

Safety and tolerability of relugolix in combination with abiraterone or apalutamide for treatment of patients with advanced prostate cancer: Data from a 52-week clinical trial

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Running Title: Relugolix in combination with antiandrogens for treatment of advanced prostate cancer

Legend to Supplemental Tables:

Suppl. Table 1a: Laboratory data by visit (Study Part 1)

Parameters are provided in alphabetic order together with the normal range and results are displayed as mean (SD) data for each parameter.

Suppl. Table 1b: Laboratory data by visit (Study Part 2)

Parameters are provided in alphabetic order together with the normal range and results are displayed as mean (SD) data for each parameter.

Suppl. Table 2: ECG data by visit

ECG interval results are displayed as mean (SD) data.

Suppl. Table 3: Vital sign data by visit

Systolic/diastolic blood pressure and hear rate results are displayed as mean (SD) data.

Suppl. Table 4: Mean steady-state plasma concentrations of relugolix, apalutamide, and N-desmethyl apalutamide by visit

Results are displayed as mean (SD) data for each analyte.

Suppl. Table 1a: Laboratory data by visit (Study Part 1)

Parameter (unit)	Normal range	Baseline	Week 4	Week 8	Week 12
Albumin (g/dL)	3.5-5.2	4.18 (0.257)	4.17 (0.294)	4.21 (0.259)	4.21 (0.184)
Alkaline Phosphatase (U/L)	40-129	93.8 (55.1)	95.0 (66.4)	101 (108)	121 (173)
ALT (U/L)	≤41	20.6 (13.3)	18.8 (7.91)	17.6 (7.37)	17.5 (12.4)
Aspartate Aminotransferase (U/L)	≤37	20.5 (7.63)	19.6 (4.94)	19.6 (5.57)	18.9 (5.68)
Bicarbonate (mEq/L)	19-29	25.9 (2.62)	25.6 (2.41)	25.5 (3.26)	24.6 (2.47)
Bilirubin - Direct (mg/dL)	≤0.3	0.200 (0.000)	0.200 (0.000)	0.200 (0.000)	0.200 (0.000)
Bilirubin - Indirect (mg/dL)	0.1-1.0	0.270 (0.171)	0.270 (0.171)	0.240 (0.184)	0.200 (0.128)
Bilirubin - Total (mg/dL)	≤1.2	0.470 (0.181)	0.450 (0.186)	0.440 (0.184)	0.410 (0.147)
Calcium (mg/dL)	8.4-10.3	9.50 (0.493)	9.49 (0.623)	9.43 (0.633)	9.35 (0.573)
Chloride (mEq/L)	97-110	103 (3.11)	102 (2.98)	102 (2.76)	103 (3.71)
Cholesterol (mg/dL)	≤199	173 (35.1)	n.a.	n.a.	170 (32.0)
Creatinine (mg/dL)	0.67-1.17	1.10 (0.285)	1.12 (0.257)	1.13 (0.275)	1.10 (0.262)
Gamma Glutamyl Transferase (U/L)	8-61	15.4 (6.22)	15.7 (6.72)	15.5 (7.14)	19.6 (26.7)
Glucose - Fasting (mg/dL)	74-106	100 (17.7)	n.a.	n.a.	99.2 (16.3)
Glucose (mg/dL)	74-106	100 (14.9)	114 (30.6)	103 (15.3)	98.4 (15.4)
HDL Cholesterol (mg/dL)	≥40	55.8 (18.3)	n.a.	n.a.	54.3 (19.1)
Lactate Dehydrogenase (U/L)	≤250	185 (35.2)	184 (31.8)	189 (33.9)	186 (37.6)
LDL Cholesterol (mg/dL)	≤129	90.3 (28.3)	n.a.	n.a.	86.5 (27.0)
Magnesium (mg/dL)	1.3-2.1	2.07 (0.214)	2.10 (0.203)	2.13 (0.176)	2.16 (0.156)
Phosphate (mg/dL)	2.5-4.5	3.57 (0.442)	3.51 (0.456)	3.48 (0.429)	3.46 (0.443)
Potassium (mEq/L)	3.3-5.1	4.20 (0.600)	4.12 (0.424)	4.10 (0.368)	4.17 (0.407)
Sodium (mEq/L)	135-147	140 (2.64)	140 (2.33)	140 (2.48)	140 (2.50)
Triglycerides (mg/dL)	≤149	136 (45.6)	n.a.	n.a.	149 (67.7)
Urea Nitrogen (mg/dL)	8-23	19.7 (6.20)	20.0 (7.10)	20.1 (5.79)	20.2 (5.27)

