2228. Treatment of Community-Acquired Bacterial Pneumonia (CABP) in Patients with Diabetes: Outcomes from a Global Phase 3 Study of Delafloxacin (DLX)

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Background. Delafloxacin (DLX) is an IV/oral anionic fluoroquinolone with no QT restrictions. It is approved for the treatment of serious skin infections including those due to MRSA and Gram-negative pathogens. A Phase 3 trial of patients with CABP was recently completed comparing DLX to moxifloxacin (MOX), including patients with diabetes (DM).

Methods. Multicenter, randomized, double-blind trial of adults with CABP with at least 2 clinical symptoms; physical signs; and radiographic evidence of pneumonia. Patients were randomized 1:1 to DLX or MOX treatment for 5–10 days. Patients received a minimum of 3 days of IV treatment, then were switched to oral at MD discretion. Key endpoints were the Early Clinical Response (ECR) at 96 ±24h and the investigator assessment of response at Test of Cure (TOC) 5–10 days after last dose in the Intent to Treat population. Clinical success was defined as complete or near resolution of signs and symptoms and no further antibiotics needed per investigator assessment.

Results. 131 DM patients were randomized. Patient characteristics: 59% male; mean age 66 (26% ≥ age 75); 40% PORT class IV/V; 29% multi-lobar pneumonia. Bacterial pathogens were identified in 59% at baseline. Patients received treatment ~8.5 days. DLX was comparable to MOX in patients with DM, with response at ECR 90% DLX vs. 88.5% MOX [1.5 (95% CI -9.6, 13.2)] as well as Clinical Success at TOC 87.1% DLX vs. 86.9% MOX [0.3 (95% CI –11.6, 12.7)]. The overall % of DM patients with at least one treatment-related adverse event (AE) was 18.6% DLX and 11.7% MOX. The most frequent treatment-related adverse events were gastrointestinal in nature including diarrhea seen in 6 DLX and 2 MOX patients.There were 3 DLX and 2 MOX deaths of patients with DM during the study (up to Day 28), unrelated to treatment. There were no cases of C diff in these patients. There were no reports of hypoglycemia on DLX. There was one discontinuation of treatment due to a related AE in each treatment group.

Conclusion. IV/oral DLX was comparable to IV/oral MOX for treatment of CABP in patients with diabetes. DLX has no preclinical signals for QT prolongation and has no QT prolongation in a validated challenge study. There were no events of hypoglycemia. DLX appears effective and well tolerated in patients with diabetes and CABP.

Disclosures. **All authors:** No reported disclosures.

2229. Relative Bioavailability of a Single Oral Dose of SUBA-Itraconazole 65 mg Capsule Compared with Conventional Itraconazole 100 mg Capsule Administered Under Fasted and Fed Conditions in Healthy Adult Volunteers

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Background. Conventional itraconazole (CI) absorption from capsules even under fed conditions is suboptimal (~55%), let alone when fasted. SUBA-itraconazole (SI) is ~1.8x's more bioavailable than CI at steady-state in a fed condition. There are, however, no data comparing these formulations under a fasted state. A single-dose PK study was performed comparing bioavailability of 65mg SI to 100mg CI under fasted or fed conditions.

Methods. This was an open-label, single-dose, randomized, four-period, four-treatment, four-sequence, crossover bioequivalence study under fasted and fed conditions in healthy adults. Subjects were administered a single dose of SI (1 × 65 mg) and CI (1 × 100 mg). Under fasted condition, subjects were administered SI or CI following an overnight fast of at least 10 hours. Subjects under fed condition were administered SI or CI after 30 minutes of consuming a standardized high fat breakfast preceded by an overnight fast of at least 10 hours. After dosing, all subjects fasted for at least 4 hours post-dose in all periods. Blood samples were collected prior to dosing and then from 1 to 120 hours. Analysis of itraconazole (IZ) and hydoxyitraconazole (HIZ) serum levels was by least-squares-geometric means of PK parameters.

Results. Under fasted condition, C_{max} and AUC_{tau} of IZ for SI were substantially higher compared with CI (Table, Figure 1). Under fed conditions, however, the C_{max} and AUC_{tau} of IZ for SI was 20% and 10% lower, respectively (table, Figure 2). Similar results were found for HIZ. The T_{max} for IZ and HIZ of SI and CI were similar under a fasted condition but extended by over 2 hours for SI vs. CI under fed conditions. Study drugs were well-tolerated under fasted and fed conditions. All TEAEs were mild and resolved at the end of the study. Fifty of 52 subjects enrolled completed the study. Two subjects did not complete the study due to not being able to finish a high fat meal and noncompliance. No SAEs were reported.

