U.S. Cooperative Group Studies

≥ 65 yrs/Non-transplant Candidates

Trials in Elderly/ Non-SCT Candidates

MPT vs MP vs Mel100[1]

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

MPR-R vs MPR vs MP[2]

- 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 MP[3]

- VMP longer med. PFS (24mos vs 16.6 mos)
- VMP higher OS @ 2 yrs (82.6% mos vs 69.5%)

[1]Facon et al. Lancet. 2007;370:1209-1218.
[2]Palumbo et al, ASH 2010: abstract 320
[3]San Miguel et al, N Engl J Med. 2008;359:906-17

MM Induction Trials in Elderly/Non-SCT

ECOG

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

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

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

Rajkumar et al. Lancet Oncol: 11(1):29-37, 2010.

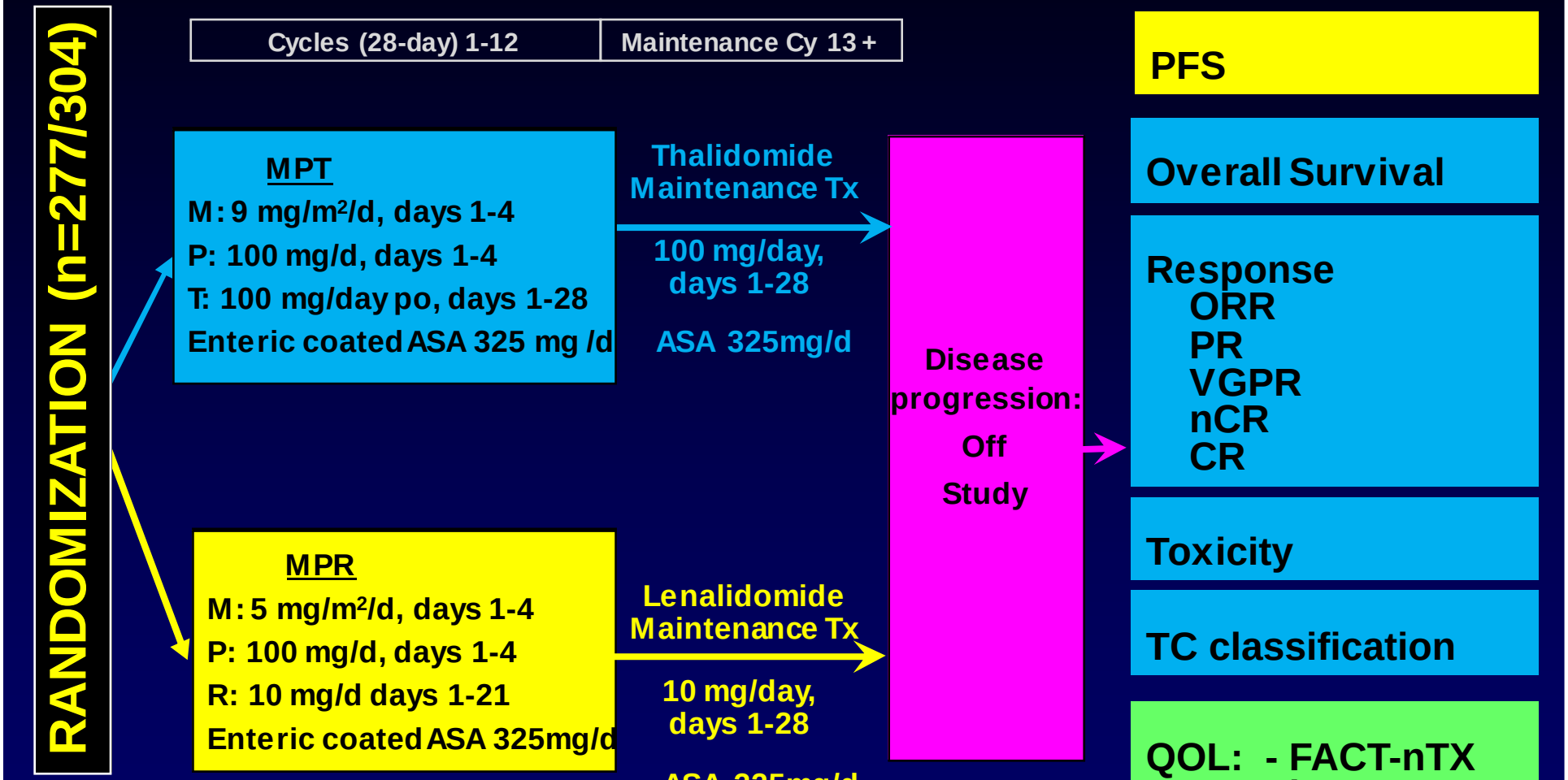
Current Questions to Consider in Non-transplant Patients with Newly Diagnosed MM

