

Appendix 1

Certainty of evidence assessments using CINeMA

1.1 CF patients

1.1.1 Change in *P. aeruginosa* sputum density in the short term (4 weeks)

Comparison	Studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
2×AZLI following TIS:3×AZLI following TIS	1	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
2×AZLI following TIS:Placebo	1	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Low
3×AZLI following TIS:Placebo	1	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Low
ALIS:Placebo	1	No concerns	Low risk	Some concerns	No concerns	No concerns	No concerns	Moderate
ALIS:TIS	1	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
AZLI:Placebo	2	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
AZLI:TIS	1	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
Cip_DPI:Placebo	1	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Col:TIS	1	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
FTI following AZLI:Placebo	1	No concerns	Low risk	Some concerns	No concerns	No concerns	No concerns	Moderate
LIS:Placebo	2	Some concerns	Low risk	Some concerns	No concerns	No concerns	No concerns	Low
LIS:TIS	1	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Low
Oral AZM with TIS:TIS	1	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Placebo:TIP	1	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Placebo:TIS	1	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
TIP:TIS	1	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Low
Indirect evidence								
2×AZLI following TIS:ALIS	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
2×AZLI following TIS:AZLI	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Low
2×AZLI following TIS:Cip_DPI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:Col	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:FTI following AZLI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:TIP	0	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
2×AZLI following TIS:TIS	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
3×AZLI following TIS:ALIS	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
3×AZLI following TIS:AZLI	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Low
3×AZLI following TIS:Cip_DPI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:Col	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
3×AZLI following TIS:FTI following AZLI	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low

3×AZLI following TIS:LIS	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
3×AZLI following TIS:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:TIP	0	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
3×AZLI following TIS:TIS	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Low
ALIS:AZLI	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
ALIS:Cip_DPI	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
ALIS:Col	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
ALIS:FTI following AZLI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
ALIS:LIS	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
ALIS:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
ALIS:TIP	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Low
AZLI:Cip_DPI	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
AZLI:Col	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
AZLI:FTI following AZLI	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
AZLI:LIS	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Low
AZLI:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Low
AZLI:TIP	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
Cip_DPI:Col	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:FTI following AZLI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:LIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Cip_DPI:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:TIP	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Low
Cip_DPI:TIS	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Low
Col:FTI following AZLI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Col:LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Col:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
Col:Placebo	0	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Col:TIP	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Low
FTI following AZLI:LIS	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:TIP	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
FTI following AZLI:TIS	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
LIS:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
LIS:TIP	0	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Oral AZM with TIS:Placebo	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
Oral AZM with TIS:TIP	0	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate

1.1.2 Change in *P. aeruginosa* sputum density in the long term (24 weeks)

Comparison	studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
Cyclical TIS:Cyclical 590mg ALIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical TIS:Cyclical TIP	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical TIS:Cyclical LIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical TIS:Placebo	1	No concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Low
Indirect evidence								
Cyclical 590mg ALIS:Cyclical TIP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical 590mg ALIS:Cyclical LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical 590mg ALIS:Placebo	0	Some concerns	Low risk	No concerns	Major concerns	Some concerns	No concerns	Very low
Cyclical TIP:Cyclical LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical TIP:Placebo	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical LIS:Placebo	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low

1.1.3 Discontinuation due to AEs in the short term (4 weeks)

Comparison	Studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
2×AZLI following TIS:3×AZLI following TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:Placebo	1	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
3×AZLI following TIS:Placebo	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI:Placebo	2	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:Placebo	1	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Col:TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:Placebo	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
LIS:Placebo	2	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Placebo:TIP	2	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Placebo:TIS	1	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Indirect evidence								
2×AZLI following TIS:AZLI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:Cip_DPI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:Col	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:FTI following AZLI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:TIP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:AZLI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:Cip_DPI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:Col	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:FTI following AZLI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:TIP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI:Cip_DPI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI:Col	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI:FTI following AZLI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
AZLI:LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI:TIP	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
AZLI:TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:Col	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:FTI following AZLI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:LIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low

Cip_DPI:TIP	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Col:FTI following AZLI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Col:LIS	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Col:Placebo	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Col:TIP	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:LIS	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:TIP	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
LIS:TIP	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
LIS:TIS	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
TIP:TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low

1.1.4 Discontinuation due to AEs in the long term (24 weeks)

Comparison	studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
Cyclical TIS:Cyclical ALIS	1	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
Cyclical TIS:Cyclical AZLI alternating with TIS	1	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical TIS:Cyclical AZLI	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical TIS:Continuous Col_DPI	1	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
Cyclical TIS:Cyclical TIP	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical TIS:Cyclical LIS	1	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
Indirect evidence								
Cyclical ALIS:Cyclical AZLI alternating with TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical ALIS:Cyclical AZLI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical ALIS:Continuous Col_DPI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical ALIS:Cyclical LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical ALIS:Cyclical TIP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI alternating with TIS:Cyclical AZLI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI alternating with TIS:Continuous Col_DPI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI alternating with TIS:Cyclical TIP	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI alternating with TIS:Cyclical LIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI:Continuous Col_DPI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI:Cyclical TIP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI:Cyclical LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Continuous Col_DPI:Cyclical LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Continuous Col_DPI:Cyclical TIP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical TIP:Cyclical LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low

1.1.5 Drug-related AEs in the short term (4 weeks)

Comparison	Studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
Cip_DPI:Placebo	1	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:Placebo	1	Major concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Placebo:TIP	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Placebo:TIS	1	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Indirect evidence								
Cip_DPI:FTI following AZLI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:TIP	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:TIS	0	Major concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
TIP:TIS	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low

1.1.6 Drug-related AEs in the long term (24 weeks)

Comparison	Studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
Continuous Col_DPI:Cyclical TIS	1	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Very low
Cyclical 590mg ALIS:Cyclical TIS	1	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
Cyclical AZLI:Cyclical TIS	1	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Very low
Cyclical AZLI alternating with TIS:Cyclical TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical TIS:Placebo	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Indirect evidence								
Continuous Col_DPI:Cyclical 590mg ALIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Continuous Col_DPI:Cyclical AZLI	0	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Very low
Continuous Col_DPI:Cyclical AZLI alternating with TIS	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
Continuous Col_DPI:Placebo	0	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Very low
Cyclical 590mg ALIS:Cyclical AZLI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical 590mg ALIS:Cyclical AZLI alternating with TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical 590mg ALIS:Placebo	0	Some concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
Cyclical AZLI:Cyclical AZLI alternating with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI:Placebo	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI alternating with TIS:Placebo	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low

1.1.7 Change in FEV1% predicted in the short term (4 weeks)

Comparison	Studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
590mg ALIS:TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI:Placebo	1	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
AZLI:TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI following TIS:Placebo	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:Placebo	1	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Col:TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:Placebo	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
LIS:Placebo	2	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Very low
LIS:TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Oral AZM with TIS:TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Placebo:TIP	2	Some concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
Placebo:TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
TIP:TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Indirect evidence								
590mg ALIS:AZLI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
590mg ALIS:AZLI following TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
590mg ALIS:Cip_DPI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
590mg ALIS:Col	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
590mg ALIS:FTI following AZLI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
590mg ALIS:LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
590mg ALIS:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
590mg ALIS:Placebo	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
590mg ALIS:TIP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI:AZLI following TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
AZLI:Cip_DPI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
AZLI:Col	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI:FTI following AZLI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
AZLI:LIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
AZLI:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI:TIP	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
AZLI following TIS:Cip_DPI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI following TIS:Col	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI following TIS:FTI following AZLI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
AZLI following TIS:LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low

AZLI following TIS:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI following TIS:TIP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI following TIS:TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:Col	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:FTI following AZLI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:LIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Cip_DPI:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:TIP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Col:FTI following AZLI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Col:LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Col:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Col:Placebo	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Col:TIP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:LIS	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:TIP	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
LIS:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
LIS:TIP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Oral AZM with TIS:Placebo	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Oral AZM with TIS:TIP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low

1.1.8 Change in FEV1% predicted in the long term (24 weeks)

Comparison	Studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
Continuous Col_DPI:Cyclical TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical 590mg ALIS:Cyclical TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical LIS:Cyclical TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical TIP:Cyclical TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical TIS:Placebo	2	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Indirect evidence								
Continuous Col_DPI:Cyclical 590mg ALIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Continuous Col_DPI:Cyclical LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Continuous Col_DPI:Cyclical TIP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Continuous Col_DPI:Placebo	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Cyclical 590mg ALIS:Cyclical LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical 590mg ALIS:Cyclical TIP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical 590mg ALIS:Placebo	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Cyclical LIS:Cyclical TIP	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical LIS:Placebo	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical TIP:Placebo	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low

1.1.9 Change in CFQR-RSS in the short term (4 weeks)

Comparison	Studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
2×AZLI following TIS:3×AZLI following TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:Placebo	1	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
3×AZLI following TIS:Placebo	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
590mg ALIS:TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI:Placebo	2	Some concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
AZLI:TIS	1	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
Cip_DPI:Placebo	1	No concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Low
FTI following AZLI:Placebo	1	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
LIS:Placebo	1	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
LIS:TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Oral AZM with TIS:TIS	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Indirect evidence								
2×AZLI following TIS:590mg ALIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:AZLI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:Cip_DPI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:FTI following AZLI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
2×AZLI following TIS:TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:590mg ALIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:AZLI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:Cip_DPI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:FTI following AZLI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
3×AZLI following TIS:TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
590mg ALIS:AZLI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
590mg ALIS:Cip_DPI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
590mg ALIS:FTI following AZLI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
590mg ALIS:LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
590mg ALIS:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
590mg ALIS:Placebo	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI:Cip_DPI	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI:FTI following AZLI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low

AZLI:LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
AZLI:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:FTI following AZLI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:LIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:Oral AZM with TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
FTI following AZLI:TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
LIS:Oral AZM with TIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Oral AZM with TIS:Placebo	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Placebo:TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low

1.1.10 Change in CFQR-RSS in the long term (24 weeks)

Comparison	Studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
Continuous Col_DPI:Cyclical TIS	1	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
Cyclical 590mg ALIS:Cyclical TIS	1	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
Cyclical LIS:Cyclical TIS	1	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
Indirect evidence								
Continuous Col_DPI:Cyclical 590mg ALIS	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
Continuous Col_DPI:Cyclical LIS	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Cyclical 590mg ALIS:Cyclical LIS	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low

1.2 NCFB patients

1.2.1 Change in *P. aeruginosa* sputum density in the short term (4 weeks)

Comparison	Studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
AZLI:Placebo	2	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Cip_DPI:Placebo	1	No concerns	Low risk	Some concerns	No concerns	No concerns	No concerns	Moderate
Col:Placebo	1	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
DRCFI:Placebo	3	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Placebo:TIP	1	No concerns	Low risk	Some concerns	No concerns	No concerns	No concerns	Moderate
Placebo:TIS	2	No concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Moderate
Indirect evidence								
AZLI:Cip_DPI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
AZLI:Col	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Low
AZLI:DRCFI	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
AZLI:TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
AZLI:TIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Cip_DPI:Col	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
Cip_DPI:DRCFI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:TIS	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Col:DRCFI	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Col:TIP	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
Col:TIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
DRCFI:TIP	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
DRCFI:TIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
TIP:TIS	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low

