Table 42: Clinical evidence profile: Comparison 3.3. Colistin versus tobramycin

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Colistin	Tobramycin	Relative (95% CI)	Absolute	Quality	Importance
Lung function: mean % change in FEV₁ % predicted (follow-up: 1 to 3 months; range of scores: 0-100; Better indicated by higher values) [COLI nebulised versus TOBI nebulised]												
1 (Hodson 2002)	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	59	50	-	MD 6.33 lower (12.7 lower to 0.04 higher)	VERY LOW	CRITICAL
Lung function: mean % change in FEV₁ % predicted (follow-up: 4 weeks; range of scores: 0-100; Better indicated by higher values) [COLI DPI versus TOBI nebulised]												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[2]	none	183	191	-	MD 1.67 lower (5.43 lower to 2.09 higher)	LOW	CRITICAL
Lung function: mean % change in FEV₁ % predicted (follow-up: 12 weeks; range of scores: 0-100; Better indicated by higher values) [COLI DPI versus TOBI nebulised]												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[2]	none	183	191	-	MD 2.63 lower (6.67 lower to 1.41 higher)	LOW	CRITICAL
Lung function: mean % change in FEV₁ % predicted (follow-up: 24 weeks; range of scores: 0-100; Better indicated by higher values) [COLI versus TOBI]												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Colistin	Tobramycin	Relative (95% CI)	Absolute	Quality	Importance
2 (COLO/DPI/02/06, Schuster 2013)	randomised trials	very serious[4]	no serious inconsistency	no serious indirectness	No serious imprecision	none	306	352	-	MD 0.99 lower (0.95 to 1.03 higher)	LOW	CRITICAL
Number of patients with 1 or more exacerbations												
NMA outcome												
Time to next pulmonary exacerbation: time to first additional anti-pseudomal treatment (Better indicated by higher values) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[5]	none	183	191	-	MD 3.49 higher (5.14 lower to 12.12 higher)	VERY LOW	CRITICAL
Suppression of the organism: change in sputum PA density Log10 CFU/ml (follow-up 4 weeks; Better indicated by higher values) [COLI nebulised versus TOBI nebulised]												
1 (Hodson 2002)	randomised trials	very serious1	no serious inconsistency	no serious indirectness	no serious imprecision	none	37	42	-	MD 0.32 higher (0.32 lower to 0.96 higher)	LOW	IMPORTANT
Nutritional status: BMI change (follow-up 24 weeks; measured with: kg; Better indicated by higher values)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[6]	none	183	191	-	MD 0.09 lower (0.26 lower to 0.88 higher)	LOW	IMPORTANT

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Colistin	Tobramycin	Relative (95% CI)	Absolute	Quality	Importance
Quality of life: change in CFQ-R physical (follow-up 24 weeks; range of scores: 0-100; Better indicated by higher values) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	Not calculable [7]	none	183	191	P=0.353	MD 1.82 higher (0 to 0 higher)	MODERATE	IMPORTANT
Quality of life: change in CFQ-R vitality (follow-up 24 weeks; range of scores: 0-100; Better indicated by higher values) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	Not calculable [7]	none	183	191	P=0.293	MD 2.27 higher (0 to 0 higher)	MODERATE	IMPORTANT
Quality of life: change in CFQ-R emotion (follow-up 24 weeks; range of scores: 0-100; Better indicated by higher values) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	Not calculable [7]	none	183	191	P=0.244	MD 1.75 higher (0 to 0 higher)	MODERATE	IMPORTANT
Quality of life: change in CFQ-R eating (follow-up 24 weeks; range of scores: 0-100; Better indicated by higher values) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	Not calculable [7]	none	181	191	P=0.925	MD 0.19 lower (0 to 0 higher)	MODERATE	IMPORTANT
Quality of life: change in CFQ-R treatment burden (follow-up 24 weeks; range of scores: 0-100; Better indicated by higher values) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	Not calculable [7]	none	183	191	P=0.091	MD 2.87 higher (0 to 0 higher)	MODERATE	IMPORTANT

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Colistin	Tobramycin	Relative (95% CI)	Absolute	Quality	Importance
Quality of life: change in CFQ-R health perception (follow-up 24 weeks; range of scores: 0-100; Better indicated by higher values) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	Not calculable [7]	none	183	191	P=0.159	MD 2.96 higher (0 to 0 higher)	MODERATE	IMPORTANT
Quality of life: change in CFQ-R social (follow-up 24 weeks; range of scores: 0-100; Better indicated by higher values) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	Not calculable [7]	none	183	191	P=0.153	MD 0.92 higher (0 to 0 higher)	MODERATE	IMPORTANT
Quality of life: change in CFQ-R body image (follow-up 24 weeks; range of scores: 0-100; Better indicated by higher values) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	Not calculable [7]	none	183	191	P=0.385	MD 1.85 higher (0 to 0 higher)	MODERATE	IMPORTANT
Quality of life: change in CFQ-R role (follow-up 24 weeks; range of scores: 0-100; Better indicated by higher values) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	Not calculable [7]	none	183	191	P=0.607	MD 1.22 lower (0 to 0 higher)	MODERATE	IMPORTANT
Quality of life: change in CFQ-R weight (follow-up 24 weeks; range of scores: 0-100; Better indicated by higher values) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	Not calculable [7]	none	183	191	P=0.461	MD 2.81 higher (0 to 0 higher)	MODERATE	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Colistin	Tobramycin	Relative (95% CI)	Absolute		
Quality of life: change in CFQ-R respiratory (follow-up 24 weeks; range of scores: 0-100; Better indicated by higher values) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	Not calculable[7]	none	183	191	P=0.756	MD 0.53 lower (0 to 0 higher)	MODERATE	IMPORTANT
Quality of life: change in CFQ-R digestion (follow-up 24 weeks; range of scores: 0-100; Better indicated by higher values) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	Not calculable[7]	none	183	191	P=0.077	MD 3.22 higher (0 to 0 higher)	MODERATE	IMPORTANT
Minor adverse events: sputum (follow-up 4 weeks) [COLI nebulised versus TOBI nebulised]												
1 (Hodson 2002)	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[8]	none	8/62 (12.9%)	6/53 (11.3%)	RR 1.14 (0.42 to 3.08)	16 more per 1000 (from 66 fewer to 235 more)	VERY LOW	IMPORTANT
Minor adverse events: pharyngitis (follow-up 4 weeks) [COLI nebulised versus TOBI nebulised]												
1 (Hodson 2002)	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[8]	none	3/62 (4.8%)	7/53 (13.2%)	RR 0.37 (0.1 to 1.35)	83 fewer per 1000 (from 119 fewer to 46 more)	VERY LOW	IMPORTANT
Minor adverse events: cough (follow-up 4 weeks) [COLI nebulised versus TOBI nebulised]												
1 (Hodson 2002)	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[8]	none	11/62 (17.7%)	5/53 (9.4%)	RR 1.88 (0.7 to 5.07)	83 more per 1000 (from 28 fewer to 384 more)	VERY LOW	IMPORTANT

