Efficacy and safety of inhaled levofloxacin versus other inhaled antibiotics in the treatment of adults with cystic fibrosis and chronic *Pseudomonas aeruginosa lung* infection: an updated network meta-analysis

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OBJECTIVES

✓ **This bayesian network meta-analysis updated the comparative efficacy and safety of inhaled levofloxacin versus other inhaled antibiotics approved in Europe in the treatment of chronic *Pseudomonas aeruginosa* (*P. aeruginosa*) lung infection in adults with cystic fibrosis (CF).**

METHODS

- PUBMED and EMBASE were searched (until January 2025) to identify trials evaluating inhaled antibiotics (levofloxacin, tobramycin inhaled powder tobramycin [TIP], tobramycin inhaled solution [TIS], colistin, and aztreonam).
- Outcomes assessed (at weeks 4 and 24) were the following:
  - Relative and absolute percent changes in forced expiratory volume in 1 second (FEV1%) predicted, *P. aeruginosa* sputum density, CF questionnaire-revised respiratory symptoms score (CFQ-R RSS), respiratory exacerbations, hospitalizations for any cause, hospitalizations for respiratory cause, additional antibiotics use,
  - Total and serious adverse events, and withdrawal rates.
- A bayesian network meta-analysis using fixed- and random-effects models was performed to pool odds ratios (ORs) and median differences with their 95% credible intervals (CrIs).

RESULTS

- Thirteen reports on twelve studies were included on the network meta-analysis.[1-13]
- At week 4, levofloxacin reduced the risk of additional antibiotics use and was more effective in improving quality of life (CFQ-R RSS) than TIS. Levofloxacin reduced the risk of hospitalizations for any cause versus aztreonam.
- At week 24, levofloxacin was associated with a lower reduction in *P. aeruginosa* sputum density versus TIP but was comparable to TIS.
- At week 24, levofloxacin increased absolute FEV1 and reduced the risk of hospitalizations for respiratory cause versus TIS.
- At week 24, levofloxacin was associated with a lower risk of respiratory exacerbations versus colistin, and a lower risk of serious adverse events than TIS.

Table 1 – Network meta-analysis results.

Levofloxacin versus		4 weeks				24 weeks			
		TIS	TIP	Aztreonam	Colistin	TIS	TIP	Aztreonam	Colistin
Additional antibiotics use	OR (CrI 95%)	**0.47 (0.31; 0.70) $**	-	1.36 (0.85; 2.19) $	-	**0.63 (0.41; 0.96) $**	**0.41 (0.24; 0.69) $**	1.39 (0.76; 2.50) $	0.63 (0.36; 1.09) $
Respiratory exacerbations	OR (CrI 95%)	-	-	-	-	0.71 (0.46; 1.09) $	-	-	**0.56 (0.31; 0.98) $**
Hospitalizations for any cause	OR (CrI 95%)	0.94 (0.48; 1.91) $	-	**0.26 (0.06; 0.94) $**	-	0.61 (0.13, 2.82) $	-	-	-
Hospitalizations for respiratory cause	OR (CrI 95%)	-	-	-	-	**0.55 (0.33; 0.90) $**	0.63 (0.34; 1.15) $	-	-
AEs	OR (CrI 95%)	-	-	-	-	0.73 (0.05; 5.83) $	0.42 (0.03; 3.50) $	-	0.36 (0.02; 3.21) $
Serious AEs	OR (CrI 95%)	-	-	-	-	**0.59 (0.37; 0.95) $**	0.66 (0.65; 1.16) $	-	0.89 (0.36; 2.28) $
Study withdrawal due to AEs	OR (CrI 95%)	-	-	2.14 (0.57; 9.29) $	-	4.30 (0.76, 75.2) $	2.54 (0.41, 45.5) $	1.52 (0.20, 28.7) $	8.52 (0.93, 188) $
P. aeruginosa sputum density	Median (CrI 95%)	0.48 (-0.68; 1.52) ¶	0.94 (-0.99; 2.74) ¶	0.26 (-1.18; 1.63) ¶	0.22 (-1.72; 2.02) ¶	0.12 (-0.2; 0.48) $	**0.54 (0.08; 1.01) $**	-	-
QoL (CFQ-R RSS)	Median (CrI 95%)	**2.78 (0.24; 5.33) $**	-	-3.39 (-6.80; 0.01) $	-	2.62 (-0.65; 2.62) $	-	-	3.15 (-1.32; 7.65) $
Absolute FEV1%	Median (CrI 95%)	-0.16 (-2.71; 2.08) ¶	-	0.30 (-3.72; 3.46) ¶	1.38 (-9.43; 12.21) ¶	**5.65 (0.90; 10.44) $**	-	0.46 (-1.63; 2.55) $	0.004 (-8.55; 8.89) $
Relative FEV1%	Median (CrI 95%)	0.49 (-3.31; 2.38) ¶	0.35 (-4.42; 5.14) ¶	-4.74 (-8.74; 0.67) ¶	5.79 (-0.94; 12.54) ¶	0.32 (-2.6; 3.09) $	-2.10 (-6.05; 1.83) $	1.93 (-2.31; 6.14) $	-

Abbreviations: AE, Adverse event; CFQ-R RSS, Cystic fibrosis questionnaire–revised respiratory symptoms score; CrI, Credible interval; FEV1, Forced expiratory volume at 1 second; OR, Odds ratio; QoL, Quality of life; TIP, Tobramycin inhaled powder; TIS, Tobramycin inhaled solution.
Legend: $ - result from a fixed-effects model NMA; ¶ - results from a random-effects model NMA.

CONCLUSIONS

Overall, the results suggest that levofloxacin may be more effective than TIS, and comparable to TIP, aztreonam and colistin, for the treatment of adults with CF and chronic *P. aeruginosa* lung infection.

REFERENCES: 1. Ramsey BW, et al. (1999); doi: 10.1056/NEJM199901073400104. **2.** Chuchalin A, et al. (2007); doi: 10.2165/00148581-200709001-00004. **3.** Hodson ME, et al. (2002); doi: 10.1183/09031936.02.00248102. **4.** McCoy KS, et al. (2008); doi: 10.1164/rccm.200712-1804OC. **5.** Nasr SZ, et al. (2010); doi: 10.1002/ppul.21188. **6.** Konstan MW, et al. (2011); doi: 10.1016/j.jcf.2010.10.003. **7.** Geller DE, et al. (2014); doi: 10.4187/respcare.02264. **8.** Schuster A, et al. (2013); doi: 10.1136/thoraxjnl-2012-202059. **9.** Assael BM, et al. (2013); doi: 10.1016/j.jcf.2012.07.006. **10.** Geller DE, et al. (2011); doi: 10.1164/rccm.201008-1293OC. **11.** Flume PA, et al. (2016); doi: 10.1016/j.jcf.2015.12.004. **12.** Elborn JS, et al. (2015); doi: 10.1016/j.jcf.2014.12.013. **13.** Bilton D, et al. (2020); doi: 10.1016/j.jcf.2019.08.001.

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CLEVIDENCE

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