Suppl. Table 1b: Laboratory data by visit (Study Part 2)

Parameter (unit)	Normal range	Baseline	Week 4	Week 8	Week 12
Albumin (g/dL)	3.5-5.2	4.35 (0.331)	4.30 (0.368)	4.33 (0.361)	4.33 (0.255)
Alkaline Phosphatase (U/L)	40-129	99.8 (53.5)	88.7 (34.3)	92.5 (33.7)	89.3 (28.6)
ALT (U/L)	≤41	18.3 (10.0)	19.0 (13.1)	17.7 (10.4)	15.2 (8.17)
Aspartate Aminotransferase (U/L)	≤37	20.1 (5.36)	21.0 (8.45)	19.9 (6.00)	19.1 (6.54)
Bicarbonate (mEq/L)	19-29	25.4 (1.77)	24.6 (3.08)	24.6 (2.02)	24.7 (1.94)
Bilirubin - Direct (mg/dL)	≤0.3	0.200 (0.020)	0.200 (0.000)	0.200 (0.000)	0.200 (0.000)
Bilirubin - Indirect (mg/dL)	0.1-1.0	0.130 (0.123)	0.100 (0.065)	0.130 (0.119)	0.120 (0.094)
Calcium (mg/dL)	≤1.2	9.57 (0.565)	9.33 (0.549)	9.53 (0.611)	9.59 (0.452)
Chloride (mEq/L)	8.4-10.3	103 (2.35)	102 (2.41)	101 (2.44)	102 (2.55)
Cholesterol (mg/dL)	97-110	182 (33.2)	n.a.	n.a.	186 (34.3)
Creatinine (mg/dL)	≤199	1.09 (0.268)	1.09 (0.271)	1.15 (0.318)	1.14 (0.317)
Gamma Glutamyl Transferase (U/L)	0.67-1.17	36.0 (50.8)	34.8 (40.4)	35.0 (46.2)	32.0 (42.1)
Glucose - Fasting (mg/dL)	8-61	112 (17.5)	n.a.	n.a.	111 (12.3)
Glucose (mg/dL)	74-106	115 (17.0)	114 (20.7)	117 (18.8)	116 (26.2)
HDL Cholesterol (mg/dL)	74-106	47.4 (9.52)	n.a.	n.a.	45.3 (9.73)
Lactate Dehydrogenase (U/L)	≥40	173 (34.0)	175 (51.3)	177 (54.0)	186 (88.3)
LDL Cholesterol (mg/dL)	≤250	101 (31.8)	n.a.	n.a.	104 (32.6)
Magnesium (mg/dL)	≤129	2.07 (0.210)	2.08 (0.191)	2.05 (0.181)	2.07 (0.214)
Phosphate (mg/dL)	1.3-2.1	3.67 (0.650)	3.64 (0.715)	3.74 (0.679)	3.67 (0.731)
Potassium (mEq/L)	2.5-4.5	4.42 (0.493)	4.52 (0.431)	4.41 (0.379)	4.56 (0.493)
Sodium (mEq/L)	3.3-5.1	140 (2.18)	139 (2.94)	139 (2.07)	140 (2.74)
Triglycerides (mg/dL)	135-147	165 (69.2)	n.a.	n.a.	189 (103)
Urea Nitrogen (mg/dL)	≤149	17.8 (6.15)	19.0 (5.98)	19.0 (6.80)	18.1 (6.57)

