

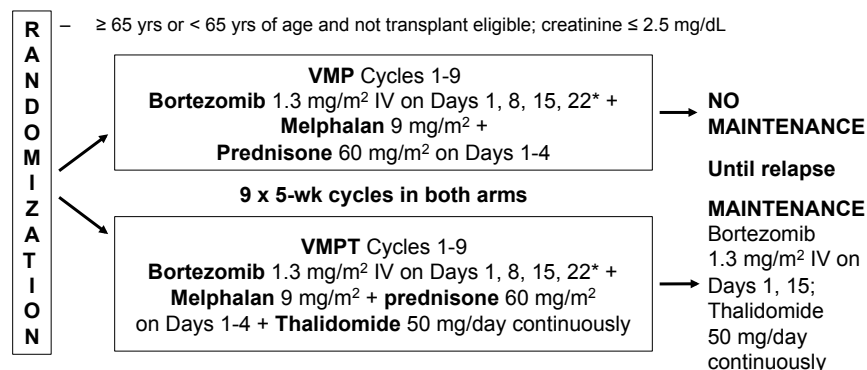
Hematology: ASCO 2009

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Multiple Myeloma

Phase III Study: VMPT Vs VMP in Newly Diagnosed Elderly MM Patients

- 511 pts (older than 65 yrs) randomized from 58 Italian centers
 - Symptomatic disease, organ damage, measurable disease
 - ≥ 65 yrs or < 65 yrs of age and not transplant eligible; creatinine ≤ 2.5 mg/dL



*64 VMP pts and 71 VMPT pts were treated with twice-wkly bortezomib.
 Palumbo A, et al. ASCO 2009. Abstract 8515. Reprinted with permission.

Efficacy and Toxicity of VMPT Vs VMP: Bortezomib Infusion Schedule

	VMPT, %		VMP, %	
	Twice Wkly (n = 71)	Wkly (n = 150)	Twice Wkly (n = 64)	Wkly (n = 165)
CR	38	32	27	20
Grade 3-4 peripheral neuropathy	18	2	14	2
Dose reduction*	42	11	35	13
Discontinuation*	10	3	15	4

*Due to peripheral neuropathy

- 25 VMPT and 19 VMP pts received both twice and once wkly

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VMPT vs VMP: Results

	VMPT, % (n = 177)	VMP, % (n = 177)	P Value
CR	35	21	< .0001
PFS at 3 yrs	71	56	.13
OS at 3 yrs	90	89	.81
Grade 3-4 peripheral neuropathy*	2	2	--
Discontinuation [§]	3	4	--

*For pts who received wkly bortezomib with VMPT and VMP.

[§]Due to peripheral neuropathy.

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Lenalidomide, Bortezomib, and Dex in Relapsed/Refractory MM: Study Design

- Accrual target: N = 65

Up to 8 cycles (21 days per cycle)
Bortezomib 1.0 mg/m² on Days 1, 4, 8, 11 +
Lenalidomide 15 mg/day on Days 1-14 +
Dexamethasone 40 mg/day* (cycles 1-4) and
 20 mg/day (cycles 5-8) on Days 1-2, 4-5, 8-9, 11-12

*Safety data indicated dexamethasone 40 mg not well tolerated
 Protocol amendment: reduced to 20 mg in cycles 1-4 and 10 mg in cycles 5-8



Maintenance treatment following cycle 8 allowed in pts with response or SD
Bortezomib[†] and **lenalidomide** continued at doses tolerated at end of cycle 8
Dexamethasone[†] 10 mg

[†]Schedule amended: bortezomib on Days 1, 8; dexamethasone 10 mg on Days 1, 2, 8, 9.

Anderson KC, et al. ASCO 2009. Abstract 8536. Reprinted with permission.

