

Appendix 5: Adverse effects probably or possibly related to study drugs reported in the randomized controlled trials included in the meta-analysis of the effectiveness of fluoroquinolones compared with other antibiotics (part 1 of 2)

Study	Adverse effects related to study drugs n/N (%)	Withdraw due to adverse events n/N (%)	Photo-sensitivity n/N (%)	Diarrhea n/N (%)	Liver function test abnormalities n/N (%)	Headache n/N (%)	Insomnia n/N (%)	Rash n/N (%)	Nausea/vomiting n/N (%)
Carbon et al ¹	97/348 (28) v. 50/168 (30)	13/348 (4) v. 5/168 (3)	NA	NA	NA	NA	NA	6/348 (2) v. 3/168 (2)	NA
D'Ignazio et al ²	26/212 (12) v. 42/211 (20)	0/212 (0) v. 0/211 (0)	NA	10/212 (5) v. 26/211 (12)	NA	NA	NA	NA	< 2% in both groups
Erard et al ³	5/79 (6) v. 2/37 (5)	0/79 (0) v. 0/37 (0)	NA	2/79 (3) v. 0/37 (0)	NA	NA	NA	NA	2/79 (3) v. 1/37 (3)
File et al ⁴	17/291 (6) v. 25/293 (9)	8/291 (3) v. 9/293 (3)	NA	4/291 (1) v. 11/293 (4)	NA	NA	NA	NA	1/104 (1) v. 5/96 (6) *
Finch et al ⁵	117/301 (39) v. 125/321 (39)	15/301 (5) v. 13/321 (4)	0/301 (0) v. 0/321 (0)	NA	NA	NA	NA	NA	NA
Fogarty et al ⁶	98/132 (74) v. 96/137 (70)	3/132 (2) v. 12/137 (9)	NA	NA	NA	NA	NA	NA	NA
Fogarty et al ⁷	84/235 (35) v. 83/238 (34)	6/235 (2) v. 12/238 (5)	NA	19/235 (8) v. 21/238 (9)	NA	NA	NA	NA	21/235 (9) v. 19/238
Frank et al ⁸	6/113 (5) v. 11/118 (9)	5/110 (5) v. 5/114 (5)	NA	0/113 (0) v. 11/118 (4)	NA	NA	1/113 (1) v. 0/118 (0)	1/113 (1) v. 0/118 (0)	0/113 (0) v. 1/118 (1)
Geijo Martinez et al ⁹	1/20 (5) v. 2/29 (7)	NA	NA	1/20(5) v. 2/29(7)	NA	NA	NA	0/20 (0) v. 1/29 (3)	NA
Gotfried et al ¹⁰	29/143 (20) v. 41/156 (26)	1/143 (1) v. 2/156 (1)	NA	9/143 (6) v. 9/156 (6)	NA	6/143 (4) v. 5/156 (3)	NA	NA	4/143 (3) v. 5/156 (3)
Hoeffken et al ¹¹	166/453 (37) v. 81/222 (36)	16/453 (4) v. 5/222 (2)	0/453 (0) v. 0/222 (0)	32/453 (7) v. 8/222 (4)	24/453 (5) v. 13/222 (6)	11/453 (2) v. 4/222 (2)	NA	NA	33/453 (7) v. 17/222 (8)
Kalbermatter et al ¹²	0/28 (0) v. 0/56 (0)	NA	NA	NA	NA	NA	NA	NA	NA
Katz et al ¹³	30/167 (18) v. 27/168 (16)	6/167 (4) v. 3/168 (2)	NA	2/167 (1) v. 10/168 (6)	NA	2/167 (1) v. 4/168 (2)	NA	3/167 (2) v. 1/168 (1)	4/167 (2) v. 6/168 (4)

Continued

Appendix 5: Adverse effects probably or possibly related to study drugs reported in the randomized controlled trials included in the meta-analysis of the effectiveness of fluoroquinolones compared with other antibiotics (part 2 of 2)

