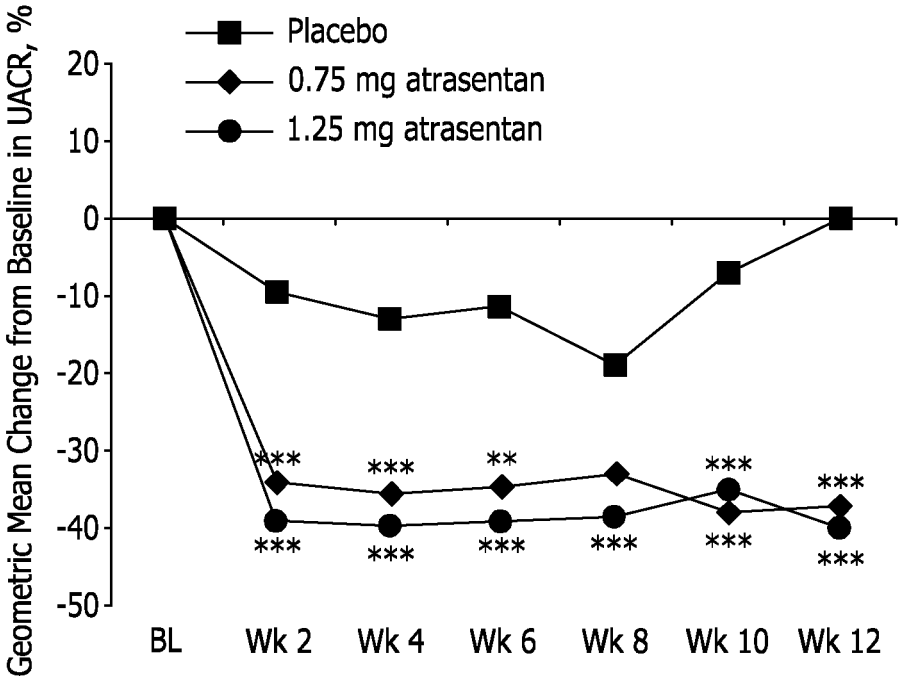


*,**,*** *P* ≤0.05, 0.01, 0.001 for difference from placebo.

FIG. 1

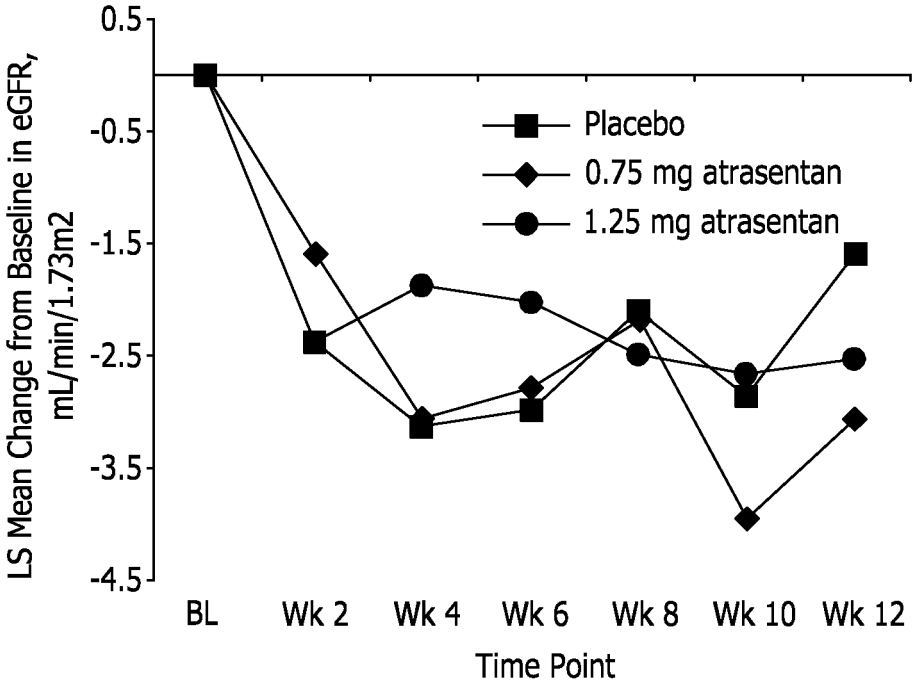


FIG. 2

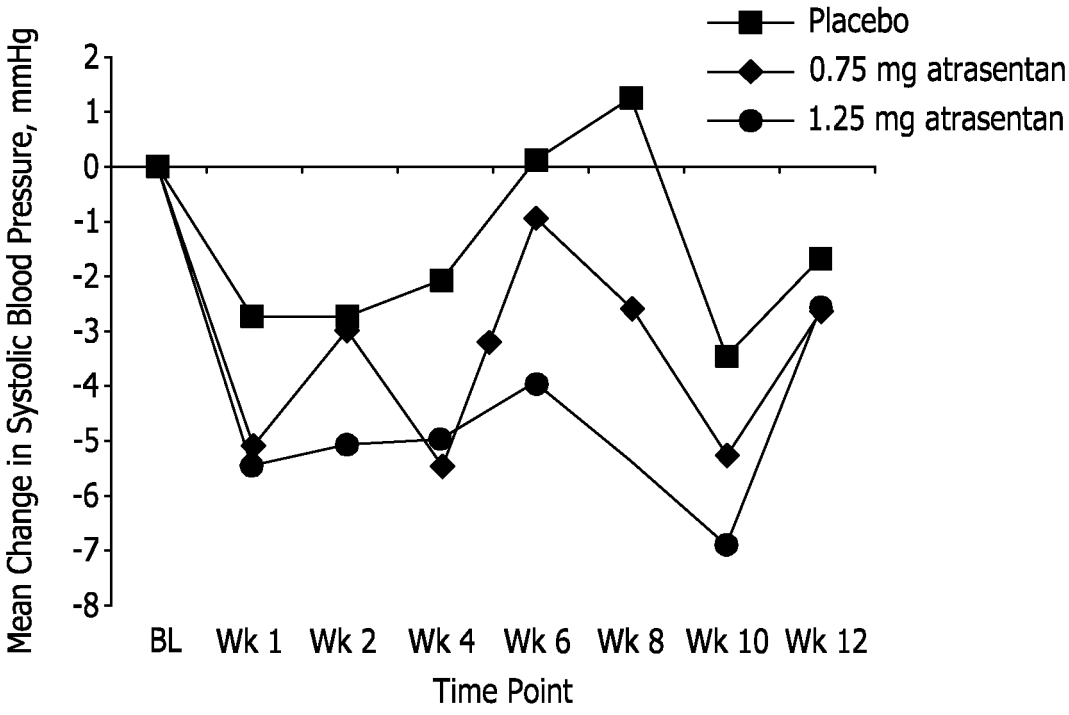
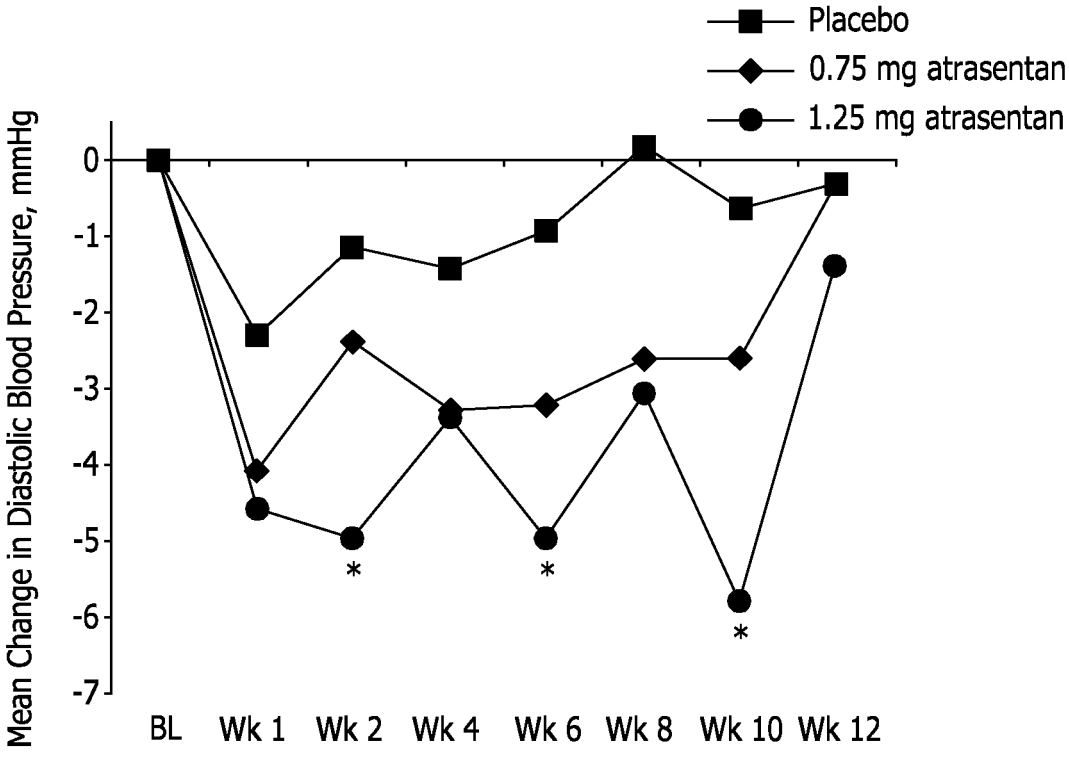


