

U.S. Cooperative Group Studies

≥ 65 yrs/Non-transplant Candidates



Trials in Elderly/ Non-SCT Candidates

MPT vs MP vs Mel100¹

MPT longer med.PFS

MPT longer med.OS (58.6 vs 33.2 vs 38.3 mos)

MPR-R vs MPR vs MP²

MPR-R higher overall response (77% vs 50% MP)

MPR-R faster response (median 2 mos.)

MPR-R highest 2 yr PFS (55% vs 16% for MP)

VMP vs MP³

VMP longer med. PFS (24mos vs 16.6 mos)

VMP higher OS @ 2 yrs (82.6% mos vs 69.5%)

¹Facon et al. Lancet. 2007;370:1209-1218.

²Palumbo et al, ASH 2010: abstract 320

³San Miguel et al, N Engl J Med. 2008;359:906-17

MM Induction Trials in Elderly/Non-SCT

ECOG

Lenalidomide - low-dose dexamethasone
(Ld) Vs. Lenalidomide – high-dose
dexamethasone (LD)

All pts: Ld higher 1 yr OS (96%) than LD (87%)
2 yr OS (87%) Vs (75%)

>65 yrs: Ld higher 1 yr OS (94%) than LD (83%)

Current Questions to Consider in Non-transplant Patients with Newly Diagnosed MM

- What are the best IMiD and bortezomib-based regimens for patients not proceeding to AuSCT?
- Where does quality of life fit in?
- Can we identify optimal regimens for subgroups?



MPT

VMP

Rd

MPR

RVD

BD



ECOG:E1A06: MPT Vs MPR

RANDOMIZATION (n=277/304)

Cycles (28-day) 1-12	Maintenance Cy 13 +
----------------------	---------------------

MPT
M: 9 mg/m²/d, days 1-4
P: 100 mg/d, days 1-4
T: 100 mg/day po, days 1-28
Enteric coated ASA 325 mg /d

**Thalidomide
Maintenance Tx**
100 mg/day,
days 1-28
ASA 325mg/d

MPR
M: 5 mg/m²/d, days 1-4
P: 100 mg/d, days 1-4
R: 10 mg/d days 1-21
Enteric coated ASA 325mg/d

