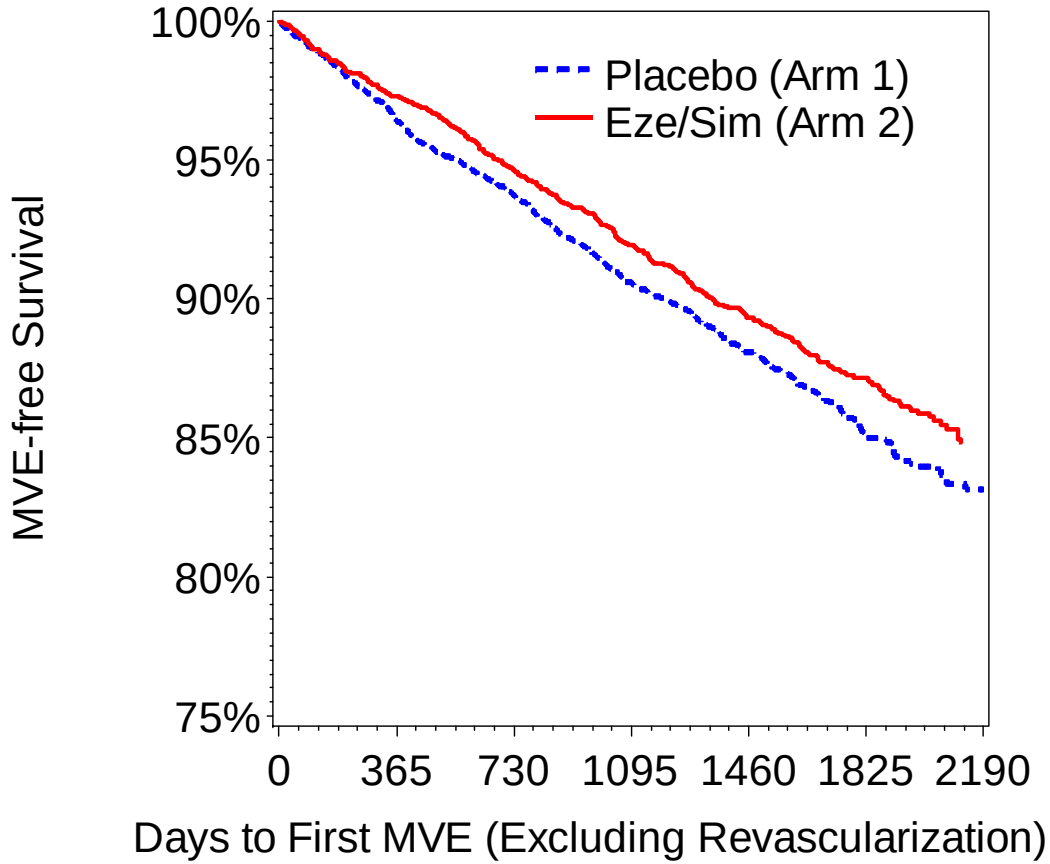
FDA Backup Slides
EMDAC November 2, 2011

FDA Exploratory Analysis: MVE without Revascularization



Eze/Sim (Arm 2)	Placebo (Arm 1)
480/4193 (11.4%)	544/4191 (13.0%)

Rate Ratio 0.88

95% CI: 0.77-0.99

Log-rank P=0.03

Events Composing First MAE

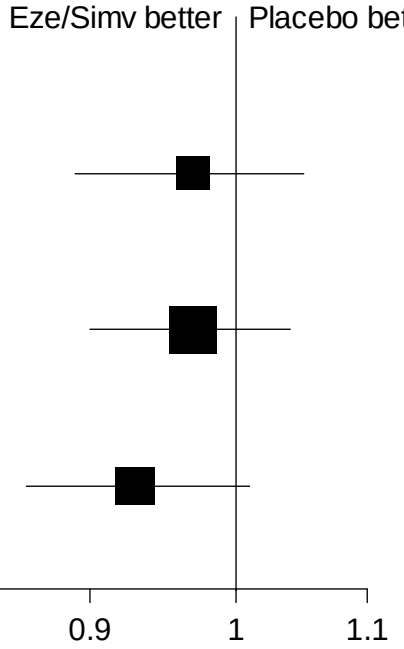
	Placebo (Arm 1)	Eze/Sim (Arm 2)
~~Non-CHD Death~~	~~143~~	~~124~~
Nonfatal MI	130	111
Ischemic CVA	126	96
Vascular Surgery/Intervention	99	75
PCI	75	59 **+ 1**
CHD Death	54	58
Non-traumatic Amputation	40	47
~~Hemorrhagic CVA~~	~~33~~	~~31~~
CABG	36	27
Unknown CVA	13 **+ 1**	11 **+ 1**
TOTAL	**574**	**486**

