-nonsusceptible [MRSA], coagulase negative staphylococci, *Streptococcus pneumoniae* and beta hemolytic streptococci. The parenteral cephem ceftaroline fosamil is approved for treatment of patients with community-acquired bacterial pneumonia caused by *S. pneumoniae* (including cases with concurrent bacteremia), MSSA, *Haemophilus influenzae*, and some species of Enterobacterales. Limited data have been published on the *in vitro* activity of ceftaroline against recent gram-positive clinical isolates known to be frequent bacterial causes of blood stream infections.

Methods. Standard CLSI broth microdilution MIC determinations (M07) were performed with ceftaroline and comparator agents. MICs were interpreted using 2021 CLSI MIC breakpoints. Clinically relevant, non-duplicate, isolates cultured from blood by clinical laboratories in 2012-2019 were tested by the ATLAS (Antimicrobial Testing Leadership and Surveillance) program central laboratory (IHMA, Inc., Schaumburg, IL, USA). In total, 21,967 non-duplicate isolates of *S. aureus*, *S. epidermidis*, *S. pneumoniae* and beta hemolytic streptococci from BSI collected between 2012 and 2019 were tested. Isolates came from (n/%): Asia/South Pacific (2,970/13.5%), Europe (13,691/62.3%), Latin America (2,824/12.9%), MidEast/Africa (1,498/6.8%), and North America (Canada only) (984/4.5%).

Results. Ceftaroline and comparator agent activities are summarized in the following table.

Results Table

Organism (n)*	MIC₉₀ (µg/mL)/%Susceptible				
	CPT	CRO	LZD	DAP	ERY
Staphylococcus aureus, MRSA (2,831)	1/90.8	> 64/na	2/100	1/99.7	> 8/35.4
Staphylococcus aureus, MSSA (3,969)	0.25/100	4/na	2/100	1/99.9	> 4/75.8
Staphylococcus epidermidis (2,344)	0.5/na	> 32/na	2/98.2	1/99.8	> 8/30.8
Streptococcus pneumoniae (2,861)	0.12/99.9	0.5/96.9	1/100	0.5/na	> 1/77.6
Beta-hemolytic streptococci (1,698)†	0.015/100	0.12/99.9	1/100	0.5/100	> 1/80.6

* n refers to number of isolates tested against ceftaroline; numbers may vary for comparators (range 901-6635); †includes *S. agalactiae* (n=466), *S. dysgalactiae* (n=343), and *S. pyogenes* (n=872).
CPT, ceftaroline; CRO, ceftriaxone; LZD, linezolid; DAP, daptomycin; ERY, erythromycin; na, no MIC breakpoints available.

Conclusion. Greater than 99% of *S. pneumoniae,* beta-hemolytic streptococci and MSSA isolates included in a 2012-2019 collection of gram-positive blood stream pathogens were susceptible to ceftaroline. 90.8% of MRSA were susceptible, and 9.1% isolates categorized as susceptible-dose dependent (MIC, 2-4 µg/mL); four isolates (two from Thailand and one each from China and S. Korea) were resistant to ceftaroline (MIC >4 µg/mL). The ceftaroline MIC₉₀ for *S. epidermidis* was 0.5 µg/mL, with 97.7% of MICs ≤1 µg/mL. Ceftaroline continues to demonstrate potent *in vitro* activity against clinically relevant pathogens associated with BSI.

Disclosures. **Meredith Hackel, PhD MPH**, IHMA (Employee)**Pfizer, Inc.** (Independent Contractor) **Gregory Stone, PhD**, **AztraZeneca** (Shareholder, Former Employee)**Pfizer, Inc.** (Employee) **Daniel F. Sahm, PhD**, IHMA (Employee)**Pfizer, Inc.** (Independent Contractor)

1225. *In Vitro* Activity of Aztreonam-Avibactam and Comparator Agents Against Enterobacterales Collected from Geriatric Patients in ICU and non-ICU wards, ATLAS Surveillance Program 2016-2019

Sibylle Lob, PhD[1]; Krystyna Kazmierczak, PhD[1]; Francis Arhin, PhD[2];
Daniel F. Sahm, PhD[1]; [1]IHMA, Inc., Schaumburg, IL; [2]Pfizer Canada, Kirkland, Quebec, Canada

Session: P-72. Resistance Mechanisms

Background. Elevated resistance rates have been reported in ICUs. Aztreonam (ATM) combined with avibactam (AVI) is being developed for use against drug-resistant Enterobacterales (Ebact), including metallo-β-lactamase (MBL)-positive isolates. We examined the activity of ATM-AVI and comparators against Ebact isolates collected from geriatric patients in ICU and non-ICU wards as part of the ATLAS surveillance program.

