

In vitro activity of the new fluoroketolide solithromycin against a large collection of clinically resistant *Neisseria gonorrhoeae* strains - potential treatment option for gonorrhoea?

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Purpose

To investigate the *in vitro* activity of the new fluoroketolide solithromycin (CEM-101), which is entering Phase 3 studies for bacterial pneumonia, against *Neisseria gonorrhoeae* isolates, including strains with various high-level antimicrobial resistance, relative to other antimicrobials previously or currently recommended for gonorrhoea treatment and telithromycin (the first developed ketolide).

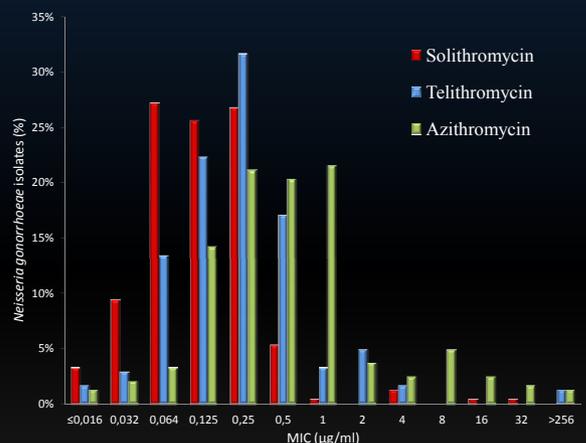
Table. Minimum inhibitory concentrations of solithromycin, relative to antimicrobials previously or currently used for treatment of gonorrhoea.

Antimicrobial	MIC (µg/ml)			Resistance (%)
	Range	50%	90%	
Solithromycin	0.001-32	0.125	0.25	ND
Azithromycin	0.001->256	0.5	8	37.8
Telithromycin	0.001->256	0.25	1	ND
Erythromycin	0.064->2	>2	>2	94.3
Cefixime	<0.016-8	0.032	0.25	6.5
Ceftriaxone	<0.002-4	0.016	0.125	1.2
Ampicillin	<0.016->256	1	16	24.4
Ciprofloxacin	0.002->32	4	>32	64.2
Spectinomycin	4->1024	16	16	2.0
Tetracycline	0.125-256	4	64	69.5

Conclusions

- Solithromycin has superior *in vitro* activity compared to azithromycin, other macrolides, and also many other classes of antimicrobials.
- Solithromycin, the new fluoroketolide, might be an effective option for treatment of gonorrhoea, as single antimicrobial therapy especially for cephalosporin-resistant gonorrhoea cases and in dual antimicrobial combination therapy.

Figure. MIC distributions for solithromycin, azithromycin and telithromycin for clinical *N. gonorrhoeae* isolates (n=218) and *N. gonorrhoeae* international reference strains (n=28).



Introduction

Resistance in *N. gonorrhoeae* to penicillins, tetracyclines, fluoroquinolones, macrolides, and early-generation cephalosporins is common worldwide. Recently, clinical high-level resistance to the currently recommended extended-spectrum cephalosporins (ESCs), which are the last remaining treatment options, has been reported. Accordingly, gonorrhoea may become untreatable and new treatment strategies and/or treatment options are essential!

Methods

- A global collection of 246 *N. gonorrhoeae* clinical isolates and reference strains were tested, including the extensively-drug resistant (XDR) H041 (Ohnishi, *et al.* AAC. 2011) and F89 (Unemo, *et al.* AAC. 2011).
- The MICs of solithromycin, azithromycin, erythromycin, and telithromycin were determined by agar dilution. MICs of cefixime, ceftriaxone, ampicillin, ciprofloxacin, spectinomycin, and tetracycline were determined using Etest. Where available, interpretative criteria from the CLSI were applied

Results

- All MIC results for the 246 *N. gonorrhoeae* isolates are summarized in the **Table**.
- Only 2.4% of the isolates had an MIC of >0.5 µg/ml for solithromycin (**Figure**) while 11%, 37.8%, and 94.3% of all the tested isolates had an MIC of >0.5 µg/ml for telithromycin, azithromycin and erythromycin, respectively.
- For the XDR *N. gonorrhoeae* strains H041 and F89, which both are highly resistant to cefixime (4-6 µg/ml) and ceftriaxone (2-4 µg/ml), the MIC of solithromycin was only 0.064 µg/ml and 0.125 µg/ml, respectively.