Supporting Slides

Endpoint Committee Definitions (1) Hospitalization for Heart Failure

- Cardiogenic shock or CV collapse with insufficient pressure to maintain clinically adequate perfusion
- Symptomatic pulmonary edema
- Heart failure symptoms and signs requiring intermittent or continuous IV therapy or adjustment of other medications for heart failure
- Hospitalization§ is defined as an overnight stay even if total duration is < 24 hours
  - Includes overnight stays in emergency room or observation units

§Hospitalizations for CHF treatment-related complications were not included in this category.

Time to First HF Hospitalization Endpoint Committee Versus Investigator Assessment

Time to first event	Patients, n (%)		Comparison (valsartan versus placebo)		
	Valsartan N = 2,511	Placebo N = 2,499	Risk ratio§	95% CI§	Log-rank *P* value
HF-related hospitalizations					
Endpoint committee‖	349 (13.9)	463 (18.5)	0.725	(0.631, 0.833)	.00001*
Investigator assessment‖	525 (20.9)	613 (24.5)	0.832	(0.740, 0.935)	.00236*

*Statistical significance at $P < .05$.
‖Cutoff date is 03 May 2000.
§Cox regression model.

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US Versus Non-US Subgroup Interaction

Endpoint	Subgroup	Hazard ratio§	95% CI	Interaction *P* value
Mortality	US	1.015	(0.84, 1.22)	.9430
Non-US	1.027	(0.87, 1.22)		
Morbidity	US	0.905	(0.78, 1.05)	.5267
	Non-US	0.844	(0.73, 0.97)	
1st HF hospitalization	US	0.798	(0.66, 0.97)	.4375
	Non-US	0.667	(0.55, 0.81)	

§Cox regression model.

Mortality by Baseline Cotherapy Groups and Subgroups (Val-HeFT)

	Valsartan N = 2,511	Placebo N = 2,499	Deaths, %		Hazard ratio§	95% CI	Log rank *P* value
			Val	Plc			
Groups							
ACEI (yes)	2,326	2,318	19.9	18.8	1.055	(0.925, 1.203)	.346
ACEI (no)	185	181	17.3	27.1	0.669	(0.424, 1.056)	.017*
BB (yes)	867	883	16.4	12.5	1.357	(1.057, 1.742)	.018*
BB (no)	1,644	1,616	21.5	23.1	0.922	(0.797, 1.067)	.220
Subgroups							
ACEI (no), BB (no)	112	114	17.0	31.6	0.582	(0.330, 1.025)	.012*
ACEI (yes), BB(no)	1,532	1,502	21.8	22.5	0.959	(0.824, 1.116)	.561
ACEI (no), BB (yes)	73	67	17.8	19.4	0.807	(0.364, 1.793)	.578
ACEI (yes), BB (yes)	794	816	16.2	11.9	1.421	(1.092, 1.851)	.009*
All subgroups except ACEI (yes), BB (yes)							
	1,717	1,683	21.3	23.0	0.924	(0.800, 1.066)	.192

*$P < .05$.
§Cox regression.

