

**Table S2. Characteristics of the substantial decliners' cohort at the enrollment in the study.**

Study ID <sup>a</sup>	Age (years)	Gender	CFTR Genotype	FEV <sub>1</sub> (%predicted)	BMI	Microflora	Maintenance antimicrobial therapy
BSD9 (I)	23	F	F508del/1717-1G>A	84	21.0	<i>Mycobacterium abscessus</i> , <i>Veillonella atypica</i> , <i>Prevotella salivae</i> , <i>Pseudallescheria boydii</i>	aerosolized colistimethate, aerosolized tobramycin
BSD10 (I)	23	F	F508del/1717-1G>A	84	21.0	<i>M. abscessus</i> , <i>Prevotella melaninogenica</i> , <i>P. boydii</i>	aerosolized colistimethate aerosolized tobramycin
BSD13 (I)	29	M	F508del/G542X	71	22.0	<i>Pseudomonas aeruginosa</i> , <i>Veillonella dispar</i> , <i>Candida albicans</i>	aerosolized tobramycin
BSD22 (I)	21	F	F508del/G85E	81	22.1	<i>Staphylococcus aureus</i> , <i>Rothia mucilaginosa</i> , <i>Prevotella denticola</i> , <i>Neisseria perflava</i> , <i>Neisseria macacae</i> , <i>Neisseria mucosa</i> , <i>Haemophilus parainfluenzae</i> , <i>Streptococcus salivarius</i> , <i>Candida glabrata</i>	aerosolized tobramycin, azithromycin
BSD28 (I)	20	M	F508del/F508del	75	23.0	<i>S. aureus</i> , <i>Streptococcus viridans</i> , <i>Bacillus licheniformis</i> , <i>Neosartoria pseudofischeri</i>	aerosolized colistimethate, aerosolized tobramycin, azithromycin
GSD5 (I)	24	M	F508del/12491G>A	72	22.7	<i>Pseudomonas</i> spp., <i>S. aureus</i> , <i>S. viridians</i> , <i>Prevotella intermedia</i> , <i>Streptococcus pneumoniae</i>	none
GSD6 (I)	17	F	F508del/F508del	91	20.2	<i>S. aureus</i> , <i>Prevotella nanceiensis</i> , <i>Streptococcus peroris</i> , <i>Streptococcus pseudopneumoniae</i> , <i>S. pneumoniae</i> , <i>Aspergillus fumigatus</i>	none
GSD7 (I)	37	F	G542X/D1152H	78	19.4	<i>S. viridans</i> , <i>Stenotrophomonas maltophilia</i> , <i>P. nanceiensis</i> , <i>S. pseudopneumoniae</i> , <i>Streptococcus oralis</i> , <i>Granulicatella elegans</i> , <i>Prevotella nigrescens</i>	none