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Colistin	Tobramycin	Relative (95% CI)	Absolute	Quality	Importance
Minor adverse events: productive cough (follow-up 24 weeks) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[8]	none	38/187 (20.3%)	44/193 (22.8%)	RR 0.89 (0.61 to 1.31)	25 fewer per 1000 (from 89 fewer to 71 more)	VERY LOW	IMPORTANT
Minor adverse events: chest discomfort (follow-up 24 weeks) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[8]	none	26/187 (13.9%)	34/193 (17.6%)	RR 0.79 (0.49 to 1.26)	37 fewer per 1000 (from 90 fewer to 46 more)	VERY LOW	IMPORTANT
Minor adverse events: vomiting (follow-up 24 weeks) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[8]	none	6/187 (3.2%)	8/193 (4.1%)	RR 0.77 (0.27 to 2.19)	10 fewer per 1000 (from 30 fewer to 49 more)	VERY LOW	IMPORTANT
Serious adverse events: patients with >1 serious AE (follow-up 4 weeks) [COLI nebulised versus TOBI nebulised]												
1 (Hodson 2002)	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[8]	none	7/62 (11.3%)	8/53 (15.1%)	RR 0.75 (0.29 to 1.93)	38 fewer per 1000 (from 107 fewer to 140 more)	VERY LOW	IMPORTANT
Serious adverse events: patients withdrawn (follow-up 24 weeks) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	22/187 (11.8%)	5/193 (2.6%)	RR 4.54 (1.76 to 11.74)	92 more per 1000 (from 20 more to 278 more)	MODERATE	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Colistin	Tobramycin	Relative (95% CI)	Absolute		
Serious adverse events: haemoptysis (follow-up 24 weeks) [COLI nebulised versus TOBI nebulised]												
1 (Hodson 2002)	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[6]	none	20/187 (10.7%)	13/193 (6.7%)	RR 1.59 (0.81 to 3.1)	40 more per 1000 (from 13 fewer to 141 more)	VERY LOW	IMPORTANT
Serious adverse events: dyspnoea (follow-up 4 weeks) [COLI nebulised versus TOBI nebulised]												
1 (Hodson 2002)	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[8]	none	7/62 (11.3%)	5/53 (9.4%)	RR 1.2 (0.4 to 3.55)	19 more per 1000 (from 57 fewer to 241 more)	VERY LOW	IMPORTANT
Serious adverse events: dyspnoea (follow-up 24 weeks) [COLI DPI versus TOBI nebulised)												
1 (COLO/DPI/02/06)	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[8]	none	49/187 (26.2%)	52/193 (26.9%)	RR 0.97 (0.7 to 1.36)	8 fewer per 1000 (from 81 fewer to 97 more)	VERY LOW	IMPORTANT
Emergence of resistant organisms: emergence of highly tobramycin-resistant _P aeruginosa_ (follow-up 24 weeks) [COLI nebulised versus TOBI nebulised]												
1 (Hodson 2002)	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	Not calculable	none	0/62 (0%)	0/53 (0%)	-	-	LOW	IMPORTANT

Abbreviations: CFQ-R: cystic fibrosis questionnaire revised; CI: confidence interval; COLI: colistin; DPI: dry powder for inhalation; FEV$_1$: forced expiratory volume in 1 second; MD: mean difference; RR: risk ratio; TOBI: tobramycin

1 The quality of the evidence was downgraded by 2 because this is an open trial, and risk of bias for randomisation and allocation concealment was unclear

2 The quality of the evidence was downgraded by 1 as the 95% CI crossed 1 clinical MID

3 The quality of the evidence was downgraded by 1 because this is an open trial, and risk of bias for randomisation was unclear

4 The quality of the evidence was downgraded by 2 because both studies were open trials, and risk of bias for randomisation and allocation concealment was unclear

5 The quality of the evidence was downgraded by 2, as the 95% CI is very large and crossed the line of no effect

6 The quality of the evidence was downgraded by 1 as the 95% CI crossed 1 default MID
7 Not calculable, p-value > 0.05
8 The quality of the evidence was downgraded by 2 as the 95% CI crossed 2 default MIDs