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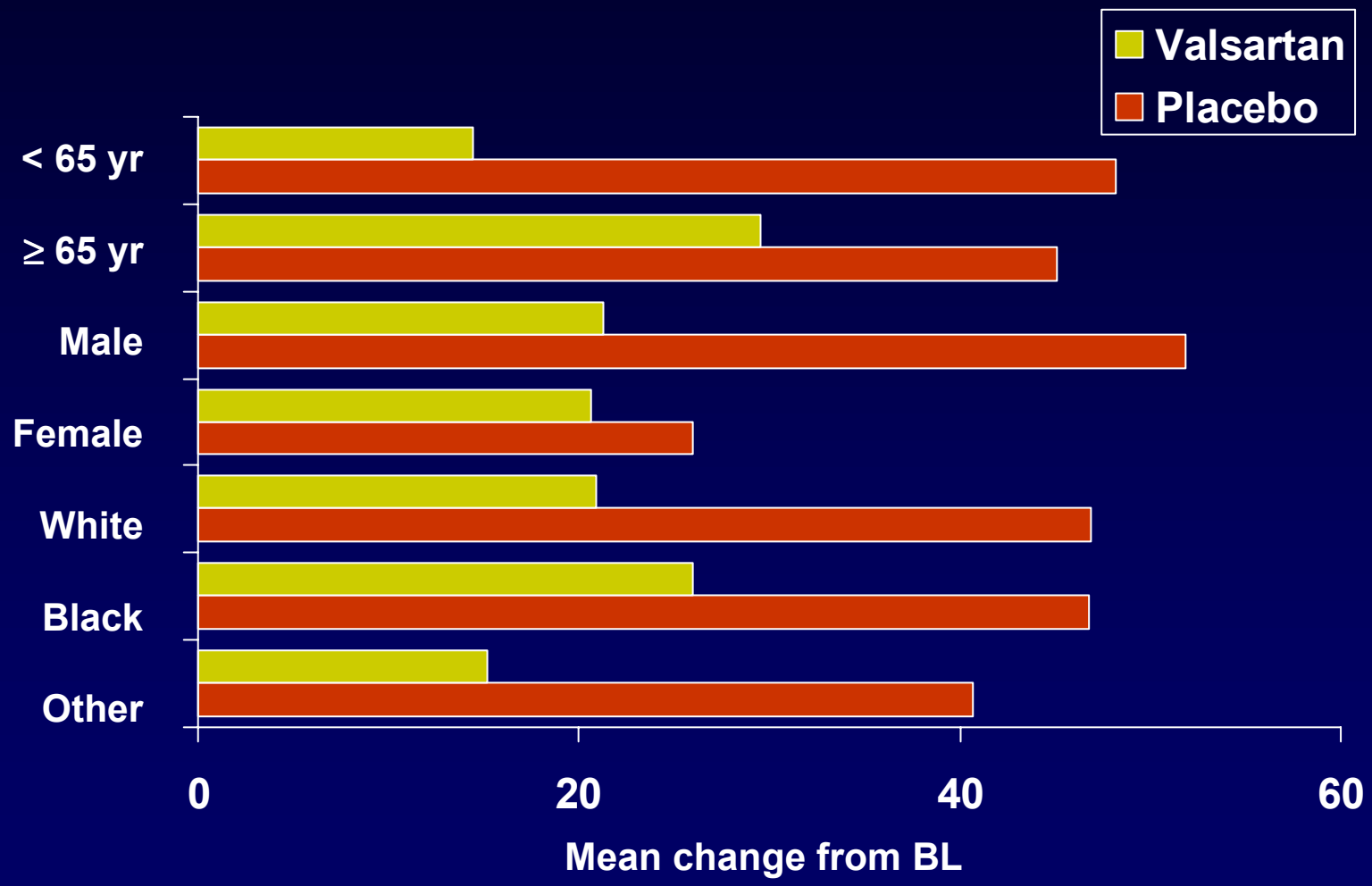
Plasma Norepinephrine Mean Change From Baseline at Endpoint by Demographics (Val-HeFT)