Study (ref)	Adverse effects related to study drugs n/N (%)	Withdraw due to adverse events n/N (%)	Photo-sensitivity n/N (%)	Diarrhea n/N (%)	Liver function test abnormalities n/N (%)	Headache n/N (%)	Insomnia n/N (%)	Rash n/N (%)	Nausea/vomiting n/N (%)
Leophonte et al ¹⁴	31/167 (19) v. 35/153 (23)	14/167 (8) v. 15/153 (10)	2/167 (1) v. 0/153 (0)	10/167 (6) v. 17/153 (11)	1/167 (1) v. 4/153 (3)	1/167 (1) v. 2/153 (1)	NA	5/167 (3) v. 3/153 (2)	5/167 (3) v. 5/153 (3)
Lin et al ¹⁵	0/26 (0) v. 0/24 (0)	0/26 (0) v. 0/24 (0)	0/26 (0) v. 0/24 (0)	0/26 (0) v. 0/24 (0)	0/26 (0) v. 0/24 (0)	0/26 (0) v. 0/24 (0)	0/26 (0) v. 0/24 (0)	0/26 (0) v. 0/24 (0)	0/26 (0) v. 0/24 (0)
Lode et al ¹⁶	28/169 (17) v. 37/172 (22)	14/172 (8) v. 15/173 (9)	NA	7/169 (4) v. 11/172 (6)	7/169 (4) v. 12/172 (7)	NA	NA	5/169 (3) v. 2/172 (1)	NA
Norrby et al ¹⁷	68/314 (22) v. 79/305 (26)	15/314 (5) v. 20/305 (7)	6/314 (2) v. 3/305 (1)	6/314 (2) v. 14/305 (5)	26/314 (8) v. 34/305 (11)	NA	NA	6/314 (2) v. 3/305 (1)	9/314 (3) v. 7/305 (2)
Petitpretz et al ¹⁸	56/200 (28) v. 42/208 (20)	8/200 (4) v. 8/208 (4)	0/200 (0) v. 0/208 (0)	14/200 (7) v. 8/208 (7)	12/200 (6) v. 15/208 (7)	2/200 (1) v. 2/208 (2)	NA	3/200 (2) v. 3/208 (1)	20/200 (10) v. 2/208 (1)
Portier et al ¹⁹	42/171 (25) v. 50/175 (29)	9/171 (5) v. 10/175 (6)	NA	3/171 (2) v. 32/175 (18)	2/171 (1) v. 0/175 (0) **	2/171 (1) v. 0/175 (0)	NA	5/171 (3) v. 2/175 (1)	7/171 (4) v. 7/175 (4)
Torres et al ²⁰	55/274 (20) v. 86/279 (31)	25/274 (9) v. 23/279 (8)	NA	13/274 (5) v. 22/279 (8)	NA	5/274 (2) v. 4/279 (1)	NA	NA	10/274 (4) v. 5/279 (2)
Welte et al ²¹	65/200 (33) v. 76/197 (39)	11/200 (6) v. 18/197 (9)	NA	NA	18/200 (9) v. 33/197 (17)	NA	NA	NA	NA
Xu et al ²²	2/20 (10) v. 1/20 (5)	0/20 (0) v. 0/20 (0)	0/20 (0) v. 0/20 (0)	0/20 (0) v. 0/20 (0)	0/20 (0) v. 0/20 (0)	0/20 (0) v. 0/20 (0)	0/20 (0) v. 0/20 (0)	0/20 (0) v. 0/20 (0)	1/20 (5) v. 0/20 (0)
Zervos et al ²³	36/102 (34) v. 49/110 (39)	3/102 (3) v. 10/110 (9)	NA	NA	NA	NA	NA	NA	NA
Pooled OR (95% CI)	0.86 (0.78-0.96)	0.85 (0.69-1.06)	2.35 (0.67-8.24)	0.55 (0.35-0.88)	0.68 (0.51-0.91)	1.76 (0.49-6.34)	NA	1.67 (0.95-2.94)	1.17 (0.69-1.98)

Note: CI = confidence interval, NA = not available.

*Adverse effects reported for the clinically evaluable populations.

†Refers to cholestatic jaundice only.

‡Abnormalities detected in the results of liver function tests.

References:

