SUPPLEMENTAL TABLE 1: 4-year Analysis Included and Excluded *R117H* or *F508del* Patient Demographic and Clinical Characteristics.

CFTR gene mutation	*R117H* (≥ 6 years old)			*F508del* (≥ 6 years old)			*R117H* vs. *F508del*
Characteristic	**Patients Included in the 4-year analysis (n=156)**	**Patients Excluded from the 4-year analysis (n=335)**	**Included vs. Excluded Patients *P*-value***	**Patients Included in the 4-year analysis (n=6,251)**	**Patients Excluded from the 4-year analysis (n=3,793)**	**Included vs. Excluded Patients *P*-value***	**Excluded Patients *P*-value***
Age, years		[n=304]			[n=3,119]	<0.001	<0.001
mean (SD)	29.2 (17.2)	30.5 (15.7)	0.39	17.0 (9.1)	21.1 (10.4)		
Female, %	51.9	51.3	0.90	47.3	46.1	0.24	0.067
Year of CF diagnosis							
median	1998	2002	<0.001	1992	1987	<0.001	<0.001
min, max	1958, 2006	1957, 2010		1949, 2006	1947, 2010		
Sweat chloride	[n=126]	[n=248]		[n=5,729]	[n=3,369]		
mmol/L, mean (SD)	77.8 (23.9)	69.5 (23.9)	0.001	102.6 (16.3)	103.4 (17.2)	0.021	<0.001
Height *z*-score		[n=304]			[n=3,119]	0.036	<0.001
mean (SD)	0.11 (1.03)	0.07 (1.09)	0.70	-0.51 (1.01)	-0.55 (1.05)		
Weight *z*-score		[n=301]			[n=3,114]	<0.001	<0.001
mean (SD)	0.46 (1.14)	0.62 (1.25)	0.18	-0.41 (1.02)	-0.69 (1.22)		
BMI *z*-score	0.41 (1.07)	0.56 (1.21)	0.21	-0.20 (0.96)	-0.52 (1.20)	<0.001	<0.001
mean (SD)							
ppFEV$_1$ baseline first visit		[n=304]			[n=3,119]		
mean (SD)	79.0 (22.2)	79.4 (24.7)	0.86	77.3 (23.0)	63.7 (27.5)	<0.001	<0.001

						<0.001	<0.001
ppFEV$_1$ best baseline year value		[n=304]			[n=3,119]		
mean (SD)	83.9 (22.4)	84.1 (24.3)	0.93	84.8 (22.3)	70.1 (28.0)		
CF related diabetes, %	7.1	3.9	0.13	15.5	19.7	<0.001	<0.001
Liver disease, %	0.6	1.5	0.67	4.1	4.4	0.47	0.010
Microbiology	[n=152]	[n=268]		[n=6,130]	[n=2,935]		
Staphylococcus aureus, %	36.2	37.7	0.76	54.1	51.4	0.017	<0.001
Pseudomonas aeruginosa, %	29.6	21.3	0.056	49.2	57.5	<0.001	<0.001
Candida species, %	7.2	5.2	0.40	3.3	4.0	0.067	0.34
Stenotrophomonas maltophilia, %	5.3	6.0	0.76	7.7	6.6	0.071	0.69
Aspergillus species, %	3.9	3.4	0.75	8.9	7.6	0.041	0.010
Haemophilus influenzae, %	3.3	6.0	0.23	6.1	4.6	0.003	0.31
≥1 IV treatment for PEx, %	28.2	17.3	0.006	45.9	42.3	<0.001	<0.001
≥1 hospitalization, %	21.2	14.3	0.058	40.8	38.3	0.012	<0.001
≥1 home IV antibiotic treatment, %	18.6	10.7	0.017	26.3	24.1	0.014	<0.001
IV treatment for PEx events/year, mean (SD)	0.44 (0.84)	0.36 (1.12)	0.40	0.87 (1.31)	1.08 (1.76)	<0.001	<0.001
Hospitalization events/year, mean (SD)	0.32 (0.74	0.27 (0.96)	0.60	0.75 (1.22)	0.92 (1.63)	<0.001	<0.001
Home IV antibiotic events/year, mean (SD)	0.25 (0.60)	0.19 (0.67)	0.30	0.41 (0.84)	0.45 (1.02)	0.012	<0.001
IV treatment in patients with ≥1 PEx, mean (SD)	1.57 (0.87)	2.07 (1.94)	0.11	1.90 (1.33)	2.56 (1.89)	<0.001	0.052