**Lenalidomide
Maintenance Tx**
10 mg/day,
days 1-28
ASA 325mg/d

Disease
progression:
Off
Study

PFS

Overall Survival

Response
ORR
PR
VGPR
nCR
CR

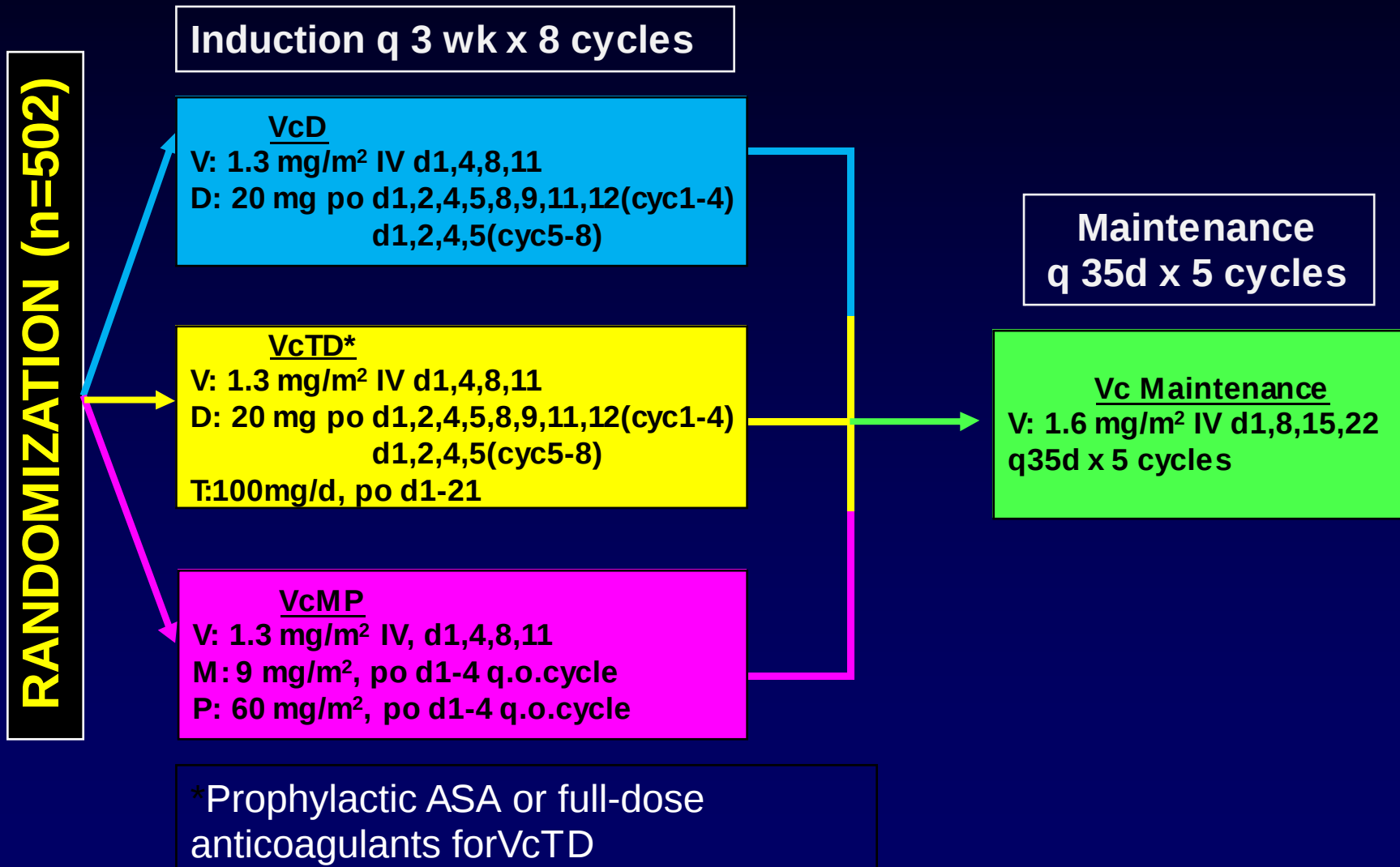
Toxicity

TC classification

QOL: - FACT-nTX
- by response
- by MM
attributes

Stratified by ISS Stage (I/II Vs III) and Age (<65 or ≥65)

Elderly Untreated MM: UPFRONT Phase 3b Trial: Community-based Trial of 3 Bortezomib-based Regimens



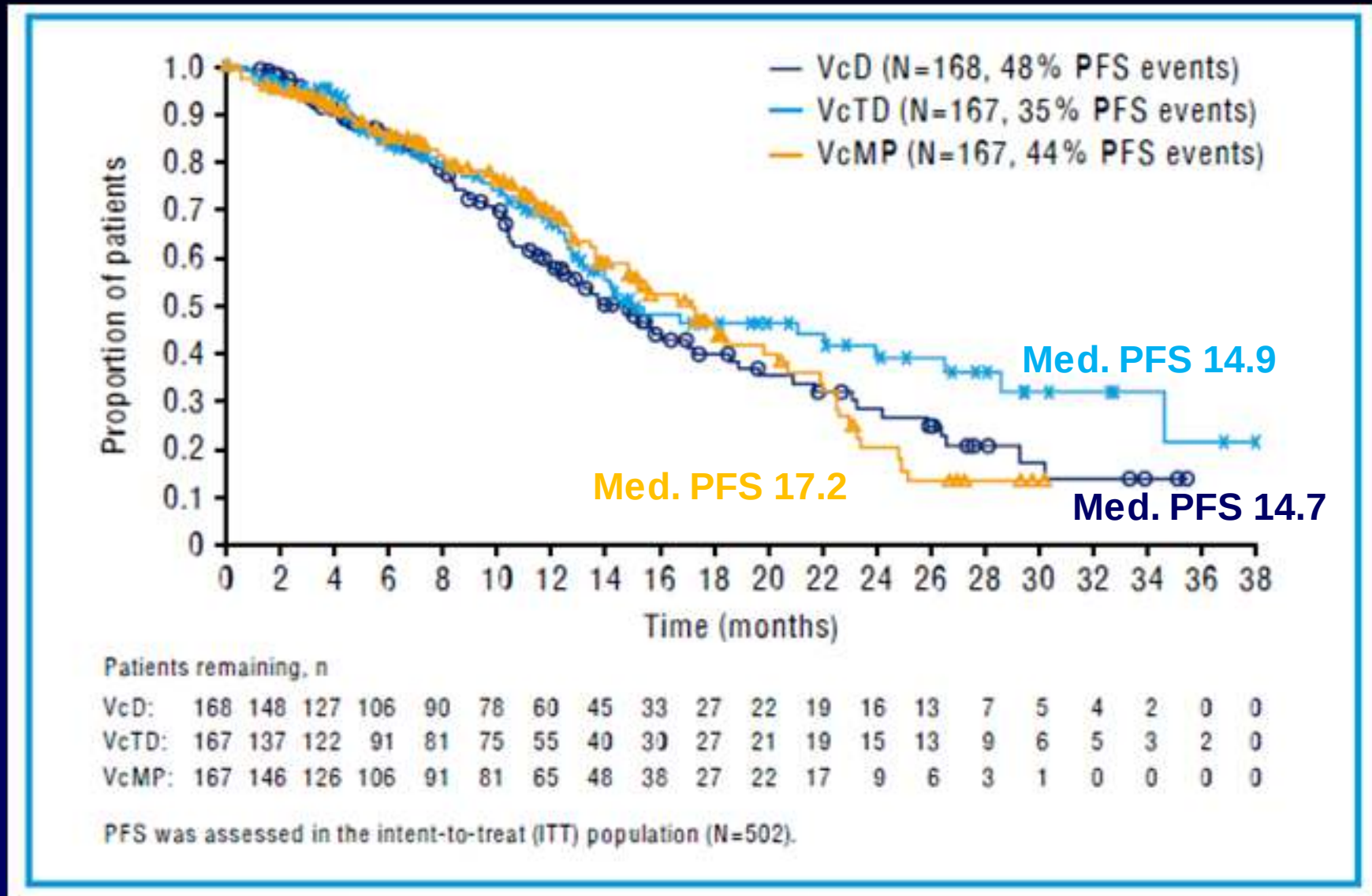
Elderly Untreated MM: UPFRONT Phase 3b Trial: Community-based Trial of 3 Bortezomib-based Regimens Efficacy