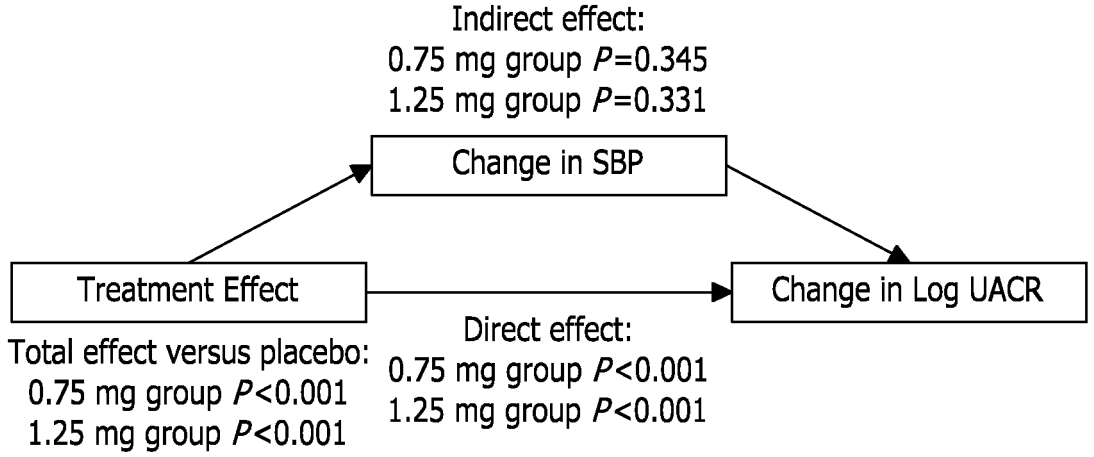
FIG. 3



* $P \leq 0.05$, 0.01 for difference from placebo.

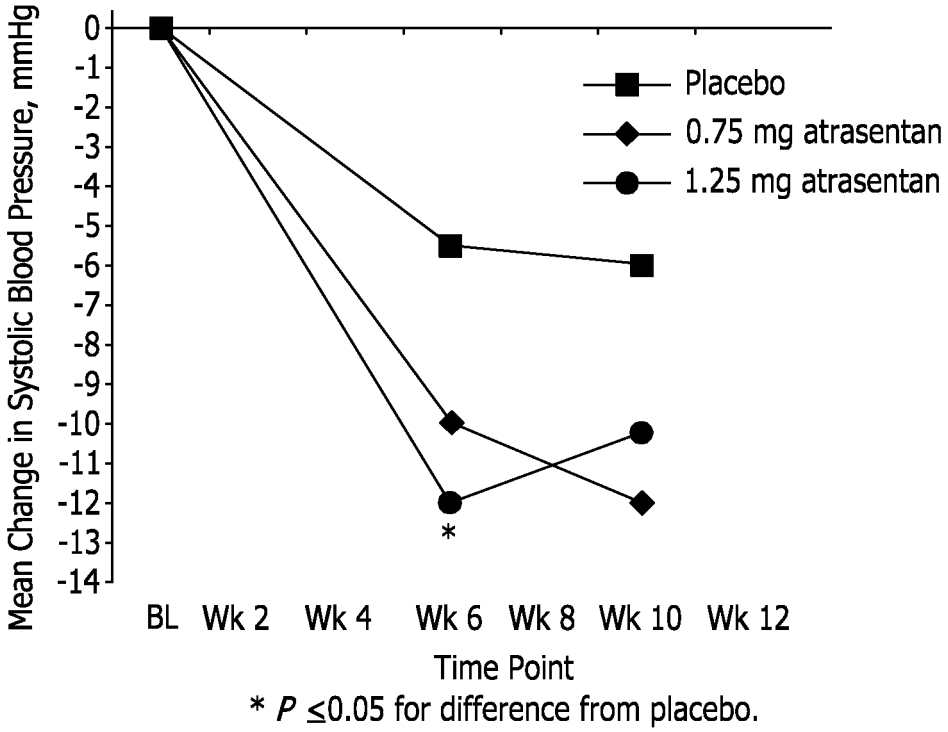
FIG. 4

Path Analysis: Evaluation of Treatment Effect on Change in UACR After Accounting for the Treatment Effect on Change in Systolic Blood Pressure in Example 1



