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Efficacy of Solithromycin versus Moxifloxacin in the Treatment of CABP by Baseline PORT Risk Class: Results from 2 Large, Multinational Studies

D. Mildvan[1], J. McKinnell[2], K. Aggarwal[3], B. Jamieson[3], D. Oldach[3], P. Fernandes[3]

[1]Mount Sinai Beth Israel Medical Center, New York, NY; [2]LA BioMed Research Institute at Harbor-UCLA, Los Angeles, CA; [3]Cempra, Inc., Chapel Hill, NC

Brian Jamieson
Cempra, Inc.
bjamieson@cempra.com

Introduction and Objective

Community-acquired bacterial pneumonia (CABP) is a common and serious respiratory infection. The pneumonia severity index (PSI) and corresponding Patients Outcomes Research Team (PORT) risk classes are validated tools for estimation of mortality and morbidity outcomes in CABP patients. Patients in PORT Classes I or II are considered lower risk and are often treated as outpatients. PORT Classes III, IV, and V indicate progressively higher risk, with patients more likely to be hospitalized. We evaluated the efficacy of solithromycin versus moxifloxacin, a potent fluoroquinolone, by baseline PORT risk class from a pooled Phase 3 dataset.

Solithromycin is a fourth-generation macrolide antibiotic, and the first fluoroketolide, and has been evaluated in two global Phase 3 CABP trials. These randomized, blinded trials enrolled >1700 adults with CABP between 2013 and 2015. SOLITAIRE-Oral evaluated a 5-day oral solithromycin regimen compared to a 7-day oral moxifloxacin regimen[1]. SOLITAIRE-IV evaluated 7-day IV or IV-to-Oral regimens of solithromycin compared to moxifloxacin[2].

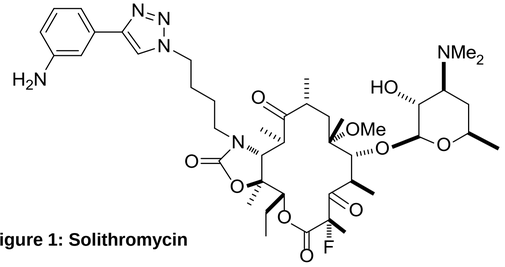


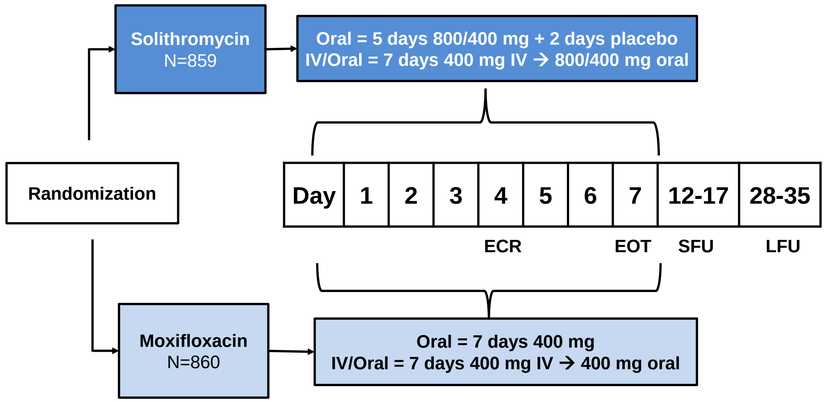
Figure 1: Solithromycin

Methods

Subgroup analyses were conducted based on baseline PORT scores from two phase 3, randomized, double-blind, non-inferiority studies. Both studies enrolled adult CABP patients in PORT Classes II, III, or IV with randomization stratified by region, history of asthma and/or COPD, and PORT Class (II vs. III/IV). In SOLITAIRE-Oral, patients received oral solithromycin for 5 days (+2 days placebo) or oral moxifloxacin for 7 days. In SOLITAIRE-IV, patients received IV solithromycin or IV moxifloxacin for 7 days and were eligible to be switched to oral therapy within the 7 day treatment period when clinically stable. The primary endpoint for both studies was Early Clinical Response (ECR), defined as improvement at 72 [-12/+36] hours after the first dose in at least 2 of the following cardinal symptoms: cough, shortness of breath, chest pain, and difficulty with sputum production.