	VcD* (n=99)		VcTD* n=93)		VcMP* (n=99)	
Age (med.yrs)	73.5		73		72	
Stage II/III Patients	55/29		33/31		43/31	
No. of Treatments (med cycles received)	9 (1-13)		6 (1-13)		7 (1-13)	
% pts. Receiving Vc maintenance	56		33		43	
	I	I+M	I	I+M	I	I+M
Response Rate						
≥ PR (%)	68	71	78	79	71	73
CR/nCR (%)	24	31	36	38	31	34
≥ VGPR (%)	36	39	44	47	40	44
PR	32	32	34	32	31	29

*Interim analysis after 70 pts/arm enrolled

Niesvizky et al, IMW 2011: abstract P-228

Elderly Untreated MM: UPFRONT Phase 3b Trial: Progression-Free Survival



Med. Follow-up 18.8 mos.

Niesvizky et al, IMW 2011: abstract P-228

Elderly Untreated MM: UPFRONT Phase 3b Trial: Community-based Trial of 3 Bortezomib-based Regimens Toxicity

TOXICITY	VcD	VcTD	VcMP
At least 1 $\geq$ Gr 3 Adverse Event	77	90	81
At Least 1 SAE	62	72	54
All Gr peripheral neuropathy	52	65	48
$\geq$ Gr 3 Peripheral Neuropathy (%)	15	26	20
$\geq$ Gr3 PN during maintenance (%)	5	6	2
All gr PN resulting in d/c all study drugs	7 + 4	18	18
	I + M		
Any Gr Thromboembolic events (%)	9 + 2	5	3

SWOG S0777: Lenalidomide-Dexamethasone (LLD) Vs Bortezomib-Lenalidomide-Dexamethasone (BLLD)

RANDOMIZATION (n=375/484)

Induction q 28d x 6 cycles

LLD

L: 25 mg/d po/d d1-21

D: 40 mg po/d d1,8,15,22

ASA 325 mg po daily

*qmo. pamidronate/zoledronic acid if bone disease

Induction q 21d x 8 cycles

BLLD

V: 1.3 mg/m² IV d1,4,8,11

L: 25 mg/d po d1-14

D: 20 mg po d1,2,4,5,8,9,11,12

ASA 325 mg po daily

*qmo. pamidronate/zoledronic acid if bone disease

**Maintenance
w/ LLD
Until
Disease
Progression**

PFS

Overall Survival

Response IMWG

**Bank specimens for
future translational
research**

**SNP/GEP for
prognosis, biology,
risk factors,
response for each
regimen**

70 GEP validation

Stratified by ISS Stage (I Vs II Vs III) and Intent to transplant

Durie et al, SWOG, S0777

Conclusions in Non-transplant Patients

- What are the best IMiD + bortezomib-based regimens?
- Can we identify optimal regimens for subgroups?
- Are 3-drug regimens better than novel agent 2 drug regimens?

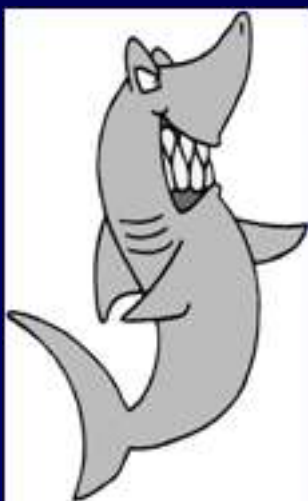
Conclusions in Non-transplant Patients

ECOG Age > 65 : Landmark Survival Probability

	Regimen	1 YR	2 YR	3 YR
No AuSCT	ALL	.94	.81	.69
	LD	.92	.77	.70
	Ld	.95	.86	.67
AuSCT	ALL	.95	.91	.83
	LD	.92	.92	.92
	Ld	1.00	.90	.75

Siegel et al, ASH 2010: abstract 38

Revisit myeloablative therapy with autologous stem cell transplant for age > 65 yrs old?



Acknowledgements



Patients Across the US