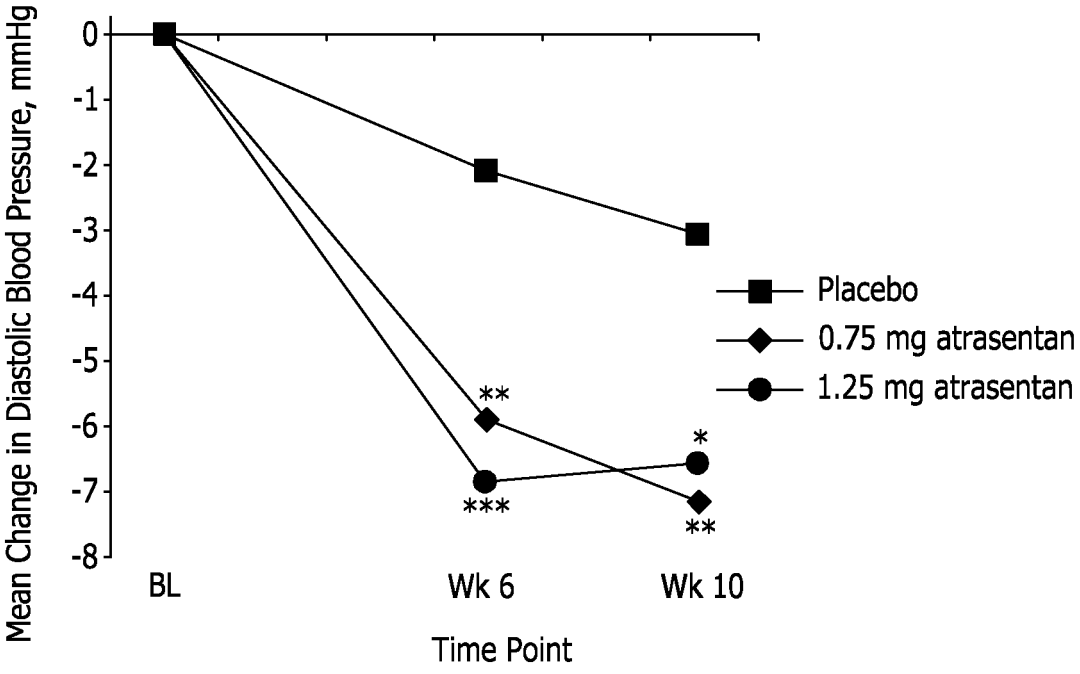
SBP = systolic blood pressure

FIG. 5



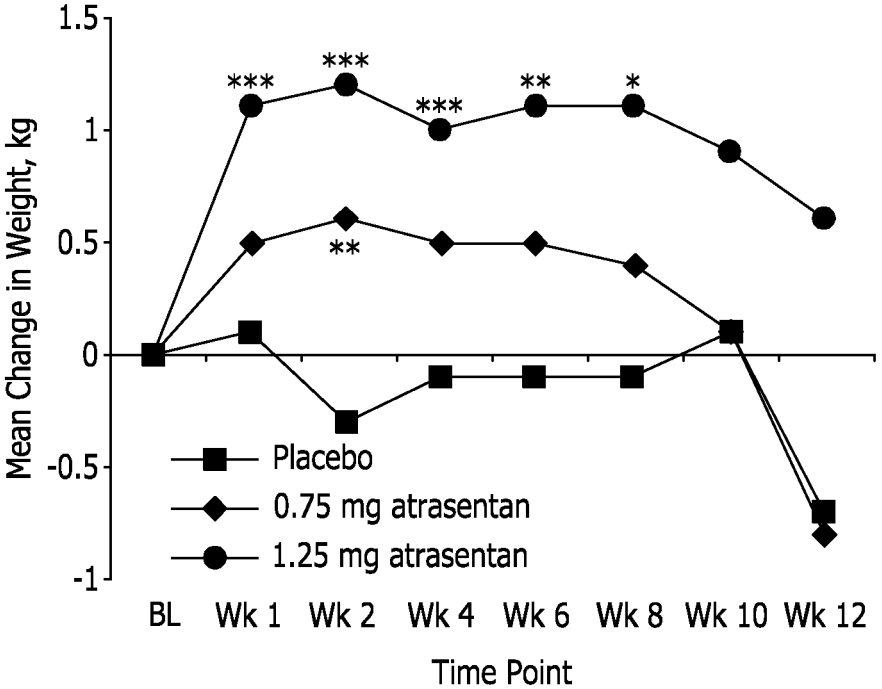
* $P \leq 0.05$ for difference from placebo.

FIG. 6



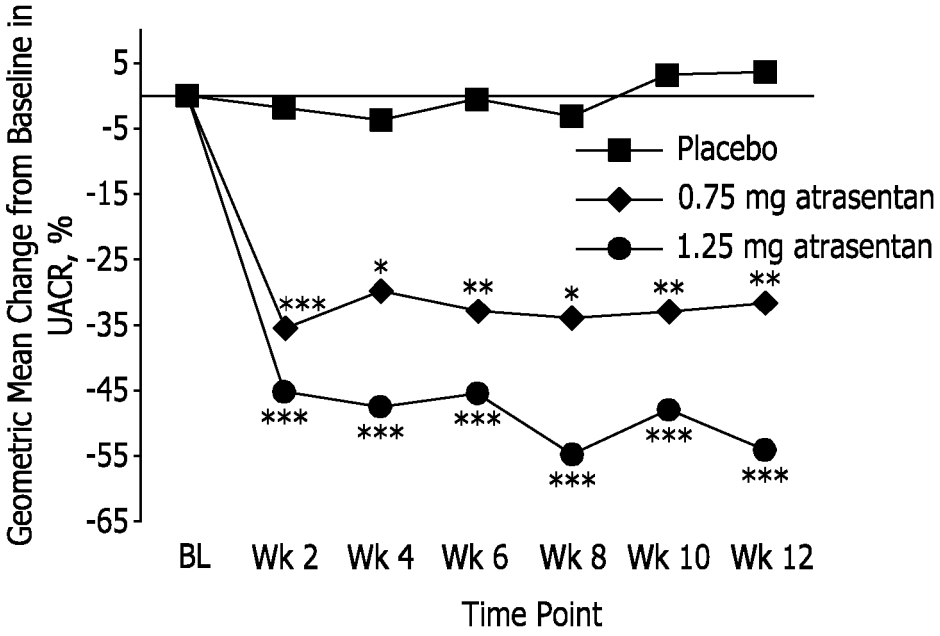
*,**,*** *P* ≤0.05, 0.01, 0.001 for difference from placebo.

FIG. 7



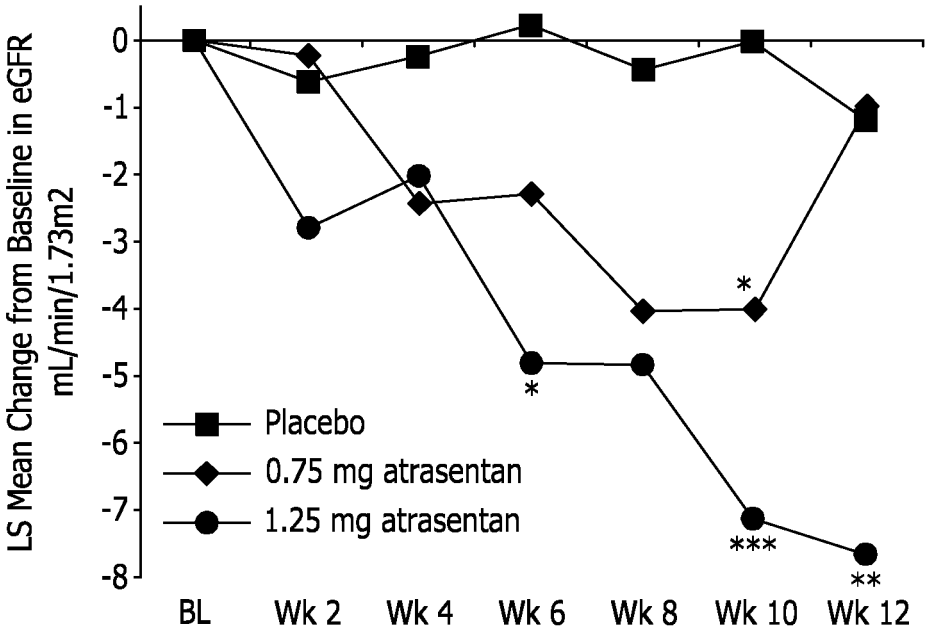
*,**,*** *P* ≤0.05, 0.01, 0.001 for difference from placebo.