Methods. 23754 non-duplicate Ebact isolates were collected in 53 countries in Asia/Pacific (excluding mainland China and India), Europe, Latin America, and Middle East/Africa from patients ≥65 years with lower respiratory tract (LRTI), urinary tract (UTI), skin and soft tissue (SSTI), intra-abdominal (IAI), and bloodstream (BSI) infections. Susceptibility testing was performed by CLSI broth microdilution and values interpreted using CLSI 2021 breakpoints. PCR and sequencing were used to determine the β-lactamase genes present in isolates with meropenem MIC >1 µg/mL, and *Escherichia coli*, *Klebsiella* spp. and *Proteus mirabilis* with ATM or ceftazidime MIC >1 µg/mL.

Results. Susceptibility of the studied comparator agents was generally slightly lower among Ebact from BSI than other infection types (Table). Susceptibility was also generally lower among Ebact from ICU than non-ICU wards by up to 10 percentage points, and MIC₉₀ values were up to 32-fold higher. ATM-AVI MIC₉₀ values were within one doubling-dilution across all studied strata (0.12-0.25 µg/mL), were comparable to or lower than for meropenem in all strata, and were 2 to ≥9 dilutions lower than all other tested comparators. MBL-positive Ebact were found in 1.5% of LRTI (n=91), 1.2% of UTI (n=70), 1.1% of SSTI (n=52), 1.3% of BSI (n=49), and 0.7% of IAI isolates (n=22). MBL-positive rates were higher among ICU (1.7%, n=101) than non-ICU isolates (1.0%, n=183). ATM-AVI MIC₉₀ values were 0.5 µg/mL against MBL-positive isolates from all ward and infection types except SSTI (MIC₉₀ 0.25 µg/mL) and BSI (MIC₉₀ 1 µg/mL), 2-4 dilutions lower than tigecycline and at least 5-10 dilutions lower than the other comparators.

Results Table

	MIC₉₀/% Susceptible (Infection Type/Ward Type)									
	All	LRTI		UTI		SSTI		BSI		IAI	
		ICU	Non-ICU	ICU	Non-ICU	ICU	Non-ICU	ICU	Non-ICU	ICU	Non-ICU
Drug	(n=23754)	(n=2799)	(n=3464)	(n=674)	(n=4969)	(n=673)	(n=4050)	(n=893)	(n=2924)	(n=738)	(n=2570)
ATM-AVI	0.12/NA	0.25/NA	0.12/NA	0.25/NA	0.12/NA	0.25/NA	0.12/NA	0.25/NA	0.12/NA	0.25/NA	0.25/NA
ATM	64/73.9	128/68.7	64/74.9	128/70.8	64/74.9	128/72.1	64/78.2	128/64.1	64/74.1	128/71.5	64/75.9
FEP	>16/77.0	>16/74.8	>16/78.1	>16/71.4	>16/75.7	>16/75.8	>16/80.4	>16/66.5	>16/76.2	>16/77.5	>16/80.9
MEM	0.12/95.7	0.12/94.0	0.12/96.0	0.25/93.3	0.12/96.5	0.12/93.5	0.12/96.6	4/88.7	0.12/96.0	0.12/94.6	0.12/97.4
AMK	8/97.4	8/96.6	4/97.9	8/96.6	8/97.2	8/97.5	4/97.7	8/94.3	8/98.2	4/97.7	4/98.2
TGC	2/96.8	2/97.0	1/97.1	2/96.4	2/96.5	2/93.8	2/95.7	2/96.8	1/98.0	1/97.8	1/97.9

LRTI, lower respiratory tract infection; UTI, urinary tract infection; SSTI, skin and soft tissue infection; BSI, bloodstream infection; IAI, intra-abdominal infection; ATM-AVI, aztreonam-avibactam; ATM, aztreonam, FEP, cefepime; MEM, meropenem; AMK, amikacin; TGC, tigecycline.
Isolates for which data regarding infection type and ward type were not available were excluded from the analysis.