*P-value obtained from t-test or chi-square test. Patients EXCLUDED from the 4-year analysis are all patients not included in the primary analysis <u>and</u> who were born before 2000 <u>and</u> without CFTR related metabolic syndrome (see text). P-values for INCLUDED *R117H* vs *F508del* patients are in Table 1.

CF, cystic fibrosis; CFTR, CF transmembrane conductance regulator; BMI, body mass index; max, maximum; min, minimum; ppFEV$_1$, percentage of predicted forced expiratory volume in 1 second; IV, intravenous; PEx, pulmonary exacerbation; SD, standard deviation.

SUPPLEMENTAL TABLE 2: 2-Year Analysis, Age Group Specific Estimated Percentage of Predicted FEV$_1$ Intercept and Slope for *R117H* Patients and *F508del* Patients.*

Parameter	Estimate	Standard Error	*P*-value	Lower 95% CI	Upper 95% CI
6-12 year olds (*R117H* n=108, *F508del* n=4,178)					
Intercept (ppFEV$_1$)					
R117H	94.18	1.93	<0.001	90.40	97.95
F508del	88.69	0.30	<0.001	88.10	89.29
Difference	5.48	1.95	0.005	1.66	9.31
Slope (ppFEV$_1$/year)					
R117H	0.58	0.92	0.52	-1.21	2.38
F508del	-1.29	0.13	<0.001	-1.55	-1.04
Difference	1.88	0.93	0.043	0.06	3.69
13-17 year olds (*R117H* n=65, *F508del* n=3,324)					
Intercept (ppFEV$_1$)					
R117H	93.32	2.76	<0.001	87.91	98.73
F508del	78.06	0.38	<0.001	77.33	78.80
Difference	15.26	2.78	<0.001	9.80	20.72
Slope (ppFEV$_1$/year)					
R117H	-0.39	1.01	0.70	-2.36	1.59
F508del	-2.07	0.11	<0.001	-2.30	-1.85
Difference	1.69	1.02	0.096	-0.30	3.68
18-24 year olds (*R117H* n=65, *F508del* n=3,258)					
Intercept (ppFEV$_1$)					
R117H	85.55	3.12	<0.001	79.44	91.65
F508del	66.73	0.42	<0.001	65.91	67.55
Difference	18.82	3.41	<0.001	12.66	24.98
Slope (ppFEV$_1$/year)					
R117H	-2.50	0.99	0.012	-4.45	-0.56
F508del	-2.49	0.11	<0.001	-2.70	-2.27
Difference	-0.02	1.00	0.99	-1.98	1.94
≥25 year olds (*R117H* n=138, *F508del* n=2,560)					
Intercept (ppFEV$_1$)					
R117H	73.74	1.99	<0.001	69.85	77.64
F508del	56.21	0.45	<0.001	55.33	57.09
Difference	17.53	2.04	<0.001	13.54	21.53

Slope (ppFEV$_1$/year)					
R117H	-0.59	0.58	0.32	-1.73	0.56
F508del	-1.46	0.11	<0.001	-1.67	-1.25
Difference	0.88	0.59	0.14	-0.29	2.04

*Repeated measures models adjusted for correlation within patient. Starting year of 2-year period and mutation were fixed effects. All 2-way and 3-way interactions were included.
CI, confidence interval; ppFEV$_1$, percentage of predicted forced expiratory volume in 1 second.