Table S1a. Other pulmonary function tests (ITT)

	CDPI (n=183)	TIS (n=191)	Total (n=370)
Mean (SD) FEV_1 (litres)			
at baseline	1.65 (0.669)	1.60 (0.621)	1.62 (0.644)
at week 24	1.61 (0.663)	1.64 (0.696)	1.62 (0.679)
Mean (SD) FVC (litres)			
at baseline	2.52 (1.044)	2.49 (0.973)	2.50 (1.007)
at week 24	2.51 (1.034)	2.51 (0.999)	2.51 (1.015)
Mean (SD) FEF_{25-75} (litres)			
at baseline	1.23 (0.851)	1.12 (0.719)	1.17 (0.787)
at week 24	1.14 (0.785)	1.20 (0.838)	1.17 (0.812)

Table S1b. Other pulmonary function tests (PP)

	CDPI (n=141)	TIS (n=157)	Total (n=298)
Mean (SD) FEV_1 (litres)			
at baseline	1.59 (0.651)	1.56 (0.618)	1.58 (0.633)
at week 24	1.57 (0.647)	1.63 (0.708)	1.60 (0.680)
Mean (SD) FVC (litres)			
at baseline	2.46 (1.043)	2.46 (0.980)	2.46 (1.009)
at week 24	2.46 (1.007)	2.50 (1.014)	2.48 (1.009)
Mean (SD) FEF_{25-75} (litres)			
at baseline	1.20 (0.877)	1.08 (0.687)	1.14 (0.784)
at week 24	1.12 (0.799)	1.16 (0.819)	1.14 (0.808)

Table S2. Mean MIC_{50} and MIC_{90} values of respiratory isolates of *P aeruginosa* (ITT population)

	MIC_{50} (mg/L)		MIC_{90} (mg/L)	
	CDPI group (N = 183)	**TNSI group (N = 191)**	**CDPI group (N = 183)**	**TNSI group (N = 191)**
Colistin				
Baseline	0.38	0.38	0.50	0.75
Week 4	0.38	0.38	0.75	0.50
Week 8	0.38	0.38	1.00	0.75
Week 16	0.38	0.38	1.00	0.75
Week 20	0.38	0.38	1.00	0.75
Week 24	0.38	0.38	0.75	0.75
Tobramycin				
Baseline	1.00	1.00	12.00	12.00
Week 4	1.00	1.00	12.00	96.00
Week 8	1.00	1.00	12.00	16.00
Week 16	1.50	1.00	12.00	16.00
Week 20	1.00	1.50	8.00	16.00
Week 24	1.00	1.50	16.00	16.00

Parenteral breakpoints:

≤4mg/L susceptible, >4mg/L resistant for colistin;
≤2mg/L susceptible, ≥8mg/L resistant for tobramycin.

Table S3. Mean MIC_{50} and MIC_{90} values of respiratory isolates of *P aeruginosa* (ITT population)

	MIC_{50} (mg/L)		MIC_{90} (mg/L)	
	CDPI group (N = 183)	**TNSI group (N = 191)**	**CDPI group (N = 183)**	**TNSI group (N = 191)**
Colistin				
Baseline	0.38	0.38	0.50	0.75
Week 4	0.38	0.38	0.75	0.50
Week 8	0.38	0.38	1.00	0.75
Week 16	0.38	0.38	1.00	0.75
Week 20	0.38	0.38	1.00	0.75
Week 24	0.38	0.38	0.75	0.75
Tobramycin				
Baseline	1.00	1.00	12.00	12.00
Week 4	1.00	1.00	12.00	96.00
Week 8	1.00	1.00	12.00	16.00
Week 16	1.50	1.00	12.00	16.00
Week 20	1.00	1.50	8.00	16.00
Week 24	1.00	1.50	16.00	16.00

Breakpoints:

≤4mg/L susceptible, >4mg/L resistant for colistin;
≤2mg/L susceptible, ≥8mg/L resistant for tobramycin.

Table S4. Mean time in days to first acute respiratory exacerbation (ITT population)

	CDPI (n=183)	TIS (n=191)	Overall (n=374)
Protocol defined			
N	57	50	107
Mean (SD)	66.09 (47.907)	59.88 (46.473)	63.19 (47.122)
Median	57.00	56.50	57.00
Min, max	1.0, 169.0	1.0, 157.0	1.0, 169.0
Non-protocol defined			
n	22	32	54
Mean (SD)	83.32 (53.567)	67.06 (43.452)	73.69 (48.024)
Median	86.50	60.00	62.00
Min, max	1.0, 165.0	1.0, 141.0	1.0, 165.0
Overall			
N	69	75	144
Mean (SD)	63.70 (46.603)	59.39 (43.457)	61.45 (44.885)
Median	57.00	57.00	57.00
Min, max	1.0, 169.0	1.0, 157.0	1.0, 169.0

A protocol-defined acute respiratory exacerbation was defined if at least four of the symptoms described in the protocol were present; a non-protocol-defined acute respiratory exacerbation was defined by fewer than four symptoms being present.

In the ITT population, the mean period of time to acute respiratory exacerbation (overall) was slightly longer in the CDPI group (63.70 days) than in the TIS group (59.39 days). The difference was particularly noticeable with respect to non-protocol-defined acute exacerbations: the mean period of time was 83.32 days in the CDPI group compared to 67.06 days in the TIS group.