Conclusion. ATM-AVI could provide a valuable therapeutic option for treatment of infections caused by Ebact in patients ≥65 years old in both ICU and non-ICU wards.

Disclosures. **Sibylle Lob, PhD**, IHMA (Employee)**Pfizer, Inc.** (Independent Contractor) **Krystyna Kazmierczak, PhD**, IHMA (Employee)**Pfizer, Inc.** (Independent Contractor) **Francis Arhin, PhD**, Pfizer, Inc. (Employee) **Daniel F. Sahm, PhD**, IHMA (Employee)**Pfizer, Inc.** (Independent Contractor)

1226. In Vitro Activity of Tebipenem and Comparators Against *Enterobacterales* Collected from Patients with Bloodstream Infections as Part of the 2019 Global STEWARD Surveillance Program

Ian A. Critchley, Ph.D.[1]; Nicole Cotroneo[1]; Rodrigo E. Mendes, PhD[2];
Michael J. Pucci, PhD[1]; [1]Spero Therapeutics, Cambridge, Massachusetts; [2]JMI Laboratories, North Liberty, Iowa

Session: P-72. Resistance Mechanisms

Background. Bloodstream infections (BSI) are a significant cause of morbidity and mortality. *Enterobacterales* (ENT) are frequently implicated in BSI with an increase in organisms producing extended-spectrum β-lactamase (ESBL). This challenges a possible transition to current oral agents due to co-resistance. Carbapenems are active against ESBL-ENT and tebipenem (TBP) is a new oral carbapenem in clinical development. The aim of the study was to assess resistance (R) among BSI isolates and activity of TBP and comparators against ENT collected in a 2019 surveillance study.

Methods. 2612 ENT from BSI were centrally tested by reference broth microdilution. Isolates were from medical centers in the US, Europe (EU), Latin America (LA) and Asia Pacific (AP). MIC results were interpreted according to CLSI, including ESBL assignment. CRE were sequenced to identify carbapenemase genes.

Results. Among the ENT, non-susceptibility (NS) rates to ceftazidime, levofloxacin were 20.4 and 27.0%, respectively, and R to trimethoprim-sulfamethoxazole was 31.1%. NS rates for ertapenem (ETP) and MER were 4.9 and 2.7%, respectively. MIC₉₀s for TBP, ETP and MER were 0.12, 0.12 and 0.06 µg/mL, respectively. The MIC₉₀ for TBP was 0.06 µg/mL for ENT from the US and 0.12 µg/mL for isolates from EU, LA and AP. *Escherichia coli* (EC) was the most prevalent (52% of ENT isolates) and the MIC₉₀ for TBP ranged from 0.015 µg/mL for isolates in the US/EU to 0.03 µg/mL for isolates in LA/AP. ESBL-EC ranged from 15.7% in US to 34.3% in LA. TBP was active against ESBL-EC with an MIC₉₀ of 0.03 µg/mL. *Klebsiella pneumoniae* (KP) accounted for 22.7% of BSI caused by ENT and TBP MIC₉₀ ranged from 0.06 µg/mL for KP in US to >8 µg/mL in EU, LA and AP. MER-R KP ranged from 2.4% in US to 14.9% in LA. KPC-2, -3 and NDM were the most prevalent carbapenemases. TBP MIC₉₀ values for MER-S ESBL KP in EU, LA and AP were ≤0.12 µg/mL.

Conclusion. TBP activity was similar to ETP and MER against ENT responsible for BSI. R to oral agents was compromised by ESBL co-resistance. TBP was among the most active agents against EC isolates and ESBL phenotypes. Among KP, TBP was more active against isolates from US where prevalence of CRE was lower than EU, LA and AP. TBP may be considered as an alternative oral option for BSI caused by non-CRE ESBL-producing ENT.

