

**Pharmacokinetics of Fentanyl Sublingual Spray in Opioid-Naïve Participants: Results of a
Phase 1, Multiple Ascending Dose Study**

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Supplemental Tables

Supplemental Table 1 Demographic and baseline characteristics for participants treated with fentanyl sublingual spray 100 mcg (safety population)

Characteristic	Safety population			
	Cohort 1 100 mcg q4h (N=6)	Cohort 2 100 mcg q2h (N=6)	Cohort 3 100 mcg q1h (N=6)	Cohort 4 100 mcg q0.5h (N=6)
Age, y				
n	6	6	6	6
Mean (SD)	37.3 (8.26)	32.3 (7.23)	31.5 (4.93)	30.3 (7.58)
Median	38.5	31.0	31.0	32.0
Min, Max	27, 45	24, 45	26, 39	21, 39
Sex, n (%)				
Male	5 (83.3)	5 (83.3)	4 (66.7)	6 (100.0)
Female	1 (16.7)	1 (16.7)	2 (33.3)	0
Race, n (%)				
Asian	0	0	0	1 (16.7)
Black or African American	4 (66.7)	2 (33.3)	4 (66.7)	3 (50.0)
White	2 (33.3)	3 (50.0)	2 (33.3)	2 (33.3)
Other	0	1 (16.7)	0	0
Ethnicity, n (%)				
Hispanic or Latino	2 (33.3)	1 (16.7)	0	2 (33.3)
Non-Hispanic / Non-Latino	4 (66.7)	5 (83.3)	6 (100.0)	4 (66.7)

Weight (kg)				
n	6	6	6	6
Mean (SD)	86.73 (16.377)	74.62 (15.946)	76.92 (9.740)	81.15 (10.287)
Median	91.40	75.52	74.62	84.14
Min, Max	65.3, 102.1	54.4, 92.1	67.6, 91.2	61.0, 89.8
Height (cm)				
n	6	6	6	6
Mean (SD)	179.28 (9.173)	175.79 (10.688)	176.95 (8.820)	177.08 (10.892)
Median	183.52	178.44	177.42	178.44
Min, Max	167.6, 188.0	159.4, 189.2	167.6, 190.0	160.0, 192.0
BMI (kg/m ²)				
n	6	6	6	6
Mean (SD)	26.75 (2.886)	23.90 (2.961)	24.66 (3.294)	25.86 (2.415)
Median	26.64	23.55	25.09	25.93
Min, Max	23.2, 29.8	19.4, 28.3	18.7, 27.9	22.9, 29.7
Body Temperature (°C)				
n	6	6	6	6
Mean (SD)	37.07 (0.082)	36.73 (0.197)	36.67 (0.339)	36.82 (0.264)
Median	37.05	36.80	36.65	36.80
Min, Max	37.0, 37.2	36.4, 36.9	36.1, 37.1	36.4, 37.1

q every; *SD* standard deviation; *BMI* body mass index

Supplemental Table 2 Demographic and baseline characteristics for participants treated with fentanyl sublingual spray 200 mcg (safety population)

Characteristic	Safety population			
	Cohort 1 200 mcg q4h (N=6)	Cohort 2 200 mcg q2h (N=6)	Cohort 3 200 mcg q1h (N=6)	Cohort 4 200 mcg q0.5h (N=6)
Age, y				
n	6	6	6	6
Mean (SD)	43.5 (9.07)	44.3 (11.25)	31.7 (10.71)	41.2 (10.55)
Median	47.5	50.5	29.5	44.5
Min, Max	31, 51	28, 54	20, 52	25, 55
Sex, n (%)				
Male	6 (100.0)	5 (83.3)	2 (33.3)	2 (33.3)
Female	0	1 (16.7)	4 (66.7)	4 (66.7)
Race, n (%)				
Asian	1 (16.7)	0	1 (16.7)	0
Black or African American	2 (33.3)	3 (50.0)	1 (16.7)	1 (16.7)
White	3 (50.0)	3 (50.0)	4 (66.7)	4 (66.7)
Other	0	0	0	1 (16.7)
Ethnicity, n (%)				
Hispanic or Latino	3 (50.0)	1 (16.7)	1 (16.7)	2 (33.3)
Non-Hispanic / Non-Latino	3 (50.0)	5 (83.3)	5 (83.3)	4 (66.7)

Weight (kg)				
n	6	6	6	6
Mean (SD)	74.88 (11.605)	76.18 (10.558)	63.88 (9.081)	75.30 (4.919)
Median	72.42	78.70	64.19	74.62
Min, Max	59.9, 91.7	61.1, 88.5	51.0, 78.9	69.4, 81.2
Height (cm)				
n	6	6	6	6
Mean (SD)	174.41 (12.155)	169.59 (6.637)	167.29 (9.068)	168.17 (7.935)
Median	176.91	168.28	165.10	169.23
Min, Max	152.4, 188.0	160.0, 177.8	156.2, 182.9	157.5, 177.8
BMI (kg/m ²)				
n	6	6	6	6
Mean (SD)	24.57 (2.388)	26.54 (3.849)	22.81 (2.496)	26.73 (2.479)
Median	24.40	26.21	22.96	26.87
Min, Max	21.7, 28.0	21.3, 31.5	18.7, 26.4	22.8, 29.6
Body Temperature (°C)				
n	6	6	6	6
Mean (SD)	36.72 (0.313)	36.78 (0.343)	36.83 (0.258)	36.93 (0.225)
Median	36.75	36.85	36.80	37.05
Min, Max	36.2, 37.0	36.2, 37.1	36.6, 37.1	36.6, 37.1

q every; *SD* standard deviation; *BMI* body mass index

Supplemental Table 3 Demographic and baseline characteristics for participants treated with fentanyl sublingual spray 400 mcg (safety population)

