

ONLINE SUPPLEMENT

**Hemodynamic and Hormonal Changes to Dual Renin Angiotensin System
Inhibition in Experimental Hypertension**

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Short Title: *Combination of Valsartan/Aliskiren*

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Supplemental Tables and Figures

Table S1. Effects of treatments on RAS components in plasma, left ventricle and kidney cortex

Variable	Vehicle (n=9)	Valsartan (n=10)	Combination (n=10)
Plasma			
Ang-(1-12), <i>fmol/mL</i>	159.5 ± 5.2	170.3 ± 10.1	173.6 ± 8.5
Left ventricle			
Ang-(1-12), <i>fmol/mg protein</i>	25.3 ± 2.7	20.6 ± 1.8	26.7 ± 3.1
Ang II, <i>fmol/mg protein</i>	16.1 ± 1.9	14.2 ± 1.5	16.2 ± 2.2
Ang-(1-7), <i>fmol/mg protein</i>	14.5 ± 1.6	15.7 ± 1.4	15.7 ± 1.9
ACE mRNA, <i>units</i>	1.00 ± 0.06	0.88 ± 0.03	0.81 ± 0.03
ACE2 mRNA, <i>units</i>	1.00 ± 0.06	0.85 ± 0.06	0.81 ± 0.07
Kidney cortex			
Ang-(1-12), <i>fmol/mg protein</i>	147.0 ± 17.0	134.8 ± 10.0	179.8 ± 8.9 [†]
Ang II, <i>fmol/mg protein</i>	24.8 ± 2.3	12.9 ± 0.5 ^{***}	12.0 ± 1.2 ^{***}
Ang-(1-7), <i>fmol/mg protein</i>	12.9 ± 0.9	12.7 ± 0.5	13.0 ± 1.3
ACE mRNA, <i>units</i>	1.00 ± 0.10	1.11 ± 0.06	0.92 ± 0.06
ACE2 mRNA, <i>units</i>	1.00 ± 0.09	1.04 ± 0.07	0.75 ± 0.09 [†]