Treatment Effect by Baseline "at-goal" LDL & Dialysis Status

	LDL ≤ 100	**LDL > 100**
Non-dialysis (n=6028)	0.90 (0.73, 1.12) (N=2348)	0.71 (0.60, 0.85) (N=3680)
Dialysis (n=2864)	0.98 (0.78, 1.22) (N=1537)	0.86 (0.68, 1.08) (N=1327)
ALL (n=8892)	0.95 (0.81, 1.10) (N=3885)	0.76 (0.66, 0.87) (N=5007)

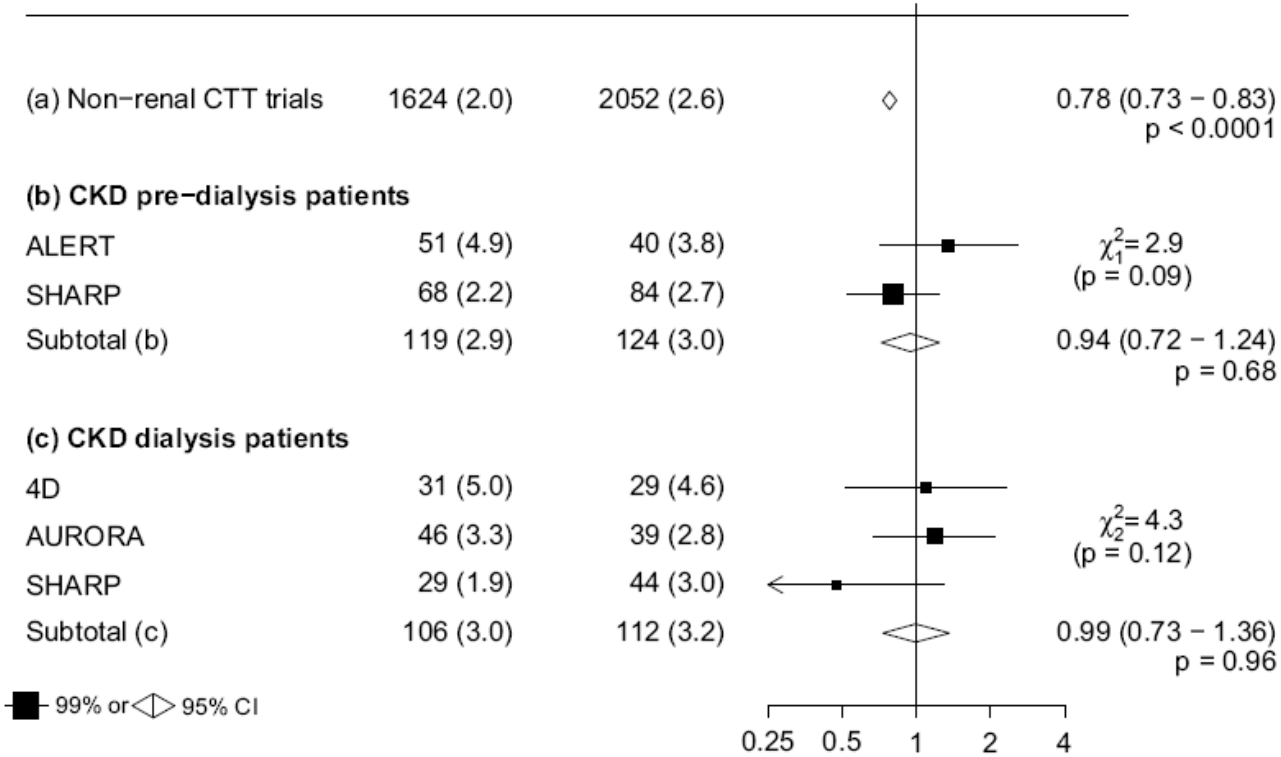
Renal Outcomes

Event	Eze/Simv (N=3117)	Placebo (N=3130)	RR & 95% CI	P
ESRD	1057 (33.9%)	1084 (34.6%)	0.97 (0.89-1.05)	P=0.414
ESRD or Death	1477 (47.4%)	1513 (48.3%)	0.97 (0.9-1.04)	P=0.35
ESRD or Doubled Cr	1190 (38.2%)	1257 (40.2%)	0.93 (0.86-1.01)	P=0.094