Lenalidomide, Bortezomib, and Dex in Relapsed/Refractory MM: Results

- 62 pts evaluable for response in current analysis
 - ORR (CR/nCR + PR + minor response): 84%
 - CR/nCR: 26%
 - CR/nCR/VGPR/PR: 69%
- Durable response
 - Median duration of response: 11.0 mos
 - Median time to response: 1.4 mos (range: 0.7-11.2)

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Lenalidomide, Bortezomib, and Dex in Relapsed/Refractory MM: Results

- Response rate
 - ORR: 81% in pts with normal cytogenetics and 91% in pts with abnormal cytogenetics
- Comparable response rates in pts with chromosome 13 deletion vs normal chromosome 13 assessed by FISH
- Median OS: 29 mos at a median follow-up of 17 mos
 - Median TTP (n = 34): 12 mos
 - Median PFS (n = 36): 12 mos
- Grade 1/2 hematologic toxicity most common adverse event

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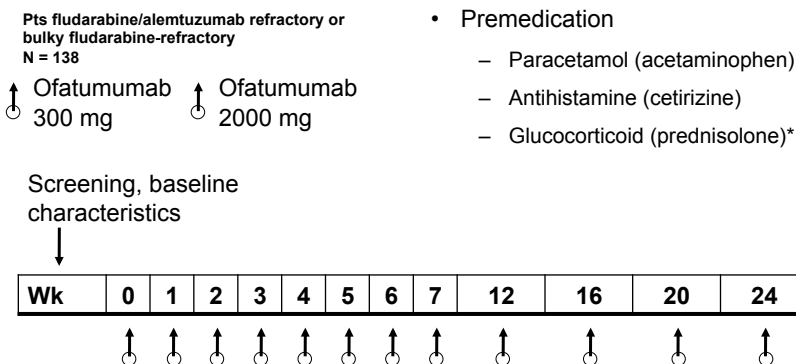
Lenalidomide, Bortezomib, and Dex in Relapsed/Refractory MM: Conclusions

- Lenalidomide, bortezomib, dexamethasone combination active and tolerable in pts with relapsed and/or refractory MM
 - Poor-risk pts and those previously treated with lenalidomide, thalidomide, bortezomib, stem cell transplantation also benefited
 - Responses durable
- Treatment generally well tolerated
 - Dose reduction for dexamethasone required for some patients

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Leukemias

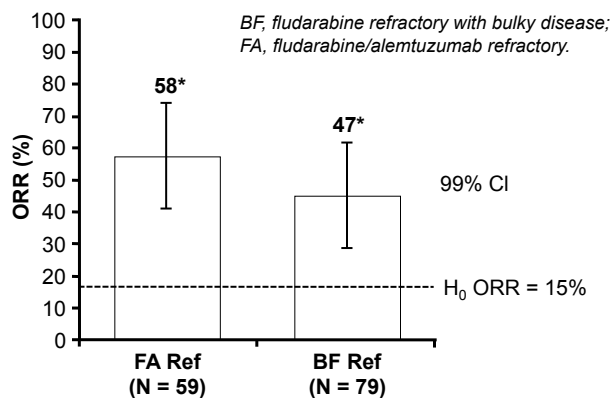
Novel CD20 mAb: Ofatumumab— Study Design



*Prednisolone 100 mg (or equivalent) prior to infusions 1, 2 and 9; if initial infusions were well tolerated, glucocorticoid dose could be reduced to < 100 mg for other infusions.

Kipps T, et al. ASCO 2009. Abstract 7043. Wierda W, et al. ASCO 2009. Abstract 7044. Reprinted with permission.

Ofatumumab: ORR



*P < .0001 vs null hypothesis (2-sided exact test)

Kipps T, et al. ASCO 2009. Abstract 7043. Wierda W, et al. ASCO 2009. Abstract 7044. Reprinted with permission.

Ofatumumab Study: Results

- Median OS (95% CI)
 - 13.7 mos (9.4-upper limit not yet reached) in the FA-ref group
 - 15.4 mos (10.2-20.2) in the BF-ref group
- Average tumor burden decreased rapidly in pts with lymphadenopathy at baseline
- Most pts with splenomegaly and hepatomegaly at baseline experienced a reduction in spleen/liver size
- Improvements in hematologic parameters observed
 - For pts with baseline neutropenia, median neutrophil counts remained stable
 - For pts with baseline thrombocytopenia or anemia, improvements occurred rapidly by Wk 8 of treatment

