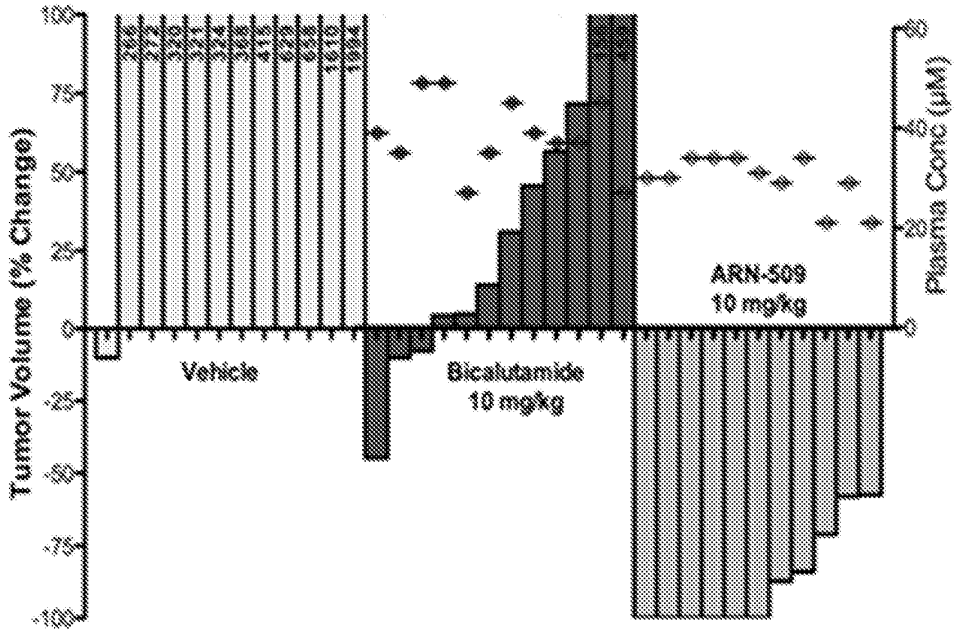

Tumor Volume (% Change)
Plasma Conc (μM)
100
75
50
25
0
-25
-50
-75
-100
60
40
20
0
Vehicle
Bicalutamide
10 mg/kg
ARN-509
10 mg/kg