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						<i>Actinomyces graevenitzii</i> , <i>S. pneumoniae</i>	
GSD8 (I)	13	F	F508del/E585X	74	18.2	<i>S. maltophilia</i> , <i>P. aeruginosa</i> , <i>S. viridans</i> , <i>S. aureus</i> , <i>P. nanceiensis</i> , <i>G. sanguinis</i>	none
GSD9 (I)	10	F	2183AA>G/I148-3199DEL6	77	17.9	<i>P. aeruginosa</i> , <i>S. aureus</i> , <i>Actinomyces odontolyticus</i>	aerosolized colistimethate, azithromycin
GSD17 (I)	18	M	F508del/F508del	85	20.7	<i>S. aureus</i> , <i>Ralstonia</i> spp., <i>Delftia acidovorans</i> , <i>P.</i> <i>nanceiensis</i> , <i>Capnocytophaga</i> <i>ochracea</i> , <i>C. albicans</i>	none
MSD2 (I)	28	F	N1303K/L1065P	75	21.5	<i>P. aeruginosa</i> , <i>S. aureus</i> , <i>Lactobacillus suebicus</i> , <i>P. nigrescens</i> , <i>S. oralis</i> , <i>P. pseudopneumoniae</i> , <i>A. fumigatus</i>	aerosolized tobramycin, azithromycin
MSD8 (I)	16	M	F508del/N1303K	75	19.8	<i>S. aureus</i> , <i>A. fumigatus</i>	aerosolized aztreonam
BSD11 (II)	24	F	G542X/UN	60	21.6	<i>P. aeruginosa</i> , <i>S. aureus</i> , <i>P. melaninogenica</i> , <i>S. salivarius</i>	aerosolized colistimethate, aerosolized tobramycin, azithromycin
BSD12 (II)	17	F	G542X/W1282R	49	17.9	<i>P. aeruginosa</i> , <i>R. mucilaginosa</i> , <i>P. denticola</i> , <i>S. oralis</i> , <i>C. albicans</i>	aerosolized tobramycin, azithromycin
BSD14 (II)	18	F	F508del/R533X	69	20.0	<i>P. aeruginosa</i> , <i>S. aureus</i> , <i>R. mucilaginosa</i> , <i>P. denticola</i> , <i>V. atypica</i> , <i>P. melaninogenica</i> , <i>Neisseria flava</i> , <i>N. macacae</i> , <i>C. albicans</i>	aerosolized colistimethate
BSD16 (II)	28	F	F508del/4016insT	53	19.1	<i>P. aeruginosa</i> , <i>R. mucilaginosa</i> , <i>Actinomyces</i> spp., <i>S. peroris</i> , <i>C. albicans</i>	aerosolized aztreonam, aerosolized colistimethate
BSD18 (II)	18	F	G542X/N1303K	54	20.8	<i>S. aureus</i> , <i>R. mucilaginosa</i> , <i>Rothia aerea</i> , <i>H. parainfluenzae</i> , <i>S. oralis</i> , <i>S. pseudopneumoniae</i>	aerosolized tobramycin
BSD23 (II)	16	M	F508del/G542X	53	16.0	<i>P. aeruginosa</i>	aerosolized tobramycin

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GSD12 (II)	59	F	F508del/F508del	44	21.9	<i>S. pseudopneumoniae</i> , <i>C. albicans</i> <i>S. viridans</i> , <i>S. aureus</i> , Enterobacteriaceae, <i>P. aeruginosa</i>	azithromycin
GSD13 (II)	20	F	F508del/F508del	67	20.7	<i>S. aureus</i> , <i>P. melaninogenica</i> , <i>S. pneumoniae</i> , <i>C. albicans</i>	azithromycin
GSD22 (II)	30	M	DEL2,3(21KB)/L1077P	46	18.5	<i>P. aeruginosa</i> , <i>Staphylococcus</i> coagulase negative, <i>P. melaninogenica</i>	aerosolized tobramycin, azithromycin
GSD23 (II)	25	F	F508del/F508del	42	17.4	<i>P. aeruginosa</i> , <i>Escherichia coli</i>	azithromycin
GSD24 (II)	48	F	F508del/F508del	35	17.3	<i>S. aureus</i> , <i>P. aeruginosa</i> , <i>S. viridans</i> , <i>P. denticola</i> , <i>S. pneumoniae</i>	aerosolized colistimethate, azithromycin
GSD25 (II)	32	M	F508del/G542X	37	21.5	<i>S. aureus</i> , <i>P. aeruginosa</i> , <i>S. viridans</i> , <i>Prevotella pallens</i> , <i>A. odontolyticus</i> , <i>Atopobium rimae</i>	aerosolized colistimethate, azithromycin
MSD9 (II)	12	F	F508del/F508del	53	19.3	<i>S. aureus</i> , <i>S. maltophilia</i> , <i>Granulicatella adiacens</i>	aerosolized aztreonam, aerosolized tobramycin
BSD15 (III)	46	F	F508del/UN	37	19.7	<i>P. aeruginosa</i> , <i>S. aureus</i> , <i>C. albicans</i> , <i>C. dubliniensis</i>	aerosolized colistimethate, azithromycin
BSD20 (III)	24	M	F508del/F508del	36	23.3	<i>P. aeruginosa</i> , <i>Enterococcus</i> <i>faecalis</i> , <i>S. maltophilia</i> , <i>Staphylococcus epidermidis</i> , <i>R. mucilaginosa</i> , <i>P. salivae</i> , <i>Veillonella parvula</i> , <i>S. pseudopneumoniae</i> , <i>C. parapsilosis</i> , <i>C. albicans</i> , <i>A. fumigatus</i>	aerosolized aztreonam, aerosolized colistimethate
BSD37 (III)	24	F	F508del/UN	39	20.5	<i>Achromobacter xylosoxidans</i> , <i>Corynebacterium amicolatum</i> , <i>R. mucilaginosa</i> , <i>Rothia</i> <i>dentocariosa</i> , <i>V. parvula</i> , <i>P. denticola</i> , <i>S. salivarius</i> , <i>S. pseudopneumoniae</i> , <i>Scedosporium prolificans</i>	aerosolized colistimethate, aerosolized tobramycin