1. Carbon C, Ariza H, Rabie WJ, et al. Comparative study of levofloxacin and amoxicillin/clavulanic acid in adults with mild-to-moderate community-acquired pneumonia. *Clin Microbiol Infect* 1999;5:724-32.
2. D'Ignazio J, Camere MA, Lewis DE, et al. Novel, single-dose microsphere formulation of azithromycin versus 7-day levofloxacin therapy for treatment of mild to moderate community-acquired pneumonia in adults. *Antimicrob Agents Chemother* 2005;49:4035-41.
3. Erard V, Lamy O, Bochud PY, et al. Full-course oral levofloxacin for treatment of hospitalized patients with community-acquired pneumonia. *Eur J Clin Microbiol Infect Dis* 2004;23:82-8.
4. File TM Jr, Segreti J, Dunbar L, et al. A multicenter, randomized study comparing the efficacy and safety of intravenous and/or oral levofloxacin versus ceftriaxone and/or cefuroxime axetil in treatment of adults with community-acquired pneumonia. *Antimicrob Agents Chemother* 1997;41:1965-72.
5. Finch R, Schurmann D, Collins O, et al. Randomized controlled trial of sequential intravenous (i.v.) and oral moxifloxacin compared with sequential i.v. and oral co-amoxiclav with or without clarithromycin in patients with community-acquired pneumonia requiring initial parenteral treatment. *Antimicrob Agents Chemother* 2002;46:1746-54.
6. Fogarty C, Siami G, Kohler R, et al. Multicenter, open-label, randomized study to compare the safety and efficacy of levofloxacin versus ceftriaxone sodium and erythromycin followed by clarithromycin and amoxicillin-clavulanate in the treatment of serious community-acquired pneumonia in adults. *Clin Infect Dis* 2004;38(Suppl 1):S16-23.
7. Fogarty C, Grossman C, Williams J, et al. Efficacy and safety of moxifloxacin vs clarithromycin for community-acquired pneumonia. *Infect Med* 1999;16:748-63.
8. Frank E, Liu J, Kinasewitz G, et al. A multicenter, open-label, randomized comparison of levofloxacin and azithromycin plus ceftriaxone in hospitalized adults with moderate to severe community-acquired pneumonia. *Clin Ther* 2002;24:1292-308.
9. Geijo Martinez MP, Diaz de Tuesta Chow-Quan AM, Herranz CR, et al. Levofloxacin versus beta-lactamic therapy in community acquired pneumonia that requires hospitalization. *Med Interna* 2002;19:621-5.
10. Gotfried MH, Dattani D, Riffer E, et al. A controlled, double-blind, multicenter study comparing clarithromycin extended-release tablets and levofloxacin tablets in the treatment of community-acquired pneumonia. *Clin Ther* 2002;24:736-51.
11. Hoeffken G, Meyer HP, Winter J, et al.; Community-acquired Pneumonia Study Group. The efficacy and safety of two oral moxifloxacin regimens compared to oral clarithromycin in the treatment of community-acquired pneumonia. *Respir Med* 2001;95:553-64.
12. Kalbermatter V, Bagilet D, Diab M, et al. Oral levofloxacin versus intravenous ceftriaxone and amoxicillin/clavulanic acid in the treatment of community-acquired pneumonia that requires hospitalization. *Med Clin (Barc)* 2000;115:561-3.
13. Katz E, Larsen LS, Fogarty CM, et al. Safety and efficacy of sequential i.v. to p.o. moxifloxacin versus conventional combination therapies for the treatment of community-acquired pneumonia in patients requiring initial i.v. therapy. *J Emerg Med* 2004;27:395-405.
14. Leophonte P, File T, Feldman C. Gemifloxacin once daily for 7 days compared to amoxicillin/clavulanic acid thrice daily for 10 days for the treatment of community-acquired pneumonia of suspected pneumococcal origin. *Respir Med* 2004;98:708-20.
15. Lin TY, Lin SM, Chen HC, et al. An open label randomized comparison of levofloxacin and amoxicillin/clavulanate plus clarithromycin for the treatment of hospitalized patients with community-acquired pneumonia. *Chang Gung Med J* 2007;30:321-32.

16. Lode H, File TM Jr, Mandell L, et al.; 185 Gemifloxacin Study Group. Oral gemifloxacin versus sequential therapy with intravenous ceftriaxone/oral cefuroxime with or without a macrolide in the treatment of patients hospitalized with community-acquired pneumonia: a randomized, open-label, multicenter study of clinical efficacy and tolerability. *Clin Ther* 2002;24:1915-36.
17. Norrby SR, Petermann W, Willcox PA, et al. A comparative study of levofloxacin and ceftriaxone in the treatment of hospitalized patients with pneumonia. *Scand J Infect Dis* 1998;30:397-404.
18. Petitpretz P, Arvis P, Marel M, et al.; CAP5 Moxifloxacin Study Group. Oral moxifloxacin vs high-dosage amoxicillin in the treatment of mild-to-moderate, community-acquired, suspected pneumococcal pneumonia in adults. *Chest* 2001;119:185-95.
19. Portier H, Brambilla C, Garre M, et al. Moxifloxacin monotherapy compared to amoxicillin-clavulanate plus roxithromycin for nonsevere community-acquired pneumonia in adults with risk factors. *Eur J Clin Microbiol Infect Dis* 2005;24:367-76.
20. Torres A, Muir JF, Corris P, et al. Effectiveness of oral moxifloxacin in standard first-line therapy in community-acquired pneumonia. *Eur Respir J* 2003;21:135-43.
21. Welte T, Petermann W, Schurmann D, et al.; MOXIRAPID Study Group. Treatment with sequential intravenous or oral moxifloxacin was associated with faster clinical improvement than was standard therapy for hospitalized patients with community-acquired pneumonia who received initial parenteral therapy. *Clin Infect Dis* 2005;41:1697-705.
22. Xu S, Xiong S, Xu Y, et al. Efficacy and safety of intravenous moxifloxacin versus cefoperazone with azithromycin in the treatment of community acquired pneumonia. *J Huazhong Univ Sci Technolog Med Sci* 2006;26:421-4.
23. Zervos M, Mandell LA, Vrooman PS, et al. Comparative efficacies and tolerabilities of intravenous azithromycin plus ceftriaxone and intravenous levofloxacin with step-down oral therapy for hospitalized patients with moderate to severe community-acquired pneumonia. *Treat Respir Med* 2004;3:329-36.