FIG. 1

FIG. 2

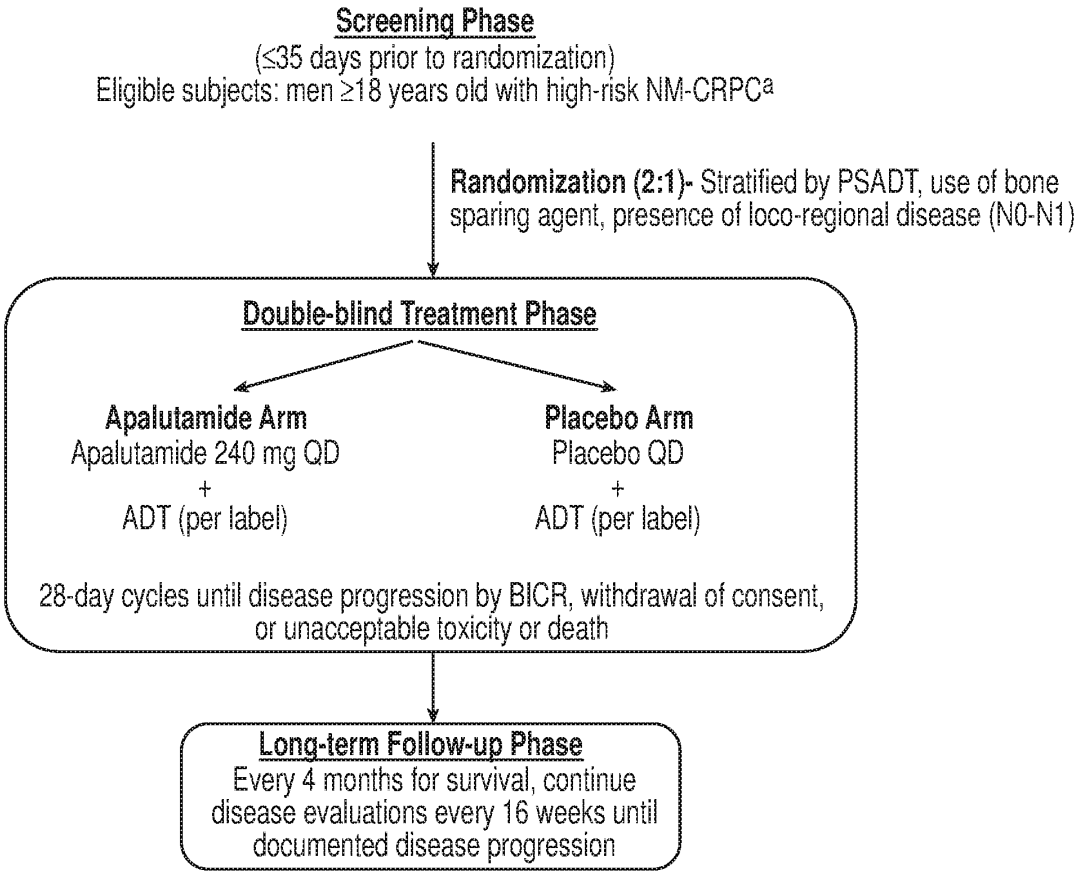

Screening Phase
(≤35 days prior to randomization)
Eligible subjects: men ≥18 years old with high-risk NM-CRPC[a]
Randomization (2:1)- Stratified by PSADT, use of bone sparing agent, presence of loco-regional disease (N0-N1)
Double-blind Treatment Phase
Apalutamide Arm
Apalutamide 240 mg QD
+
ADT (per label)
Placebo Arm
Placebo QD
+
ADT (per label)
28-day cycles until disease progression by BICR, withdrawal of consent, or unacceptable toxicity or death
Long-term Follow-up Phase
Every 4 months for survival, continue disease evaluations every 16 weeks until documented disease progression

