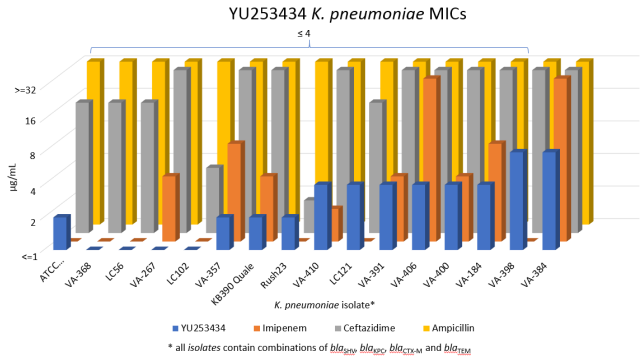

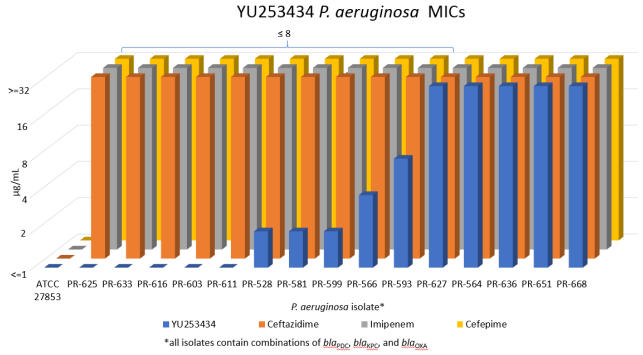

Disclosures. **All authors:** No reported disclosures.

699. Hepatobiliary Safety in Adults With Community-Acquired Bacterial Pneumonia (CABP) Treated With Lefamulin (LEF) or Moxifloxacin (MOX): Pooled Analysis of Lefamulin Evaluation Against Pneumonia (LEAP) 1 and LEAP 2 Study Results

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Background. LEF efficacy and safety were shown in 2 noninferiority trials (LEAP 1/2) vs. MOX in adults with CABP. We assessed the hepatobiliary safety of LEF based on pooled analyses of LEAP 1/2 data.

Methods. In LEAP 1, PORT III–V patients received LEF 150 mg IV q12h for 5–7 days or MOX 400 mg IV q24h for 7 days, with optional IV-to-oral switch (600 mg LEF q12h or 400 mg MOX q24h). In LEAP 2, PORT II–IV patients received oral LEF 600 mg q12h for 5 days or oral MOX 400mg q24h for 7 days. Exclusion criteria included infection with HBV/HCV, acute hepatitis, cirrhosis, AST or ALT >5xULN, total bilirubin >3xULN (unless Gilbert's disease), AST or ALT >3xULN and total bilirubin >2xULN, and manifestation of end-stage liver disease. Hepatic safety was assessed from baseline (BL) and multiple post-BL blood samples using a central laboratory, TEAEs, and expert consultant adjudication. Pooled analyses included all randomized/treated patients (safety population).

Results. Of 1282 randomized/treated patients, 1251 had BL and post-BL hepatobiliary data (table). Post-BL distribution of ALT/AST was generally similar for both groups, although ALT >AST in the absence of muscle injury or alcohol use. Overall, rates of patients experiencing an increase in ALT/AST >3xULN, ALP >2xULN, or total bilirubin >1.5xULN were low (table). Patients with elevated vs. normal BL transaminases (TAs) were more likely to have post-BL elevations >3xULN, but the vast majority remained <5xULN. Among patients with ALT >5xULN, peak increases were generally seen in the first week after the first LEF dose and declined to within/near normal levels by late follow-up (day 28); for MOX, time to peak ALT was less consistent (figure). No LEF pt and 1 MOX pt met laboratory criteria for Hy's Law. Elevations in TAs were reversible, with no evidence of chronic injury. The LEF injury pattern was predominantly hepatocellular (50.0%)/mixed (40.0%), with no apparent gender, age, or ethnic predominance. TEAEs in the hepatobiliary disorders system organ class were reported in 6 (0.9%) LEF patients and 6 (0.9%) MOX patients, with similar levels seen in patients with elevated BL TAs. There were no symptomatic patients, severe disease, or evidence of hypersensitivity.