Non-hemorrhagic CVA per mmol/L LDL-C Reduction

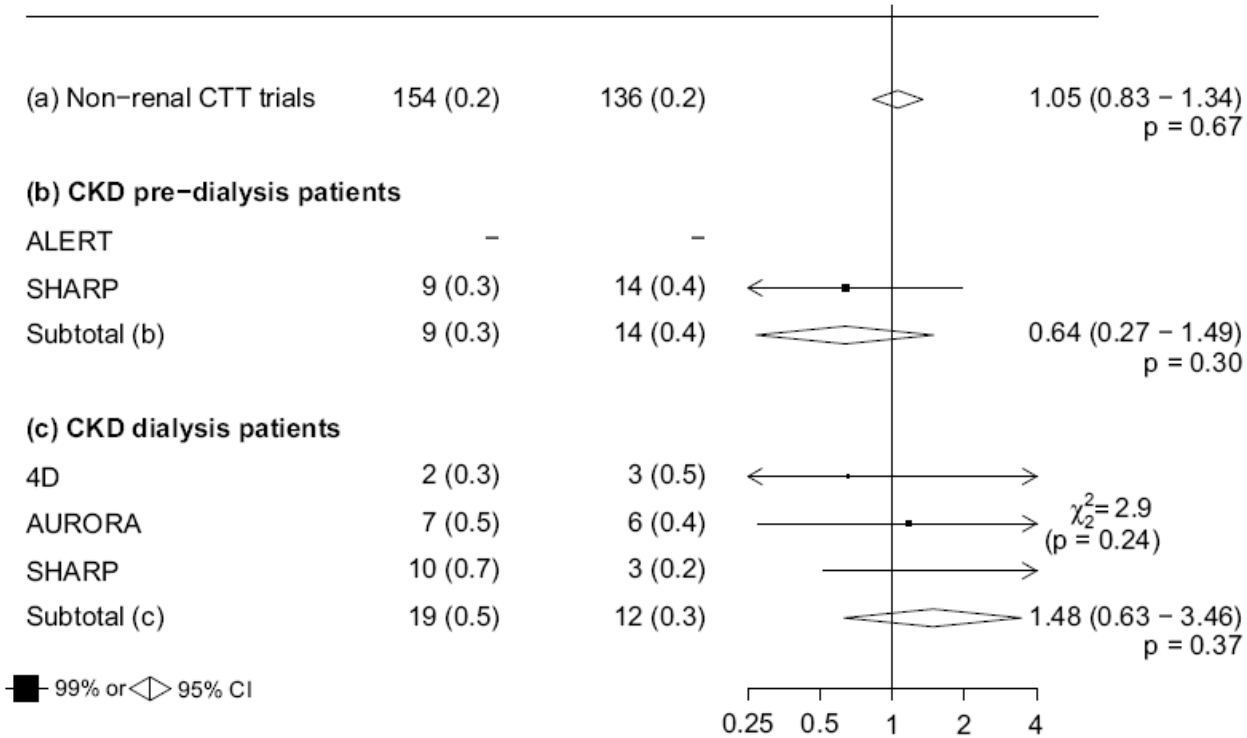
Trial	Events (%) Statin/more intensive	Events (%) Control/less intensive	Rate ratio (RR) per mmol/L LDL−C reduction
(a) Non−renal CTT trials	1624 (2.0)	2052 (2.6)	0.78 (0.73 − 0.83) p < 0.0001
(b) CKD pre−dialysis patients			
ALERT	51 (4.9)	40 (3.8)	χ^2_1= 2.9 (p = 0.09)
SHARP	68 (2.2)	84 (2.7)	
Subtotal (b)	119 (2.9)	124 (3.0)	0.94 (0.72 − 1.24) p = 0.68
(c) CKD dialysis patients			
4D	31 (5.0)	29 (4.6)	
AURORA	46 (3.3)	39 (2.8)	χ^2_2= 4.3 (p = 0.12)
SHARP	29 (1.9)	44 (3.0)	
Subtotal (c)	106 (3.0)	112 (3.2)	0.99 (0.73 − 1.36) p = 0.96



Heterogeneity between (a), (b) and (c): χ^2_2= 3.9 (p = 0.14)
Difference between (b) and (c): χ^2_1= 0.1 (p = 0.81)
Weighted by 2.5 year LDL difference for SHARP and 1 year for all the other trials