1.2.2 Change in *P. aeruginosa* sputum density in the long term (≥ 16 weeks)

Comparison	Studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
Continuous Col:Placebo	1	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Continuous GM:Placebo	1	Some concerns	Low risk	Major concerns	Some concerns	No concerns	No concerns	Very low
Continuous TIP:Cyclical TIP	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIP:Placebo	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI:Placebo	2	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Cyclical TIP:Placebo	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical TIS:Placebo	1	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Indirect evidence								
Continuous Col:Continuous GM	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous Col:Continuous TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous Col:Cyclical AZLI	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Continuous Col:Cyclical TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous Col:Cyclical TIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Continuous GM:Continuous TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous GM:Cyclical AZLI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous GM:Cyclical TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous GM:Cyclical TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIP:Cyclical AZLI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIP:Cyclical TIS	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI:Cyclical TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI:Cyclical TIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Cyclical TIP:Cyclical TIS	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low

1.2.3 Change in QoL-B-RSS in the short term (4 weeks)

Comparison	Studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
AZLI:Placebo	2	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Placebo:TIP	1	No concerns	Low risk	Some concerns	Some concerns	No concerns	No concerns	Low
Placebo:TIS	1	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Indirect evidence								
AZLI:TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
AZLI:TIS	0	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
TIP:TIS	0	No concerns	Low risk	Some concerns	Some concerns	No concerns	No concerns	Low

1.2.4 Change in QoL-B-RSS in the long term (≥ 16 weeks)

Comparison	Studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
14-day cyclical Cip_DPI:Placebo	1	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
28-day cyclical Cip_DPI:Placebo	1	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
Continuous TIP:Cyclical TIP	1	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIP:Placebo	1	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIS:Placebo	1	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Cyclical AZLI:Placebo	2	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Cyclical DRCFI:Placebo	2	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Cyclical TIP:Placebo	1	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Cyclical TIS:Placebo	1	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Indirect evidence								
14-day cyclical Cip_DPI:28-day cyclical Cip_DPI	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
14-day cyclical Cip_DPI:Continuous TIP	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
14-day cyclical Cip_DPI:Continuous TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
14-day cyclical Cip_DPI:Cyclical AZLI	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
14-day cyclical Cip_DPI:Cyclical DRCFI	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
14-day cyclical Cip_DPI:Cyclical TIP	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
14-day cyclical Cip_DPI:Cyclical TIS	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
28-day cyclical Cip_DPI:Continuous TIP	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
28-day cyclical Cip_DPI:Continuous TIS	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
28-day cyclical Cip_DPI:Cyclical AZLI	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
28-day cyclical Cip_DPI:Cyclical DRCFI	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
28-day cyclical Cip_DPI:Cyclical TIP	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
28-day cyclical Cip_DPI:Cyclical TIS	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
Continuous TIP:Continuous TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIP:Cyclical AZLI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIP:Cyclical DRCFI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIP:Cyclical TIS	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Continuous TIS:Cyclical AZLI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIS:Cyclical DRCFI	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Continuous TIS:Cyclical TIP	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIS:Cyclical TIS	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Cyclical AZLI:Cyclical DRCFI	0	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Cyclical AZLI:Cyclical TIP	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI:Cyclical TIS	0	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Cyclical DRCFI:Cyclical TIP	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Cyclical DRCFI:Cyclical TIS	0	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Cyclical TIP:Cyclical TIS	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low

1.2.5 Pulmonary exacerbations per patient-year in the long term (≥ 16 weeks)

Comparison	Studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
14-day cyclical Cip_DPI:Placebo	2	No concerns	Low risk	Some concerns	No concerns	Some concerns	No concerns	Low
28-day cyclical Cip_DPI:Placebo	2	No concerns	Low risk	Some concerns	No concerns	Some concerns	No concerns	Low
Continuous GM:Placebo	1	Some concerns	Low risk	Major concerns	No concerns	No concerns	No concerns	Very low
Continuous TIP:Cyclical TIP	1	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Continuous TIP:Placebo	1	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Cyclical AZLI:Placebo	2	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Cyclical DRCFI:Placebo	2	No concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Moderate
Cyclical TIP:Placebo	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical TIS:Placebo	1	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Indirect evidence								
14-day cyclical Cip_DPI:28-day cyclical Cip_DPI	0	No concerns	Low risk	Some concerns	Some concerns	No concerns	No concerns	Low
14-day cyclical Cip_DPI:Continuous GM	0	Some concerns	Low risk	Major concerns	No concerns	No concerns	No concerns	Very low
14-day cyclical Cip_DPI:Continuous TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
14-day cyclical Cip_DPI:Cyclical AZLI	0	No concerns	Low risk	Some concerns	No concerns	Some concerns	No concerns	Low
14-day cyclical Cip_DPI:Cyclical DRCFI	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
14-day cyclical Cip_DPI:Cyclical TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
14-day cyclical Cip_DPI:Cyclical TIS	0	No concerns	Low risk	Some concerns	Some concerns	No concerns	No concerns	Low
28-day cyclical Cip_DPI:Continuous GM	0	Some concerns	Low risk	Major concerns	No concerns	No concerns	No concerns	Very low
28-day cyclical Cip_DPI:Continuous TIP	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
28-day cyclical Cip_DPI:Cyclical AZLI	0	No concerns	Low risk	Some concerns	Some concerns	No concerns	No concerns	Low
28-day cyclical Cip_DPI:Cyclical DRCFI	0	No concerns	Low risk	Some concerns	Some concerns	No concerns	No concerns	Low
28-day cyclical Cip_DPI:Cyclical TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
28-day cyclical Cip_DPI:Cyclical TIS	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Continuous GM:Continuous TIP	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Continuous GM:Cyclical AZLI	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	No concerns	Low
Continuous GM:Cyclical DRCFI	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	No concerns	Low
Continuous GM:Cyclical TIP	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
Continuous GM:Cyclical TIS	0	Some concerns	Low risk	Some concerns	No concerns	No concerns	No concerns	Low
Continuous TIP:Cyclical AZLI	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Continuous TIP:Cyclical DRCFI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIP:Cyclical TIS	0	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Cyclical AZLI:Cyclical DRCFI	0	No concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Moderate
Cyclical AZLI:Cyclical TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI:Cyclical TIS	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Low
Cyclical DRCFI:Cyclical TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical DRCFI:Cyclical TIS	0	No concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
Cyclical TIP:Cyclical TIS	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low

1.2.6 Discontinuation due to AEs in the short term (4 weeks)

Comparison	Number of studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
Cip_DPI:Placebo	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
DRCFI:Placebo	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Placebo:TIS	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Indirect evidence								
Cip_DPI:DRCFI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cip_DPI:TIS	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
DRCFI:TIS	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low

1.2.7 Discontinuation due to AEs in the long term (≥ 16 weeks)

Comparison	Studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
14-day cyclical Cip_DPI:Placebo	2	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
28-day cyclical Cip_DPI:Placebo	2	No concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
Continuous Col:Placebo	1	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Continuous GM:Placebo	1	Some concerns	Low risk	Major concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIP:Cyclical TIP	1	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIP:Placebo	1	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
Continuous TIS-QD:Placebo	1	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI:Placebo	2	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Cyclical DRCFI:Placebo	3	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Cyclical TIP:Placebo	1	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
Cyclical TIS:Placebo	1	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Indirect evidence								
14-day cyclical Cip_DPI:28-day cyclical Cip_DPI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
14-day cyclical Cip_DPI:Continuous Col	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
14-day cyclical Cip_DPI:Continuous GM	0	Some concerns	Low risk	Major concerns	Major concerns	No concerns	No concerns	Very low
14-day cyclical Cip_DPI:Continuous TIP	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
14-day cyclical Cip_DPI:Continuous TIS-QD	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
14-day cyclical Cip_DPI:Cyclical AZLI	0	No concerns	Low risk	Some concerns	No concerns	No concerns	No concerns	Very low
14-day cyclical Cip_DPI:Cyclical DRCFI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
14-day cyclical Cip_DPI:Cyclical TIP	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
14-day cyclical Cip_DPI:Cyclical TIS	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
28-day cyclical Cip_DPI:Continuous Col	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
28-day cyclical Cip_DPI:Continuous GM	0	Some concerns	Low risk	Major concerns	Major concerns	No concerns	No concerns	Very low
28-day cyclical Cip_DPI:Continuous TIP	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
28-day cyclical Cip_DPI:Continuous TIS-QD	0	Some concerns	Low risk	Some concerns	Some concerns	Some concerns	No concerns	Very low
28-day cyclical Cip_DPI:Cyclical AZLI	0	No concerns	Low risk	Some concerns	No concerns	No concerns	No concerns	Moderate
28-day cyclical Cip_DPI:Cyclical DRCFI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
28-day cyclical Cip_DPI:Cyclical TIP	0	No concerns	Low risk	Some concerns	No concerns	Some concerns	No concerns	Low
28-day cyclical Cip_DPI:Cyclical TIS	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
Continuous Col:Continuous GM	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous Col:Continuous TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous Col:Continuous TIS-QD	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous Col:Cyclical AZLI	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Continuous Col:Cyclical DRCFI	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low

Continuous Col:Cyclical TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous Col:Cyclical TIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Continuous GM:Continuous TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous GM:Continuous TIS-QD	0	Some concerns	Low risk	Major concerns	Major concerns	No concerns	No concerns	Very low
Continuous GM:Cyclical AZLI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous GM:Cyclical DRCFI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous GM:Cyclical TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous GM:Cyclical TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIP:Continuous TIS-QD	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIP:Cyclical AZLI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIP:Cyclical DRCFI	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
Continuous TIP:Cyclical TIS	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIS-QD:Cyclical AZLI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIS-QD:Cyclical DRCFI	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIS-QD:Cyclical TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Continuous TIS-QD:Cyclical TIS	0	Some concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI:Cyclical DRCFI	0	No concerns	Low risk	No concerns	No concerns	No concerns	No concerns	High
Cyclical AZLI:Cyclical TIP	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical AZLI:Cyclical TIS	0	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Cyclical DRCFI:Cyclical TIP	0	No concerns	Low risk	Some concerns	No concerns	Some concerns	No concerns	Low
Cyclical DRCFI:Cyclical TIS	0	No concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Low
Cyclical TIP:Cyclical TIS	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low

1.2.8 Drug-related AEs in the long term (≥ 16 weeks)

Comparison	Studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
14-day cyclical Cip_DPI:Placebo	2	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
28-day cyclical Cip_DPI:Placebo	2	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
Cyclical DRCFI:Placebo	2	No concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Cyclical TIS:Placebo	1	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Indirect evidence								
14-day cyclical Cip_DPI:28-day cyclical Cip_DPI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
14-day cyclical Cip_DPI:Cyclical DRCFI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
14-day cyclical Cip_DPI:Cyclical TIS	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
28-day cyclical Cip_DPI:Cyclical DRCFI	0	No concerns	Low risk	Some concerns	Major concerns	No concerns	No concerns	Very low
28-day cyclical Cip_DPI:Cyclical TIS	0	No concerns	Low risk	Some concerns	No concerns	Major concerns	No concerns	Very low
Cyclical DRCFI:Cyclical TIS	0	No concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low

Table S1 List of terms of the search strategy

Web of science (adapted for other databases)