Disclosures. **Ian A. Critchley, Ph.D.**, Spero Therapeutics (Employee, Shareholder) **Nicole Cotroneo**, Spero Therapeutics (Employee, Shareholder) **Rodrigo E. Mendes, PhD**, **AbbVie** (Research Grant or Support)**AbbVie (formerly Allergan)** (Research Grant or Support)**Cipla Therapeutics** (Research Grant or Support)**Cipla USA Inc.** (Research Grant or Support)**ContraFect Corporation** (Research Grant or Support)**GlaxoSmithKline, LLC** (Research Grant or Support)**Melinta Therapeutics, Inc.** (Research Grant or Support)**Melinta Therapeutics, LLC** (Research Grant or Support)**Nabriva Therapeutics** (Research Grant or Support)**Pfizer, Inc.** (Research Grant or Support)**Shionogi** (Research Grant or Support)**Spero Therapeutics** (Research Grant or Support)

1227. A Survey Study of Healthcare Resource Use, and Direct and Indirect Costs, Among Females with an Uncomplicated Urinary Tract Infection in the United States

Jeffrey Thompson, PhD[1]; Alen Marijam, MSc[2]; Fanny S. Mitrani-Gold, MPH[3]; Jonathon Wright, BSc[1]; Ashish V. Joshi, PhD[3]; [1]Kantar Health, New York, NY, USA, New York, New York; [2]GlaxoSmithKline plc., Collegeville, PA, USA, Collegeville, Pennsylvania; [3]GlaxoSmithKline plc, Collegeville, PA, USA, Chicago, Illinois

Session: P-72. Resistance Mechanisms

Background. Uncomplicated urinary tract infections (uUTI) account for a large proportion of primary care antibiotic (AB) prescriptions. This study assessed uUTI-related healthcare resource use (HRU) and costs in US females with a self-reported uUTI.

Methods. We surveyed US females aged ≥ 18 years who participated in web-based surveys (fielded August 28–September 28, 2020 by Dynata, EMI, Lucid/Federated, and Kantar Profiles). Participants had a self-reported uUTI ≤ 60 days prior, and took ≥ 1 oral AB for their uUTI. Those reporting signs of complicated UTI were excluded. HRU was measured via self-reported primary care provider (PCP), specialist, urgent care, emergency room (ER) visits, and hospitalizations. Direct costs were calculated as sum of self-reported and HRU monetized with Medical Expenditure Panel Survey estimates. Indirect costs were calculated via Work Productivity and Impairment metrics monetized with Bureau of Labor Statistics estimates. Participants were stratified by number of oral ABs prescribed (1/2/3+) and therapy appropriateness (1 AB [1st line/2nd line]/multiple [any line] AB) for most recent uUTI. Multivariable regression modeling was used to compare strata; 1:1 propensity score matching assessed uUTI burden vs matched population (derived from the 2020 National Health and Wellness Survey [NHWS]).

Results. In total, 375 participants were eligible for this analysis. PCP visits (68.8%) were the most common HRU. Across participants, there were an average of 1.46 PCP, 0.31 obstetrician/gynecologist, 0.41 urgent care and 0.08 ER visits, and 0.01 hospitalizations for most recent uUTI (Table 1). Total mean uUTI-related direct and indirect costs were $1289 and $515, respectively (Table 1). Adjusted mean total direct costs were significantly higher (Table 2) for participants in the '2 AB' cohort vs the '1 AB' cohort ($2090 vs $776, p < 0.0001), and for the 'multiple AB' vs '1 AB, 1st line' cohorts ($1642 vs $875, p=0.002). Participants in the uUTI cohort reported worse absenteeism (+15.3%), presenteeism (+46.5%), overall work impairment (+52.4%), and impact on daily activities (+50.7%) vs NHWS cohort (p < 0.0001, Table 3).

Table 1. Overall mean uUTI-related healthcare resource use, direct, and indirect cost data

	N=375
uUTI-related HRU, visits in prior 12 months, mean (SD)	
Primary care physician	1.46 (5.34)
OB/GYN	0.31 (2.91)
Urgent care facility	0.41 (2.64)
Emergency room visit	0.08 (0.34)
Hospital (admitted/hospitalized)	0.01 (0.09)
uUTI-related direct costs ($), mean (SD)	
Total OOP costs	90 (168)
PCP visit-related costs	491 (1828)
OB/GYN visit-related costs	105 (966)
Urgent care visit-related costs	390 (2049)
ER visit-related costs	96 (421)
Hospitalization-related costs	118 (1315)
Total direct costs	1289 (3960)
uUTI-related indirect costs ($), mean (SD)	
Cost of presenteeism	348 (230)
Cost of absenteeism	166 (228)
Total indirect cost	515 (311)
WPAI, % impairment (SD)	
Absenteeism	15.9 (21.2)
Presenteeism	50.9 (27.8)
Overall work impairment	56.2 (29.1)
Impact on daily activities	55.0 (26.8)