Hemorrhagic CVA per mmol/L LDL-C Reduction

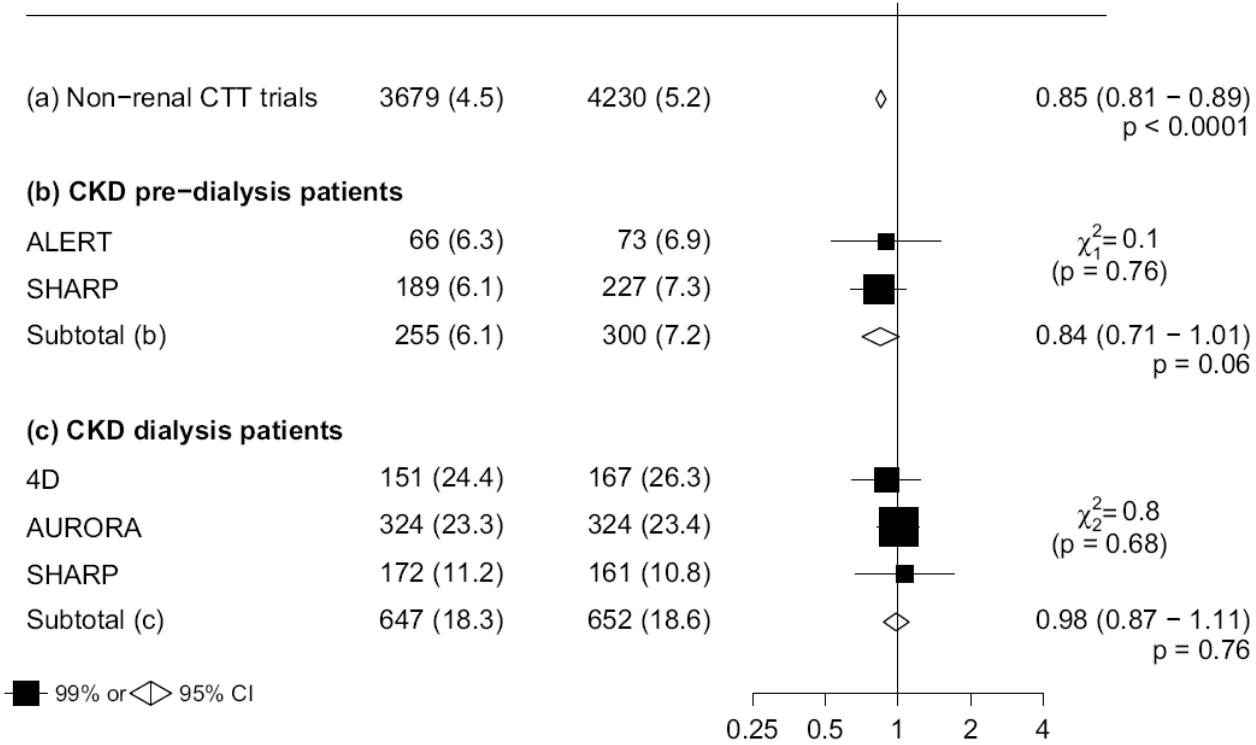
Trial	Events (%) Statin/more intensive	Events (%) Control/less intensive	Rate ratio (RR) per mmol/L LDL−C reduction
(a) Non−renal CTT trials	154 (0.2)	136 (0.2)	1.05 (0.83 − 1.34) p = 0.67
(b) CKD pre−dialysis patients			
ALERT	−	−	
SHARP	9 (0.3)	14 (0.4)	
Subtotal (b)	9 (0.3)	14 (0.4)	0.64 (0.27 − 1.49) p = 0.30
(c) CKD dialysis patients			
4D	2 (0.3)	3 (0.5)	
AURORA	7 (0.5)	6 (0.4)	χ^2_2= 2.9 (p = 0.24)
SHARP	10 (0.7)	3 (0.2)	
Subtotal (c)	19 (0.5)	12 (0.3)	1.48 (0.63 − 3.46) p = 0.37



Heterogeneity between (a), (b) and (c): χ^2_2=2.0 (p = 0.38)
Difference between (b) and (c): χ^2_1= 1.9 (p = 0.17)
Weighted by 2.5 year LDL difference for SHARP and 1 year for all the other trials

Vascular Death per mmol/L LDL-C Reduction

Trial	Events (%) Statin/more intensive	Events (%) Control/less intensive	Rate ratio (RR) per mmol/L LDL−C reduction
(a) Non−renal CTT trials	3679 (4.5)	4230 (5.2)	0.85 (0.81 − 0.89) p < 0.0001
(b) CKD pre−dialysis patients			
ALERT	66 (6.3)	73 (6.9)	χ^2_1= 0.1 (p = 0.76)
SHARP	189 (6.1)	227 (7.3)	
Subtotal (b)	255 (6.1)	300 (7.2)	0.84 (0.71 − 1.01) p = 0.06
(c) CKD dialysis patients			
4D	151 (24.4)	167 (26.3)	
AURORA	324 (23.3)	324 (23.4)	χ^2_2= 0.8 (p = 0.68)
SHARP	172 (11.2)	161 (10.8)	
Subtotal (c)	647 (18.3)	652 (18.6)	0.98 (0.87 − 1.11) p = 0.76



Heterogeneity between (a), (b) and (c): χ^2_2=4.8 (p = 0.09)
Difference between (b) and (c): χ^2_1= 1.9 (p = 0.17)
Weighted by 2.5 year LDL difference for SHARP and 1 year for all the other trials