#1	((ALL=(inhal*)) OR ALL=(nebuli*)) OR ALL=(aerosol*)
#2	((ALL=(Cystic Fibrosis)) OR ALL=(Mucoviscidosis)) OR ALL=(Fibrocytic Disease*
#3	ALL=(Bronchiectas*)
#4	((ALL=(Pseudomonas aeruginosa)) OR ALL=(Pseudomonas polycolor)) OR ALL=(Bacillus pyocyaneu*) OR ALL=(Bacterium aeruginosu*)
#5	(ALL=(multidrug resistant bacteria)) OR ALL=(extensively drug resistant bacteria)
#6	#2 OR #3 OR #4 OR #5
#7	(((((ALL=(antibiotic*)) OR ALL=(antibacterial)) OR ALL=(anti-bacterial)) OR ALL=(antimicrobial)) OR ALL=(anti-microbial)) OR ALL=(aminoglycoside*)
#8	((ALL=(Ciprofloxacin)) OR ALL=(Cipro)) OR ALL=(Ciprinol)
#9	(((((ALL=(Tobramycin)) OR ALL=(Nebamycin Factor 6)) OR ALL=(Obracin)) OR ALL=(Tobracin)) OR ALL=(Brulamycin)) OR ALL=(Nebcin)) OR ALL=(Nebicin)
#10	((ALL=(Colisti*)) OR ALL=(Polymyxin E)) OR ALL=(Colimycin)) OR ALL=(Totazina)
#11	((ALL=(Aztreonam)) OR ALL=(Azthreonam)) OR ALL=(Urobactam)) OR ALL=(Azactam)
#12	(ALL=(Levofloxacin)) OR ALL=(Ofloxacin)
#13	(ALL=(Amika*)) OR ALL=(Yectamid)
#14	(ALL=(Ceftazidime)) OR ALL=(Tazidime)
#15	((ALL=(Genta*)) OR ALL=(Garamycin)) OR ALL=(Genticin)
#16	ALL=(Fosfomycin)
#17	#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16
#18	((TS=(single)) OR TS=(double)) OR TS=(treble)) OR TS=(triple)
#19	(TS=(mask*)) OR TS=(blind*)
#20	#18 AND #19
#21	((((((((((SO=(randomized controlled trial)) OR SO=(controlled clinical trial)) OR TS=(clinical trial*)) OR TS=(random*)) OR TS=(research design)) OR TS=(comparative stud*)) OR TS=(evaluation stud*)) OR TS=(controlled trial*)) OR TS=(follow-up stud*)) OR TS=(prospective stud*)) OR TS=(placebo*)) OR TS=(clinical stud*)) OR ALL=(open label)
#22	#20 OR #21
#23	#1 AND #6 AND #17 AND #22

Table S2. Definition of outcomes.

Outcome	Definition
Primary outcomes	
Change in <i>P aeruginosa</i> sputum density	Change in <i>P aeruginosa</i> sputum density was measured as the reduction in log ₁₀ CFU/g of sputum at 4 weeks and the end of the treatment period.
Discontinuation due to AEs	Number of patients with premature treatment discontinuation due to any adverse event during the treatment period.
Secondary outcomes	
Exacerbation frequency per patient-year	Number of pulmonary exacerbation events per patient-year during the treatment period. To meet the definition of a pulmonary exacerbation, patients must concurrently have had at least 4 of the 12 symptoms/signs: <ul style="list-style-type: none">• Change in sputum• New or increased hemoptysis;• Increased cough;• Increased dyspnea;• Malaise, fatigue or lethargy;• Temperature above 38 °C;• Anorexia or weight loss;• Sinus pain or tenderness;• Change in sinus discharge;• Change in physical examination of the chest;• Decrease in pulmonary function by 10% or more from a previously recorded value;• Radiographic changes indicative of pulmonary infection.
Change in CFQR-RSS	In the CF Questionnaire Revised Respiratory Symptom Score (CFQR-RSS) questionnaire, higher scores indicate more improvements in respiratory symptoms. Change in CFQR-RSS and QoL-B-RSS is calculated from baseline to the end of the treatment.
Change in QoL-B-RSS	In the quality-of-life bronchiectasis respiratory symptom score (QoL-B-RSS), higher scores indicate more improvements in respiratory symptoms. Change in QoL-B-RSS is calculated from baseline to the end of the treatment.
Change in FEV ₁ % predicted	Change in FEV ₁ % predicted was measured as the improvement of FEV ₁ % at 4 weeks and the end of the treatment period.
Drug-related AEs	Number of patients with drug-related adverse events at 4 weeks and the end of the study.

Abbreviations: CF: cystic fibrosis; AE: adverse event; FEV₁: forced expiratory volume in the first second.

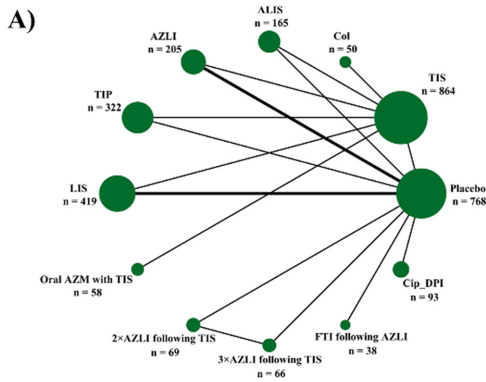
Table S3 Studies excluded at full text screening stage and reasons

Reason	Number	Reference
Not randomized-controlled trials	28	Huang2022, Stockmann2015, Emiralioğlu2016, Harrison2014, Gibson2007, Bilton2021, Elborn2016, konstan2016, Sommerwerck2016, Bilton2015, Flume2014, Bilton2014, Quintana-Gallego2014, Oermann2010, Bowman2002, Moss2002, Rietschel2016, Stass2013, Geller2011, Geller2007, Gibson2006, Geller2002, Crowther1999, Dodd1997, Terpstra2022, Loebinger2019, O'Donnell2016, Serisier2012
Wrong population	19	Langton Hewer2020, Ratjen2019, Mayer-Hamblett2018, Orriols2015, Proesmans2013, Taccetti2012, Treggiari2011, Ratjen2010, Angermair2023, Bharathi2022, Lu 2009, Rakhshan2023, Frost2021, Puvvadi2021, Ailiyaer2018, Hossain2010, Bilton2006, Semykin2010, Al-Aloul2005
Wrong intervention	10	Mayer-Hamblett2013, Eber2021, Balfour-Lynn2006, Tabernero2015, Adeboyeku2006, Orriols1999, Greenwood2017, Greenwood2016, Guidetti2021, Nikolaizik2008
No outcomes of interest	8	Gilchrist2023, Nasr2008, Quittner2002, Wiesemann1998, Lin1997, Schaad1997, Gibson2003, Twiss2022
Results from other included study	35	Terpstra2023, Alkhatib2022, McCleave2022, Ramsey2017, Flume2015, Hansen2015, Schuster2015, Antoniu2013, Fiel2013, Konstan2013, Alder2012, Galeva2012, Oermann2011, Rubin2011, Taccetti2011, Nasr2011, Couch2001, Goldman2012, Harrison2012, Alder2011, Bilton2011, Murray2009, Quittner2009, Konstan2009, Ratjen2008, McCoy2009, Oermann2009, Retsch-Bogart2008, Chuchalin2006, Lenoir2006, Gibson2002, VanDevanter2000, O'Donnell1999, Rosenfeld1999, Hung1995
Unable to retrieve full text	9	Haworth2021, Dimakou2017, Herrmann2017, Dimakou2014, Flume2011, Hampel2011, Quittner2011, O'Donnell2009, Hazinski1999

Table S4 CFTR genotypes of patients included in studies of CF

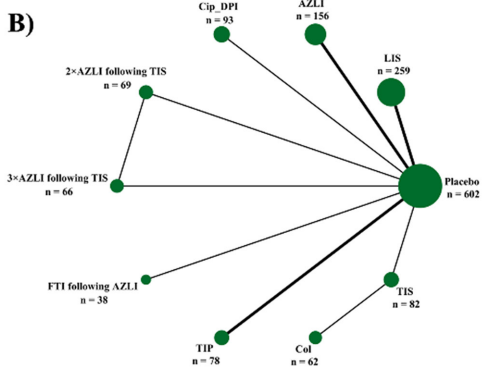
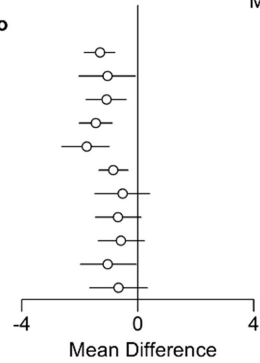
Study	Treatment	CFTR genotype, n (%)		
		ΔF508 Homozygous	ΔF508 Heterozygous	Unidentified or other
Nichols <i>et al.</i> , 2022 (TEACH)	Oral AZM (500 mg, t.i.w.) + TIS/TIP (300 mg/112 mg, b.i.d.)	38 (62.3)	17 (27.9)	6 (9.8)
	TIS/TIP (300 mg/112 mg, b.i.d.)	35 (64.8)	11 (20.4)	8 (14.9)
Bilton <i>et al.</i> , 2020 (CLEAR-108)	ALIS (590 mg, q.d.)	72 (48.6)	40 (27.0)	21 (14.2)
	TIS (300 mg, b.i.d.)	70 (47.9)	43 (29.5)	25 (17.1)
Assael <i>et al.</i> , 2013	AZLI (75 mg, t.i.d.)	64 (54.7)	36 (30.8)	17 (14.5)
	TIS (300 mg, b.i.d.)	60 (54.1)	30 (27.0)	21 (18.9)
Trapnell <i>et al.</i> , 2012	FTI (80/20 mg, b.i.d.) following AZLI (75 mg, t.i.d.)	14 (37.0)	17 (45.0)	7 (18.0)
	Placebo	15 (38.0)	14 (35.0)	11 (28.0)
Wainwright <i>et al.</i> , 2011 (AIR-CF4)	AZLI (75 mg, t.i.d.)	39 (54.2)	23 (31.9)	4 (5.8)
	Placebo	40 (57.1)	26 (37.1)	10 (13.9)
Retsch-Bogart <i>et al.</i> , 2009 (AIR-CF1)	AZLI (75 mg, t.i.d.)	38 (47.5)	21 (26.3)	21 (26.3)
	Placebo	30 (35.7)	22 (26.2)	32 (38.1)
McCoy <i>et al.</i> , 2008 (AIR-CF2)	AZLI (75 mg, b.i.d.) following TIS (300 mg, b.i.d.)	25 (36.0)	15 (22.0)	29 (42.0)
	AZLI (75 mg, t.i.d.) following TIS (300 mg, b.i.d.)	31 (47.0)	12 (18.0)	23 (35.0)
	Placebo	34 (45.0)	20 (26.0)	22 (29.0)

Abbreviations: CF: cystic fibrosis; CFTR: cystic fibrosis transmembrane conductance regulator; TIS: tobramycin inhalation solution; TIP: tobramycin inhalation powder; ALIS: amikacin liposome inhalation suspension; AZLI: aztreonam lysine for inhalation solution; FTI: fosfomycin/tobramycin for inhalation.



