were susceptible). Mecillinam showed the lowest MIC_{90} value of all single antibiotics tested. The highest MIC_{90} was 128 µg/mL for both nitrofurantoin and cefotaxime. The lowest percentage of resistance was obtained with fosfomycin (1.7%), followed by mecillinam (4%).

Table 1: Summary MIC and susceptibility data for all isolates tested (n=1075)

	MIC (µg/mL)				CLSI susceptibility			
Drug	MIC 50	MIC 90	MIN	MAX	Breakpoints (S|I|R)	%S	%I	%R
CTZ	>64	>64	≤0.25	>64	≤1 | 2 | ≥4	32.4	1.1	66.5
CTZ/CLAV [4 µg/mL]	≤0.25	1	≤0.25	32	No Breakpoints Defined	-	-	-
CTX	16	128	≤0.25	>128	≤4 | 8 | ≥16	37.4	7.1	55.5
CTX/CLAV [4 µg/mL]	≤0.25	2	≤0.25	64	No Breakpoints Defined	-	-	-
CRO	0.03	>8	≤0.015	>8	≤1 | 2 | ≥4	81.4	0.6	18.1
CIP	0.015	>8	≤0.002	>8	≤0.25 | 0.5 | ≥1	77.4	2.1	20.6
FOS	1	32	0.25	>256	≤64 | 128 | ≥256	97.6	0.7	1.7
MEC*	0.25	2	≤0.015	>128	≤8 | 16 | ≥32	95.0	1.0	4.0
NIT	16	128	≤2	>128	≤32 | 64 | ≥128	69.6	14.5	15.9
SXT (1:19)	0.12	>8	≤0.015	>8	≤2/38 | – | ≥4/76	73.8	-	26.2

*Using CLSI breakpoints for *E. coli*
CLSI: Clinical & Laboratory Standards Institute; CTZ: ceftazidime; CTZ/CLAV: ceftazidime/clavulanate; CTX: cefotaxime; CTX/CLAV: cefotaxime/clavulanate; CRO: ceftriaxone; CIP: ciprofloxacin; FOS: fosfomycin; I: intermediate; MEC: mecillinam; MIC: minimum inhibitory concentration; NIT: nitrofurantoin; R: resistance; S: susceptibility; SXT: trimethoprim/sulfamethoxazole

Conclusion. Overall, mecillinam showed excellent activity and a comparable resistance profile to fosfomycin. Resistance rates to ceftazidime, cefotaxime, ciprofloxacin and trimethoprim/sulfamethoxazole of greater than 20% are concerning due to the frequent use of these antibiotics in clinical practice to treat UTIs. Taken together, these data demonstrate that mecillinam has promising activity, with low resistance observed in Enterobacterales species causing UTIs in the USA. Clinical development of mecillinam in the USA is ongoing.

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1044. *In vitro* Activity of Tebipenem Against Relevant Clinical Isolates in the Presence of Pulmonary Surfactant

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Session: P-59. New Drug Development

Background. Tebipenem (TBP) is an orally administered broad-spectrum carbapenem antibiotic under development for the treatment of acute pyelonephritis and complicated urinary tract infections. This study evaluated the effect of bovine pulmonary surfactant (BPS) on the *in vitro* activity of TBP and ertapenem (ETP) against a recent collection of clinical isolates.

Methods. A total of 10 isolates recovered from patients with infections in 2018 were tested for antimicrobial susceptibility to TBP and ETP in the absence or presence of 1%, 5%, or 10% BPS (Infasurf; ONY Biotech). These isolates included the following species: *C. freundii*, *E. cloacae*, *E. coli*, *H. influenzae*, *H. parainfluenzae*, *K. pneumoniae*, methicillin-susceptible *S. aureus*, *M. catarrhalis*, *S. pneumoniae*, and *S. pyogenes*. Isolates were tested with the appropriate broth microdilution method for each organism as specified by CLSI. For most organisms, MICs were determined in cation-adjusted Mueller-Hinton broth (CAMHB). CAMHB was supplemented with 2.5-5% lysed horse blood for streptococci and *Haemophilus* Test Medium broth for *Haemophilus* spp. Daptomycin (DAP) was tested against *S. aureus* ATCC 29213 as a positive control.

Results. All isolates displayed TBP MIC values ranging from ≤0.004 to 0.06 mg/L in media without BPS. There were no observed MIC increases >2-fold in the presence of BPS. 4 of the 10 isolates displayed slightly higher (≥4-fold) ETP than TBP MIC values. The ETP MIC values ranged from 0.015-0.25 mg/L in media without BPS. Similarly, there were no observed instances of a >2-fold shift toward lower potency in the presence of BPS. For both TBP and ETP, MIC endpoint values were easily determined, except for in the case of the 2 *Haemophilus* strains growing in the presence of 5% or 10% BPS. For these conditions, resazurin was added to establish an MIC value. The MIC values found with this method did not differ from the MIC values found in either HTM media or HTM media with 1% BPS. As expected, the addition of BPS shifted DAP *S. aureus* MIC values to >8 mg/L for all 3 BPS concentrations.

