Supplementary Table 1: Clinical Characteristics for Cohort 3 (All Other Gating Mutations/non-G551D or R117H) Patients taking Ivacaftor

Variable	Visit	N	Mean (SD)	N	Mean	95% C.I.	P-value
						Absolute Change	
ppFEV1	Baseline	21	68 (28.4)	.	.		.
	1 month	20	77.6 (26.6)	20	9.3	(4.2, 14.4)	0.0011
	3 month	20	78.6 (25.8)	20	8.4	(1.4, 15.4)	0.0214
	6 month	17	79.8 (21.7)	17	10.9	(2.6, 19.3)	0.0134
FEV$_1$, L	Baseline	21	2 (1)	.	.		.
	1 month	20	2.3 (1)	20	0.3	(0.2, 0.4)	<.0001
	3 month	20	2.4 (0.9)	20	0.3	(0.1, 0.5)	0.0169
	6 month	17	2.5 (1)	17	0.4	(0.2, 0.6)	0.0019
ppFVC	Baseline	21	81.2 (26.4)	.	.		.
	1 month	20	89.3 (22.5)	20	7.4	(1.9, 12.9)	0.0112
	3 month	20	89.2 (21.1)	20	6.3	(1.4, 11.3)	0.0146
	6 month	17	88 (17.4)	17	6.5	(-1.8, 14.8)	0.1170
FVC, L	Baseline	21	3 (1.2)	.	.		.
	1 month	20	3.2 (1.2)	20	0.3	(0.1, 0.4)	0.0017
	3 month	20	3.3 (1.2)	20	0.3	(0.1, 0.5)	0.0017
	6 month	17	3.3 (1.3)	17	0.3	(0.1, 0.6)	0.0170
BMI, kg/m^2	Baseline	21	20.8 (4.2)	.	.		.
	1 month	21	21.4 (4.3)	21	0.6	(0.2, 0.9)	0.0023
	3 month	20	21.7 (4.6)	20	1	(0.4, 1.5)	0.0012
	6 month	17	22.1 (4.9)	17	1.4	(0.7, 2.1)	0.0009
BMI, Percentile[1]	Baseline	11	43.1 (26.6)	.	.		.
	1 month	11	46.4 (28.4)	11	3.3	(-2.0, 8.6)	0.1934
	3 month	11	48.7 (31)	11	5.6	(-2.6, 13.8)	0.1595
	6 month	9	46.7 (33.1)	9	6.2	(-4.3, 16.8)	0.2106
Weight, kg	Baseline	21	55.8 (17.7)	.	.		.
	1 month	21	57.8 (18.4)	21	2	(0.9, 3.0)	0.0008
	3 month	20	58.7 (18.7)	20	3.3	(1.8, 4.9)	0.0003
	6 month	17	60.4 (19.7)	17	5.1	(2.8, 7.3)	0.0002
Weight, Percentile[1]	Baseline	11	41 (25.8)	.	.		.
	1 month	11	44.6 (27.4)	11	3.6	(-1.5, 8.8)	0.1491
	3 month	11	48.3 (28.8)	11	7.4	(-0.8, 15.5)	0.0711
	6 month	9	50.1 (32.9)	9	9.2	(-1.7, 20.1)	0.0867
Height, Z-Score[1]	Baseline	11	-0.1 (1.1)	.	.		.
	1 month	11	-0.1 (1)	11	0	(0.0, 0.1)	0.2543
	3 month	11	0 (1.1)	11	0.1	(0.0, 0.2)	0.0655
	6 month	9	0.2 (1)	9	0.2	(0.0, 0.3)	0.0179
Height, Percentile[1]	Baseline	11	45 (32.3)	.	.		.
	1 month	11	46 (30.5)	11	1	(-1.4, 3.4)	0.3728
	3 month	11	48.2 (30.4)	11	3.1	(-0.8, 7.1)	0.1101
	6 month	9	52.5 (29.6)	9	5	(0.5, 9.5)	0.0344
Sweat Chloride, mEq/L	Baseline	19	89.6 (20)	.	.		.
	1 month	18	40 (18.3)	16	-53.5	(-63.3, -43.7)	<.0001
	3 month	19	39.3 (20.5)	17	-51.4	(-63.2, -39.5)	<.0001
	6 month	16	40.3 (29.9)	14	-48.6	(-67.4, -29.9)	<.0001
CFQR Respiratory Score	Baseline	21	62 (19.6)	.	.		.