- 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

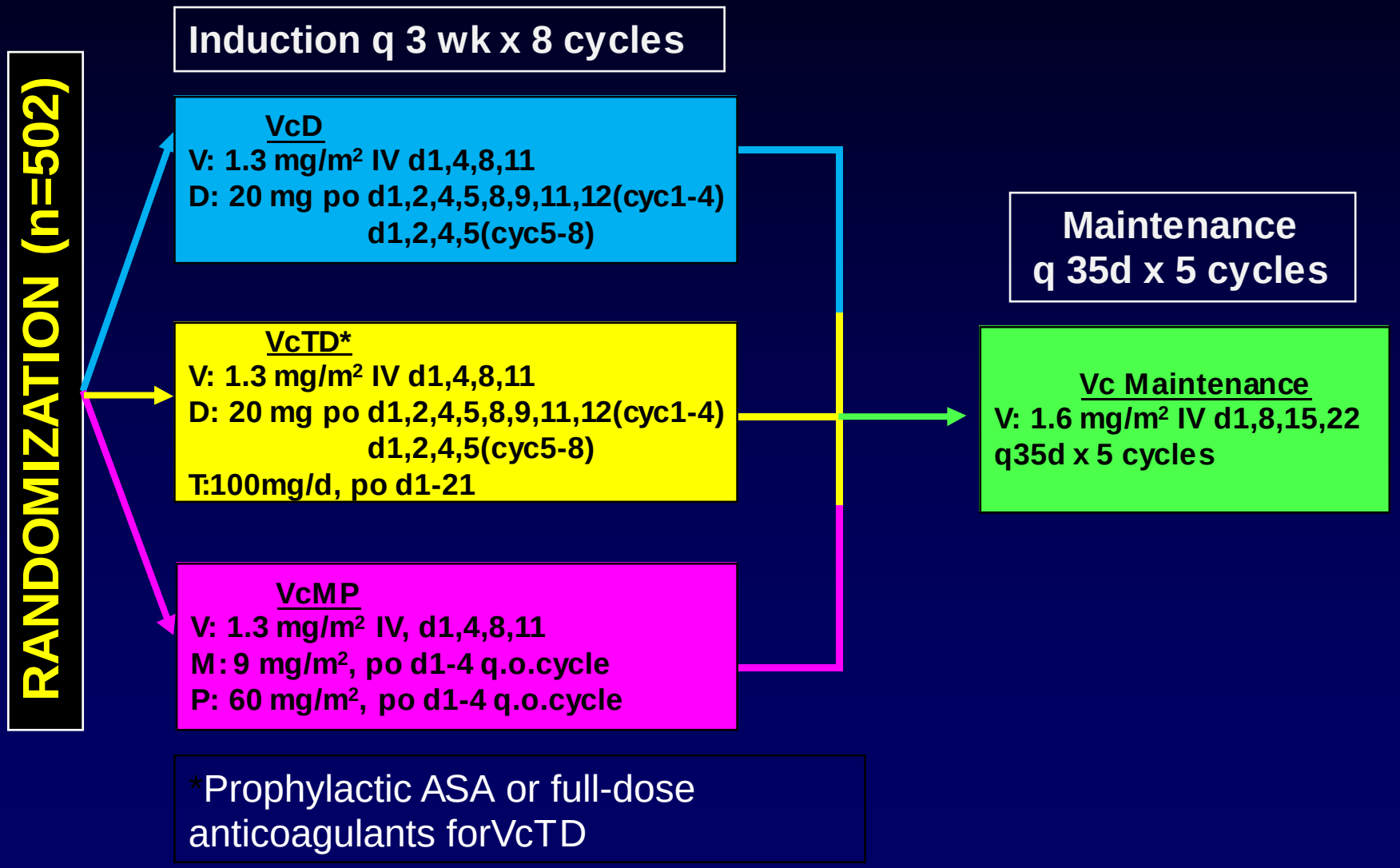
ECOG:E1A06: MPT Vs MPR



M, melphalan; P, prednisone; T thalidomide; R, lenalidomide

Stewart et al ECOG EA1A06

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