FIG. 3

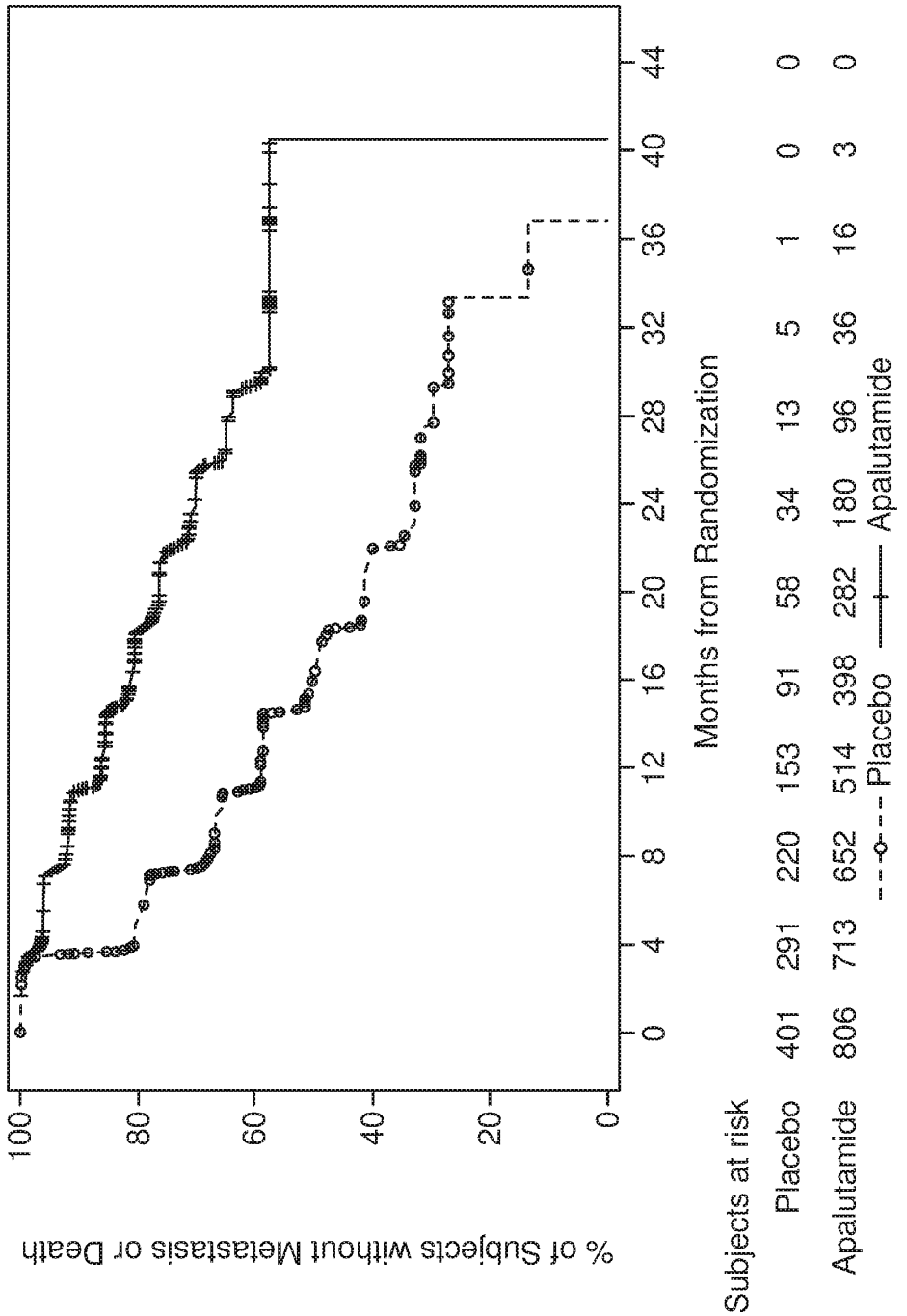