Table S5. Time to first additional anti-pseudomonal antibiotic use, days, ITT Population

	CDPI (n=183)	TIS (n=191)	Overall (n=374)	Hazard ratio	95% CI	p-value
N	92	96	188	0.871	0.653, 1.163	0.350
Mean (SD)	55.28 (43.204)	51.79 (41.867)	53.50 (42.449)			
Median	49.50	42.50	47.50			
Min, max	0.0, 153.0	1.0, 157.0	0.0, 157.0			

Hazard ratio, confidence intervals and p-value determined using Cox's proportional hazard modelling

In the ITT population, the mean time to first additional anti-pseudomonal treatment was 55.28 days in the CDPI group and 51.79 days in the TIS group. The results of the PP population were similar and confirmed the ITT results.

Table S6. Duration of additional anti-pseudomonal antibiotic use, days, ITT population

	CDPI (n=183)	TIS (n=191)	Overall (n=374)
N	269	277	546
Mean (SD)	13.6 (5.44)	14.4 (7.32)	14.0 (6.47)
Median	14.0	15.0	14.0
Min, max	1, 35	2, 81	1, 81

In the ITT population, the mean duration of use of additional anti-pseudomonal agents was slightly lower in the CDPI group (13.6 days) than in the TIS group (14.4 days). The results of the PP population were similar and confirmed the ITT results.

Quality of Life

The Cystic Fibrosis Questionnaires (CFQ) are disease-specific, developmentally appropriate QoL questionnaires designed to measure the physical, emotional and social impact of CF on patients and their families. The CFQs were recommended for use in this study by the EMEA (in a language translation appropriate to the country of use). Validated versions of the CFQs are available in US English, French and German. Spanish and Italian translations of the CFQs are available.

The Cystic Fibrosis Questionnaires (CFQ) developed in the United States by A. Quittner et al, are based on three versions of the CFQ that were first developed in France to evaluate the impact of CF on health status and QoL. The three US modified versions are:

- CFQ Teen/Adult Version (14 years of age and older), filled out by the adolescent/ adult (self-report)
- CFQ Parent Version (used in conjunction with the child questionnaire), filled out by the parent (parent-report)
- CFQ Child Version (6-13 years of age), which is provided in two different formats so that it can be either administered by an interviewer or, for children who are 12 or 13 years old, self-administered (self-report)

The CFQ are to be completed at the start of the trial (Visit 1) and at Visits 2, 5 and 6.

At Week 24/Exit, the QoL assessments were in favour of CDPI in the majority of CFQ-R domains in the ITT population. In the ITT population, detectable differences were only observed for the change in treatment burden from baseline to Week 4 (Visit 2) with CDPI being more favourable (adjusted difference: 6.27; 95% CI: 3.15, 9.40; $p<0.001$); for the change in body image from baseline to Week 4 (Visit 2) with TIS being more favourable (adjusted difference: -4.08; 95% CI: -7.73, -0.44; $p=0.028$); and for the change in digestion from baseline to last recorded result with CDPI being more favourable (adjusted difference: 3.67; 95% CI: 0.27, 7.07; $p=0.034$).

The incidence of notable differences between the treatment groups may be explained by the fact that during the first four weeks of randomised treatment the patients randomised to CDPI experienced a novel therapeutic entity, but over the course of the study, the novelty wore off.

Table S7. Adjusted mean changes in quality of life (CFQ-R) from baseline to week 24 (exist visit), ITT population

CFQ-R domain	CDPI (n=183)	TIS (n=191)	Adjusted difference	p-value
Physical	0.26	-1.56	1.82	0.353
Vitality	0.86	-1.40	2.27	0.293
Emotion	2.23	0.47	1.75	0.244
Eating	0.48	0.66	-0.19	0.925
Treatment burden	5.62	2.75	2.87	0.091
Health perceptions	0.25	-2.71	2.96	0.159
Social	3.10	0.92	2.18	0.153
Body image	7.83	5.98	1.85	0.385
Role	0.65	1.87	-1.22	0.607
Weight	0.88	-1.93	2.81	0.461
Respiratory	2.99	3.51	-0.53	0.756
Digestion	5.06	2.89	3.22	0.077

Adjusted difference (mean difference CDPI – TIS), p-value and confidence intervals determined using ANCOVA with covariates of baseline score and pooled centre.

Patient ease of use of device.

The patients were asked to assess their view of the in trial treatment (taking into account time taken to administer, ease and convenience of treatment) on a 5-point scale. The global assessment was recorded at Visit 6 (after 24 weeks of study treatment) or at exit from the study should the subject be withdrawn.

A five-point scale was used:

1 Very easy to use

2 Easy to use

3 Neither easy nor hard to use

4 Hard to use

5 Very hard to use

In the ITT population, 51.9% of the patients in the Colobreathe® group assessed their use of Colobreathe® via the Turbospin® device as 'very easy to use', whereas only 9.9% of the patients in the TIS group assessed their use of TOBI® using a PARI LC Plus® nebuliser as 'very easy to use'. In the Colobreathe® and TOBI® groups, 38.8% and 44.0% of patients, respectively, assessed the ease of use as 'easy to use', and 2.2% vs. 31.9% of patients, respectively, as 'neither easy nor hard to use'. Statistical comparison of the two treatment groups revealed a marked difference (95% CI: 4.684, 15.274; $p<0.001$) in favour of Colobreathe® via the Turbospin® device.

Table S8. Patient ease of use

Patient response, n (%)	CDPI (n=183)	TIS (n=191)	Overall (n=374)	95% CI	P=value
Very easy to use	95 (51.9)	19 (9.9)	114 (30.5)	4.684, 15.274	<0.001
Easy to use	71 (38.8)	84 (44.0)	155 (41.4)		
Neither easy nor hard to use	4 (2.2)	61 (31.9)	65 (17.4)		
Hard to use	6 (3.3)	16 (8.4)	22 (5.9)		
Very hard to use	1 (0.5)	3 (1.6)	4 (1.1)		
Missing	6 (3.3)	8 (4.2)	14 (3.7)		