	1 month	21	78.2 (22.2)	21	16.1	(6.0, 26.3)	0.0035
	3 month	20	82.4 (16.3)	20	19.2	(9.6, 28.7)	0.0005
	6 month	17	77.8 (18.3)	17	14.2	(1.0, 27.4)	0.0366
CFRSD Score	Baseline	18	35.2 (15.5)	.	.		.
	1 month	18	23.7 (15.2)	18	-11.4	(-20.4, -2.5)	0.0154
	3 month	17	19.7 (16.6)	17	-14.4	(-26.7, -2.0)	0.0259
	6 month	15	23.8 (15.3)	15	-9.3	(-21.0, 2.5)	0.1130
SNOT-20 Score	Baseline	18	1.1 (0.7)	.	.		.
	1 month	18	0.7 (0.7)	18	-0.4	(-0.7, -0.1)	0.0098
	3 month	17	0.7 (0.8)	17	-0.4	(-0.7, -0.1)	0.0168
	6 month	15	0.8 (0.8)	15	-0.2	(-0.6, 0.1)	0.1273

[1] Percentiles and z-scores derived using CDC reference equations for individuals < 20 years of age

Supplementary Table 2: Clinical Characteristics by Age Group for Cohort 3 Patients Taking Ivacaftor

Variable	Visit	Age<18 Years Absolute Change					Age≥18 Years Absolute Change				
		N	Mean (SD)	N	Mean	95% C.I.	P-value	N	Mean (SD)	N	Mean	95% C.I.	P-value
ppFEV₁	Baseline	11	88.7 (16.8)	.	.		.	10	45.2 (19.3)	.	.		.
	1 month	11	96.2 (13.3)	11	7.5	(2.0, 13.0)	0.0120	9	54.7 (19.9)	9	11.5	(1.0, 22.0)	0.0350
	3 month	11	96 (17.6)	11	7.2	(-4.6, 19.1)	0.2039	9	57.4 (16.6)	9	9.8	(0.8, 18.7)	0.0364
	6 month	9	94.6 (12.7)	9	6.1	(-4.1, 16.2)	0.2058	8	63.1 (17)	8	16.4	(1.1, 31.8)	0.0393
FEV₁, L	Baseline	11	2.5 (0.9)	.	.		.	10	1.5 (0.9)	.	.		.
	1 month	11	2.7 (0.9)	11	0.3	(0.1, 0.4)	0.0065	9	1.7 (0.8)	9	0.3	(0.1, 0.5)	0.0080
	3 month	11	2.8 (0.8)	11	0.3	(-0.1, 0.6)	0.1425	9	1.9 (0.9)	9	0.3	(0.0, 0.5)	0.0325
	6 month	9	2.8 (0.9)	9	0.3	(-0.1, 0.6)	0.0863	8	2 (1)	8	0.5	(0.1, 0.8)	0.0106
ppFVC	Baseline	11	100.6 (13.6)	.	.		.	10	59.9 (19.6)	.	.		.
	1 month	11	104.9 (13.6)	11	4.3	(-0.5, 9.2)	0.0755	9	70.1 (15.1)	9	11.2	(-0.6, 23.0)	0.0607
	3 month	11	104.1 (11.5)	11	3.5	(-3.9, 10.9)	0.3136	9	70.8 (14.2)	9	9.8	(2.6, 16.9)	0.0140
	6 month	9	100.8 (8.3)	9	1.1	(-7.0, 9.3)	0.7552	8	73.6 (13)	8	12.5	(-4.0, 29.0)	0.1158
FVC, L	Baseline	11	3.3 (1.2)	.	.		.	10	2.6 (1.2)	.	.		.
	1 month	11	3.5 (1.2)	11	0.2	(0.0, 0.4)	0.0154	9	2.8 (1)	9	0.3	(0.0, 0.7)	0.0392
	3 month	11	3.5 (1.1)	11	0.2	(0.0, 0.5)	0.0574	9	3 (1.2)	9	0.4	(0.1, 0.6)	0.0168
	6 month	9	3.5 (1.1)	9	0.2	(-0.1, 0.5)	0.1809	8	3.1 (1.4)	8	0.5	(0.0, 1.0)	0.0601
BMI, kg/m²	Baseline	11	19.1 (3.3)	.	.		.	10	22.7 (4.4)	.	.		.