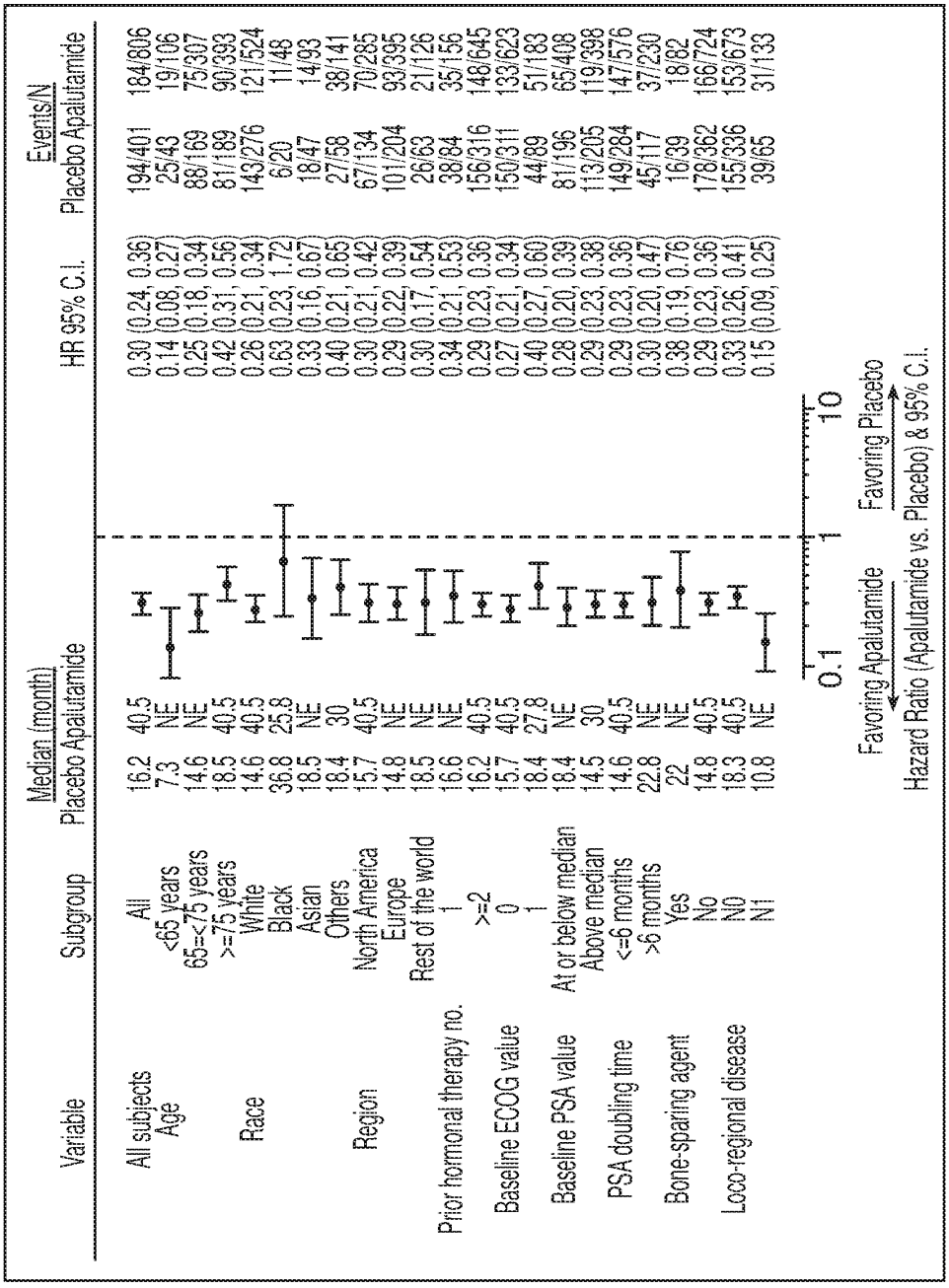

