

Supplemental Table 1: At-Home Pharmacologic Pain Management Used

	Ibuprofen Group (n=140) n (%)			Oxycodone Group (n=70) n (%)			Total Cohort (n=210) n (%)		
	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3
Ibuprofen Only	139 (99.3)	108 (77.1)	76 (54.3)	10 (14.3)	10 (14.3)	11 (15.7)	149 (71.0)	118 (56.2)	87 (41.4)
Oxycodone Only	1 (0.7)	0 (0.0)	1 (0.7)	13 (18.6)	10 (14.3)	10 (14.3)	14 (6.7)	10 (4.8)	11 (5.2)
Acetaminophen Only	0 (0)	3 (2.1)	1 (0.7)	0 (0)	10 (14.3)	12 (17.1)	0 (0.0)	13 (6.2)	13 (6.2)
Ibuprofen and Acetaminophen	0 (0)	6 (4.3)	4 (2.9)	0 (0)	0 (0)	0 (0)	1 (0.5)	6 (2.9)	4 (1.9)
Acetaminophen + Oxycodone Combination Tablet*	0 (0)	0 (0)	0 (0)	47 (67.1)	32 (45.7)	17 (24.3)	47 (22.4)	32 (15.2)	17 (8.1)
None †	N/A	23 (16.4)	58 (41.4)	N/A	8 (11.4)	20 (28.6)	N/A	31 (14.8)	78 (37.1)

*Oxycodone Group: Day 1 (n=1 also used codeine); Day 2 (n=1 also used codeine; n=2 also used ibuprofen); Day 3 (n=2 also used ibuprofen).

† Inclusion criteria required patients to have taken medication on Day 1.

Supplemental Table 2. Adverse Events on Days 1-3 by Treatment Group

Day 1		Ibuprofen Group (n=140) n (%)	Oxycodone Group (n=69) n (%)	Total Cohort (n=208) n (%)	p Value
	Any AE	74 (52.9)	54 (78.3)	128 (61.6)	<0.001
	Abdominal Pain	7 (5.0)	6 (8.7)	13 (6.2)	0.30
	Appetite Loss	34 (24.3)	26 (37.7)	60 (28.8)	0.04
	Constipation	6 (4.3)	12 (17.4)	18 (8.7)	0.002
	Dizziness	11 (7.9)	18 (26.1)	29 (13.9)	<0.001
	Drowsiness	56 (40.0)	44 (63.8)	100 (48.1)	0.001
	Nausea	13 (9.3)	21 (30.4)	34 (16.3)	<0.001
	Rash	3 (2.1)	1 (1.4)	4 (1.9)	0.73
	Vomiting	3 (2.1)	7 (10.1)	10 (4.8)	0.01
Day 2		Ibuprofen Group (n=140) n (%)	Oxycodone Group (n=66) n (%)	Total Cohort (n=206) n (%)	p Value
	Any AE	50 (35.7)	38 (57.6)	88 (42.7)	0.003
	Abdominal Pain	3 (2.1)	7 (10.6)	10 (4.9)	0.008
	Appetite Loss	21 (15.0)	15 (22.7)	36 (17.5)	0.17
	Constipation	6 (4.3)	4 (6.1)	10 (4.9)	0.58
	Dizziness	4 (2.9)	10 (15.2)	14 (6.8)	0.001

	Drowsiness	30 (21.4)	30 (45.5)	60 (29.1)	<0.001
	Nausea	6 (4.3)	10 (15.2)	16 (7.8)	0.007
	Rash	0 (0.0)	3 (4.5)	3 (1.5)	0.01
	Vomiting	0 (0.0)	1 (1.5)	1 (0.5)	0.14
Day 3		Ibuprofen Group (n=140) n (%)	Oxycodone Group (n=64) n (%)	Total Cohort (n=204) n (%)	p Value
	All	31 (22.1)	21 (32.8)	55 (27.0)	0.10
	Abdominal Pain	4 (2.9)	4 (6.2)	8 (3.9)	0.25
	Appetite Loss	13 (9.3)	9 (14.1)	22 (10.8)	0.31
	Constipation	7 (5.0)	3 (4.7)	10 (4.9)	0.92
	Dizziness	5 (3.6)	7 (10.9)	12 (5.9)	0.04
	Drowsiness	17 (12.1)	13 (20.3)	30 (14.7)	0.13
	Nausea	5 (3.6)	6 (9.4)	11 (5.4)	0.09
	Rash	1 (0.7)	2 (3.1)	3 (1.5)	0.18
	Vomiting	0 (0.0)	3 (4.7)	3 (1.5)	0.01