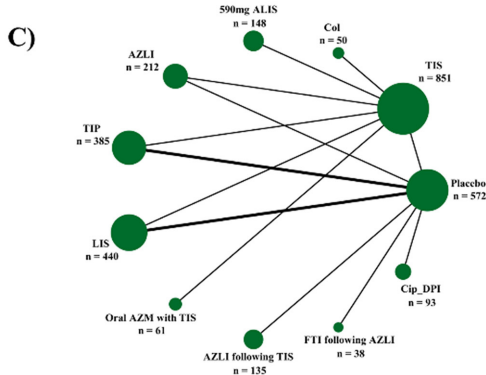
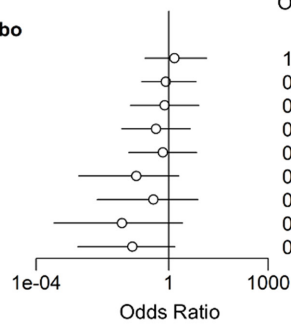
Compared with Placebo

Treatment	Mean Difference (95% CI)
TIS	-1.30 (-1.85, -0.789)
Col	-1.04 (-2.04, -0.0807)
ALIS	-1.08 (-1.79, -0.405)
AZLI	-1.45 (-2.03, -0.880)
TIP	-1.76 (-2.63, -0.991)
LIS	-0.843 (-1.35, -0.336)
Oral AZM with TIS	-0.519 (-1.48, 0.414)
2x AZLI following TIS	-0.682 (-1.47, 0.114)
3x AZLI following TIS	-0.582 (-1.37, 0.222)
FTI following AZLI	-1.03 (-1.98, -0.0550)
Cip_DPI	-0.663 (-1.66, 0.325)



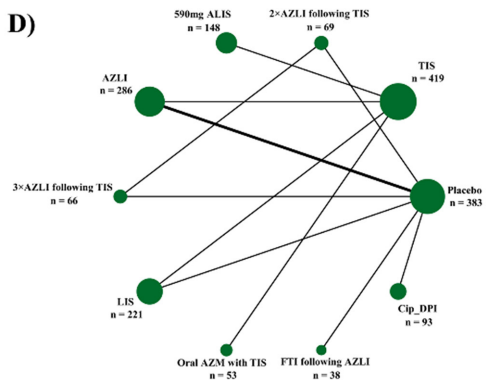
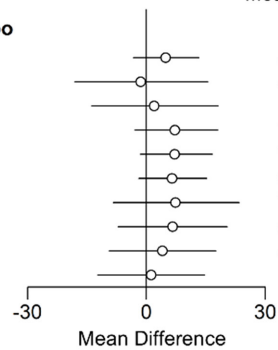
Compared with Placebo

Treatment	Odds Ratio (95% CI)
LIS	1.49 (0.189, 13.9)
AZLI	0.817 (0.152, 6.72)
Cip_DPI	0.750 (0.0693, 8.06)
2x AZLI following TIS	0.413 (0.0379, 4.44)
3x AZLI following TIS	0.663 (0.0623, 6.98)
FTI following AZLI	0.106 (0.00191, 2.01)
TIP	0.348 (0.00696, 7.58)
Col	0.0390 (0.000341, 2.60)
TIS	0.0801 (0.00182, 1.52)



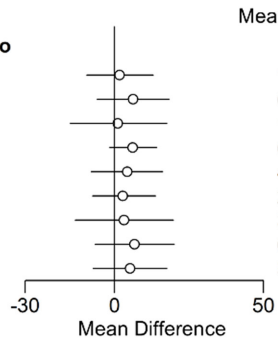
Compared with Placebo

Treatment	Mean Difference (95% CI)
TIS	4.84 (-3.31, 13.2)
Col	-1.47 (-18.1, 15.5)
590mg ALIS	1.96 (-13.8, 18.1)
AZLI	7.19 (-2.94, 18.0)
TIP	7.12 (-1.56, 16.7)
LIS	6.46 (-1.96, 15.2)
Oral AZM with TIS	7.33 (-8.40, 23.4)
AZLI following TIS	6.62 (-7.17, 20.4)
FTI following AZLI	4.04 (-9.42, 17.5)
Cip_DPI	1.21 (-12.3, 14.7)

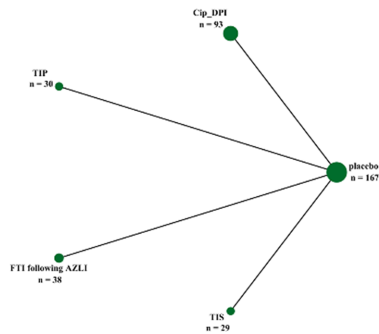


Compared with Placebo

Treatment	Mean Difference (95% CI)
TIS	1.68 (-9.36, 13.0)
2x AZLI following TIS	6.21 (-5.83, 18.2)
590mg ALIS	1.03 (-14.8, 17.5)
AZLI	6.08 (-1.66, 14.1)
3x AZLI following TIS	4.22 (-7.86, 16.2)
LIS	2.72 (-7.40, 13.7)
Oral AZM with TIS	3.16 (-13.2, 19.8)
FTI following AZLI	6.68 (-6.54, 20.0)
Cip_DPI	5.20 (-7.19, 17.5)

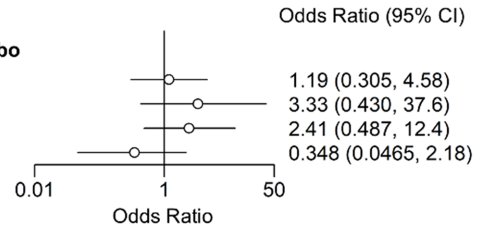


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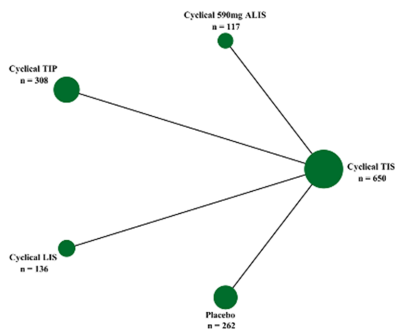


Compared with placebo

Cip_DPI
TIP
FTI following AZLI
TIS

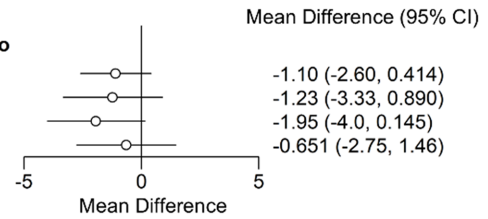


F)

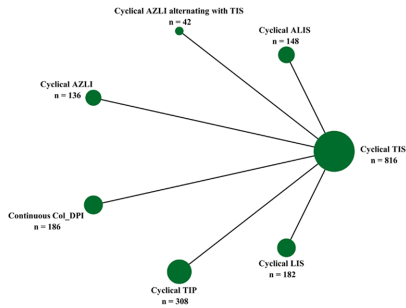


Compared with Placebo

Cyclical TIS
Cyclical 590mg ALIS
Cyclical TIP
Cyclical LIS

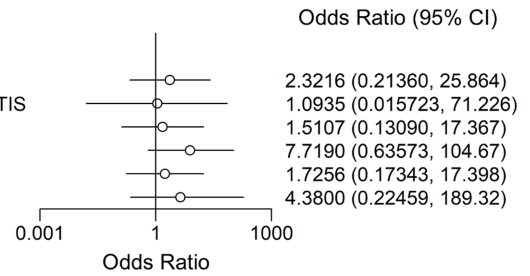


G)

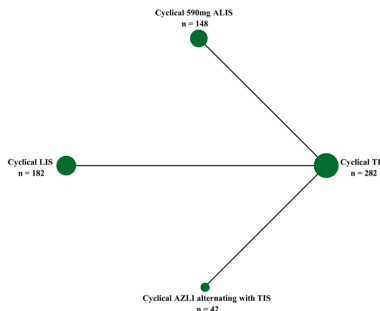


Compared with Cyclical TIS

Cyclical ALIS
Cyclical AZLI alternating with TIS
Cyclical AZLI
Continuous Col_DPI
Cyclical TIP
Cyclical LIS

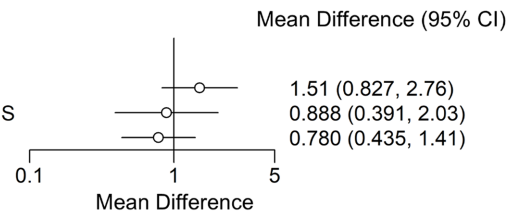


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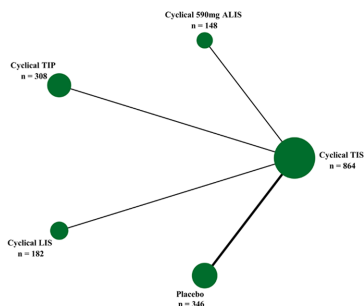


Compared with Cyclical TIS

Cyclical 590mg ALIS
Cyclical AZLI alternating with TIS
Cyclical LIS

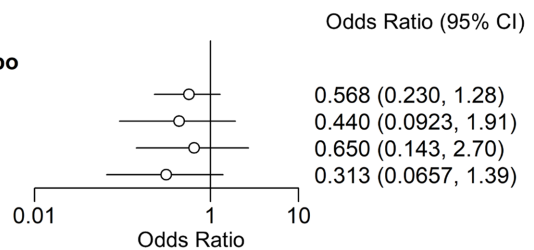


I)



Compared with Placebo

Cyclical TIS
Cyclical 590mg ALIS
Cyclical TIP
Cyclical LIS



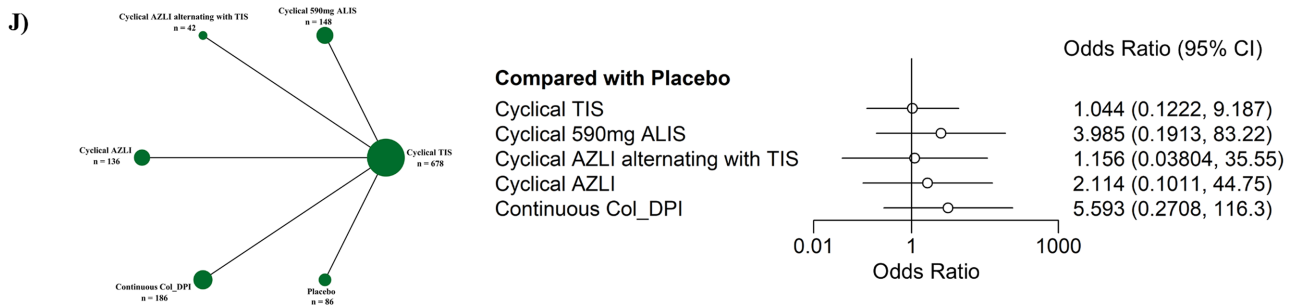
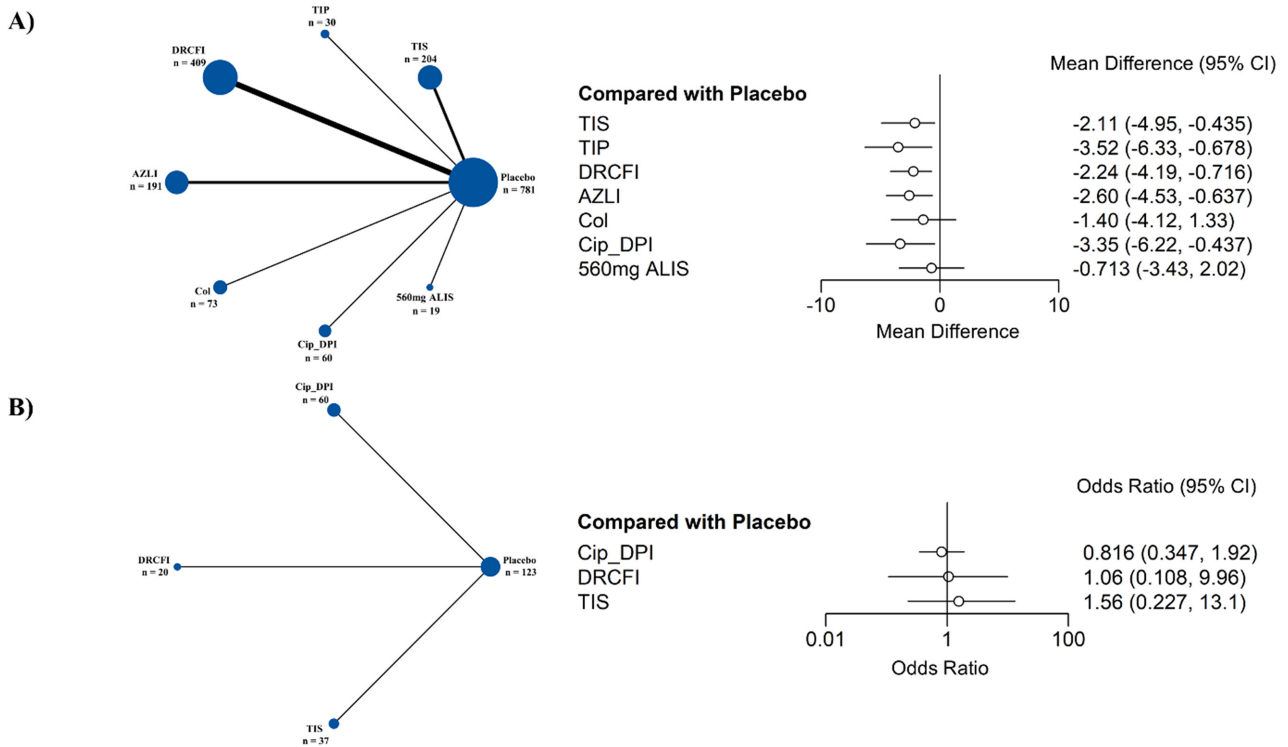
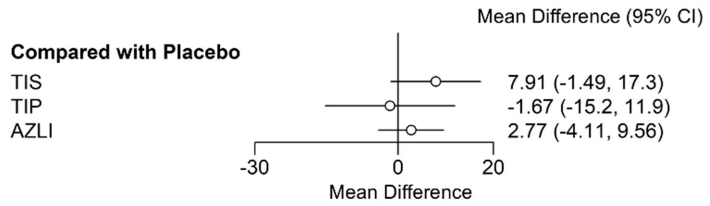
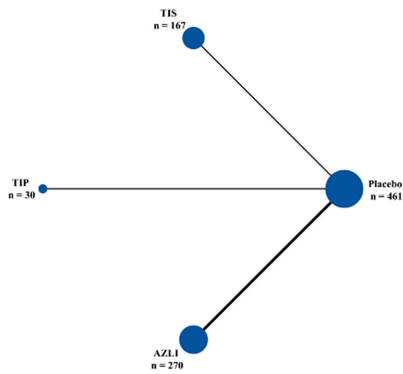