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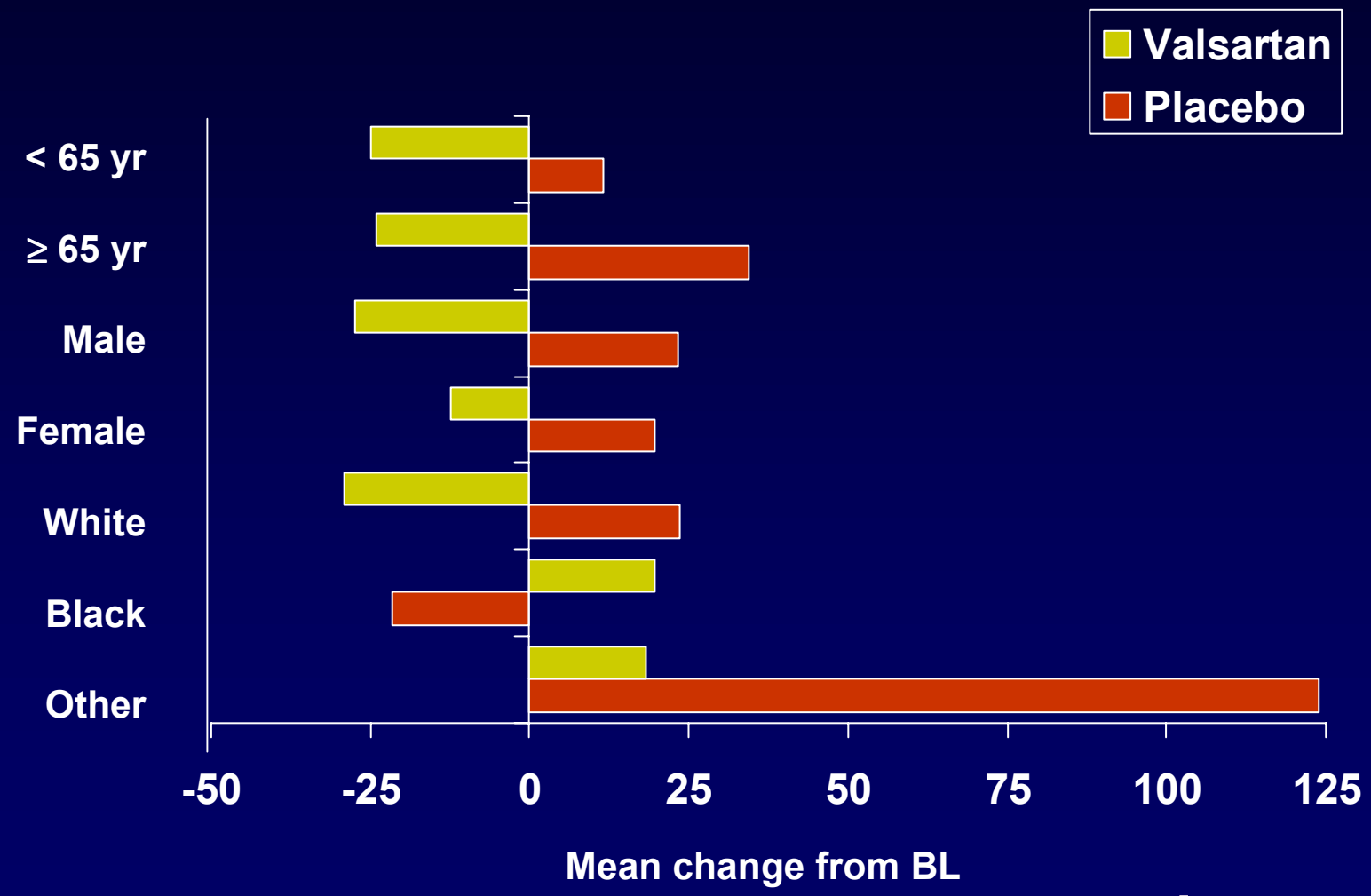
Plasma Brain Natriuretic Peptide Mean Change From Baseline at Endpoint by Demographics (Val-HeFT)



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Primary Endpoints Black Patients (Val-HeFT)

	Events, n (%)		Hazard ratio§	
	Valsartan	Placebo	(95% CI)	*P* value‖
Primary endpoints black patients				
	N = 182	N = 162		
Mortality¶	37 (20.3)	23 (14.2)	1.479 (0.87, 2.51)	.127
Morbidity#	68 (37.4)	52 (32.1)	1.112 (0.77, 1.61)	.302
Primary endpoints non-black patients				
	N = 2,329	N = 2,337		
Mortality¶	458 (19.7)	461 (19.7)	.997 (0.88, 1.14)	.911
Morbidity#	655 (28.1)	749 (32.0)	.848 (0.76, .94)	.002*

*Statistically significant vs. placebo (*P* < .025).
§Cox regression.
‖Log-rank test.
¶All cause mortality to trial end.
#First event including all cause mortality.