FIG. 8



*,**,*** *P* ≤0.05, 0.01, 0.001 for difference from placebo.

FIG. 9



*,**,*** *P* ≤0.05, 0.01, 0.001 for difference from placebo.

FIG. 10

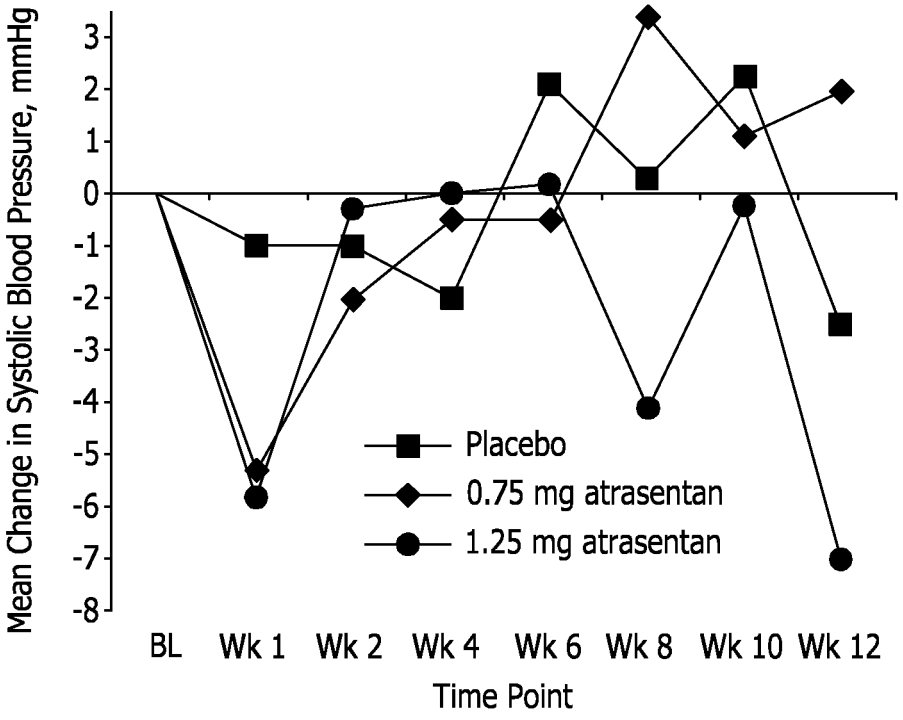

Mean Change in Systolic Blood Pressure, mmHg
3
2
1
0
-1
-2
-3
-4
-5
-6
-7
-8
Placebo
0.75 mg atrasentan
1.25 mg atrasentan
BL
Wk 1
Wk 2
Wk 4
Wk 6
Wk 8
Wk 10
Wk 12
Time Point

FIG. 11

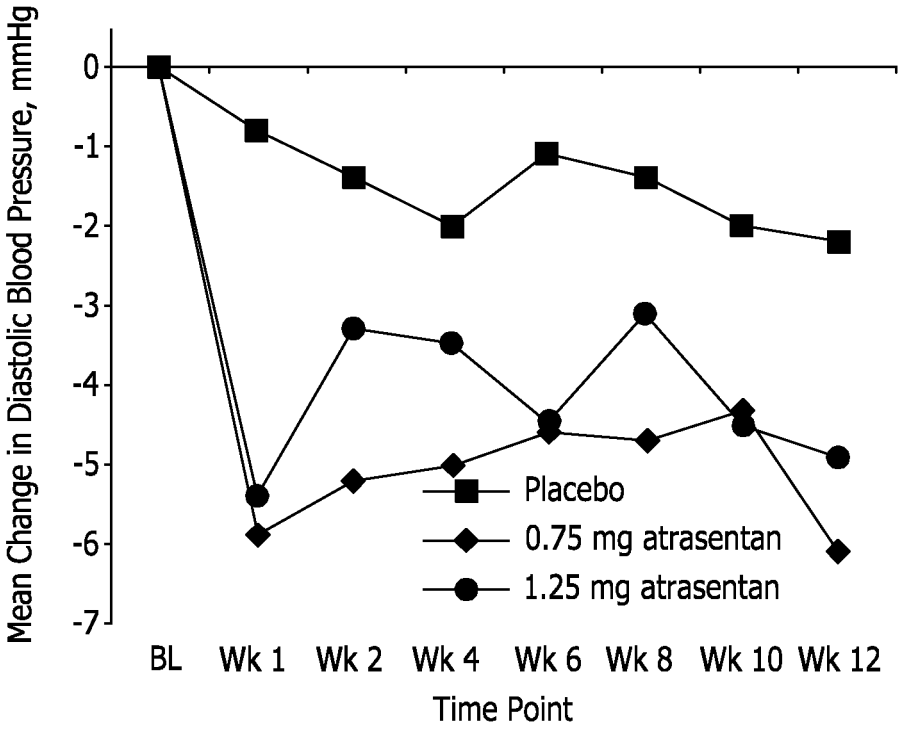

Mean Change in Diastolic Blood Pressure, mmHg
0
-1
-2
-3
-4
-5
-6
-7
Placebo
0.75 mg atrasentan
1.25 mg atrasentan
BL
Wk 1
Wk 2
Wk 4
Wk 6
Wk 8
Wk 10
Wk 12
Time Point

FIG. 12

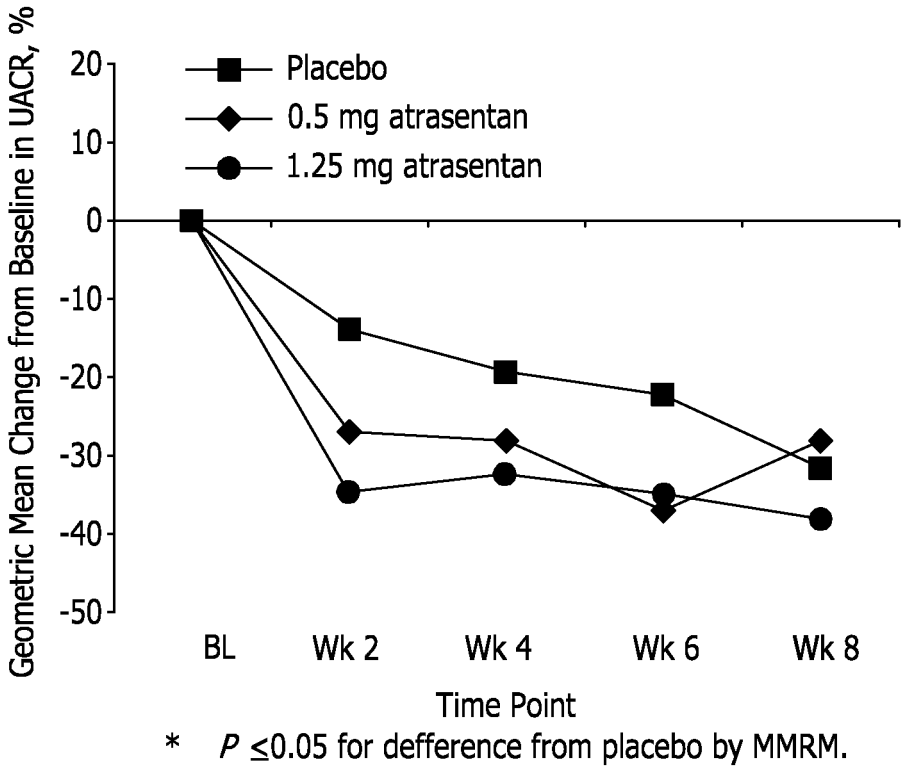

Geometric Mean Change from Baseline in UACR, %
20
10
0
-10
-20
-30
-40
-50
Placebo
0.5 mg atrasentan
1.25 mg atrasentan
BL
Wk 2
Wk 4
Wk 6
Wk 8
Time Point
* P ≤0.05 for defference from placebo by MMRM.