Conclusion. TBP displayed potent activity against all isolates tested, as all observed MIC values were ≤0.06 mg/L. The addition of BPS to the testing medium did not affect the *in vitro* MIC values of TBP or ETP against these species.

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1045. Safety of the Synthetic Saponin Adjuvant TQL1055: Preliminary Results from a First-in-humans Trial

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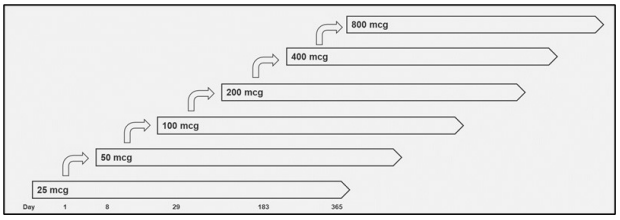
Session: P-60. New Vaccines

Background. Saponin adjuvants reliably enhance immune response to a variety of antigens, but their use is hindered by dose-limiting toxicities and supply constraints. TQL1055 is a semi-synthetic analog of the natural saponin adjuvant QS-21, rationally modified to improve tolerability and enable large-scale manufacturing. We previously showed that the combination of acellular pertussis vaccine (aP) and TQL1055 was well-tolerated and increased anti-pertussis toxin (PT) antibody responses in mice and rabbits, with a no observed adverse effect level (NOAEL) > 2000 mcg/dose.

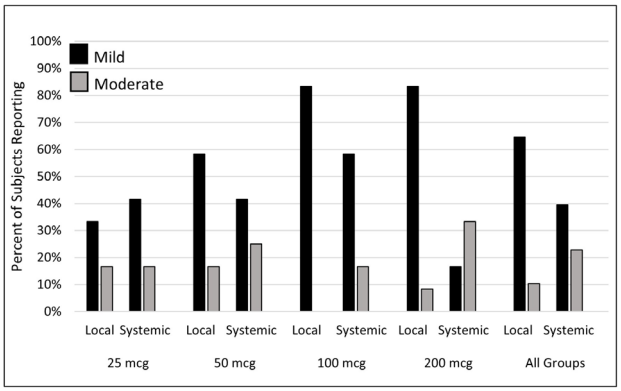
Methods. Here we report interim results from a Phase 1 first-in-humans dose-escalation study of TQL1055. Healthy adults 18 to 50 years of age were sequentially enrolled into 6 groups (n=12/group) and randomized 10:2 to receive one intramuscular dose of aP + TQL1055 or aP alone on Day 1. TQL1055 dose increased by group from 25 to 800 mcg (Figure 1). Local adverse events (AEs) (injection site pain, redness, swelling) and systemic AEs (fever, chills, headache, fatigue, myalgia, arthralgia, nausea, vomiting, diarrhea) were solicited through Day 8. Clinical laboratory panels (chemistry, hematology, coagulation) were performed on Days 1 (pre-dose), 8, and 29. Serious AEs were collected through Day 365. Antibodies to PT were assessed at all visits.

Figure 1. Study Design



Results. Blinded safety data from the first four groups (n=48) through Day 8 were analyzed, including 2 subjects/group receiving aP alone. All solicited AEs were mild or moderate (Figure 2). Local AEs, mainly injection site pain, occurred in 75% of subjects (mild 65%, moderate 10%). The incidence of total local AEs increased with TQL1055 dose, from 50% at 25 mcg to 92% at 200 mcg. The mean duration of local AEs was 1.8 days and also increased with TQL1055 dose, from 1.3 days at 25 mcg to 2.1 days at 200 mcg. Systemic AEs, mostly fatigue, headache, and nausea, occurred in 63% of subjects (mild 40%, moderate 23%), with no fevers. The mean duration of systemic AEs was 1.4 days, with no association with TQL1055 dose. No severe or serious adverse events were reported.

Figure 2. Solicited Adverse Events by Severity and TQL1055 Dose



Conclusion. In this early analysis, the safety profile of aP + TQL1055 appears similar to that of licensed aP vaccines, without severe or prolonged injection site pain. These data support further dose escalation and assessment of immunogenicity.

Disclosures. **Sean R. Bennett, MD PhD**, **Adjuvance Technologies** (Employee) **Tyler Martin, MD**, **Adjuvance Technologies** (Employee, Shareholder)

1046. Immunogenicity and Safety of a Quadrivalent Meningococcal Conjugate Vaccine (MenACYW-TT) Administered as a Booster to Adults ≥ 59 Years of Age

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