Oral Solithromycin Versus Oral Moxifloxacin for Treatment of Adult Community-Acquired Bacterial Pneumonia (CABP): Results of the Global Phase-3 Trial SOLITAIRE-ORAL

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RATIONALE: Due to rising microbial resistance and concerns with antibiotic tolerability and impact on gut flora, new CABP treatments are needed.

METHODS: Global, Phase 3, DB-RCT comparing solithromycin (5 days) to moxifloxacin (7 days) for treatment of CABP of PORT II, III, / IV severity. Etiologic agents were detected with traditional and molecular methods. Patients were evaluated at baseline, Day 4 Early Clinical Response (ECR), Day 7 End of Therapy (EOT), Day 12-17 short-term follow-up (SFU), and Day 30 late-up follow-up. ECR was defined as improvement in at least two of four cardinal symptoms (chest pain, dyspnea, sputum production and cough), without worsening in any. Success at EOT and SFU was judged by investigators. Primary objectives were demonstration of non-inferiority at ECR in the ITT population (FDA guidance), and at SFU in the ITT and CE populations (EMA guidance).

RESULTS: 860 patients from 16 countries were randomized 1:1 to receive oral solithromycin or moxifloxacin. Among patients randomized to solithromycin, mean age was 58.5, with 36.4% ≥ 65, versus mean age 56.7, with 31.6% ≥ 65 for moxifloxacin. 50.7% of solithromycin patients had PORT III/IV CABP (11.3%, PORT IV) vs. 48.6% of moxifloxacin patients (8.8% PORT IV). Regional enrollment: North America 23.7%, Europe 52.1%, Latin America 12.3%, and South Africa 11.9%. Solithromycin was non-inferior to moxifloxacin for all primary objectives (Table). Solithromycin demonstrated comparable safety to moxifloxacin in the occurrence of adverse events (AEs) (36.6% vs 35.6%), study drug related AEs (10.1% vs 12.5%), Serious Adverse Events (6.6% vs 6.3%) (none attributed to study drug) and deaths (1.4% vs 1.4%). Grade 4 ALTs (>8xULN) were observed in 5 moxifloxacin patients and 2 solithromycin patients. No patient had concomitant ALT and bilirubin elevation meeting Hy's Law criteria. Two episodes of *C. difficile* diarrhea were diagnosed, both occurring in moxifloxacin patients.

Outcome Measure	Solithromycin (%)	Moxifloxacin (%)	Delta (%)	95% CI	Interpretation
Early Clinical Response Rate (ECR), ITT Population	78.2 (333/426)	77.9 (338/434)	0.29	(-5.5, 6.1)	**Solithromycin Non-inferiority Demonstrated**
ECR, PORT II patients	80.5 (169/210)	80.7 (180/223)	-0.24	(-8.2, 7.7)	subset analysis
ECR, PORT III/IV patients	75.9 (164/216)	74.9 (158/211)	1.04	(-7.6, 9.7)	subset analysis
ECR, patients of age < 65 years	77.9 (211/271)	80.8 (240/297)	-2.95	(-10.0, 4.1)	subset analysis
ECR, patients of age 65-74 years	75.3 (70/93)	73.0 (54/74)	2.30	(-12.3, 16.9)	subset analysis
ECR, patients of age ≥ 75 years	83.9 (52/62)	69.8 (44/63)	14.03	(-2.1, 30.2)	subset analysis
Success at Short-Term Follow-Up Visit, ITT Population (SFU-ITT)	84.5 (360/426)	86.6 (376/434)	-2.13	(-7.1, 2.8)	**Solithromycin Non-inferiority Demonstrated**
SFU-ITT Success, PORT II	86.2 (181/210)	89.2 (199/223)	-3.05	(-9.7, 3.6)	subset analysis
SFU-ITT Success, PORT III/IV	82.9 (179/216)	83.9 (177/211)	-1.02	(-8.5, 6.5)	subset analysis
Success at Short-Term Follow-Up Visit, CE Population (SFU-CE)	88.1 (342/388)	91.3 (356/390)	-3.14	(-7.7, 1.4)	**Solithromycin Non-inferiority Demonstrated**
SFU-CE Success, PORT II	89.3 (175/196)	92.1 (187/203)	-2.83	(-9.0, 3.4)	subset analysis
SFU-CE Success, PORT III/IV	87.9 (167/192)	90.4 (169/187)	-3.40	(-10.3, 3.5)	subset analysis

CONCLUSIONS: Oral solithromycin was non-inferior to oral moxifloxacin for treatment of CABP. Solithromycin ECR rates were notably higher than moxifloxacin in the elderly and among patients with higher PORT scores. Safety outcomes were comparable, although among moxifloxacin patients there were more G4 ALT elevations and two episodes of *C. difficile* diarrhea. A global P3 CABP trial evaluating IV-to-Oral solithromycin versus IV-to-Oral moxifloxacin is ongoing.