FIG. 13

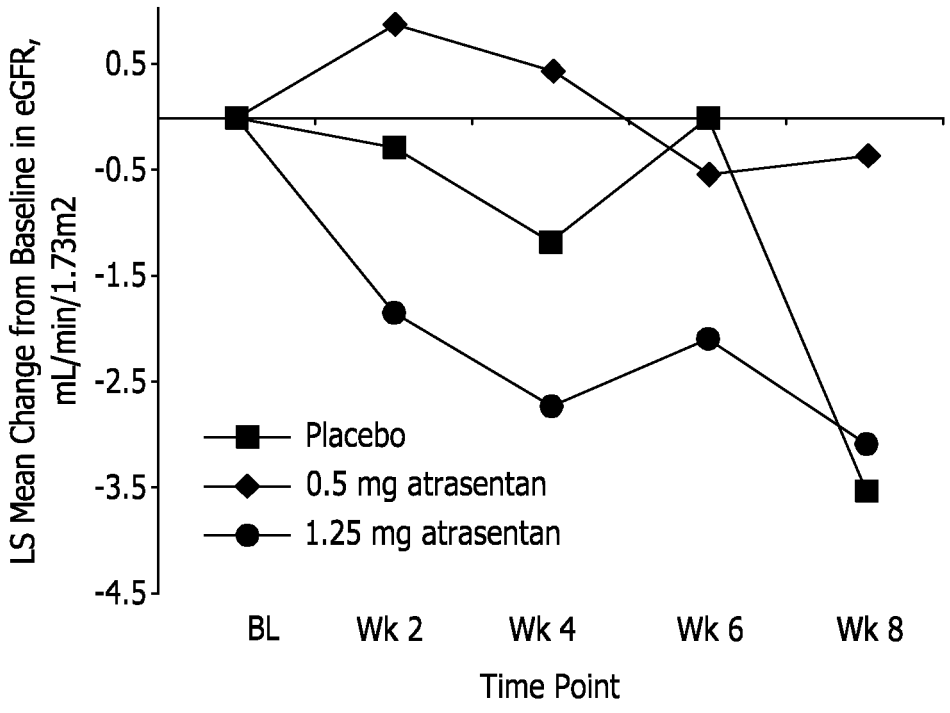

LS Mean Change from Baseline in eGFR, mL/min/1.73m2
0.5
-0.5
-1.5
-2.5
-3.5
-4.5
Placebo
0.5 mg atrasentan
1.25 mg atrasentan
BL
Wk 2
Wk 4
Wk 6
Wk 8
Time Point

FIG. 14

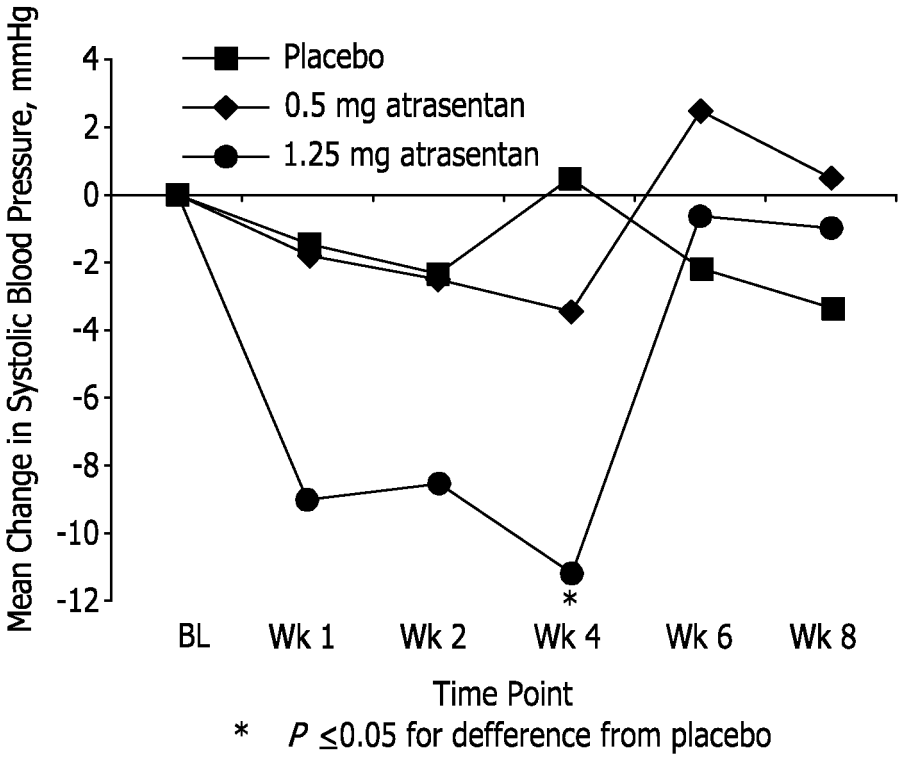

Placebo
0.5 mg atrasentan
1.25 mg atrasentan
Mean Change in Systolic Blood Pressure, mmHg
4
2
0
-2
-4
-6
-8
-10
-12
*
BL
Wk 1
Wk 2
Wk 4
Wk 6
Wk 8
Time Point
* P ≤0.05 for defference from placebo

