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Efficacy of Solithromycin for Treatment of Community-acquired Pneumonia by Patient Age: Pooled Analysis of 2 Multinational, Double-blind, Randomized, Controlled Studies

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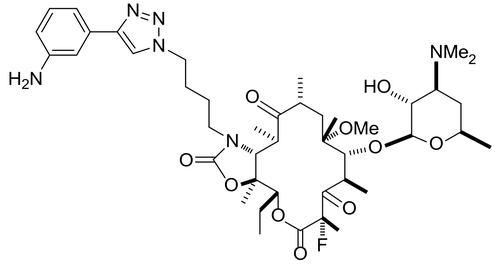
Introduction and Objective

Community-acquired pneumonia (CAP) is a common and serious pulmonary infection that disproportionately affects the elderly, with increasing morbidity and mortality by age. We evaluated the efficacy of solithromycin versus moxifloxacin, an approved and potent fluoroquinolone, for treatment of CAP in patients by age group.

Solithromycin is a fourth-generation macrolide antibiotic, and the first fluoroketolide, and has been evaluated in two global Phase 3 CAP trials. These randomized, blinded trials enrolled >1700 adults with CAP 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

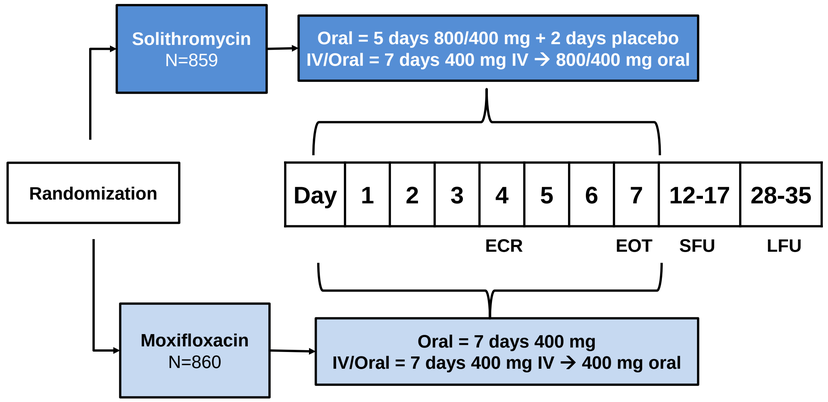


Methods

Subgroup analyses were conducted by patient age in two phase 3, randomized, double-blind, non-inferiority studies. Both studies enrolled adult patients with a diagnosis of CAP; 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. 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. Study investigators also assessed patient clinical response at a short-term follow-up visit 5 to 10 days after last dose as a secondary efficacy endpoint.

Results

Figure 2: SOLITAIRE Phase 3 Studies Design



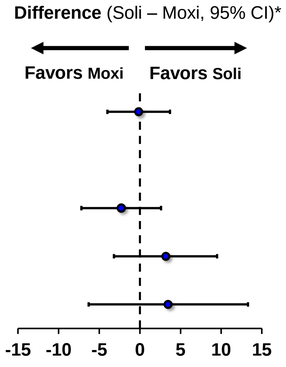
ECR = early clinical response, EOT = end of treatment, SFU = short-term follow-up, LFU = long-term follow-up

The mean age for patients treated with solithromycin was 59.5 years and with moxifloxacin was 58.9 years. The overall responder rate for the primary endpoint of ECR in the pooled data set was 78.7% (676/859) vs 78.8% (678/860) in solithromycin and moxifloxacin recipients, respectively. ECR rates for patient subgroups by age are shown in Table 1.

Table 1: Early Clinical Response Rate, by Age Subgroup

	Solithromycin		Moxifloxacin	
	n/N	%	n/N	%
ITT population (overall) [a]	676/859	**78.7**	678/860	**78.8**
Age				
<65 years	407/517	**78.7**	426/526	**81.0**
≥ 65 years	269/342	**78.7**	252/334	**75.4**
≥ 75 years	115/145	**79.3**	106/140	**75.7**

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



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

Clinical success rates as determined by the investigator 5 to 10 days after the last dose are shown in Table 2.

Table 2: Investigator-assessed Clinical Success, by Age Subgroup

	Solithromycin		Moxifloxacin	
	n/N	%	n/N	%
ITT population (overall) [a]	727/859	**84.6**	753/860	**87.6**
Age				
<65 years	430/517	**83.2**	462/526	**87.8**
≥ 65 years	297/342	**86.8**	291/334	**87.1**
≥ 75 years	122/145	**84.1**	121/140	**86.4**

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

Conclusions

- Early Clinical Response rates (Day 4) and Investigator's assessment of Clinical Success rates (Day 12-17) were comparable between age groups.
- Patients ≥ 65 and ≥ 75 years of age treated with solithromycin had equal or greater response rates at both an early and later time point compared to those patients <65 years of age.
- Solithromycin and moxifloxacin were comparably effective in the treatment of CAP across patient age subpopulations, including for at-risk elderly patients ≥ 65 or ≥ 75 years of age.

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.