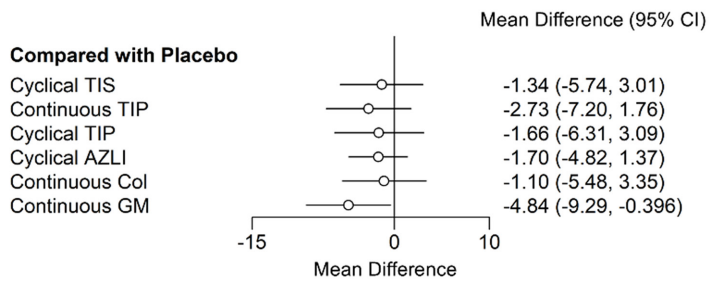
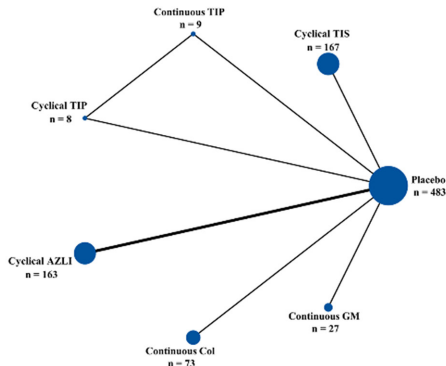
Figure S1 Network and forest plots for outcomes in patients with CF: Change in *P. aeruginosa* sputum density (A); discontinuation due to AEs (B); change in FEV1% predicted (C); change in CFQR-RSS (D); and drug-related AEs (E) all at 4 weeks. As well as change in *P. aeruginosa* sputum density (F); discontinuation due to AEs (G); change in FEV1% predicted (H); change in CFQR-RSS (I); and drug-related AEs (J) all at 24 weeks. CF: cystic fibrosis; AE: adverse event; FEV1: forced expiratory volume in the first second; CFQR-RSS: cystic fibrosis questionnaire revised respiratory symptom score; CI: confidence interval; AZM: azithromycin; TIS: tobramycin inhalation solution; TIP: tobramycin inhalation powder; ALIS: amikacin liposome inhalation suspension; AZLI: aztreonam lysine for inhalation solution; LIS: levofloxacin inhalation solution; Cip: ciprofloxacin; DPI: dry powder for inhalation; FTI: fosfomycin/tobramycin for inhalation; Col: colistimethate sodium.



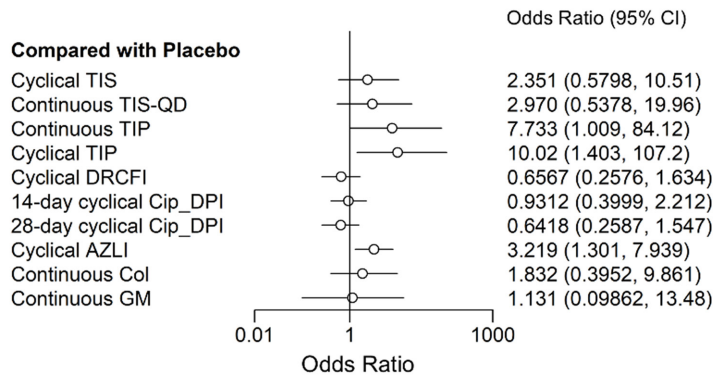
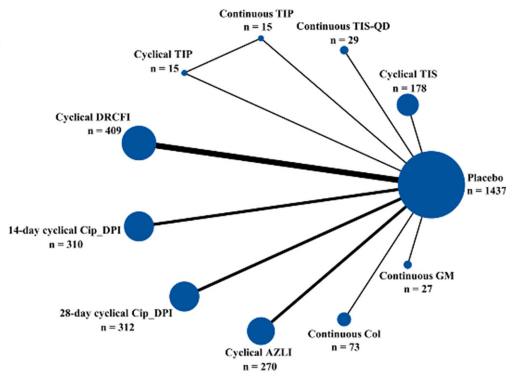
C)



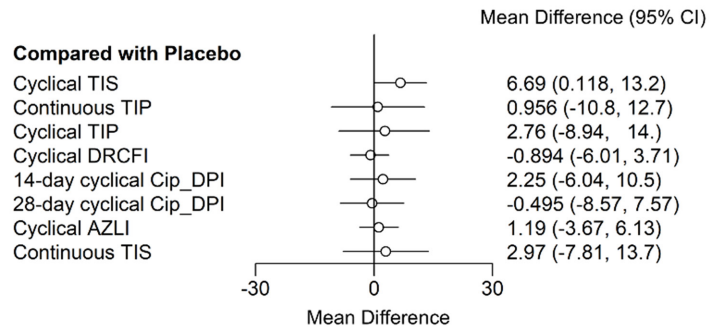
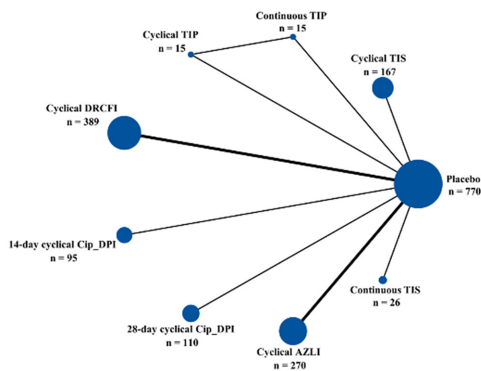
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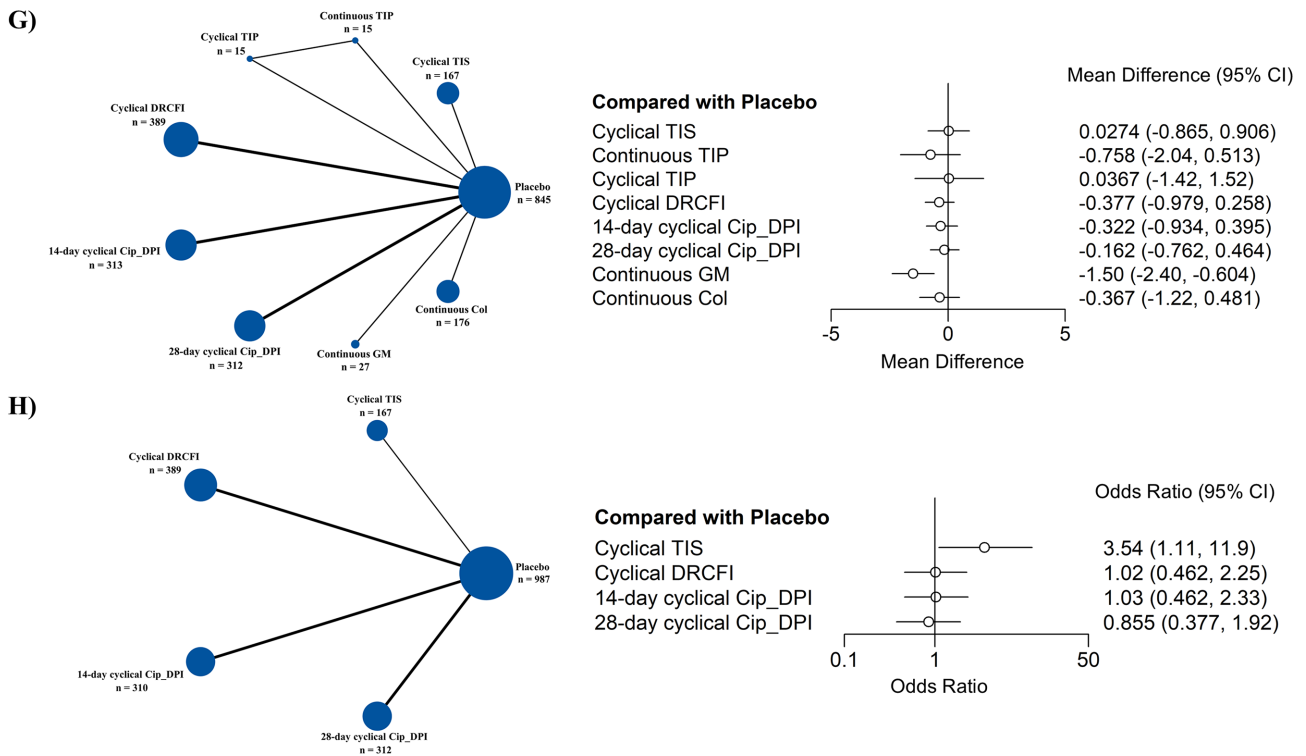


Figure S2 Network and forest plots for outcomes in patients with NCFB: Change in *P. aeruginosa* sputum density (A); discontinuation due to AEs (B); and change in QoL-B-RSS (C) all at 4 weeks, as well as change in *P. aeruginosa* sputum density (D); discontinuation due to AEs (E); change in QoL-B-RSS (F); pulmonary exacerbations per patient-year (G); and drug-related AEs (H) all at long-term timepoints (≥ 4 months). NCFB: non-cystic fibrosis bronchiectasis; AE: adverse event; QoL-B-RSS: quality-of-life bronchiectasis respiratory symptom score; CI: confidence interval; TIS: tobramycin inhalation solution; TIP: tobramycin inhalation powder; ALIS: amikacin liposome inhalation suspension; AZLI: aztreonam lysine for inhalation solution; DRCFI: dual release ciprofloxacin for inhalation; Cip: ciprofloxacin; DPI: dry powder for inhalation; Col: colistimethate sodium; GM: gentamicin.