Characteristic	Safety population			
	Cohort 1 400 mcg q4h (N=6)	Cohort 2 400 mcg q2h (N=6)	Cohort 3 400 mcg q1h (N=6)	Cohort 4 400 mcg q0.5h (N=6)
Age, y				
n	6	6	6	6
Mean (SD)	34.8 (10.15)	37.7 (13.03)	36.7 (8.76)	39.3 (6.12)
Median	33.5	37.0	35.5	39.5
Min, Max	25, 54	23, 52	24, 50	30, 48
Sex, n (%)				
Male	3 (50.0)	4 (66.7)	5 (83.3)	5 (83.3)
Female	3 (50.0)	2 (33.3)	1 (16.7)	1 (16.7)
Race, n (%)				
Asian	0	1 (16.7)	2 (33.3)	0
Black or African American	3 (50.0)	0	1 (16.7)	2 (33.3)
White	3 (50.0)	5 (83.3)	3 (50.0)	4 (66.7)
Other	0	0	0	0
Ethnicity, n (%)				
Hispanic or Latino	0	1 (16.7)	0	2 (33.3)
Non-Hispanic / Non-Latino	6 (100.0)	5 (83.3)	6 (100.0)	4 (66.7)

Weight (kg)				
n	6	6	6	6
Mean (SD)	68.87 (9.985)	72.24 (13.538)	76.32 (13.862)	75.43 (7.700)
Median	65.77	72.12	78.93	77.51
Min, Max	60.3, 85.7	56.7, 91.6	54.4, 91.6	64.0, 83.9
Height (cm)				
n	6	6	6	6
Mean (SD)	167.64 (10.255)	170.50 (8.287)	173.69 (8.286)	172.30 (9.252)
Median	167.64	170.50	173.10	173.36
Min, Max	154.9, 179.1	158.8, 181.6	160.0, 185.4	161.3, 185.4
BMI (kg/m ²)				
n	6	6	6	6
Mean (SD)	24.50 (2.601)	24.67 (2.687)	25.12 (3.001)	25.57 (3.668)
Median	24.33	24.67	25.69	24.88
Min, Max	20.5, 27.7	20.2, 27.8	21.3, 29.4	20.8, 30.8
Body Temperature (°C)				
n	6	6	6	6
Mean (SD)	36.87 (0.234)	37.03 (0.216)	36.92 (0.160)	36.87 (0.308)
Median	36.90	37.10	36.90	36.95
Min, Max	36.6, 37.1	36.6, 37.2	36.7, 37.1	36.4, 37.2

q every; *SD* standard deviation; *BMI* body mass index

Supplemental Table 4 Demographic and baseline characteristics for participants treated with fentanyl citrate IV 50 mcg (safety population)

Characteristic	Safety population			
	Cohort 1 50 mcg q4h (N=6)	Cohort 2 50 mcg q2h (N=6)	Cohort 3 50 mcg q1h (N=6)	Cohort 4 50 mcg q0.5h (N=6)
Age, y				
n	6	6	6	6
Mean (SD)	39.8 (13.88)	34.8 (6.11)	33.8 (13.20)	33.8 (9.60)
Median	44.0	33.0	30.0	33.5
Min, Max	20, 54	29, 46	21, 55	23, 47
Sex, n (%)				
Male	6 (100.0)	5 (83.3)	4 (66.7)	5 (83.3)
Female	0	1 (16.7)	2 (33.3)	1 (16.7)
Race, n (%)				
Asian	0	0	1 (16.7)	1 (16.7)
Black or African American	1 (16.7)	2 (33.3)	1 (16.7)	1 (16.7)
White	5 (83.3)	4 (66.7)	4 (66.7)	4 (66.7)
Other	0	0	0	0
Ethnicity, n (%)				
Hispanic or Latino	1 (16.7)	3 (50.0)	2 (33.3)	2 (33.3)
Non-Hispanic / Non-Latino	5 (83.3)	3 (50.0)	4 (66.7)	4 (66.7)

Weight (kg)				
n	6	6	6	6
Mean (SD)	88.71 (12.746)	79.98 (12.233)	78.04 (16.465)	74.03 (8.404)
Median	94.01	81.65	82.28	73.37
Min, Max	64.9, 98.4	61.7, 95.3	55.1, 96.2	65.2, 86.2
Height (cm)				
n	6	6	6	6
Mean (SD)	178.92 (6.017)	177.06 (12.091)	171.66 (6.734)	173.99 (7.492)
Median	180.54	182.56	170.48	172.72
Min, Max	167.6, 184.2	160.0, 188.0	165.1, 180.3	162.6, 185.4
BMI (kg/m ²)				
n	6	6	6	6
Mean (SD)	27.61 (3.130)	25.59 (3.594)	26.30 (4.296)	24.46 (2.391)
Median	28.21	26.38	26.63	24.37
Min, Max	23.1, 31.1	19.1, 29.1	20.2, 31.3	21.8, 27.3
Body Temperature (°C)				
n	6	6	6	6
Mean (SD)	36.92 (0.214)	36.70 (0.379)	37.05 (0.362)	36.75 (0.339)
Median	37.00	36.65	37.00	36.70
Min, Max	36.6, 37.1	36.1, 37.2	36.6, 37.7	36.3, 37.3

q every; *SD* standard deviation; *BMI* body mass index