FIG. 15

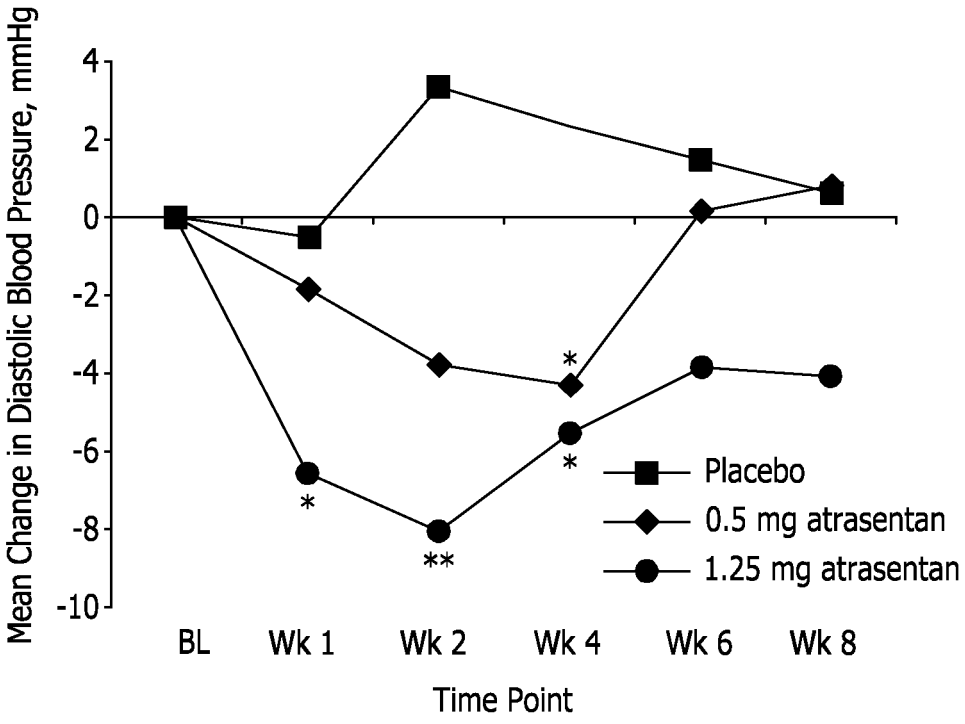

Mean Change in Diastolic Blood Pressure, mmHg
4
2
0
-2
-4
-6
-8
-10
*
*
*
**
Placebo
0.5 mg atrasentan
1.25 mg atrasentan
BL
Wk 1
Wk 2
Wk 4
Wk 6
Wk 8
Time Point

FIG. 16

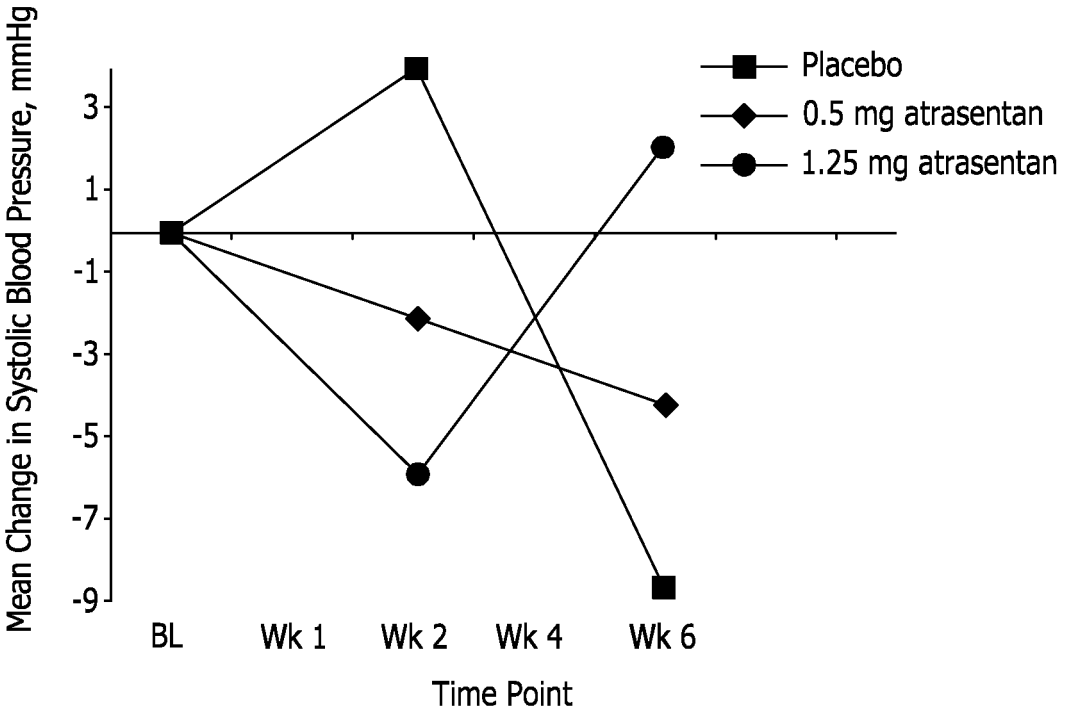

Mean Change in Systolic Blood Pressure, mmHg
3
1
-1
-3
-5
-7
-9
BL
Wk 1
Wk 2
Wk 4
Wk 6
Time Point
Placebo
0.5 mg atrasentan
1.25 mg atrasentan

FIG. 17

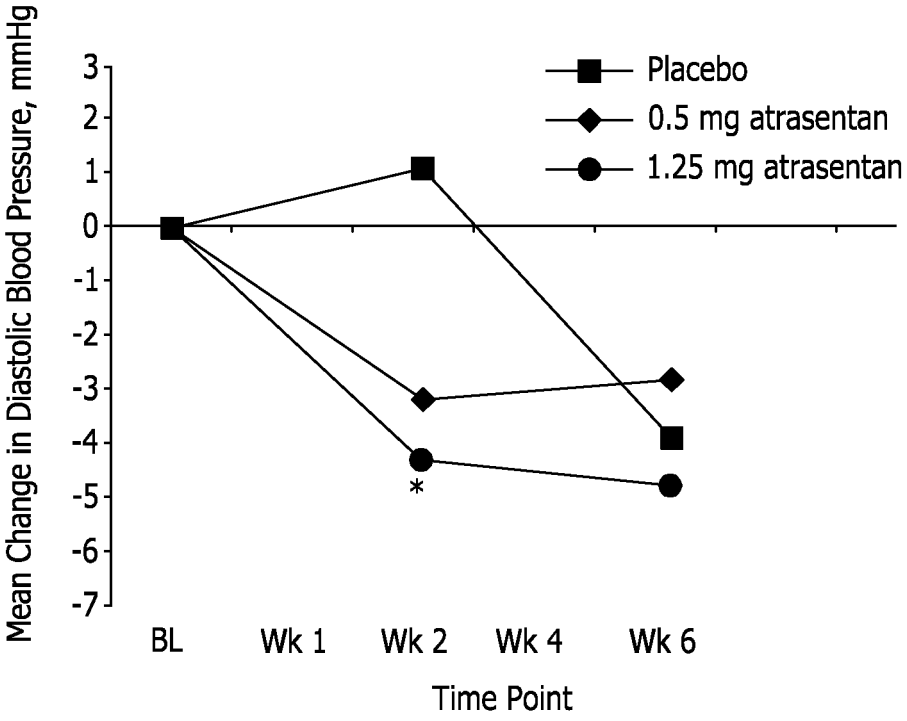

Mean Change in Diastolic Blood Pressure, mmHg
3
2
1
0
-1
-2
-3
-4
-5
-6
-7
*
BL
Wk 1
Wk 2
Wk 4
Wk 6
Time Point
Placebo
0.5 mg atrasentan
1.25 mg atrasentan