A) Change in FEV1% predicted at 4 weeks (MD, 95% CI)

Cip_DPI								
-2.8 (-21.95, 16.23)	FTI following AZLI							
-5.4 (-24.76, 13.9)	-2.6 (-21.94, 16.77)	AZLI following TIS						
-6.1 (-27.22, 14.57)	-3.3 (-24.25, 17.37)	-0.72 (-21.98, 20.24)	Oral AZM with TIS					
-5.24 (-21.44, 10.58)	-2.44 (-18.6, 13.24)	0.16 (-16.27, 16.28)	0.87 (-15.77, 17.56)	LIS				
-5.87 (-22.65, 9.92)	-3.05 (-19.83, 12.7)	-0.47 (-17.52, 15.63)	0.24 (-16.78, 16.64)	-0.63 (-12.59, 10.8)	TIP			
-5.95 (-23.44, 10.65)	-3.15 (-20.54, 13.54)	-0.57 (-18.27, 16.4)	0.13 (-17.32, 17.11)	-0.73 (-13.58, 11.78)	-0.12 (-12.92, 12.89)	AZLI		
-0.76 (-21.98, 20.09)	2.04 (-19.05, 22.77)	4.68 (-16.73, 25.66)	5.34 (-13.92, 24.61)	4.49 (-12.29, 21.25)	5.11 (-11.51, 22.33)	5.24 (-11.9, 22.71)		
2.7 (-18.96, 24.1)	5.48 (-16.17, 26.89)	8.08 (-13.84, 29.71)	8.82 (-11.19, 28.66)	7.95 (-9.62, 25.55)	8.55 (-8.79, 26.56)	8.67 (-9.31, 27.02)		
-3.63 (-19.62, 12.02)	-0.82 (-16.75, 14.86)	1.79 (-14.47, 17.8)	2.5 (-11.13, 16.09)	1.62 (-7.98, 11.32)	2.25 (-7.32, 12.44)	2.35 (-8.02, 13.19)		
1.21 (-12.32, 14.68)	4.04 (-9.42, 17.5)	6.62 (-7.17, 20.41)	7.33 (-8.4, 23.41)	6.46 (-1.96, 15.23)	7.12 (-1.56, 16.65)	7.19 (-2.94, 18.03)		
590mg ALIS								
3.46 (-16.58, 23.53)	Col							
-2.88 (-16.49, 10.82)	-6.32 (-20.98, 8.35)	TIS						
1.96 (-13.83, 18.12)	-1.47 (-18.13, 15.5)	4.84 (-3.31, 13.24)	Placebo					

B) Change in CFQR-RSS at 4 weeks (MD, 95% CI)

Cip_DPI								
-1.47 (-19.79, 16.52)	FTI following AZLI							
2.05 (-18.75, 22.51)	3.52 (-17.76, 24.53)	Oral AZM with TIS						
2.48 (-14.12, 18.26)	3.88 (-13.41, 20.47)	0.46 (-15.41, 15.62)	LIS					
0.96 (-16.19, 18.35)	2.46 (-15.39, 20.43)	-1.09 (-21.3, 19.55)	-1.51 (-17.07, 14.98)	3×AZLI following TIS				
-0.89 (-15.64, 13.59)	0.59 (-15, 15.93)	-2.94 (-18.72, 12.85)	-3.38 (-14.27, 8.18)	-1.87 (-16.44, 12.36)	AZLI			
4.17 (-16.44, 24.25)	5.61 (-15.53, 26.27)	2.09 (-14.73, 18.85)	1.6 (-13.24, 17.01)	3.15 (-17.32, 23.05)	5.02 (-10.54, 20.4)	590mg ALIS		
-1 (-18.17, 16.25)	0.46 (-17.41, 18.56)	-3.05 (-23.32, 17.64)	-3.49 (-19.06, 12.98)	-1.98 (-14.1, 10.19)	-0.12 (-14.3, 14.47)	-5.18 (-25.1, 15.34)		
3.54 (-13.3, 19.98)	4.97 (-12.44, 22.23)	1.49 (-10.56, 13.64)	0.89 (-8.34, 11.03)	2.56 (-14.09, 18.8)	4.41 (-5.76, 14.55)	-0.6 (-12.14, 11.07)		
5.2 (-7.19, 17.5)	6.68 (-6.54, 20.02)	3.16 (-13.21, 19.79)	2.72 (-7.4, 13.72)	4.22 (-7.86, 16.18)	6.08 (-1.66, 14.11)	1.03 (-14.83, 17.5)		
2×AZLI following TIS								
4.54 (-12.17, 20.76)	TIS							
6.21 (-5.83, 18.25)	1.68 (-9.36, 13.01)	Placebo						

C) Drug-related AEs at 4 weeks (OR, 95% CI)

Cyclical TIS								
0.89 (-13.57, 15.29)	Cyclical 590mg ALIS							
-5.16 (-19.55, 9.31)	-6.06 (-26.46, 14.36)	Cyclical AZLI						
-1.83 (-16.26, 12.54)	-2.75 (-23.16, 17.59)	3.3 (-17.14, 23.59)	Cyclical LIS					
0.02 (-13.91, 14.14)	-0.86 (-20.9, 19.28)	5.18 (-14.95, 25.36)	1.87 (-18.16, 22.04)	Continuous Col_DPI				
-0.77 (-15.02, 13.56)	-1.68 (-21.94, 18.65)	4.4 (-16, 24.69)	1.06 (-19.27, 21.32)	-0.8 (-20.84, 19.08)	Cyclical TIP			
7.91 (-1.86, 19.17)	6.99 (-10.02, 25.61)	13.05 (-4.01, 31.78)	9.73 (-7.32, 28.29)	7.78 (-8.91, 26.09)	8.66 (-8.17, 27.15)	Placebo		

D) Change in FEV1% predicted at 24 weeks (MD, 95% CI)

TIS					
0.14 (0.01, 1.67)	FTI following AZLI				
0.1 (0, 1.65)	0.71 (0.04, 9.66)	TIP			
0.29 (0.03, 2.86)	2.02 (0.25, 16.47)	2.85 (0.24, 43.61)	Cip_DPI		
0.35 (0.05, 2.23)	2.38 (0.49, 12.39)	3.35 (0.43, 36.41)	1.18 (0.3, 4.6)	placebo	

E) Change in CFQR-RSS at 24 weeks (MD, 95% CI)

AZLI					
1.77 (0.11, 33.11)	TIP				
3.81 (0.24, 73.18)	2.15 (0.07, 62.19)	560mg ALIS			
1.16 (0.08, 18.47)	0.65 (0.02, 16.83)	0.31 (0.01, 7.83)	Cip_DPI		
0.8 (0.18, 3.82)	0.46 (0.04, 4.53)	0.21 (0.02, 2.09)	0.69 (0.07, 6.79)	Placebo	

F) Drug-related AEs at 24 weeks (OR, 95% CI)

Cyclical TIS					
0.26 (0.03, 2.24)	Cyclical 590mg ALIS				
0.93 (0.06, 13.78)	3.51 (0.11, 107.99)	Cyclical AZLI alternating with TIS			
0.5 (0.06, 4.29)	1.88 (0.09, 39.23)	0.53 (0.02, 16.68)	Cyclical AZLI		
0.19 (0.02, 1.57)	0.71 (0.03, 14.67)	0.2 (0.01, 6.14)	0.38 (0.02, 7.85)	Continuous Col_DPI	
1.04 (0.12, 9.22)	3.96 (0.19, 82.53)	1.13 (0.04, 35.05)	2.11 (0.1, 45.46)	5.6 (0.26, 116.69)	Placebo

Figure S3 League tables for outcomes in patients with CF: Change in FEV1% predicted (A); change in CFQR-RSS (B); and drug-related AEs (C) all at 4 weeks. As well as change in FEV1% predicted (D); change in CFQR-RSS (E); and drug-related AEs (F) all at 24 weeks. Data are presented as MD (95% CI) or OR (95% CI). CF: cystic fibrosis; MD: mean difference; OR: odds ratio; AE: adverse event; FEV1: forced expiratory volume in the first second; CFQR-RSS: cystic fibrosis questionnaire revised respiratory symptom score; CI: confidence interval; AZM: azithromycin; TIS: tobramycin inhalation solution; TIP: tobramycin inhalation powder; ALIS: amikacin liposome inhalation suspension; AZLI: aztreonam lysine for inhalation solution; LIS: levofloxacin inhalation solution; Cip: ciprofloxacin; DPI: dry powder for inhalation; FTI: fosfomycin/tobramycin for inhalation; Col: colistimethate sodium.

A) Change in QoL-B-RSS at 4 weeks (MD, 95% CI)

AZLI			
4.43 (-10.7, 19.56)	TIP		
-5.14 (-16.83, 6.42)	-9.64 (-25.9, 6.71)	TIS	
2.77 (-4.11, 9.56)	-1.67 (-15.25, 11.9)	7.91 (-1.49, 17.27)	Placebo

B) Change in FEV1% predicted at long-term timepoints (≥4 months) (MD, 95% CI)

Continuous TIS							
1.76 (-10.11, 13.5)	Cyclical AZLI						
3.51 (-10.05, 16.8)	1.7 (-7.7, 11.18)	28-day cyclical Cip_DPI					
0.69 (-12.87, 14.3)	-1.04 (-10.65, 8.61)	-2.77 (-14.21, 8.86)	14-day cyclical Cip_DPI				
3.91 (-7.75, 15.77)	2.08 (-4.48, 9.26)	0.44 (-8.74, 9.94)	3.17 (-6.18, 12.92)	Cyclical DRCFI			
0.3 (-15.46, 16.09)	-1.55 (-13.77, 11.01)	-3.16 (-17.01, 11.04)	-0.46 (-14.59, 13.61)	-3.66 (-16.02, 8.72)	Cyclical TIP		
2.02 (-14.16, 17.88)	0.33 (-12.27, 12.92)	-1.49 (-15.5, 12.94)	1.28 (-13.06, 15.75)	-1.89 (-14.55, 10.59)	1.66 (-11.54, 14.98)	Continuous TIP	
-3.7 (-16.24, 8.77)	-5.5 (-13.63, 2.76)	-7.2 (-17.53, 3.12)	-4.42 (-14.97, 6.02)	-7.58 (-16.02, 0.28)	-3.96 (-17.13, 8.97)	-5.7 (-19.13, 7.45)	
2.97 (-7.81, 13.72)	1.19 (-3.67, 6.13)	-0.49 (-8.57, 7.57)	2.25 (-6.04, 10.51)	-0.89 (-6.01, 3.71)	2.76 (-8.94, 13.97)	0.96 (-10.78, 12.71)	
Cyclical TIS							
6.69 (0.12, 13.24)	Placebo						

C) Pulmonary exacerbations per patient-year at long-term timepoints (≥4 months) (MD, 95% CI)

Cyclical AZLI							
0.52 (-0.28, 1.31)	Continuous Col						
1.65 (0.8, 2.5)	1.13 (0.23, 2.04)	Continuous GM					
0.31 (-0.37, 0.98)	-0.2 (-0.97, 0.54)	-1.33 (-2.15, -0.54)	28-day cyclical Cip_DPI				
0.48 (-0.28, 1.17)	-0.04 (-0.87, 0.71)	-1.17 (-2.05, -0.37)	0.17 (-0.54, 0.81)	14-day cyclical Cip_DPI			
0.53 (-0.17, 1.21)	0.02 (-0.77, 0.76)	-1.12 (-1.95, -0.32)	0.22 (-0.42, 0.84)	0.05 (-0.61, 0.76)	Cyclical DRCFI		
0.1 (-1.35, 1.61)	-0.41 (-1.9, 1.13)	-1.54 (-3.04, 0.01)	-0.21 (-1.64, 1.29)	-0.37 (-1.8, 1.15)	-0.43 (-1.85, 1.08)	Cyclical TIP	
0.9 (-0.37, 2.16)	0.39 (-0.91, 1.68)	-0.75 (-2.07, 0.57)	0.6 (-0.64, 1.83)	0.43 (-0.81, 1.7)	0.38 (-0.86, 1.62)	0.79 (-0.53, 2.09)	
0.12 (-0.72, 0.97)	-0.4 (-1.3, 0.5)	-1.53 (-2.47, -0.59)	-0.2 (-0.98, 0.62)	-0.36 (-1.16, 0.52)	-0.41 (-1.2, 0.41)	0.01 (-1.56, 1.53)	
0.15 (-0.37, 0.67)	-0.37 (-0.97, 0.24)	-1.5 (-2.17, -0.83)	-0.17 (-0.6, 0.29)	-0.33 (-0.8, 0.22)	-0.38 (-0.82, 0.09)	0.05 (-1.39, 1.4)	
Continuous TIP							
-0.79 (-2.1, 0.54)	Cyclical TIS						
-0.76 (-1.91, 0.4)	0.03 (-0.64, 0.69)	Placebo					