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Incidence of Patients Exceeding Prespecified Percent Change at Any Timepoint: Overall Population Versus Background Spironolactone (Val-HeFT)

	Patients, %			
	All patients		Background spironolactone	
	Valsartan N = 2,307-2,480	Placebo N = 2,295-2,475	Valsartan N = 108-120	Placebo N = 117-125
Potassium§ (> 20% increase)	34.3	20.9	36.8	25.0
Creatinine (> 50% increase)	14.6	6.1	22.5	4.8
BUN (> 50% increase)	46.8	26.7	59.2	24.8
Uric Acid (> 50% increase)	10.1	7.9	16.7	9.4

§Excluding values ≥ 7 mEq/L.

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Number of Patients Requiring Dialysis

	Valsartan		Placebo	
	N	n (%)	N	n (%)
Total	3,282	12 (0.4)	2,740	12 (0.4)
103, 104, 106, 110	776	1 (0.1)	246	0 (0.0)
Val-HeFT	2,506	11 (0.4)	2,494	12 (0.5)

Most Frequent AEs (≥ 5%, Overall Valsartan Group) by Race (Val-HeFT) (1)

	Patients, %					
	Valsartan			Placebo		
	N = 2,250	N = 182	N = 74	N = 2,268	N = 162	N = 64
	White	Black	Oriental/ Other	White	Black	Oriental/ Other
Total patients with AEs, %	91.2	94.0	95.9	89.2	93.2	96.9
Dizziness (exc vertigo)	24.8	24.7	31.1	18.2	16.0	20.3
Hypotension NOS	14.4	10.4	6.8	8.2	6.8	4.7
Chest pain NEC	12.7	22.5	13.5	13.6	21.6	12.5
Congestive cardiac failure aggravated	10.5	18.1	8.1	14.5	22.8	34.4
Cough	9.6	18.1	12.2	10.3	14.8	14.1
Nasopharyngitis	9.8	12.6	9.5	9.1	12.3	4.7
Upper respiratory tract infection NOS	9.3	13.2	13.5	9.4	19.1	23.4
Diarrhea NOS	9.8	7.1	6.8	7.7	8.0	7.8
Nausea	8.7	11.0	4.1	9.1	14.8	7.8
Bronchitis NOS	8.0	6.0	8.1	8.6	4.3	12.5

NOS = Not otherwise specified; NEC = Not elsewhere classified.

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Goals for Heart Therapy

- Make people feel better (short-term)
- Keep people from feeling worse (intermediate-term)
- Delay death and morbidity (long-term)

Mean Change From Baseline Sitting Systolic BP to Final Visit by Cotherapy (Val-HeFT)

	Blood pressure, mm Hg					
	Valsartan			Placebo		
	N	Baseline	Change	N	Baseline	Change
ACEI (yes)	2,310	123.1	–6.9*	2,302	124.0	–3.8
ACEI (no)	184	127.4	–8.5*	180	125.2	–2.6
BB (yes)	862	122.9	–6.5*	877	123.9	–3.2
BB (no)	1,632	123.7	–7.4*	1,605	124.2	–4.0
ACEI (no), BB (no)	112	128.8	–10.2*	113	127.2	–3.8
ACEI (yes), BB (no)	1,520	123.3	–7.1*	1,492	124.0	–4.0
ACEI (no), BB (yes)	72	125.3	–5.9	67	121.7	–0.6
ACEI (yes), BB (yes)	790	122.7	–6.6*	810	124.0	–3.4

*$P < .05$, valsartan versus placebo.

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