FIG. 18

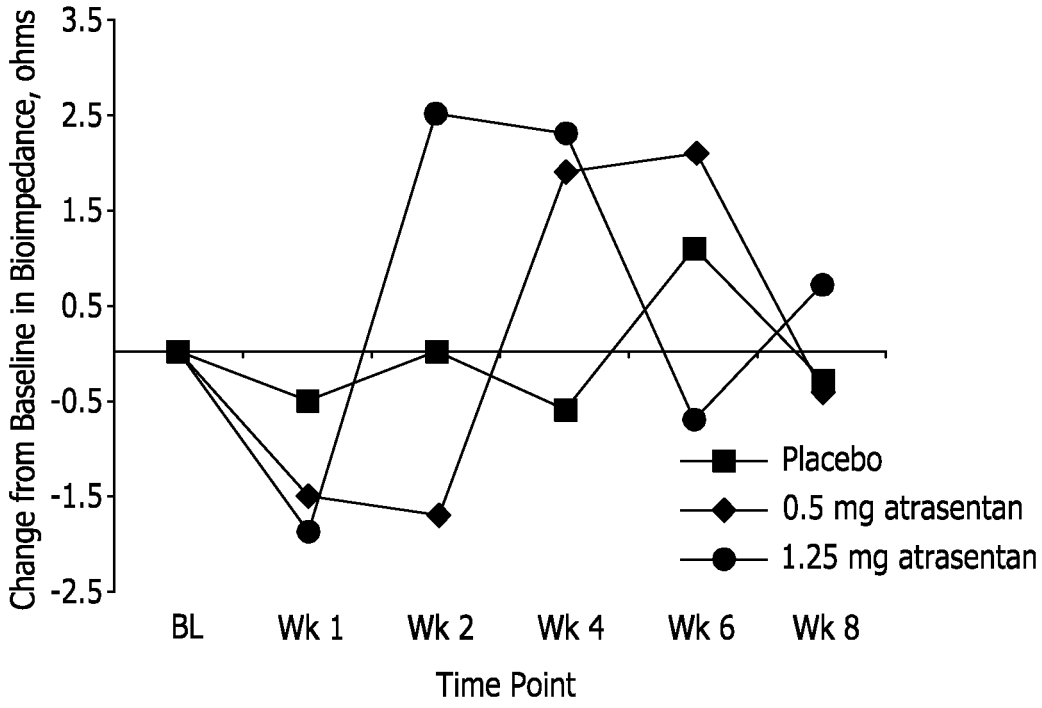

Change from Baseline in Bioimpedance, ohms
3.5
2.5
1.5
0.5
-0.5
-1.5
-2.5
BL
Wk 1
Wk 2
Wk 4
Wk 6
Wk 8
Time Point
Placebo
0.5 mg atrasentan
1.25 mg atrasentan

FIG. 19

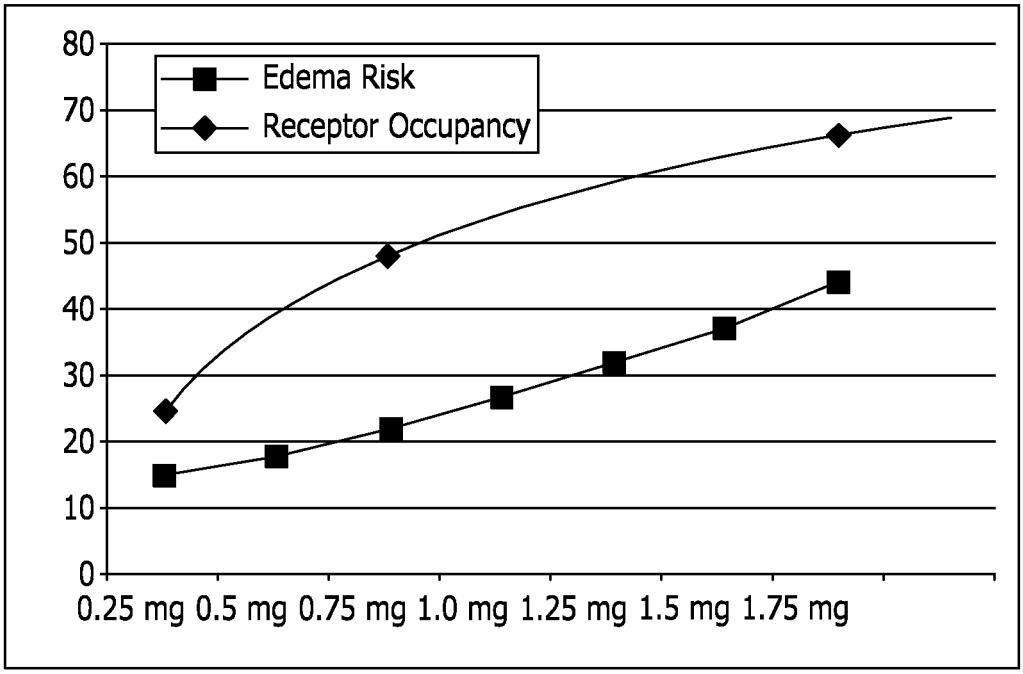

80
70
60
50
40
30
20
10
0
Edema Risk
Receptor Occupancy
0.25 mg 0.5 mg 0.75 mg 1.0 mg 1.25 mg 1.5 mg 1.75 mg

FIG. 20

	Atrasentan 0.75 mg (n = 78)	Atrasentan 0.75 mg (n = 78)	Atrasentan 0.75 mg (n = 78)
Age (years), mean ± SD	64.3 ± 9.0	65.0 ± 9.8	64.5 (8.8)
Female, n (%)	10 (20)	15 (19)	26 (31)
Race, n (%)			
White	23 (46)	36 (46)	38 (46)
Black	2 (4)	14 (18)	13 (16)
Asian	24 (48)	25 (32)	28 (34)
Other	1 (2)	3 (4)	4 (5)
Systolic BP (mm Hg), mean (SD)	136 (14)	138 (14)	136 (15)
Diastolic BP (mm Hg), mean (SD)	72 (10)	75 (10)	74 (9)
UACR (mg/g creatinine), median	671	878	826
Serum creatinine (mg/dL), mean (SD)	1.5 (0.4)	1.6 (0.4)	1.4 (0.4)
eGFR (mL/min/1.73 m2), mean (SD)	49 (13)	48 (15)	51 (14)
BNP (pg/ml), mean (SD)	62 (63)	60 (68)	46 (41)
Statins, n (%)	38 (76)	58 (74)	68 (82)
Diuretics, n (%)	46 (92)	71 (91)	73 (88)