Niesvizky et al, ASH 2009: abstract 129

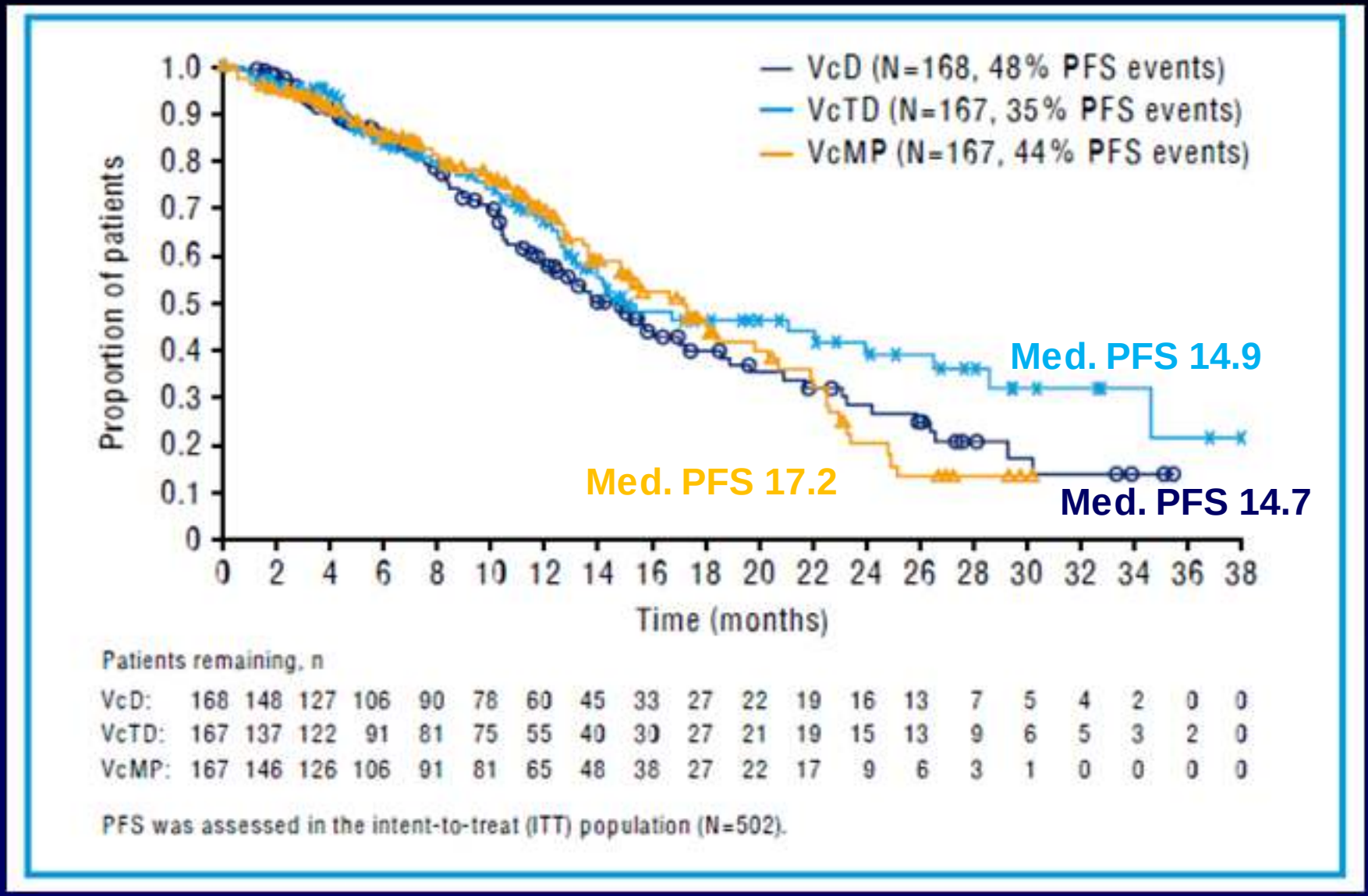
Elderly Untreated MM: UPFRONT Phase 3b Trial: Community-based Trial of 3 Bortezomib-based Regimens Efficacy

	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.

