
MR+NR	3%	3%	3%

Results (VII). Pre- and post-ASCT CR rate according to the induction regimen

	Pre-ASCT	Post-ASCT
VBMCP/VBAD+ Bortezomib	20%	43%
TD	6%	34%
VTD	30%	49%

Conclusions (I)

- In younger patients with MM, induction with either VTD or VBMCP/VBAD+Bortezomib resulted in higher CR rate than with TD.
- Patients with EMP had a higher progressive disease rate.
- Patients with poor cytogenetics showed a trend towards higher response rate with VTD.

Conclusions (II)

- The incidence of AEs was not significantly different among the three arms. However, thrombotic events were significantly higher with TD and peripheral neuropathy with VTD.
- ASCT increased the CR rate in about 20% of patients irrespective of the induction regimen used.