Suppl. Table 2: ECG data by visit

	Relugolix in combination with					
	Abiraterone and Corticosteroid (Study Part 1)			Apalutamide (Study Part 2)		
	Baseline	Week 4	Week 12	Baseline	Week 4	Week 12
PR interval (msec)	173 (37.2)	171 (36.7)	164 (33.9)	171 (33.4)	171 (26.1)	174 (25.8)
QRS duration (msec)	95.8 (19.5)	102 (21.2)	101 (19.9)	95.4 (15.8)	92.8 (14.9)	94.4 (13.5)
QTcF interval (msec)	424 (20.8)	429 (24.1)	424 (23.0)	422 (27.2)	425 (21.4)	421 (28.3)
Number (%) of patients with QTcF interval						
<450 msec	22 (91.7%)	17 (70.8%)	19 (82.6%)	20 (83.3%)	20 (90.9%)	20 (90.9%)
450 – 480 msec	2 (8.3%)	7 (29.2%)	4 (17.4%)	4 (16.7%)	2 (9.1%)	2 (9.1%)
>480 msec	0	0	0	0	0	0
≥30 msec Δ from baseline	n.a.	3 (12.5%)	2 (8.7%)	n.a.	0	0
≥60 msec Δ from baseline	n.a.	0	0	n.a.	0	0

Suppl. Table 3: Vital sign data by visit

	Relugolix in combination with									
	Abiraterone and Corticosteroid (Study Part 1)					Apalutamide (Study Part 2)				
	Baseline	Week 2	Week 4	Week 8	Week 12	Baseline	Week 2	Week 4	Week 8	Week 12
Systolic blood pressure (mmHg)	135 (14.6)	138 (20.2)	137 (17.2)	134 (12.7)	135 (11.4)	134 (18.1)	134 (15.9)	132 (20.1)	126 (13.5)	130 (18.0)
Diastolic blood pressure (mmHg)	79.2 (7.20)	81.0 (9.48)	80.3 (9.64)	77.5 (9.65)	78.0 (8.81)	80.8 (11.7)	80.4 (8.72)	79.3 (10.8)	76.1 (10.4)	78.4 (9.45)
Heart Rate (beats/min)	69.3 (12.5)	72.2 (9.76)	71.3 (13.1)	71.5 (11.1)	68.0 (11.0)	68.8 (8.92)	70.0 (10.7)	72.6 (13.6)	71.3 (11.8)	72.4 (11.1)
Number (%) of patients with										
Systolic blood pressure ≥ 140 mmHg	9 (37.5%)	11 (45.8%)	10 (41.7%)	9 (37.5%)	10 (41.7%)	9 (37.5%)	9 (37.5%)	8 (33.3%)	4 (16.7%)	6 (25.0%)
Systolic blood pressure ≥ 180 mmHg	0	0	0	0	0	0	0	0	0	0
Diastolic blood pressure ≥ 90 mmHg	1 (4.17%)	4 (16.7%)	4 (16.7%)	2 (8.3%)	2 (8.3%)	5 (20.8%)	3 (12.5%)	4 (16.7%)	2 (8.3%)	3 (12.5%)
Diastolic blood pressure ≥ 105 mmHg	0	0	0	0	0	1	0	0	0	0
Heart rate ≥ 120 beats/min	0	0	0	0	0	0	0	0	0	0
Heart rate < 45 beats/min	0	0	0	0	0	0	0	0	0	0

Suppl. Table 4: Mean steady-state plasma concentrations of relugolix, apalutamide, and N-desmethyl apalutamide by visit

	Week 2 (N=23)	Week 4 (N=23)	Week 8 (N=23)	Week 12 (N=24)
Relugolix (ng/mL)	10.9 (10.7)	9.93 (7.71)	11.2 (9.58)	11.1 (9.66)
Apalutamide (ng/mL)	4088 (1047)	3889 (761)	3650 (1471)	3666 (1154)
N-desmethyl apalutamide (ng/mL)	4767 (1133)	4988 (963)	4627 (1516)	4718 (1363)