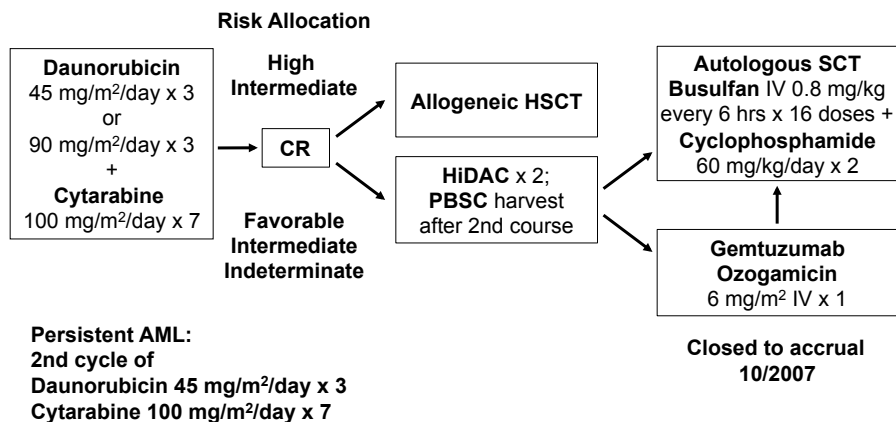
Kipps T, et al. ASCO 2009. Abstract 7043. Wierda W, et al. ASCO 2009. Abstract 7044.
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Ofatumumab Studies: Conclusions

- Ofatumumab as a single-agent produces a high ORR and improves disease symptoms in difficult-to-treat pts who are heavily pretreated and refractory to fludarabine/alemtuzumab or fludarabine refractory with bulky disease
- These findings are irrespective of previous CD20 mAb therapy with rituximab

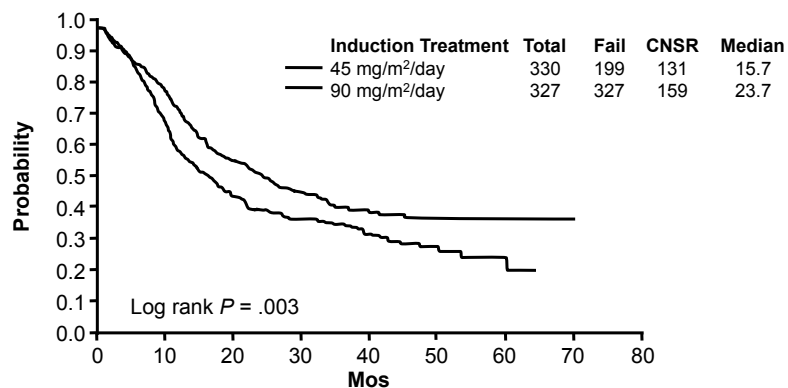
Kipps T, et al. ASCO 2009. Abstract 7043. Wierda W, et al. ASCO 2009. Abstract 7044.
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ECOG Protocol E1900: Anthracycline Dose Intensification During Induction in AML



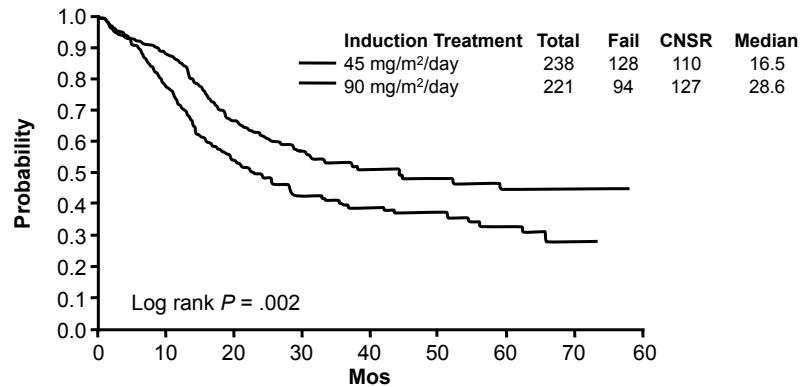
Fernandez H, et al. ASCO 2009. Abstract 7003. Reprinted with permission.

