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Multi-national Studies Comparing Solithromycin, a New Macrolide, to Moxifloxacin in the Treatment of CABP: Response by Geographic Region

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

[1]LA BioMed Research Institute at Harbor-UCLA, Los Angeles, CA; [2]Mount Sinai Beth Israel Medical Center, New York, NY; [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 infection requiring antibiotic therapy. CABP remains a prevalent illness worldwide with resistance rates to macrolides and other classes of antibiotics growing across geographic regions. Despite increasing resistance, no new oral antibiotics have been approved for CABP use in over a decade, creating a medical need for new agents.

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].

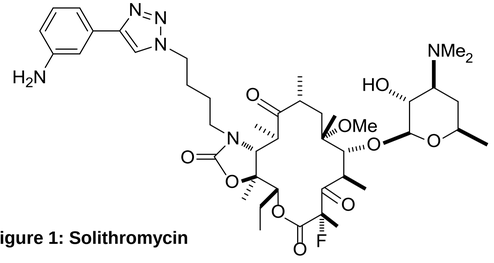


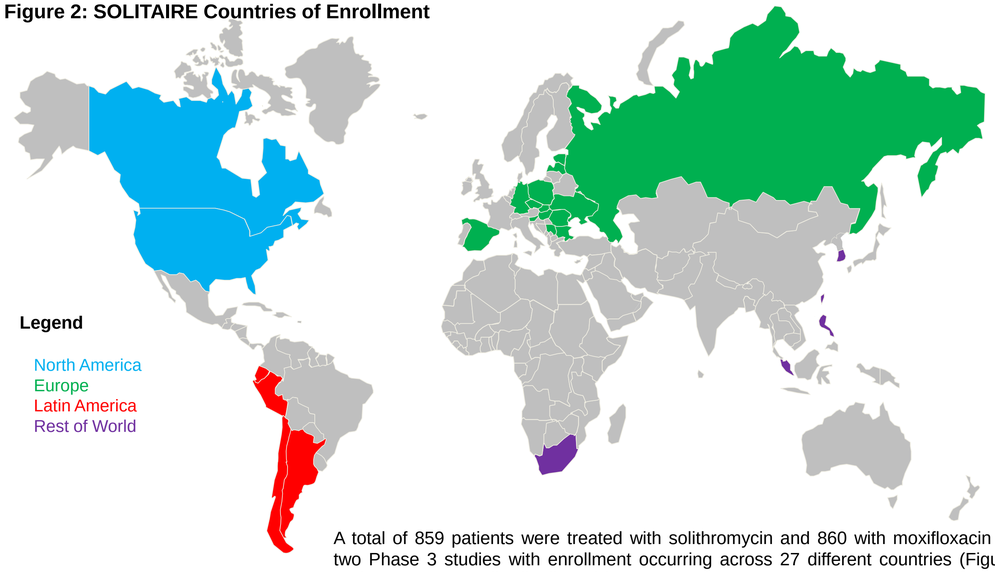
Figure 1: Solithromycin

Methods

Subgroup analyses were conducted by geographic region in two phase 3, randomized, double-blind, non-inferiority studies. Both studies enrolled adult patients with a diagnosis of CABP; randomization was stratified by geographic area, history of asthma and/or COPD, and PORT Risk Class (II vs III/IV). In SOLITAIRE-Oral, patients received oral solithromycin for 5 days (+2 days placebo) or oral moxifloxacin for 7 days (Figure 3). 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 Countries of Enrollment



A total of 859 patients were treated with solithromycin and 860 with moxifloxacin in the two Phase 3 studies with enrollment occurring across 27 different countries (Figure 2). Patients were equally distributed between treatment groups across geographic regions: Europe (solithromycin 60.9%, moxifloxacin 58.4%), North America (solithromycin 14.9%, moxifloxacin 15.9%), Latin America (solithromycin 6.6%, moxifloxacin 7.6%) and rest of world (solithromycin 14.9%, moxifloxacin 15.9). Early Clinical Response rates by geographic region are shown in Table 1.

Table 1: Early Clinical Response Rate, by Geographic Region

	Solithromycin		Moxifloxacin	
	n/N	%	n/N	%
ITT population (overall) [a]	676/859	**78.7**	678/860	**78.8**
Geographic Region				
North America	110/151	**72.8**	103/156	**66.0**
Europe	420/523	**80.3**	418/502	**83.3**
Latin America	42/57	**73.7**	48/65	**73.8**
Rest of World	104/128	**81.3**	109/137	**79.6**

[a] Pooled data from two Phase 3 studies with similar designs and identical endpoints

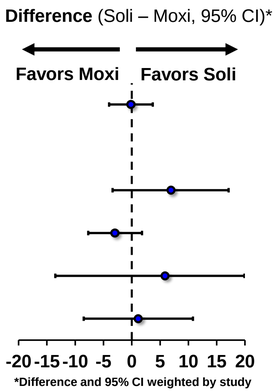
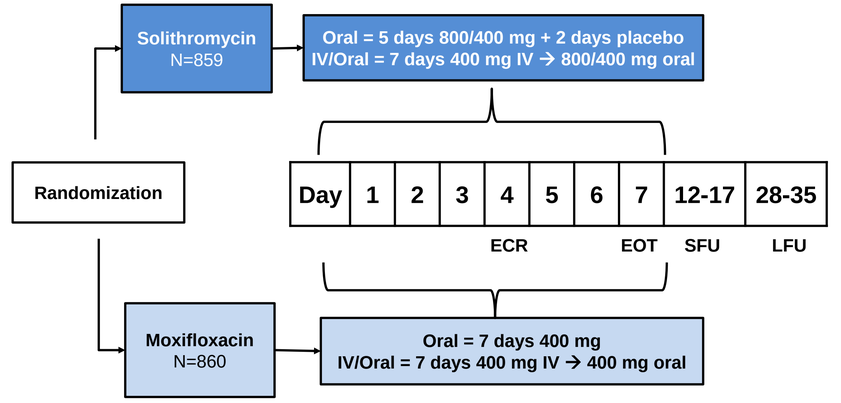


Figure 3: SOLITAIRE Phase 3 Studies Design



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

Conclusions

- Effective new antibiotic treatments are needed for CABP due to growing antimicrobial resistance in regions across the globe.
- Solithromycin, a new macrolide antibiotic, demonstrated non-inferiority to moxifloxacin, a potent fluoroquinolone, in the treatment of CABP in multinational studies conducted in 27 enrolling countries.
- Solithromycin demonstrated a comparable treatment effect to moxifloxacin in each geographic region where the studies were conducted, indicating it is a promising potential new empiric therapy for CABP.

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 phase 3 CABP 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.