Supp.2 Meta-analyses and subgroup analyses for safety profiles comparing morning dosing versus bedtime dosing

Variable	No. of Trials	No. of subjects (M/E)	Heterogeneity (I^2)	RR	95%CI	P-value
Overall drug-related AEs						
Total	**14**	**1146/1147**	**Chi^2=18.70, I^2=41.0%**	**0.81**	**(0.60, 1.10)**	**P=0.17**
ACEIs	5	209/213	Chi^2=0.34, I^2=0.0%	0.35	(0.09, 1.40)	P=0.14
ARBs	2	300/294	Chi^2=2.55, I^2=61.0%	1.28	(0.32, 5.22)	P=0.73
Diuretics	2	88/91	Chi^2=0.17, I^2=0.0%	1.67	(0.57, 4.88)	P=0.35
CCBs	3	253/245	Chi^2=1.75, I^2=0.0%	0.32	(0.17, 0.62)	P=0.0007
ARBs+CCBs	2	296/304	Chi^2=0.83, I^2=0.0%	1.20	(0.80, 1.82)	P=0.38
Overall withdrawals						
Total	**13**	**876/872**	**Chi^2=4.69, I^2=0.0%**	**0.58**	**(0.36, 0.93)**	**P=0.02**
ACEIs	3	67/70	Chi^2=0.85, I^2=0.0%	0.68	(0.20, 2.31)	P=0.54
ARBs	3	408/404	Chi^2=0.37, I^2=0.0%	0.64	(0.36, 1.13)	P=0.13
Diuretics*	2	88/91	NA	NA	-	-
CCBs	2	133/127	Chi^2=2.71, I^2=63%	0.29	(0.04, 1.95)	P=0.20
Combination*	3	180/180	NA	NA	-	-
Serious AEs						
Total	**2**	**497/499**	**Chi^2=1.60, I^2=37.0%**	**0.66**	**(0.23, 1.90)**	**P=0.44**
ARBs	1	229/221	NA	0.14	(0.01, 2.65)	P=0.19
ARBs+CCBs	1	268/278	NA	1.04	(0.30, 3.54)	P=0.95

*The data in this row could not available;

AEs=adverse events; ACEIs= angiotensin converting enzyme inhibitor; ARB=angiotensin II receptor blockers; CCBs=calcium channel blockers; No. of trials=number of trials; No. of subjects=number of subjects; M/E=morning/evening; RR=risk ratio; CI=confidence interval; NA=not available.