Conclusion. Total and peak IZ/HIZ exposure was substantially higher for SI under fasted conditions compared with CI, but slightly lower under fed conditions with similar safety profiles. This study demonstrates the unique nature of the SI formulation compared with CI under fasted conditions and may lead to less variability if patients are not adherent to dietary requirements when taking itraconazole.

Table:

	Fasted				Fed			
	SI: 65mg itraconazole	CI: 100mg itraconazole			SI: 65mg itraconazole	CI: 100mg itraconazole		
Parameter	Geometric Mean	Geometric Mean	SI/CI Ratio	90% Confidence Interval	Geometric Mean	Geometric Mean	SI/CI Ratio	90% Confidence Interval
Cmax,ss (ng/mL)	101.612	62.821	161.75%	141.40-185.02	43.563	54.279	80.26 %	67.61-95.27
AUCtau (hr*ng/mL)	864.483	700.82	123.35%	110.68-137.47	564.352	625.683	90.20 %	78.22-104.01
T_{max} (h) Median (Range)	2.50 (1.50-5.00)	3.00 (1.50-4.52)			7.50 (4.50-24.00)	5.00 (2.50-11.00)		

Fig 1: Mean Itraconazole Plasma Concentration-Time Profiles (A: n = 51 / B: n = 50 / C: n = 52 / D: n = 51)

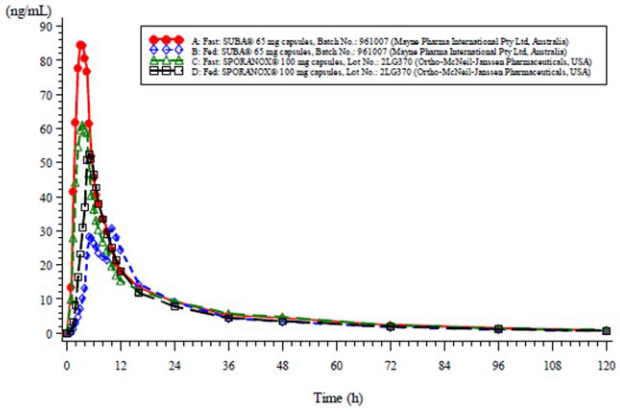
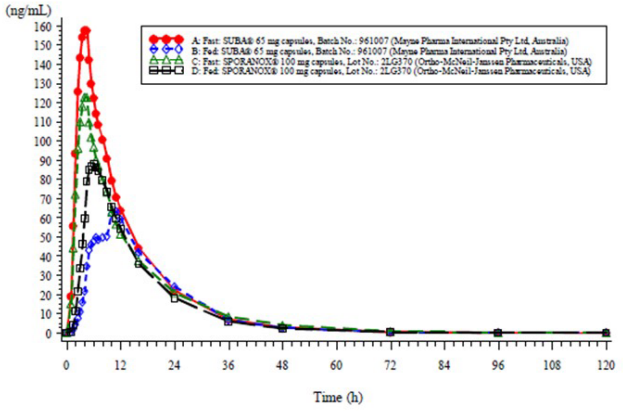


Fig 2: Mean Hydroxy-itraconazole Plasma Concentration-Time Profiles (A: n = 51 / B: n = 50 / C: n = 52 / D: n = 51)



Disclosures. **All authors:** No reported disclosures.

2230. Analysis of the Microbiological Data from the Delafloxacin (DLX) Phase 3 Community-acquired Bacterial Pneumonia (CABP) Trial

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Background. DLX is a novel fluoroquinolone (FQ) antibiotic with Gram-positive/MRSA, Gram-negative and atypical activity. It offers IV and oral treatment with no QT restrictions. In a Phase 3 study in CABP patients, DLX was non-inferior to moxifloxacin (MOX) in the primary endpoint, early clinical response at 96 ± 24 hours (88.9 vs. 89.0; 95% CI: −4.4, 4.1) in the intent-to-treat (ITT) population. A detailed microbiological analysis was conducted.

Methods. CABP pathogens were identified by culture/non-culture methods. Pathogens identified by non-culture methods included *Streptococcus pneumoniae* (Sp; culture, urinary antigen [UA], nasopharyngeal [NP] swab *lytA* PCR), *Legionella pneumophila* (Lp) (culture, UA, serology), *Mycoplasma pneumoniae* (Mp; culture, serology), and *Chlamydia pneumoniae* (Cp; serology). All other pathogens were identified using