% of Subjects without Metastasis or Death
100
80
60
40
20
0
0
4
8
12
16
20
24
28
32
36
40
44
Months from Randomization
Subjects at risk
Placebo 401 291 220 153 91 58 34 13 5 1 0 0
Apalutamide 806 713 652 514 398 282 180 96 36 16 3 0
Placebo
Apalutamide

FIG. 4


Variable
Subgroup
Median (month)
Placebo Apalutamide
HR 95% C.I.
Events/N
Placebo Apalutamide
All subjects
All
16.2
40.5
0.30 (0.24, 0.36)
194/401
184/806
Age
<65 years
7.3
NE
0.14 (0.08, 0.27)
25/43
19/106
65=<75 years
14.6
NE
0.25 (0.18, 0.34)
88/169
75/307
>=75 years
18.5
40.5
0.42 (0.31, 0.56)
81/189
90/393
Race
White
14.6
40.5
0.26 (0.21, 0.34)
143/276
121/524
Black
36.8
25.8
0.63 (0.23, 1.72)
6/20
11/46
Asian
18.5
NE
0.33 (0.16, 0.67)
18/47
14/93
Others
18.4
30
0.40 (0.21, 0.65)
27/58
38/141
Region
North America
15.7
40.5
0.30 (0.21, 0.42)
67/134
70/285
Europe
14.8
NE
0.29 (0.22, 0.39)
101/204
93/395
Rest of the world
18.5
NE
0.30 (0.17, 0.54)
26/63
21/126
Prior hormonal therapy no.
1
16.6
NE
0.34 (0.21, 0.53)
38/84
35/156
>=2
16.2
40.5
0.29 (0.23, 0.36)
156/316
148/645
Baseline ECOG value
0
15.7
40.5
0.27 (0.21, 0.34)
150/311
133/623
1
18.4
27.8
0.40 (0.27, 0.60)
44/89
51/183
Baseline PSA value
At or below median
18.4
NE
0.28 (0.20, 0.39)
81/196
65/408
Above median
14.5
30
0.29 (0.23, 0.38)
113/205
119/398
PSA doubling time
<=6 months
14.6
40.5
0.29 (0.23, 0.36)
149/284
147/576
>6 months
22.8
NE
0.30 (0.20, 0.47)
45/117
37/230
Bone-sparing agent
Yes
22
NE
0.38 (0.19, 0.76)
16/39
18/82
No
14.8
40.5
0.29 (0.23, 0.36)
178/362
166/724
Loco-regional disease
N0
18.3
40.5
0.33 (0.26, 0.41)
155/336
153/673
N1
10.8
NE
0.15 (0.09, 0.25)
39/65
31/133
0.1
1
10
Favoring Apalutamide
Favoring Placebo
Hazard Ratio (Apalutamide vs. Placebo) & 95% C.I.