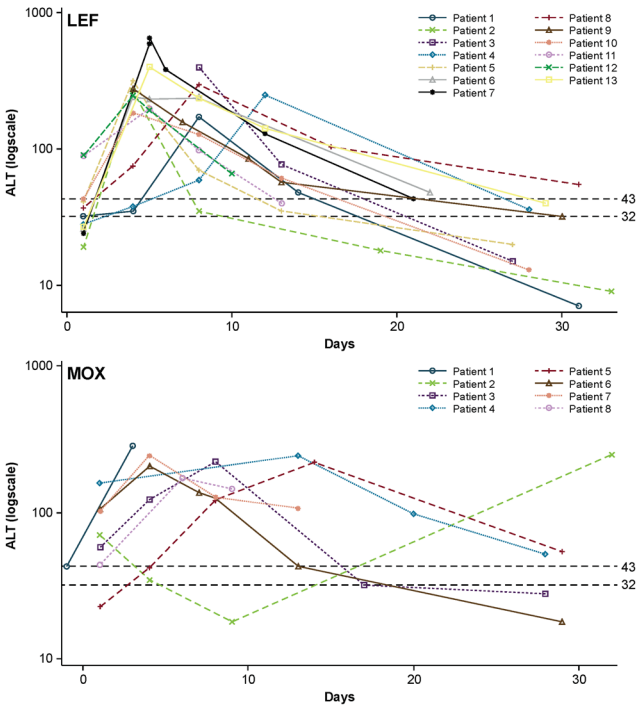
Conclusion. Low incidences of hepatobiliary parameter elevations and TEAEs were observed, with no apparent differences between LEF and MOX.

Table. Maximum Postbaseline Increases in Hepatobiliary Parameters

	LEAP 1		LEAP 2		Pooled	
n (%)	LEF (n=268)	MOX (n=267)	LEF (n=355)	MOX (n=361)	LEF* (n=623)	MOX† (n=628)
ALT >3×ULN	19 (7.1)	17 (6.4)	15 (4.2)	17 (4.7)	34 (5.5)	34 (5.4)
ALT >5×ULN	6 (2.2)	5 (1.9)	7 (2.0)	3 (0.8)	13 (2.1)	8 (1.3)
ALT >10×ULN	1 (0.4)	0	1 (0.3)	0	2 (0.3)	0
AST >3×ULN	11 (4.1)	7 (2.6)	12 (3.4)	8 (2.2)	23 (3.7)	15 (2.4)
AST >5×ULN	2 (0.7)	2 (0.7)	6 (1.7)	5 (1.4)	8 (1.3)	7 (1.1)
AST >10×ULN	1 (0.4)	0	1 (0.3)	0	2 (0.3)	0
ALP >2×ULN	5 (1.9)	5 (1.9)	14 (3.9)‡	6 (1.7)‡	19 (3.0)‡	11 (1.7)‡
Total bilirubin >1.5×ULN	3 (1.1)	3 (1.1)	3 (0.8)	3 (0.8)	6 (1.0)	6 (1.0)
Total bilirubin >2×ULN	0	2 (0.7)	2 (0.6)	0	2 (0.3)	2 (0.3)

ALP=alkaline phosphatase; ALT=alanine aminotransferase; AST=aspartate aminotransferase; LEF=lefamulin; MOX= moxifloxacin; ULN=upper limit of normal.
*Lefamulin 150 mg IV / 600 mg oral.
†Moxifloxacin 400 mg IV / 400 mg oral.
‡For LEAP 2: LEF, n=357; MOX, n=362. For pooled analysis: LEF, n=625; MOX, n=629.

Figure. Individual ALT Values for Patients With Postbaseline ALT >5xULN



ALT=alanine aminotransferase; LEF=lefamulin; MOX=moxifloxacin; ULN=upper limit of normal.
Note: The ALT ULN range for the central laboratory is 32-43 U/L, depending on age and sex.

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700. Safety and Efficacy of Omadacycline in Patients with Diabetes in Phase 3 Clinical Studies

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Background. The risk of serious infections and poor treatment outcomes is reported to be higher in patients with diabetes compared with the general population. Omadacycline (OMC) is an intravenous (IV) and oral aminomethylcycline antibiotic approved in the US to treat acute bacterial skin and skin structure infections (ABSSSI) and community-acquired bacterial pneumonia (CABP) in adults. Here we assessed safety and efficacy results from OMC Phase 3 studies (ABSSSI: Omadacycline in Acute Skin and skin structure Infections Study [OASIS]-1 and OASIS-2; CABP: Omadacycline for Pneumonia Treatment In the Community study [OPTIC]), by diabetes history.

Methods. In OASIS-1 (IV to optional oral medication) and OASIS-2 (oral only), patients were randomized to OMC or linezolid (LZD) for 7–14 days. In OPTIC, patients were randomized to IV OMC or moxifloxacin (MOX) for 7–14 days, with optional transition to oral medication. Data from OASIS-1 and OASIS-2 were pooled, and patient