Title: # 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).

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Abstract: **BACKGROUND**: Community-acquired bacterial pneumonia (CABP) is a leading cause of morbidity and mortality, and treatment recommendations, each with specific limitations, vary globally. We aimed to compare the efficacy and safety of solithromycin, a novel macrolide, with moxifloxacin for treatment of CABP.

METHODS: We did this global, double-blind, double-dummy, randomised, active-controlled,

non-inferiority trial at 114 centres in North America, Latin America, Europe, and South Africa. Patients (aged >=18 years) with clinically and radiographically confirmed pneumonia of Pneumonia Outcomes Research Team (PORT) risk class II, III, or IV were randomly assigned (1:1), via an internet-based central block randomisation procedure (block size of four), to receive either oral solithromycin (800 mg on day 1, 400 mg on days 2-5, placebo on days 6-7) or oral moxifloxacin (400 mg on days 1-7). Randomisation was stratified by geographical region, PORT risk class (II vs III or IV), and medical history of asthma or chronic obstructive pulmonary disease. The study sponsor, investigators, staff, and patients were masked to group allocation. The primary outcome was early clinical response, defined as an improvement in at least two of four symptoms (cough, chest pain, sputum production, dyspnoea) with no worsening in any symptom at 72 h after the first dose of study drug, with a 10% non-inferiority margin. The primary analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT-01756339.

FINDINGS: Between Jan 3, 2013, and Sept 24, 2014, we randomly assigned 860 patients to receive solithromycin (n=426) or moxifloxacin (n=434). Patients were followed up to days 28-35 after first dose. Solithromycin was non-inferior to moxifloxacin in achievement of early clinical response: 333 (78.2%) patients had an early clinical response in the solithromycin group versus 338 (77.9%) patients in the moxifloxacin group (difference 0.29, 95% CI -5.5 to 6.1). Both drugs had a similar safety profile. 43 (10%) of 155 treatment-emergent adverse events in the solithromycin group and 54 (13%) of 154 such events in the moxifloxacin group were deemed to be related to study drug. The most common adverse events, mostly of mild severity, were gastrointestinal disorders, including diarrhoea (18 [4%] patients in the solithromycin group vs 28 [6%] patients in the moxifloxacin group), nausea (15 [4%] vs 17 [4%] patients) and vomiting (ten [2%] patients in each group); and nervous system disorders, including headache (19 [4%] vs 11 [3%] patients) and dizziness (nine [2%] vs seven [2%] patients).

INTERPRETATION: Oral solithromycin was non-inferior to oral moxifloxacin for treatment of patients with CABP, showing the potential to restore macrolide monotherapy for this indication.

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