	1 month	11	19.5 (3.5)	11	0.4	(0.0, 0.9)	0.0628	10	23.4 (4.3)	10	0.8	(0.2, 1.4)	0.0201
	3 month	11	20 (3.9)	11	0.9	(0.0, 1.7)	0.0470	9	23.8 (4.7)	9	1.1	(0.3, 1.9)	0.0126
	6 month	9	20.3 (4.5)	9	1.3	(0.0, 2.7)	0.0516	8	24.1 (4.7)	8	1.4	(0.6, 2.2)	0.0042
Weight, kg	Baseline	11	48.1 (15.6)	.	.		.	10	64.3 (16.6)	.	.		.
	1 month	11	49.8 (16.1)	11	1.6	(0.3, 2.9)	0.0180	10	66.6 (17.3)	10	2.3	(0.4, 4.2)	0.0234
	3 month	11	51.7 (16.7)	11	3.6	(1.1, 6.0)	0.0084	9	67.3 (18.2)	9	3	(0.6, 5.3)	0.0185
	6 month	9	54 (18.2)	9	5.8	(1.6, 9.9)	0.0123	8	67.7 (19.8)	8	4.3	(1.8, 6.7)	0.0046
Sweat Chloride, mEq/L	Baseline	10	99 (12.2)	.	.		.	9	79.2 (22.5)	.	.		.
	1 month	11	36.2 (19.1)	10	-60.9	(-73.9, -47.8)	<.0001	7	46 (16.6)	6	-41.3	(-53.0, -29.5)	0.0003
	3 month	11	42.5 (24)	10	-55.9	(-76.0, -35.7)	0.0001	8	35.1 (15)	7	-44.9	(-56.3, -33.6)	<.0001
	6 month	9	37.3 (30.3)	8	-57.3	(-85.8, -28.7)	0.0021	7	44.1 (31.3)	6	-37.2	(-67.5, -6.8)	0.0253
CFQR Respiratory Score	Baseline	11	74 (15.2)	.	.		.	10	48.9 (15.2)	.	.		.
	1 month	11	85.1 (25.8)	11	11.1	(-2.4, 24.6)	0.0973	10	70.6 (15.3)	10	21.7	(4.2, 39.1)	0.0202
	3 month	11	83.6 (20.5)	11	9.6	(-1.3, 20.5)	0.0781	9	80.9 (10.1)	9	30.9	(15.9, 45.8)	0.0014
	6 month	9	82.7 (11.8)	9	7.1	(-3.3, 17.5)	0.1526	8	72.2 (23.2)	8	22.2	(-6.3, 50.7)	0.1080
CFRSD Score	Baseline	8	26.9 (7.8)	.	.		.	10	41.8 (17.3)	.	.		.
	1 month	8	14.8 (13.1)	8	-12.1	(-20.1, -4.2)	0.0087	10	30.9 (13.3)	10	-10.9	(-27.6, 5.8)	0.1730
	3 month	8	16.3 (16.5)	8	-10.6	(-26.7, 5.5)	0.1630	9	22.8 (17.1)	9	-17.7	(-39.5, 4.2)	0.0995
	6 month	7	19.7 (11)	7	-5.7	(-15.7, 4.3)	0.2104	8	27.4 (18.2)	8	-12.4	(-35.7, 10.9)	0.2497
SNOT-20 Score	Baseline	8	0.8 (0.5)	.	.		.	10	1.4 (0.7)	.	.		.
	1 month	8	0.4 (0.4)	8	-0.4	(-0.8, 0.0)	0.0338	10	0.9 (0.8)	10	-0.4	(-0.9, 0.1)	0.1090
	3 month	8	0.4 (0.4)	8	-0.4	(-0.7, 0.0)	0.0446	9	1 (0.9)	9	-0.4	(-0.9, 0.2)	0.1498
	6 month	7	0.4 (0.2)	7	-0.4	(-1.0, 0.1)	0.0915	8	1.2 (0.8)	8	-0.1	(-0.6, 0.4)	0.6920