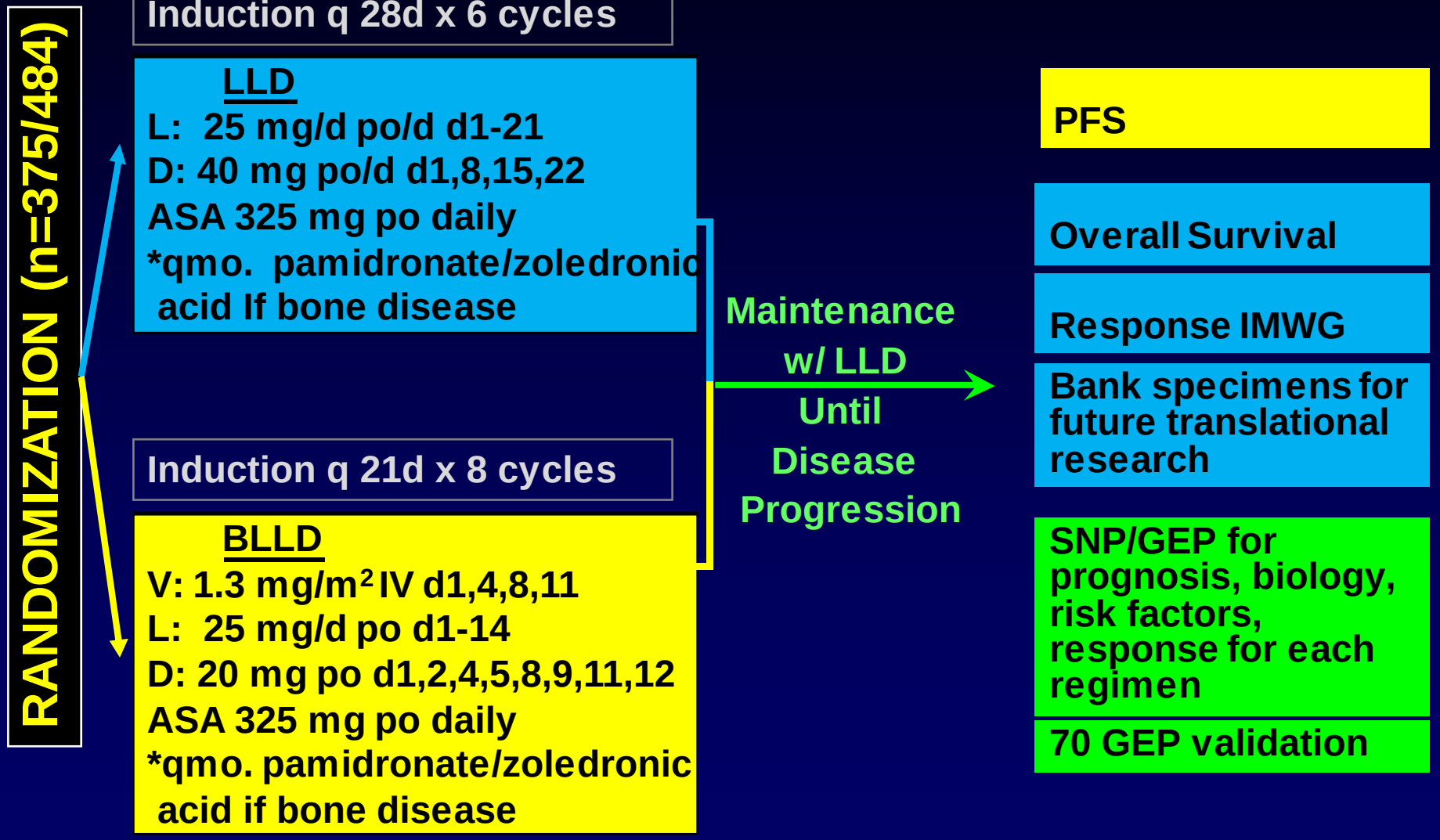
Niesvizky et al, IMW 2011: abstract P-228

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

TOXICITY	VcD	VcTD	VcMP
At least 1 ≥ Gr 3 Adverse Event	77	90	81
At Least 1 SAE	62	72	54
All Gr peripheral neuropathy	52	65	48
≥ Gr 3 Peripheral Neuropathy (%)	15	26	20
≥ 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

Niesvizky et al, IMW 2011: abstract P-228

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



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

Durie et al, SWOG, S0777

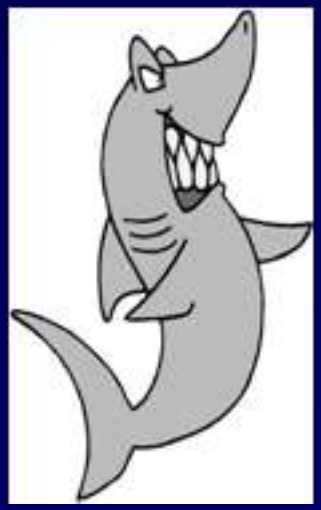
Conclusions in Non-transplant Patients

- 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