Results

Figure 2: SOLITAIRE Phase 3 Studies Design



ECR = early clinical response, EOT = end of treatment, SFU = short-term follow-up, LFU = long-term follow-up

The majority of CABP patients in the pooled analysis were in the PORT III or IV risk classes (>60%). The SOLITAIRE-Oral study included a higher proportion of PORT II patients (approximately 50%) compared with the SOLITAIRE-IV trial where PORT II patient enrollment was limited to 25% of enrollment. PORT class distribution was balanced between treatment groups in each study. The ECR rate in the pooled data, by PORT risk class, is shown in Table 1.

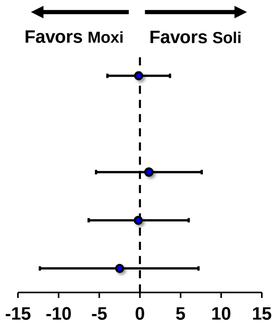
Table 1: Early Clinical Response Rate, by PORT Risk Class

	Solithromycin		Moxifloxacin	
	n/N	%	n/N	%
ITT population (overall) [a]	676/859	**78.7**	678/860	**78.8**
PORT Score (PSI) [b]				
II (51-70)	255/314	**81.2**	254/317	**80.1**
III (71-90)	286/364	**78.6**	296/376	**78.7**
IV (91-130)	132/178	**74.2**	125/163	**76.7**

[a] Pooled data from two Phase 3 studies with similar designs and identical endpoints
[b] Data does not include 1 PORT I and 6 PORT V patients

PORT = Pneumonia Patients Outcomes Research Team; PSI = Pneumonia Severity Index

Difference (Soli – Moxi, 95% CI)*



***Difference and 95% CI weighted by study**

Baseline CURB scores were also evaluated as a subgroup analysis in this pooled dataset. CURB-65 scores are assessed by scoring one point for each of the following 5 criteria: **C**onfusion of new onset; Blood **U**rea nitrogen greater than 7 mmol/l (19 mg/dL); **R**espiratory rate of 30 breaths per minute or greater; **B**lood pressure less than 90 mmHg systolic or diastolic blood pressure 60 mmHg or less; Age **65** or older. The ECR rate, by baseline CURB-65 score, is shown in Table 2.

Table 2: Early Clinical Response Rate, by CURB-65 Score

	Solithromycin		Moxifloxacin	
CURB-65 Score	n/N	%	n/N	%
0	162/213	**76.1**	166/219	**75.8**
1	274/347	**79.0**	270/331	**81.6**
2	182/228	**79.8**	187/235	**79.6**
3	30/37	**81.1**	31/44	**70.5**
4	2/2	**100.0**	2/2	**100.0**

Conclusions

- Solithromycin was non-inferior to moxifloxacin in the treatment of CABP
- ECR rates across PORT risk classes were consistent and similar in PORT II patients and higher risk patients in the PORT III and IV risk classes.
- Solithromycin had ECR rates similar to moxifloxacin in subgroup analyses by baseline CURB-65 Score

References

1. Barrera CM, Mykietiuk A, Metev H, Nitu MF, Karimjee N, Doreski PA, et al. Efficacy and safety of oral solithromycin versus oral moxifloxacin for treatment of community-acquired bacterial pneumonia: a global, double-blind, multicentre, randomised, active-controlled, non-inferiority trial (SOLITAIRE-ORAL). *Lancet Infect Dis* 2016 16(4):421:430.
2. File TM, Rewerska B, Vucinic-Mihailovic V, Gonong JR, Das AF, Keedy K, Taylor D, Sheets A, Fernandes P, Oldach D, Jamieson BD. SOLITAIRE-IV: A Randomized, Double-Blind, Multi-Center Study Comparing the Efficacy and Safety of Intravenous-to-Oral Solithromycin to Intravenous-to-Oral Moxifloxacin for Treatment of Community-acquired Bacterial Pneumonia. *Clin Infect Dis.* 2016 Oct 15;63(8): 1007-1016.

Disclosures

These trials were conducted by and funded by Cempra, Inc. Brian Jamieson and David Oldach are employees of Cempra, Inc. Kavita Aggarwal and Prabhavathi Fernandes are former employees of Cempra, Inc.