FIG. 21

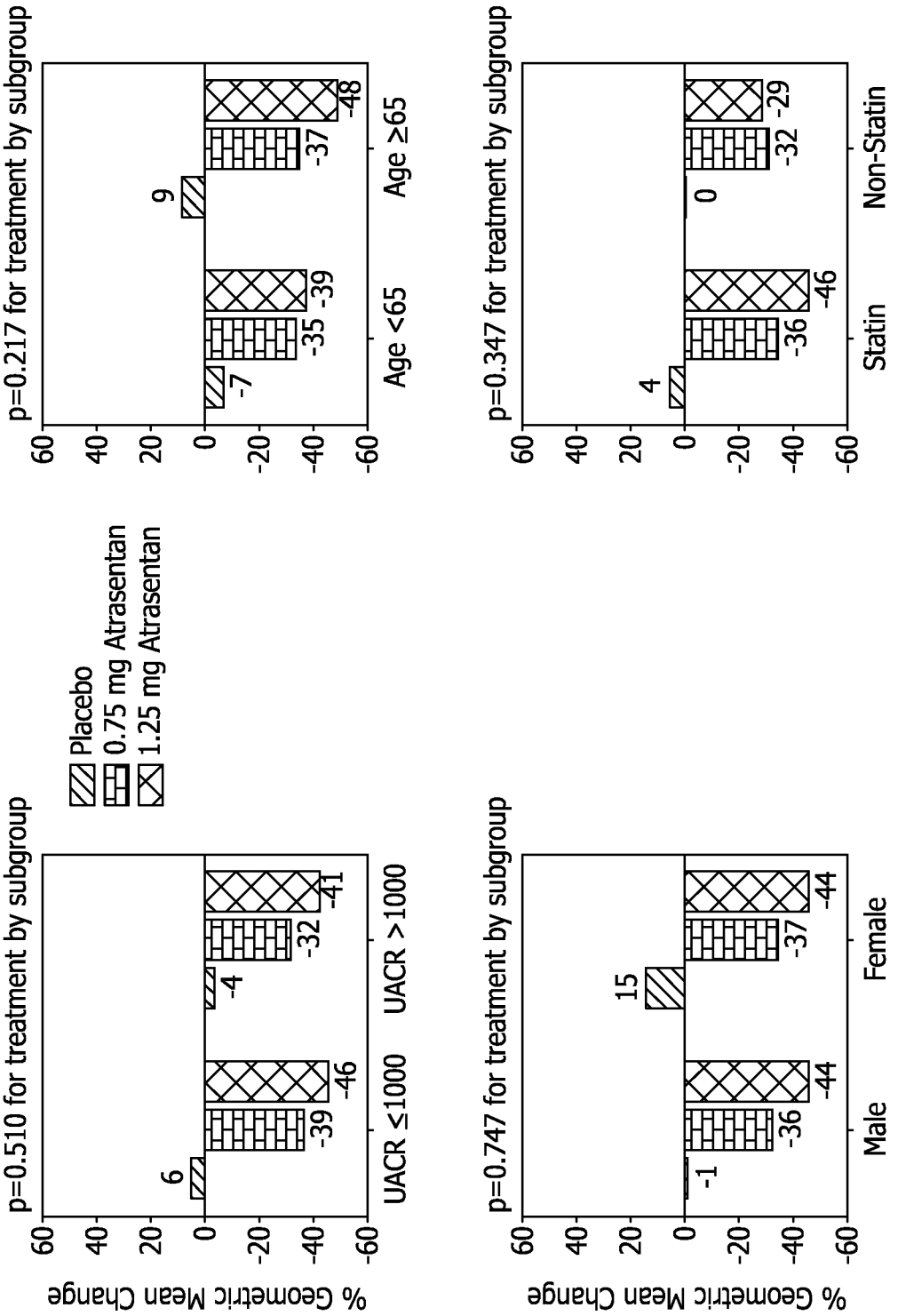

p=0.510 for treatment by subgroup
% Geometric Mean Change
60
40
20
0
-20
-40
-60
6
-39
-46
-4
-32
-41
UACR ≤1000
UACR >1000
Placebo
0.75 mg Atrasentan
1.25 mg Atrasentan
p=0.217 for treatment by subgroup
-7
-35
-39
9
-37
-48
Age <65
Age ≥65
p=0.747 for treatment by subgroup
-1
-36
-44
15
-37
-44
Male
Female
p=0.347 for treatment by subgroup
4
-36
-46
0
-32
-29
Statin
Non-Statin

FIG. 22

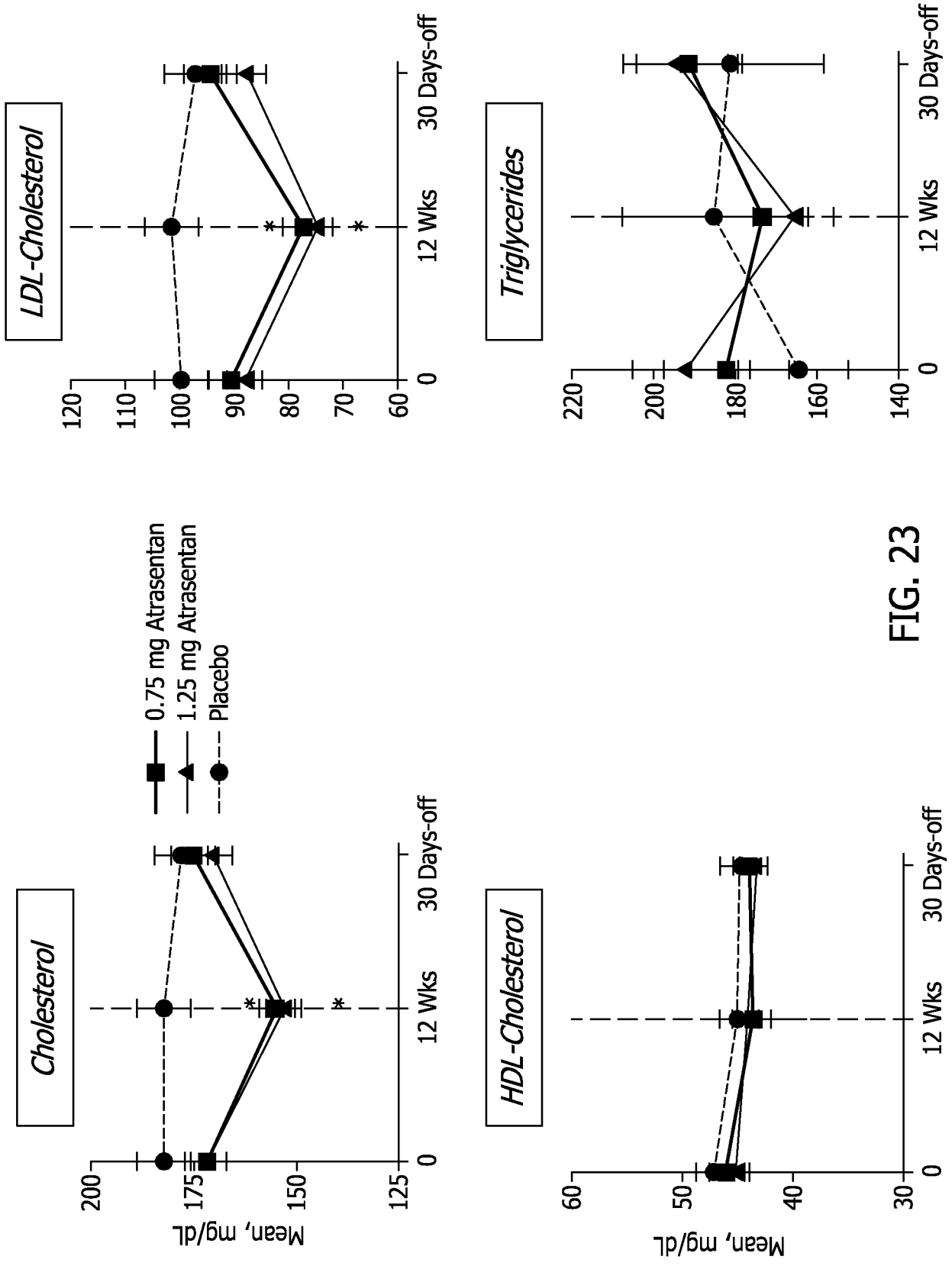

Cholesterol
LDL-Cholesterol
Triglycerides
HDL-Cholesterol
Mean, mg/dL
0.75 mg Atrasentan
1.25 mg Atrasentan
Placebo
0
12 Wks
30 Days-off
*

FIG. 23