D) Drug-related AEs at long-term timepoints (≥4 months) (OR, 95% CI)

28-day cyclical Cip_DPI				
0.83 (0.26, 2.57)	14-day cyclical Cip_DPI			
0.84 (0.27, 2.61)	1.01 (0.33, 3.16)	Cyclical DRCFI		
0.24 (0.06, 1)	0.29 (0.07, 1.22)	0.29 (0.07, 1.17)	Cyclical TIS	
0.85 (0.38, 1.92)	1.03 (0.46, 2.33)	1.02 (0.46, 2.25)	3.54 (1.11, 11.91)	Placebo

Figure S4 League tables for outcomes in patients with NCFB: Change in QoL-B-RSS (A) all at 4 weeks, as well as change in QoL-B-RSS (B); pulmonary exacerbations per patient-year (C); and drug-related AEs (D) all at long-term timepoints (≥4 months). Data are presented as MD (95% CI) or OR (95% CI). NCFB: non-cystic fibrosis bronchiectasis; MD: mean difference; OR: odds ratio; AE: adverse event; QoL-B-RSS: quality-of-life bronchiectasis respiratory symptom score; CI: confidence interval; TIS: tobramycin inhalation solution; TIP: tobramycin inhalation powder; ALIS: amikacin liposome inhalation suspension; AZLI: aztreonam lysine for inhalation solution; DRCFI: dual release ciprofloxacin for inhalation; Cip: ciprofloxacin; DPI: dry powder for inhalation; Col: colistimethate sodium; GM: gentamicin.

Table S5 SUCRA values of outcomes in patients with CF

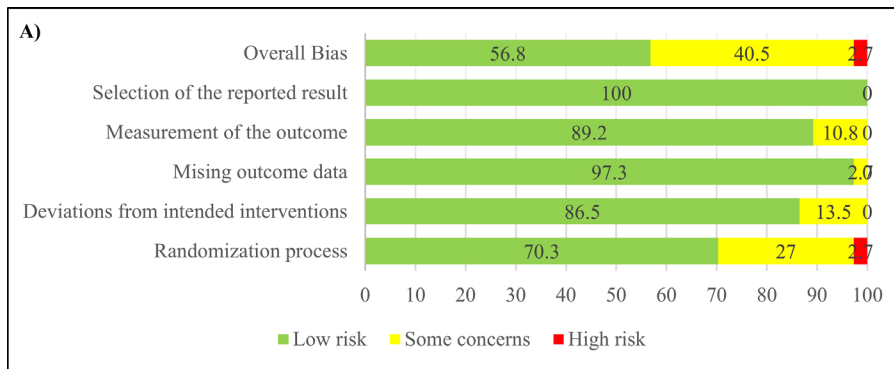
Change in <i>P. aeruginosa</i> sputum density		Discontinuation due to AEs						Change in FEV1% predicted				Change in CFQR-RSS				Drug-related AEs			
At 4 weeks		At 24 weeks		At 4 weeks		At 24 weeks		At 4 weeks		At 24 weeks		At 4 weeks		At 24 weeks		At 4 weeks		At 24 weeks	
Treatment	SUCRA (%)	Treatment	SUCRA (%)	Treatment	SUCRA (%)	Treatment	SUCRA (%)	Treatment	SUCRA (%)	Treatment	SUCRA (%)	Treatment	SUCRA (%)	Treatment	SUCRA (%)	Treatment	SUCRA (%)	Treatment	SUCRA (%)
TIP	94.48	Cyclical TIP	90.54	Col	83.95	Cyclical TIS	75.69	AZLI	68.45	Cyclical AZLI	80.16	AZLI	68.78	Cyclical ALIS	83.28	TIS	90.78	Cyclical TIS	73.55
AZLI	82.27	Cyclical ALIS	60.97	TIS	78.1	Cyclical AZLI alternating with TIS	63.22	TIP	68.34	Cyclical LIS	62.11	FTI following AZLI	66.09	Cyclical LIS	51.95	placebo	62.59	Placebo	71.52
TIS	75.11	Cyclical TIS	55.44	FTI following AZLI	75.31	Cyclical AZLI	58.77	Oral AZM with TIS	66.6	Cyclical TIP	55.66	2×AZLI following TIS	65.87	Cyclical TIS	34.48	Cip_DPI	52.2	Cyclical AZLI alternating with TIS	65.24
ALIS	59.68	Cyclical LIS	32.99	TIP	54.1	Cyclical TIP	54.75	LIS	64.59	Cyclical TIS	49.63	Cip_DPI	59.33	Continuous Col_DPI	30.29	FTI following AZLI	25.38	Cyclical AZLI	46.25
FTI following AZLI	56.74	Placebo	10.07	2×AZLI following TIS	52.63	Cyclical ALIS	46.28	AZLI following TIS	62.74	Continuous Col_DPI	49.62	3×AZLI following TIS	53.26			TIP	19.05	Cyclical ALIS	26.58
Col	56.45			3×AZLI following TIS	39.47	Cyclical LIS	32.77	TIS	53.4	Cyclical ALIS	43.96	Oral AZM with TIS	48.16					Continuous Col_DPI	16.87
LIS	43.84			Cip_DPI	36.58	Continuous Col_DPI	18.52	FTI following AZLI	48.87	Placebo	8.86	LIS	45.12						
Cip_DPI	36.1			AZLI	33.8			ALIS	37.94			TIS	36.07						
2×AZLI following TIS	36.06			Placebo	26.04			Cip_DPI	33.93			ALIS	34.77						
3×AZLI following TIS	29.84			LIS	20.02			Col	23.74			Placebo	22.55						
Oral AZM with TIS	26.19							Placebo	21.41										
Placebo	3.23																		

Treatments producing the better performance in the target outcome were listed first. Abbreviations: CF: cystic fibrosis; SUCRA: surface under the cumulative ranking curve; AE: adverse event; FEV1: forced expiratory volume in the first second; CFQR-RSS: cystic fibrosis questionnaire revised respiratory symptom score; AZM: azithromycin; TIS: tobramycin inhalation solution; TIP: tobramycin inhalation powder; ALIS: amikacin liposome inhalation suspension; AZLI: aztreonam lysine for inhalation solution; LIS: levofloxacin inhalation solution; Cip: ciprofloxacin; DPI: dry powder for inhalation; FTI: fosfomycin/tobramycin for inhalation; Col: colistimethate sodium.

Table S6 SUCRA values of outcomes in patients with NCFB

Change in P. aeruginosa sputum density				Discontinuation due to AEs				Change in QoL-B-RSS				Exacerbations per patient-year		Drug-related AEs	
In 4 weeks		At endpoint		In 4 weeks		At endpoint		In 4 weeks		At endpoint		At endpoint		At endpoint	
Treatment	SUCRA(%)	Treatment	SUCRA(%)	Treatment	SUCRA(%)	Treatment	SUCRA(%)	Treatment	SUCRA(%)	Treatment	SUCRA(%)	Treatment	SUCRA(%)	Treatment	SUCRA(%)
TIP	84.18	Continuous GM	92.16	Cip_DPI	66.37	28-day cyclical Cip_DPI	85.62	TIS	90.61	Cyclical TIS	86.52	Continuous GM	97.84	28-day cyclical Cip_DPI	74.65
Cip_DPI	80.64	Continuous TIP	69.62	Placebo	50.49	Cyclical DRCFI	84.42	AZLI	56.89	Continuous TIS	58.98	Continuous TIP	75.52	Placebo	59
AZLI	65.7	Cyclical AZLI	51.34	DRCFI	49.92	14-day cyclical Cip_DPI	71.56	Placebo	26.66	Cyclical TIP	57	Cyclical DRCFI	63.26	Cyclical DRCFI	57.2
DRCFI	56.05	Cyclical TIP	47.57	TIS	33.23	Placebo	68.18	TIP	25.85	14-day cyclical Cip_DPI	55.57	Continuous Col	61.37	14-day cyclical Cip_DPI	56.24
TIS	53.84	Cyclical TIS	42.19			Continuous GM	62.66			Cyclical AZLI	49.15	14-day cyclical Cip_DPI	57.96	Cyclical TIS	2.91
Col	34.48	Continuous Col	36.38			Continuous Col	47.61			Continuous TIP	45.84	28-day cyclical Cip_DPI	43.14		
ALIS	20.48	Placebo	10.75			Cyclical TIS	39.74			Placebo	35.93	Cyclical TIP	32.65		
Placebo	4.62					Continuous TIS-QD	34.12			28-day cyclical Cip_DPI	34.2	Cyclical TIS	26.51		
						Cyclical AZLI	29.64			Cyclical DRCFI	26.81	Placebo	25.2		
						Continuous TIP	15.98					Cyclical AZLI	16.54		
						Cyclical TIP	10.46								

Treatments producing the better performance in the target outcome were listed first. Abbreviations: NCFB: non-cystic fibrosis bronchiectasis; SUCRA: surface under the cumulative ranking curve; AE: adverse event; QoL-B-RSS: quality-of-life bronchiectasis respiratory symptom score; TIS: tobramycin inhalation solution; TIP: tobramycin inhalation powder; ALIS: amikacin liposome inhalation suspension; AZLI: aztreonam lysine for inhalation solution; DRCFI: dual release ciprofloxacin for inhalation; Cip_DPI: ciprofloxacin dry powder for inhalation; Col: colistimethate sodium; GM: gentamicin.



B)

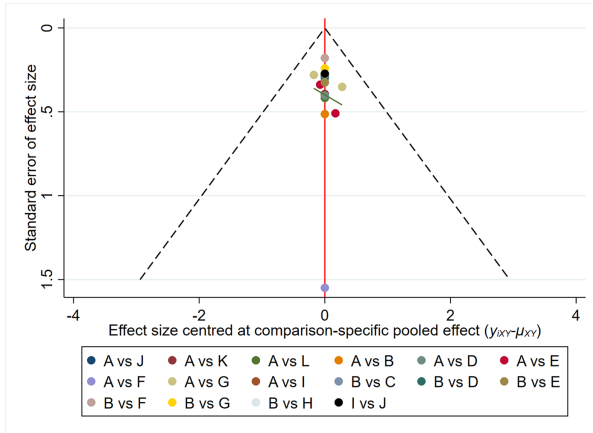
Author, Year	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall
Ramsey et al., 1999	+	+	+	+	+	+
Bilton et al., 2020	+	!	+	!	+	!
Flume et al., 2016	+	+	+	+	+	+
Flume et al., 2016	+	+	+	+	+	+
Elborn et al., 2015	+	!	+	!	+	!
Assael et al., 2013	+	!	+	!	+	!
Clancy et al., 2013	+	+	+	+	+	+
Schuster et al., 2013	+	!	+	!	+	!
Trapnell et al., 2012	+	+	+	+	+	+
Konstan et al., 2010	+	+	+	+	+	+
Konstan et al., 2011	!	+	+	+	+	!
McCoy et al., 2008	!	+	+	+	+	!
Galeva et al., 2013	?	+	+	+	+	?
Hodson et al., 2002	!	+	+	+	+	!
Retsch-Bogart et al., 2009	!	+	+	+	+	!
Wainwright et al., 2011	!	+	+	+	+	!
Geller et al., 2011	!	+	+	+	+	!
Lenoir et al., 2007	!	+	+	+	+	!
Chuchalin et al., 2007	!	+	+	+	+	!
Nichols et al., 2022	!	+	+	+	+	!
Dorkin et al., 2015	+	+	+	+	+	+
Haworth et al., 2019	+	+	+	+	+	+
Serisier et al., 2013	+	+	+	+	+	+
De Soya et al., 2018	+	+	+	+	+	+
Aksamit et al., 2018	+	+	+	+	+	+
Wilson et al., 2013	+	+	+	+	+	+
Barker et al., 2014	+	+	+	+	+	+
Haworth et al., 2014	+	+	+	+	+	+
Barker et al., 2000	+	+	+	+	+	+
Guan et al., 2023	+	+	+	+	+	+
Murray et al., 2011	!	!	!	+	+	!
Loebinger et al., 2021	+	+	+	+	+	+
Terpstra et al., 2022	+	+	+	+	+	!