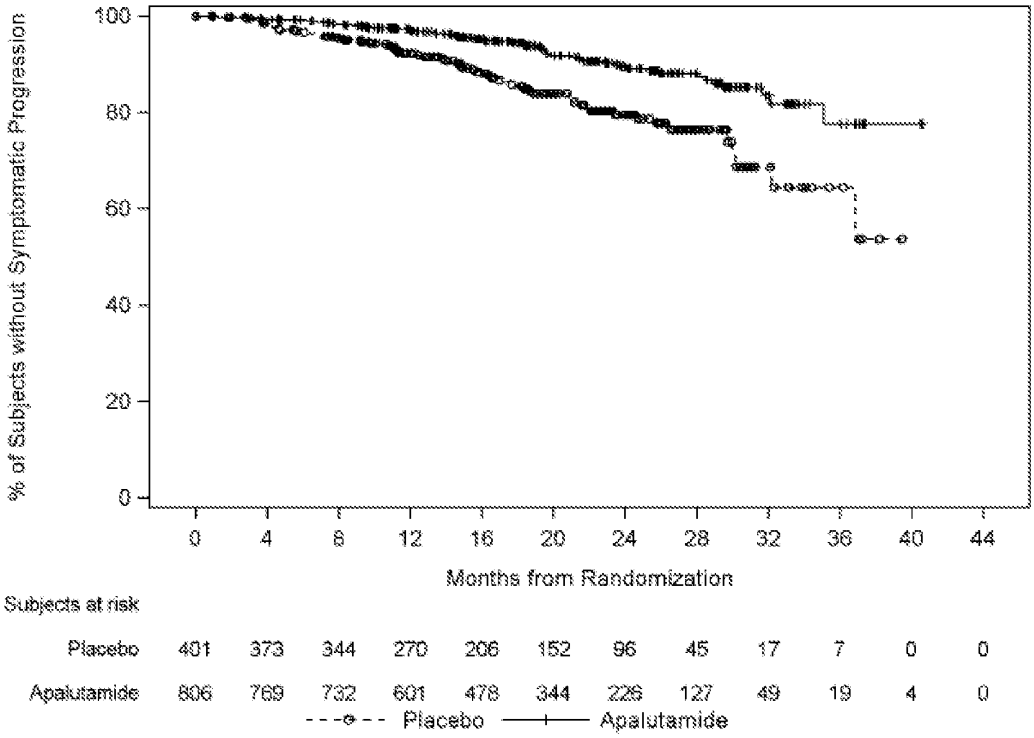
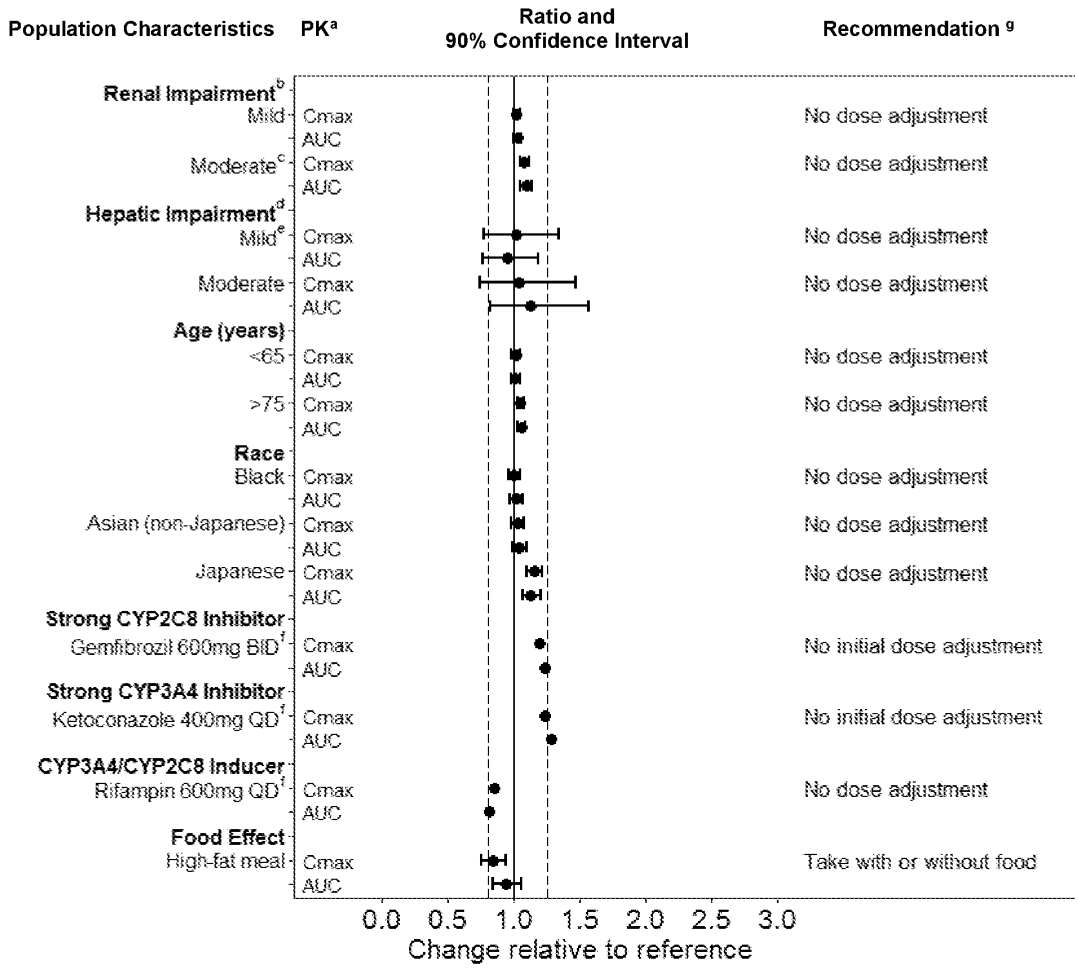