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BSD38 (III)	18	M	N1303K/F508del	35	16.6	<i>A. xylosoxidans</i> , <i>P. aeruginosa</i> , <i>V. dispar</i> , <i>Bifidobacterium breve</i> <i>R. mucillaginosa</i> , <i>Streptococcus gordonii</i> , <i>S.</i> <i>pseudopneumoniae</i> , <i>S. peroris</i> , <i>Streptococcus constellatus</i>	aerosolized tobramycin
BSD49 (III)	26	M	N1303K/G85E	29	19.9	<i>Burkholderia cepacia</i> complex, <i>P. aeruginosa</i> , <i>P. denticola</i> , <i>P. melaninogenica</i> , <i>Bifidobacterium dentum</i> , <i>Lactobacillus gasseri</i> , <i>Peptoniphilus haeri</i>	aerosolized colistimethate
GSD15 (III)	29	M	F508del/F508del	36	27.1	<i>S. aureus</i> , <i>P. aeruginosa</i> , <i>A. xylosoxydans</i> , <i>Cryseobacterium</i> spp.	aerosolized colistimethate, azithromycin
GSD26 (III)	45	M	F508del/H939R+H949L	28	19.2	<i>P. aeruginosa</i> , <i>P. melaninogenica</i> , <i>Parvimonas</i> <i>micra</i> , <i>Campylobacter concisus</i> , <i>A. odontolyticus</i>	aerosolized colistimethate
GSD27 (III)	25	M	F508del/F508del	29	22.5	<i>S. aureus</i> , <i>P. aeruginosa</i> , <i>A. xylosoxidans</i> , <i>Streptococcus</i> spp., <i>S. oralis</i> , <i>S. salivarius</i> , <i>B. breve</i>	none
MSD11 (III)	31	M	4169delCTAAGCC/E585X	33	11.4	<i>A. xylosoxidans</i> , <i>S. pneumoniae</i> , <i>S. peroris</i>	aerosolized tobramycin, azithromycin
MSD12 (III)	37	F	F508del/del Exon 2	32	25.9	<i>P. aeruginosa</i> , <i>S. pneumoniae</i>	aerosolized colistimethate, azithromycin
MSD13 (III)	18	M	1898+1G>A/1898+1G>A	33	16.3	<i>P. aeruginosa</i> , <i>S. aureus</i>	azithromycin
MSD15 (III)	49	M	G1244E/del Exons 14a, 14b,15, 16, 17a, 17b	32	15.4	<i>P. aeruginosa</i> , <i>S. aureus</i> , <i>C. albicans</i>	azithromycin

<sup>a</sup>In parenthesis, the FEV<sub>1</sub> group: I = normal/mild (FEV<sub>1</sub>% > 70); II = moderate (70 ≥ FEV<sub>1</sub>% ≥ 40); III = severe (FEV<sub>1</sub>% < 40)