ECOG E1900: OS by Induction: All Patients



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ECOG E1900: OS by Induction < 55 Yrs



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ECOG E1900: Results: Toxicity

- Similar death rates in both induction arms
 - 45 mg/m²/day: 4.5%
 - 90 mg/m²/day: 5.5%
- Grade 3/4 toxicity similar
- High-dose daunorubicin arm
 - Cardiac toxicity not increased
 - Did not impact delivery of HSCT

Fernandez H, et al. ASCO 2009. Abstract 7003. Reprinted with permission.

ECOG E1900: Conclusions

- In AML patients < 60 yrs, induction therapy with daunorubicin 90 mg/m²/day
 - Safe
 - Improved CR rates: 70.6% vs 57.3%
 - Improved OS: 23.7 vs 15.7 mos
- 45 mg/m²/day no longer standard dose

Fernandez H, et al. ASCO 2009. Abstract 7003. Reprinted with permission.

Omacetaxine in Pts With T315I-Mutated CML: Rationale

- First-in-class cetaxine, inhibitor of protein elongation^[1]
- Potent inhibitory activity against leukemic cells, including T315I+ cells^[1]
- Activity independent of Bcr-Abl binding activity
- Induces apoptosis by inhibiting the antiapoptotic oncoprotein Mcl-1^[2]
- Clinical activity in CML after imatinib failure^[3]

1. Chen R, et al. Cancer Res. 2006;66:19059-19066. 2. Tang R, et al. Mol Cancer Ther. 2006;5:723-731.
3. Quintas-Cardama A, et al. Cancer. 2007;109:248-255.

Omacetaxine Study: Design

- Induction therapy
 - 1.25 mg/m² BID SC
 - 14 consecutive days every cycle (28 days)
 - Until CHR, HI, or cytogenetic response
- Maintenance therapy
 - 1.25 mg/m² BID SC
 - 7 consecutive days every 28 days for up to 24 mos
- Self-administered at home
- Dosing adjustments by decreasing or increasing number of dosing days per cycle

Cortes JE, et al. ASCO 2009. Abstract 7008. Reprinted with permission.

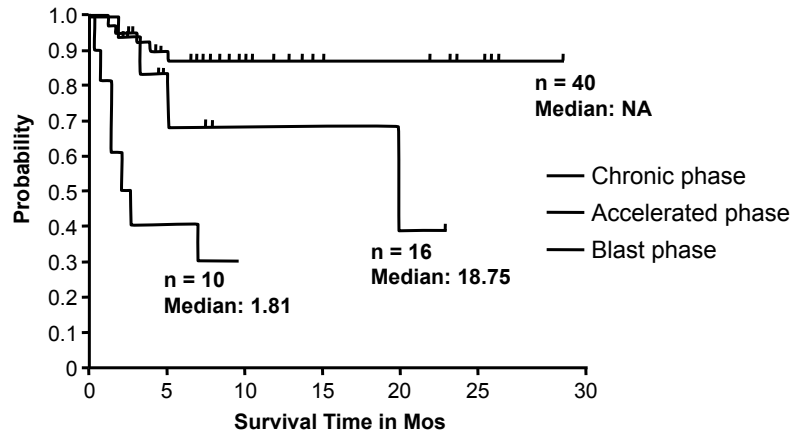
Omacetaxine Study: Response to Therapy

Response, n (%)	Chronic Phase (n = 40)	Accelerated Phase (n = 16)	Blast Phase (n = 10)
Hematologic	34 (85)	8 (50)	4 (40)
▪ CHR	34 (85)	5 (31)	2 (20)
▪ HI	NA	2 (13)	1 (10)
▪ RCP	NA	1 (6)	1 (10)
Cytogenetic	11 (28)	1 (6)	--
▪ MCyR	6 (15)	--	--
• CCyR	4 (10)	1 (6)	--
• PCyR	2 (5)	--	--
▪ Minimal	5 (13)	--	--

Data independently adjudicated by safety and data monitoring committee

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Omacetaxine Study: OS



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Omacetaxine Study: Grade 3-4 Hematologic Adverse Events*

Adverse Event, %	CP (n = 40)	AP (n = 16)	BP (n = 10)	Total (N = 66)
Thrombocytopenia	70	38	40	58
Anemia	55	19	20	41
Neutropenia	43	19	40	36
Febrile neutropenia	10	19	30	15

*Regardless of relationship to omacetaxine treatment.

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