% of Subjects without Symptomatic Progression
100
80
60
40
20
0
0 4 8 12 16 20 24 28 32 36 40 44
Months from Randomization
Subjects at risk
Placebo 401 373 344 270 206 152 96 45 17 7 0 0
Apalutamide 806 769 732 601 478 344 226 127 49 19 4 0
Placebo
Apalutamide

FIG. 5



[a] Pharmacokinetic (PK) parameters (C_{max} and AUC) are for apalutamide, except in the drug interaction studies, where they are for active moieties (i.e., unbound apalutamide + potency adjusted unbound N-desmethyl apalutamide)

[b] Degree of renal impairment was determined based on eGFR using the modification of diet in renal disease (MDRD) study equation; normal (≥90 mL/min/1.73m^2), mild (60-89 mL/min/1.73m^2), moderate (30-59 mL/min/1.73m^2)

[c] Data included 2 subjects with severe renal impairment (≤29 mL/min/1.73m^2)

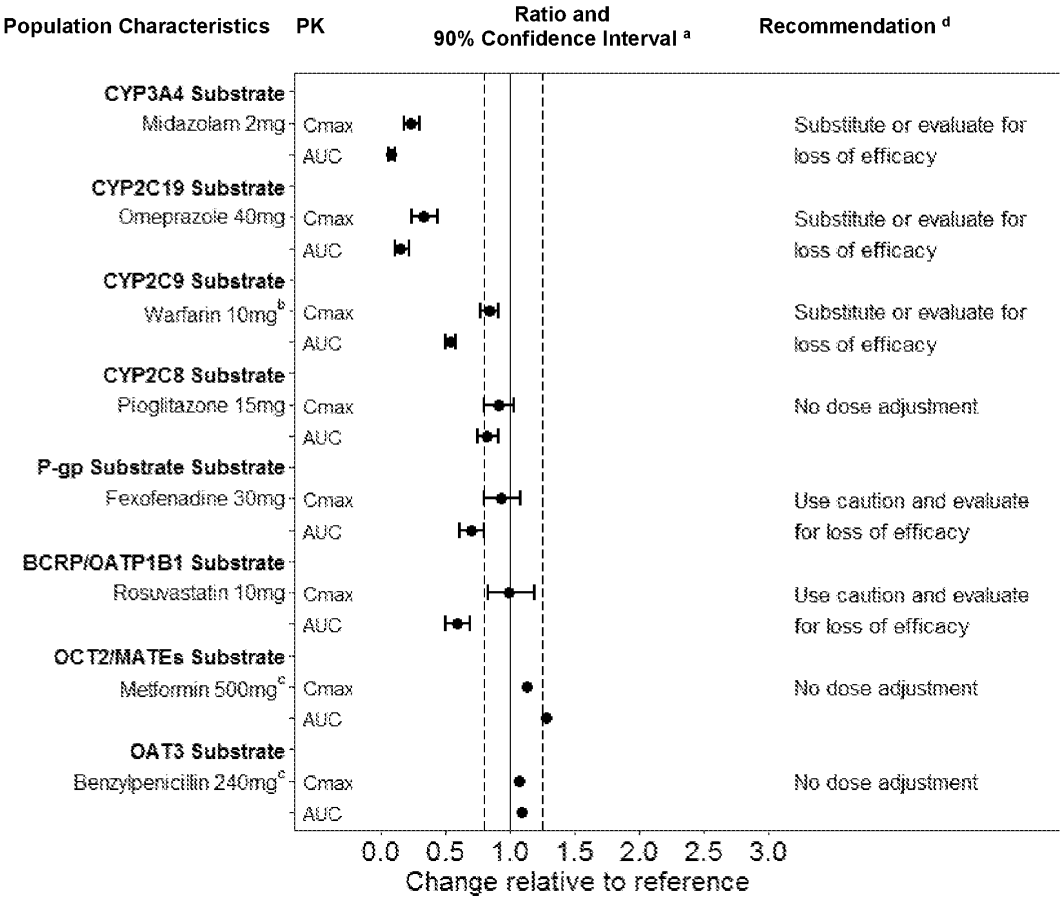
[d] Degree of hepatic impairment was determined based on Child-Pugh classification; mild (Child-Pugh A), moderate (Child-Pugh B)

[e] A population PK analysis demonstrated that mild hepatic impairment (based on the National Cancer Institute criteria) does not influence the exposure of apalutamide

[f] Effects on steady-state PK of active moieties based on simulations

[g] See Drug Interactions (7.1 and 7.2) and Use in Specific Populations (8.6 and 8.7)

FIG. 6



[a] combination/no combination
[b] S-warfarin was measured in the study
[c] based on simulations
[d] see Drug Interactions (7.3 and 7.4)

FIG. 7