HRU, healthcare resource use; OB/GYN, obstetrician/gynecologist; OOP, out of pocket; PCP, primary care practitioner; SD, standard deviation; uUTI, uncomplicated urinary tract infection; WPAI, Work Productivity and Activity Impairment survey.

Table 2. Estimated uUTI-related direct costs stratified by (A) number of AB and (B) appropriateness of AB therapy used to treat last uUTI

Cohort		Estimate (SE)	p-value	Adj mean cost (SE), $
(A)	3+ AB, any line (n=52)	0.29 (0.23)	0.197	1041 (215)
	2 AB, any line (n=88)	0.99 (0.19)	< 0.0001*	2090 (343)
	1 AB, any line (n=235)	Reference		776 (76)
(B)	Multiple AB, any line (n=140)	0.63 (0.20)	0.002*	1642 (217)
	1 AB, 2nd line (n=112)	-0.26 (0.21)	0.204	673 (98)
	1 AB, 1st line (n=123)	Reference		875 (125)

*Statistically significant (p < 0.05). Number of AB used for most recent uUTI based on self-report from participants; '1 AB, 1st line' defined as only one 1st line oral AB used (self-reported) to treat last uUTI (trimethoprim-sulfamethoxazole, nitrofurantoin, fosfomycin); '1 AB, 2nd line' defined as only one 2nd line oral AB used (self-reported) to treat last uUTI (ciprofloxacin, ofloxacin, levofloxacin, amoxicillin-clavulanate, cefdinir, cefaclor, cefpodoxime-proxetil, cephalexin); 'Multiple AB, any line' defined as two or more different AB (any line) used (self-reported) for most recent uUTI. '1 AB, any line' is the reference group for part (A) of the table, '1 AB, 1st line' is the reference group for part (B) of the table.

AB, antibiotic(s); Adj, adjusted; SE, standard error; uUTI, uncomplicated urinary tract infection.

Table 3. Mean Work Productivity and Activity Impairment data for uUTI and NHWS cohorts

Outcomes (adjusted)	uUTI cohort Mean score (SD)	NHWS cohort Mean score (SD)	p-value	Incremental burden of uUTI (%)	Interpretation
Absenteeism	16.4 (3.4)	1.1 (0.2)	< 0.0001*	15.3	Approximately 6 hours of missed work in uUTI cohort
Presenteeism	53.8 (6.7)	7.4 (0.9)	< 0.0001*	46.5	Ability to work while working impacted by ~47% in uUTI cohort
Overall work impairment	60.6 (7.4)	8.2 (1.0)	< 0.0001*	52.4	Overall ability to work impacted by ~52% in uUTI cohort
Impact on daily activities	59.0 (7.1)	8.3 (1.0)	< 0.0001*	50.7	Overall daily activities impacted by ~51% in uUTI cohort

*Statistically significant (p < 0.05).

NHWS, National Health and Wellness Survey; SD, standard deviation; uUTI, uncomplicated urinary tract infection.

Conclusion. Inadequate treatment response, evident by multiple AB use, was associated with an increase in uUTI-related costs, including productivity loss.

1228. Outcomes Associated with Empiric Cefepime or Meropenem for Bloodstream Infections Caused by Ceftriaxone-Resistant, Cefepime-Susceptible *Escherichia coli* and *Klebsiella pneumoniae*

Brian E. Frescas, PharmD[1]; Christopher McCoy, PharmD, BCIDP[1]; James Kirby, MD, D(ABMM)[1]; Robert Bowden, BS[1]; Nicholas J. Mercuro, PharmD[1]; [1]Beth Israel Deaconess Medical Center, Boston, Massachusetts

Session: P-72. Resistance Mechanisms

Background. Cefepime is a 4th generation cephalosporin frequently used for empiric sepsis therapy. Dose- and MIC-dependent efficacy of cefepime is supported by the Clinical & Laboratory Standards Institute, however its use in infections due to extended-spectrum beta-lactamase-producing *Enterobacterales* is controversial. This study aims to compare outcomes in patients given empiric meropenem or cefepime for bloodstream infections (BSI) caused by ceftriaxone-resistant *E. coli* and *K. pneumoniae*.

