A Randomized, Double-Blind, Multi-Center Study to Evaluate the Efficacy and Safety of Oral Solithromycin (CEM-101) Compared to Oral Levofloxacin in the Treatment of Patients with Community-Acquired Bacterial Pneumonia

Abstract P719

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Trial Design:

This was a multi-center, Phase 2, double-blind, randomized, efficacy and safety study to evaluate oral solithromycin versus oral levofloxacin in the treatment of adults with moderate to moderately severe community-acquired bacterial pneumonia (CABP). [Clinical Trials registration NCT01168713]

Methods:

Patients with CABP were enrolled and randomized (1:1) to either: solithromycin 800 mg orally (PO) on Day 1 followed by 400 mg PO daily on Days 2 to 5 or levofloxacin 750 mg PO daily on Days 1 to 5. Randomization was stratified by age (<50 or ≥50 years) and pneumonia severity index (PORT) score. Co-primary efficacy outcome measures were Investigator's assessment of clinical success at test-of-cure (TOC; 4 to 11 days after the last dose of study drug) in the Intent-to-Treat (ITT) and Clinically Evaluable (CE) populations. Early response success (at Day 3) was defined as improvement in at least two cardinal symptoms (cough, sputum production, chest pain, or dyspnea) without worsening in any.

Results:

The 132 patients randomized were primarily (95%) from U.S. sites, 50.7% male, and 82.6% Caucasian, with a mean age of 55. Randomized patients had PORT scores of II (73%), III (20%), or IV (5%). Clinical success rates, presented in the table below, were comparable across the analysis populations, at both early response (Day 3) and TOC visits, as well as among subgroups with a baseline elevated procalcitonin (PCT) and with an identified pneumococcal infection.

More levofloxacin recipients experienced one or more treatment-emergent adverse events (TEAEs) during the study (45.6%) than did solithromycin recipients (29.7%). The majority of TEAEs were gastrointestinal, were of mild or moderate intensity, and included nausea (1.6% solithromycin; 10.3% levofloxacin), diarrhea (7.8% solithromycin; 5.9% levofloxacin), and vomiting (0% solithromycin; 4.4% levofloxacin). Six patients, all receiving levofloxacin, discontinued study drug due to an AE. There was one death in the trial, attributed to a pulmonary embolism, in a levofloxacin recipient.

Conclusions:

Solithromycin demonstrated efficacy comparable to levofloxacin and a favorable safety and tolerability profile, with a lower incidence of treatment-emergent adverse events than levofloxacin. These findings strongly support the further study of solithromycin in Phase 3 clinical trials for the treatment of CABP.

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Table

Clinical Success Rates Visit: Population	**Solithromycin** **n/N (%)**	**Levofloxacin** **n/N (%)**
TOC: ITT (co-primary efficacy outcome)	55/65 (84.6)	58/67 (86.6)
CE (co-primary efficacy outcome)	46/55 (83.6)	54/58 (93.1)
microITT	14/18 (77.8)	10/14 (71.4)
ME	12/15 (80.0)	10/13 (76.9)
TOC: ITT, Baseline Plasma PCT ≥ 0.2 ng/mL	22/25 (88.0)	24/27 (88.9)
TOC: ITT, Baseline Plasma PCT ≥ 0.5 ng/mL	14/15 (93.3)	12/13 (92.3)
TOC: *Streptococcus pneumoniae* diagnosis	5/7 (71.4) *	2/3 (66.7)
Day 3: ITT	47/65 (72.3)	48/67 (71.6)

* includes one patient who missed EOT visit, but was considered a success when evaluated at TOC.
Notes: n/N (%): n=number of patients in the specific category; N=number of patients with an assessment of the specified parameter; percentage=100 x (n/N). PCT=procalcitonin. *S. pneumoniae* diagnoses were established by blood or sputum culture, or by detection of streptococcal capsular antigen in urine (BINAX assay). Success at Day 3 was defined as improvement in at least two cardinal symptoms (cough, sputum production, chest pain, or dyspnea) without worsening in any.