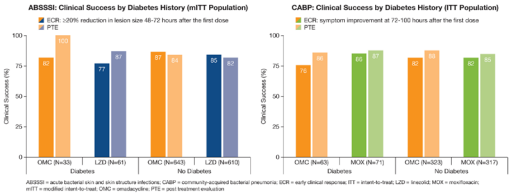
subgroups were defined by any medical history of diabetes (type 1, type 2, or unspecified), or no medical history of diabetes. Efficacy outcomes were early clinical response (ECR) and investigator's assessment of clinical response at post-treatment evaluation (PTE), as defined for each indication. Safety was assessed by treatment-emergent adverse events (TEAEs) and laboratory measures, and data were pooled across the three studies.

***Results.*** A total of 2,150 patients were included, of whom 238 (11.1%) had any history of diabetes ($n$ = 105 for ABSSSI, $n$ = 133 for CABP). In the pooled ABSSSI studies and the CABP study, clinical success at ECR and PTE was similar between patients with or without diabetes, and between OMC and the respective comparator (figure). TEAEs and serious TEAEs, respectively, were reported in similar numbers of OMC-, LZD-, and MOX-treated patients with diabetes (41.8–49.3%, 4.5–7.0%) and without (41.2–48.3%, 1.6–6.9%). Rates of nausea and vomiting, respectively, in patients with diabetes were similar across treatment arms: OMC (5.0%, 5.0%), LZD (7.5%, 6.0%), MOX (7.0%, 2.8%).

***Conclusion.*** Omadacycline efficacy and safety were similar and consistent in patients with or without diabetes.




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

### 701. Comparison of MIC Results for Gepotidacin by Agar Dilution and Broth Microdilution Methods

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**Session:** 68. Novel Antimicrobials and Approaches Against Resistant Bugs
*Thursday, October 3, 2019: 12:15 PM*

***Background.*** Gepotidacin (GSK2140944) is a novel triazaacenaphthylene bacterial type II topoisomerase inhibitor in clinical development for the treatment of gonorrhea and uncomplicated UTI (acute cystitis). Gepotidacin selectively inhibits bacterial DNA gyrase and topoisomerase IV by a unique mechanism not utilized by any currently approved therapeutic agent and demonstrates *in vitro* activity against most target pathogens resistant to established antibacterials, including fluoroquinolones. This study tested the equivalency of minimal inhibitory concentrations (MICs) obtained by 2 reference susceptibility testing methods, agar dilution (AD) and broth microdilution (BMD), for gepotidacin against Gram-positive and Gram-negative organisms.

***Methods.*** Susceptibility testing for both methods was performed on a total of 733 clinical isolates recovered largely in 2016 from over 120 medical centers worldwide. For *N. gonorrhoeae*, only the AD method is recommended by CLSI, therefore BMD was performed using Fastidious Broth for comparison purposes. Essential agreement (EA) based on evaluable results was calculated as the number of isolates with MICs within one 2-fold dilution of the reference method divided by the total number of results. Equivalency was defined using the 95% criteria from the FDA's class II controls document.

***Results.*** The EA observed for gepotidacin with these 2 methods was 85.8% overall and 98.3% when *H. influenzae* and *N. gonorrhoeae* isolates were excluded. Slightly higher gepotidacin MICs were observed when tested by BMD for each of these species/groups; this trend was especially prominent for *E. coli* and *S. pyogenes*. Gepotidacin tested against *H. influenzae* (73.1%) or *N. gonorrhoeae* (28.6%) species had much lower EAs.

***Conclusion.*** Equivalency (EA >95%) was established between AD and BMD methods for determining gepotidacin susceptibility results against *Staphylococcus* spp., *Streptococcus* spp. and *E. coli*. However, for *N. gonorrhoeae* and *H. influenzae*, equivalency between the 2 methods was not established; therefore, future antimicrobial susceptibility testing for gepotidacin against these organisms should adhere to the methods for which quality control ranges and breakpoints are approved.

| Organism / organism group (number of organisms) | % essential agreement[b] | No. of isolates ($log_2$ difference[a]) Higher agar ← dilution MIC | | | | Higher broth microdilution MIC → | | |
|---|---|---|---|---|---|---|---|---|
| | | ≤ -3 | -2 | -1 | 0 | 1 | 2 | ≥ 3 |
| **Gepotidacin** | | | | | | | | |
| All isolates (718) | 85.8 | 16 | 80 | 97 | 318 | 201 | 5 | 1 |
| Isolates excluding *H. influenzae* and *N. gonorrhoeae* (523) | 98.3 | 1 | 2 | 14 | 302 | 198 | 5 | 1 |
| *E. coli* (102) | 97.1 | | | | 48 | 51 | 3 | |
| *Staphylococcus* spp. (110) | 98.2 | | | 3 | 71 | 34 | 2 | |
| *S. aureus* (80) | 97.5 | | | 2 | 53 | 23 | 2 | |
| *S. saprophyticus* (30) | 100.0 | | | 1 | 18 | 11 | | |
| *Streptococcus* spp. (311) | 98.7 | 1 | 2 | 11 | 183 | 113 | | 1 |
| *S. pneumoniae* (101) | 100.0 | | | 4 | 79 | 18 | | |
| β-hemolytic streptococci (105) | 100.0 | | | | 45 | 60 | | |
| *S. pyogenes* (77) | 100.0 | | | | 27 | 50 | | |
| *S. agalactiae* (28) | 100.0 | | | | 18 | 10 | | |
| Viridans group streptococci (105) | 96.2 | 1 | 2 | 7 | 59 | 35 | | 1 |
| *H. influenzae* (104) | 73.1 | 2 | 26 | 64 | 12 | | | |
| *N. gonorrhoeae* (91) | 28.6 | 13 | 52 | 19 | 4 | 3 | | |

[a] The $log_2$ dilution difference calculated as the $log_2$ difference between the broth microdilution and agar dilution MIC value.