Domain:
 1. Randomization process
 2. Deviations from intended interventions
 3. Missing outcome data
 4. Measurement of the outcome
 5. Selection of the reported result

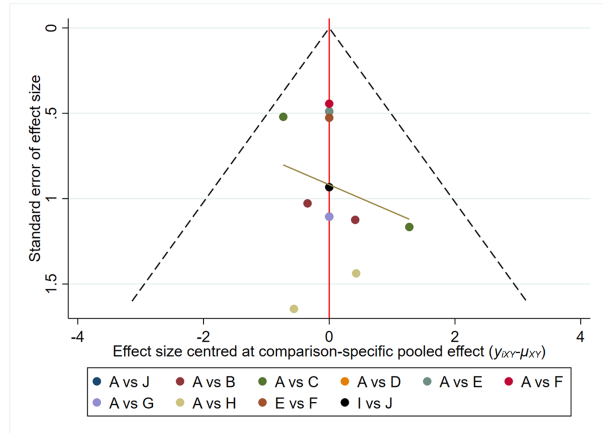
Low risk
 Some concerns
 High risk

Figure S5 Results of the quality assessment: “Risk of bias” graph (A), “Risk of bias” summary (B).

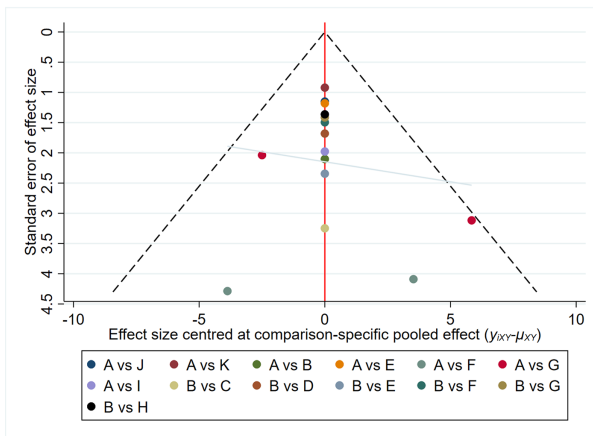
A) Change in *P. aeruginosa* sputum density



B) Discontinuation due to AEs



C) Change in FEV1% predicted



D) Change in CFQR-RSS

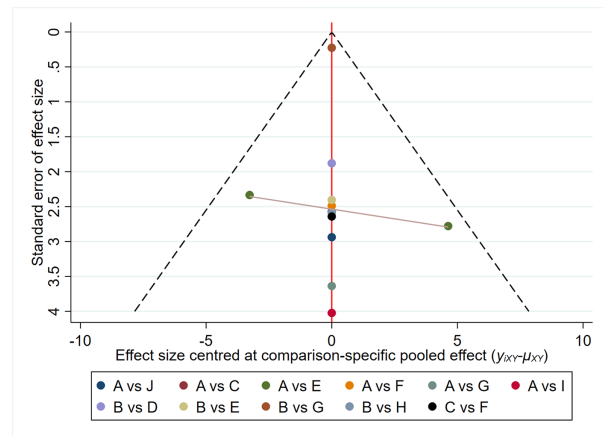
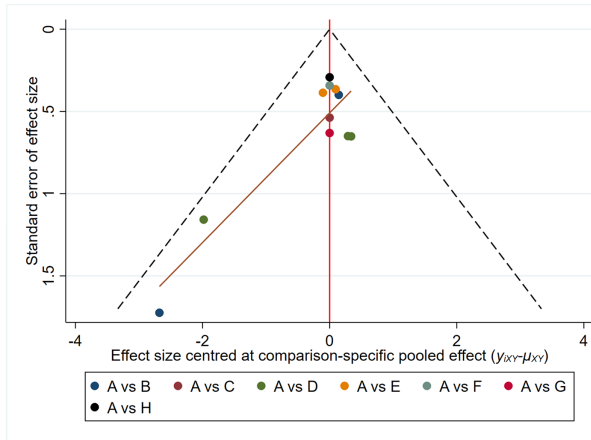
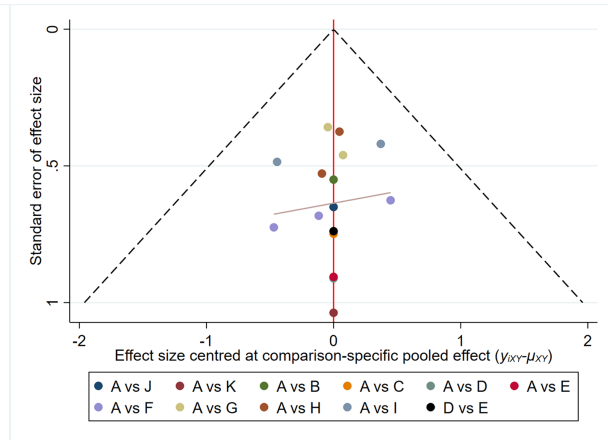


Figure S6 Funnel plots for some outcomes in patients with CF: Change in *P. aeruginosa* sputum density (A); discontinuation due to AEs (B); change in FEV1% predicted (C); and change in CFQR-RSS (D) all in the short term (4 weeks). Each of the points represents a published study. CF: cystic fibrosis; AE: adverse event; FEV1: forced expiratory volume in the first second; CFQR-RSS: cystic fibrosis questionnaire revised respiratory symptom score.

A) Change in *P. aeruginosa* sputum density



B) Discontinuation due to AEs



C) Pulmonary exacerbations per patient-year

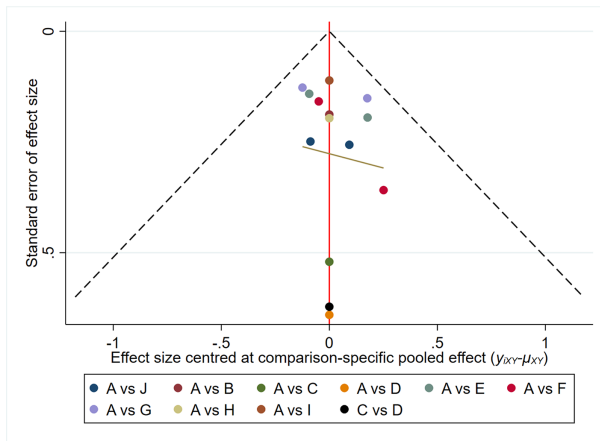
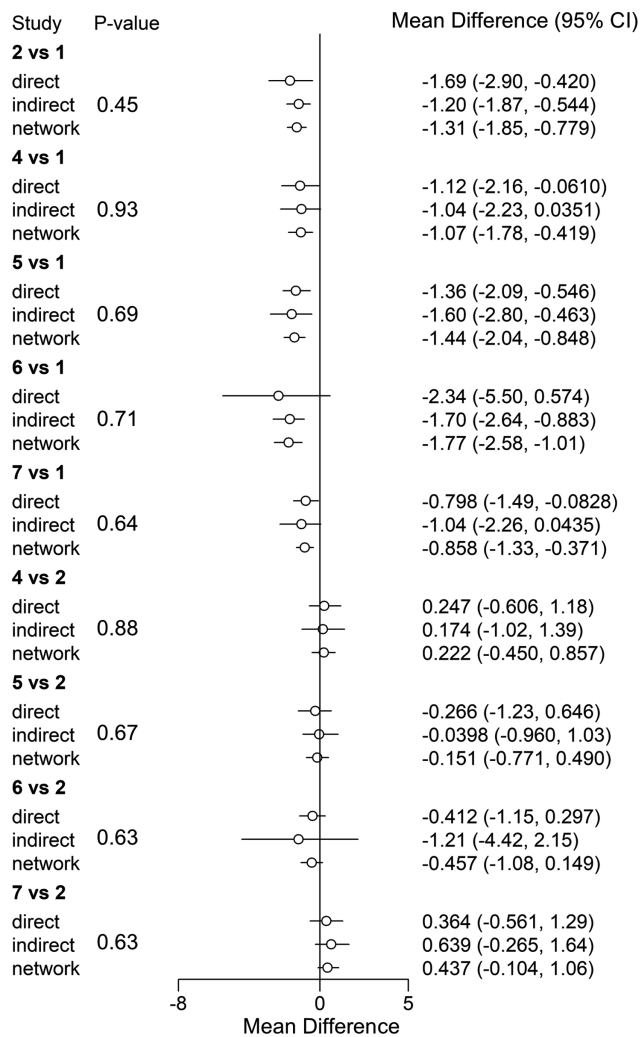


Figure S7 Funnel plots for some outcomes in patients with NCFB: Change in *P. aeruginosa* sputum density in the short term (4 weeks) (A); as well as discontinuation due to AEs (B); and pulmonary exacerbations per patient-year (C) all in the long term (≥ 16 weeks). Each of the points represents a published study. NCFB: non-cystic fibrosis bronchiectasis; AE: adverse event.

A) Microbiological efficacy



B) Change in FEV1% predicted

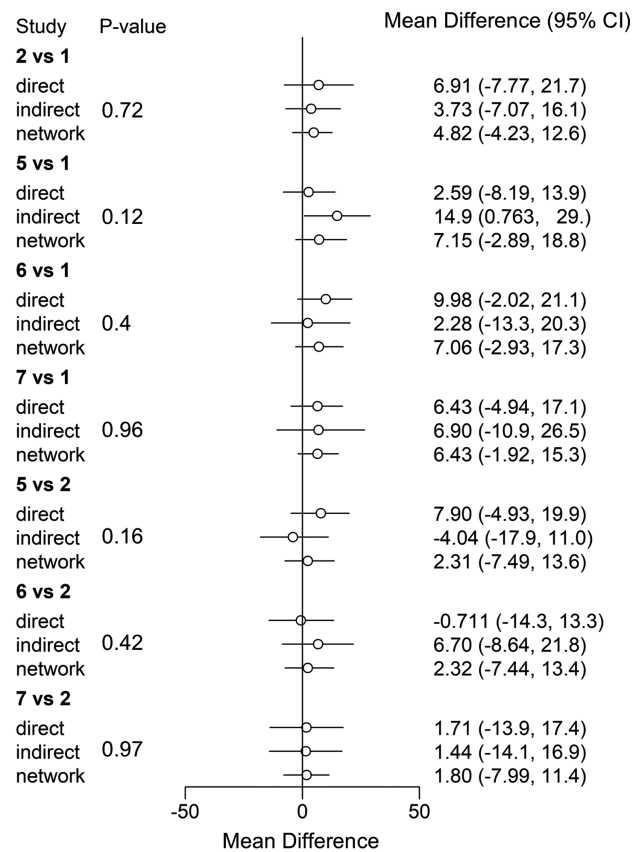


Figure S8 Node-splitting analysis of some outcomes at 4 weeks in patients with CF. CF: cystic fibrosis; FEV1: forced expiratory volume in the first second; CI: confidence interval.