Values are means ± SEM. mRNA values , relative gene expression as described in

Methods. †: P<0.05 vs valsartan, ***: P<0.001 vs vehicle

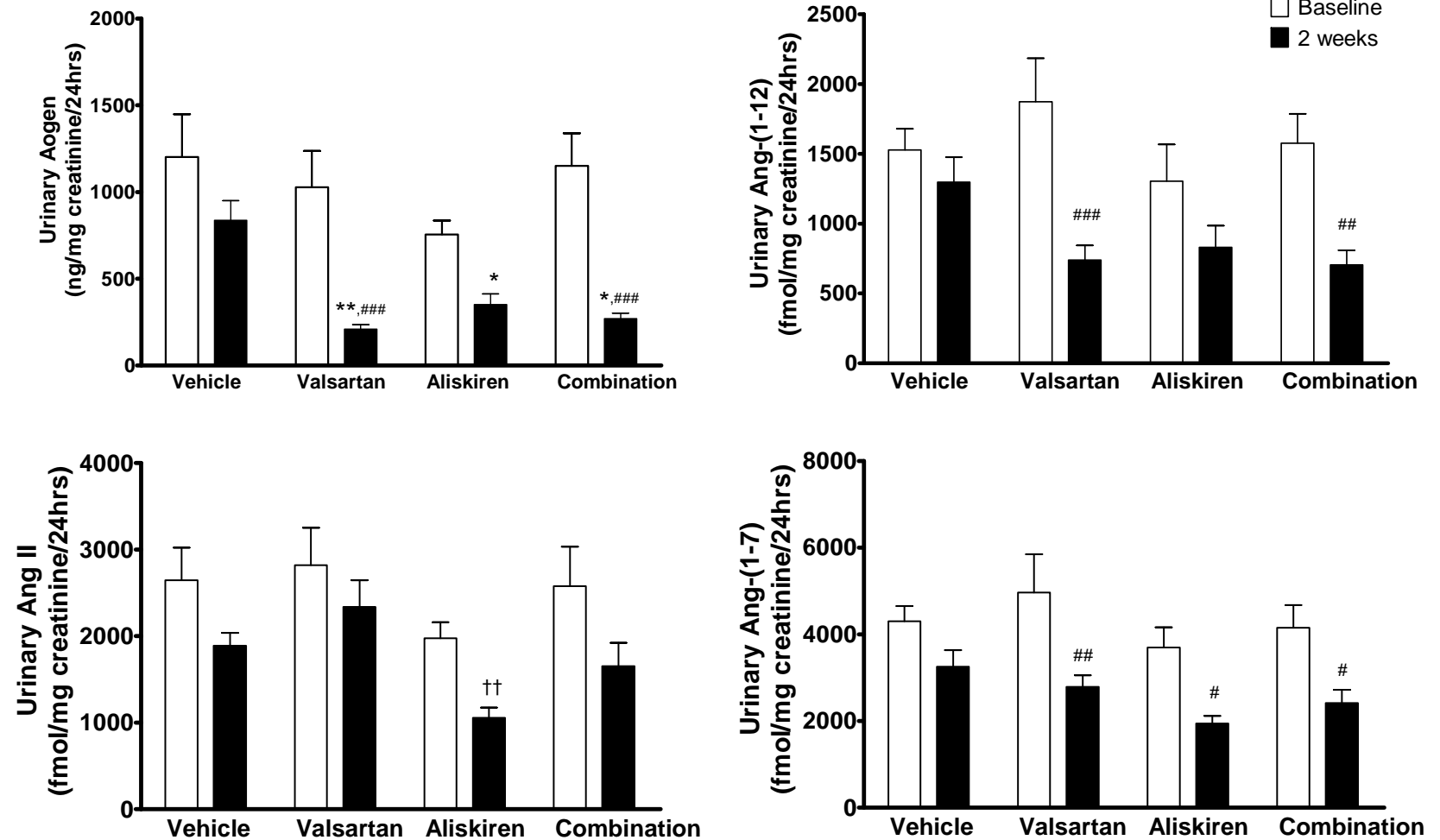


Figure S1. Patterns of urinary excretion rates of angiotensinogen (Aogen), angiotensin-(1-12) [Ang-(1-12)], Ang II, and Ang-(1-7) in mRen2.Lewis rats medicated with valsartan, aliskiren, or the combination of valsartan/aliskiren. Values are means ± SEM. *: P<0.05 vs vehicle, #: P<0.05 vs before treatment, **: P<0.01 vs vehicle, ††: P<0.01 vs valsartan, ###:

P<0.01 vs before treatment, ###: P<0.001 vs before treatment.

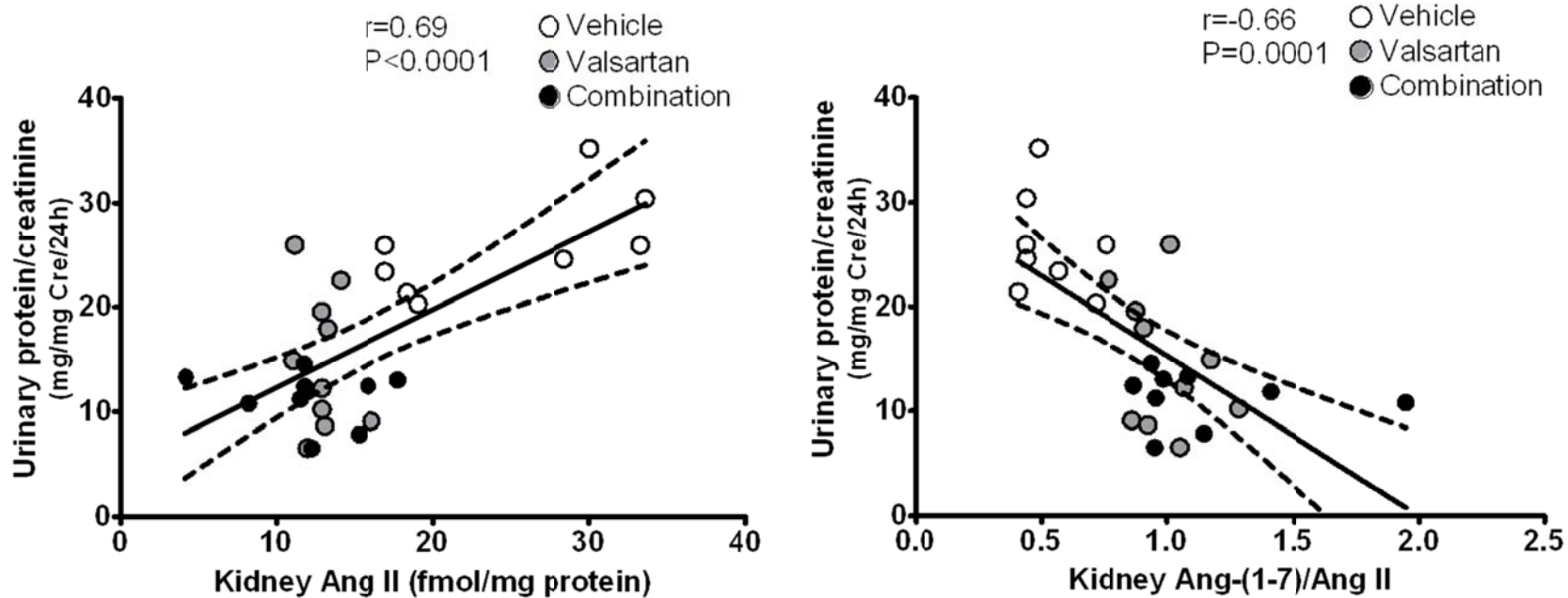


Figure S2. Correlations between urinary protein/creatinine ratio and kidney Ang II level (left panel) or kidney Ang-(1-7)/Ang II ratio (right panel).