Methods. This single-center retrospective cohort included adults hospitalized from 2010 - 2020 and received empiric cefepime or meropenem for BSI caused by ceftriaxone-resistant *E. coli* or *K. pneumoniae*. In the cefepime group, only organisms with MIC ≤ 2 mg/L were included. Patients who received the empiric agent for < 48 hours, or received an additional active agent within 48 hours were excluded. The primary outcome was 30-day mortality; secondary outcomes were recurrent infection, readmission, and time to clinical stability. Chi-squared or Fisher's exact was used for categorical variables and Mann-Whitney-U for continuous variables. Inverse probability treatment weighing was used to determine the impact of empirical therapy on clinical stability at 48 hours.

Results. Fifty-four patients were included: 36 received empiric meropenem, 18 received cefepime. There were no significant differences in baseline severity of illness or comorbid conditions. Urinary source was less common in the meropenem group compared to cefepime (52.8 vs 83.8%, p=0.028) (Table 1). There was no difference in 30-day mortality between meropenem and cefepime (2.8 vs 11.1%, p = 0.255). More patients achieved clinical stability at 48 hours on empiric meropenem compared to cefepime (75 vs 44.4%, p = 0.027), and time to clinical stability was significantly shorter (median 21.3 vs 38.5 hours, p = 0.016). Most patients in the meropenem and cefepime groups completed definitive treatment with a carbapenem (88.9 vs 72.2%, p=0.142).

Table 1: Results

Outcomes	Total (n=54)	Meropenem (n=36)	Cefepime (n=18)	p
30-day mortality, n (%)	3 (5.6%)	1 (2.8%)	2 (11.1%)	0.255
14-day mortality, n (%)	2 (3.7%)	1 (2.8%)	1 (5.6%)	1.000
Recurrent BSI in 90 days, n (%)	5 (9.8%)	3 (8.6%)	2 (12.5%)	0.643
Recurrent infection with same organism in 90 days, n (%)	16 (31.4%)	8 (22.9%)	8 (50%)	0.053
90-day Readmission, n (%)	23 (45.1%)	14 (40%)	9 (56.3%)	0.279
90-day Readmission for infection from same organism, n (%)	13 (56.5%)	7 (50%)	6 (66.7%)	0.669
Clinical stability at 48 hours, n (%)	35 (64.8%)	27 (75%)	8 (44.4%)	0.027
Time to clinical stability, hours (IQR)	30.6 [4.1 - 51.4]	21.3 [3.2-48.6]	38.5 [18.9-73.2]	0.016
Time to resolution of signs/symptoms of infection, hours (IQR)	34.3 [21.3 - 59.6]	32.8 [18.5-57.5]	48.6 [33.5-87.4]	0.264
Clostridioides difficile infection, n (%)	2 (3.7%)	0 (0%)	2 (11.1%)	0.107

Summary of primary and secondary outcomes

Conclusion. There was no difference in mortality between patients receiving empiric cefepime for BSI due to ceftriaxone-resistant *Enterobacterales*, with cefepime MIC ≤ 2 mg/L, compared to meropenem; however, time to clinical stability was significantly delayed.

1229. Antimicrobial Activity of Plazomicin against Multidrug-resistant *Enterobacterales*: Results from 3 Years of Surveillance in Hospitals in the United States (2018–2020)

Cecilia G. Carvalhaes, MD, PhD[1]; Jaideep Gogtay, n/a[2]; Cheung Yee, MSc, PhD[3]; Sandhya Das, n/a[2]; Mariana Castanheira, PhD[4]; Mariana Castanheira, PhD[4]; Rodrigo E. Mendes, PhD[4]; Helio S. Sader, MD, PhD, FIDSA[4]; [1]JMI Laboratories, Inc., North Liberty, Iowa; [2]Cipla Ltd., Mumbai, Maharashtra, India; [3]Cipla Therapeutics, Warren, New Jersey; [4]JMI Laboratories, North Liberty, IA