[b] Essential agreement calculated as the number of broth microdilution and agar dilution MIC values for each isolate that are ±1 $log_2$ dilution (shaded values), divided by the total number of isolates.

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### 702. Hepatic Safety Among Patients Treated with Anti-Fungal Triazole Agent Posaconazole: Characterization of Adverse events in a Manufacturer's Safety Database

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**Session:** 68. Novel Antimicrobials and Approaches Against Resistant Bugs
*Thursday, October 3, 2019: 12:15 PM*

***Background.*** Second-generation triazoles including posaconazole are highly efficacious for the prophylaxis and salvage treatment of life-threatening invasive fungal diseases. All triazoles have been associated with hepatic adverse events (AEs), which may affect their clinical use; however, risk factors for those AEs are poorly defined.

***Methods.*** Reports of hepatobiliary AEs for posaconazole from clinical trials and post-market use in our company's global safety database were reviewed to characterize concomitant medical conditions and drug exposure.

***Results.*** As of 2018, 444 cases of hepatic AEs were reported; 139 (31%) led to discontinuation of posaconazole. Most hepatic AEs had a time to onset >20 days (55.5%). The most frequent AEs reported (per Medical Dictionary for Regulatory Activities) were: Hyperbilirubinaemia (17%); Hepatotoxicity (13.5%); Hepatic function abnormal (11.5%); and Hepatocellular injury (11.3%). Most patients were adults (18–64 years old) (65%). Hematological malignancy (128 cases, 29%) and hematopoietic stem cell transplant (91 cases, 20%) were leading concurrent medical conditions. Notably, 75% of the cases reported exposure to other drugs (often multiple ones) with known risks for drug-induced liver injury (DILI, e.g., acetaminophen, cytarabine, cyclosporine). Among 139 cases in which posaconazole treatment was discontinued due to hepatic AEs, 6 of the 20 most frequently used co-medications (used by >4.5% of the cases) were classified by the FDA in its DILIRank as "Most-DILI-Concern" (resulting in drug withdrawal, or prominent labeling for severe DILI risk in boxed warning or warnings and precautions), and 7 were "Less-DILI-concern" drugs (DILI risk language in warnings and precautions or adverse reactions). Similarly, of the top 35 concomitant medications for the entire group, 9 are classified as "Most-DILI-Concern" and 12 are "Less-DILI Concern" drugs.

***Conclusion.*** The use of concomitant medications with known risks for hepatic injury appears to be an important contributor to the development of hepatotoxicity in patients treated with posaconazole. Co-administration of these drugs with anti-fungal triazole agents such as posaconazole, when needed, will continue to be carefully monitored.

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

### 703. *In Vitro* Activity of Lefamulin Against Bacterial Pathogens Causing Community-Acquired Bacterial Pneumonia (CABP): SENTRY Surveillance 2017–2018 Results From the United States (US)

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**Session:** 68. Novel Antimicrobials and Approaches Against Resistant Bugs
*Thursday, October 3, 2019: 12:15 PM*

***Background.*** Lefamulin (LEF), a novel pleuromutilin protein synthesis inhibitor in development for use as an empiric IV and oral monotherapy for CABP, recently demonstrated safety and efficacy in two phase 3 trials in adults with CABP (PORT II–V). LEF IV or IV/oral (5–7 days; 10 days for methicillin-resistant *Staphylococcus aureus* [MRSA]) and LEF oral (5 days) were noninferior to MOX IV or IV/oral (7 days; 10 days for MRSA) and MOX oral (7 days) in patients with CABP caused by the most prevalent typical and atypical bacterial pathogens. This study investigated the *in vitro* activity of LEF and comparators against bacterial respiratory pathogens collected in the United States in 2017 and 2018.

***Methods.*** As part of the SENTRY Surveillance Programme, isolates ($n$ = 2299, 1/patient) were collected from 39 medical centers in the United States from patients with community-acquired respiratory tract infections (1812/2299 [78.8%]) and pneumonia in hospitalized patients (487/2299 [21.2%]). LEF and comparators were tested by broth microdilution and CLSI (2019) breakpoints were applied.

***Results.*** LEF demonstrated potent antibacterial activity against all pathogens tested and was unaffected by resistance to other antibiotic classes (table). *Streptococcus pneumoniae* isolates were largely susceptible ( >80%) to most comparators; however, 45.6% and 20.4% were resistant (R) to macrolides and tetracycline, respectively. LEF exhibited a $MIC_{50/90}$ of 0.12/0.25 mg/L for *S. pneumoniae*, including all R subsets. Among *S. aureus* isolates, and particularly MRSA, resistance to macrolides was high (48.5% and 81.2% R, respectively). LEF showed a $MIC_{50/90}$ of 0.06/0.12 mg/L for *S. aureus*, including all R subsets. *Haemophilus influenzae* isolates were susceptible to all comparators except for ampicillin (31.4% R) and trimethoprim-sulfamethoxazole (35.3% R). LEF displayed a $MIC_{50/90}$ of 0.5/2 mg/L for *H. influenzae* isolates. *Moraxella catarrhalis* isolates, which were largely β-lactamase positive (98%), were susceptible to all comparators.

***Conclusion.*** LEF displayed potent *in vitro* activity against contemporary CABP pathogens collected in the United States. LEF activity was unaffected by resistance to other antibiotic classes, including fluoroquinolones, macrolides, β-lactams, and tetracyclines.