Supplemental Table 3a. Estimates of Genomic Associations with Pain Reduction

Variable	Estimate	Standard Error	p value
CYP2C9			
CYP2C9*2	0.60	0.48	0.22
CYP2C9*3	-0.79	0.59	0.18
CYP2C9*6	-1.52	1.84	0.41
CYP2D6			
Poor Metabolizer	-0.36	1.23	0.77
Intermediate Metabolizer	-1.42	0.73	0.06
CYP3A4			
CYP3A4_20239G>A	-0.15	0.69	0.83
CYP3A4*1B	-0.11	0.86	0.90

Supplemental Table 3b. Estimates of Genomic Associations with Adverse Events

Variable	OR (95% CI)	p value
CYP2C9		
CYP2C9*2	0.72 (0.58, 0.89)	0.003
CYP2C9*3	0.80 (0.60, 1.05)	0.11
CYP2C9*6	0.54 (0.21, 1.41)	0.21
CYP2D6		
Poor Metabolizer	0.96 (0.65, 1.43)	0.85
Intermediate Metabolizer	1.16 (0.93, 1.46)	0.20
CYP3A4		
CYP3A4*_20239G>A	0.98 (0.77, 1.25)	0.88
CYP3A4*1B	0.97 (0.73, 1.29)	0.84

Supplemental Table 4a. Estimates of Genomic Associations with Pain Reduction Adjusted by Clinical Factors

Variable	Estimate	Standard Error	p value
Ibuprofen			
Age	-0.05	0.05	0.30
Sex	0.12	0.37	0.76
Fracture Location	-0.44	0.43	0.31
Fracture Reduction	-0.08	0.38	0.83
Non-Pharmacologic Management	-1.34	1.10	0.23
Ethnicity	0.05	0.26	0.86
CYP2C9*2	0.66	0.50	0.19
CYP2C9*3	-0.79	0.62	0.21
CYP2C9*6	-1.55	1.93	0.42
Oxycodone – CYP2D6			
Age	-0.26	0.14	0.06
Sex	-1.81	0.90	0.05
Fracture Location	-1.05	0.97	0.29
Fracture Reduction	-0.73	0.74	0.31
Non-Pharmacologic Management	-4.56	1.82	0.02
Ethnicity	0.04	0.92	0.96
CYP2D6 Intermediate	0.84	1.34	0.53
CYP2D6 Normal	2.18	1.28	0.10

Supplemental Table 4b. Estimates of Genomic Associations with Adverse Events Adjusted by Clinical Factors

Variable	OR (95% CI)	p value
Ibuprofen		
Age	1.00 (0.97, 1.02)	0.76
Sex	0.92 (0.78, 1.09)	0.35
Fracture Location	1.14 (0.93, 1.39)	0.21
Sedation in ED	1.07 (0.89, 1.28)	0.50
Ethnicity	0.98 (0.88, 1.10)	0.77
CYP2C9*2	0.73 (0.58, 0.90)	0.005
CYP2C9*3	0.78 (0.58, 1.04)	0.09
CYP2C9*6	0.57 (0.21, 1.54)	0.27
Oxycodone – CYP2D6		
Age	0.97 (0.93, 1.02)	0.24
Sex	1.24 (0.93, 1.66)	0.15
Fracture Location	1.12 (0.82, 1.52)	0.48
Sedation in ED	1.05 (0.83, 1.33)	0.67
Ethnicity	1.36 (0.99, 1.87)	0.07
CYP2D6 Intermediate	1.09 (0.69, 1.71)	0.71
CYP2D6 Normal	0.90 (0.58, 1.39)	0.64