Terms. We excluded 80 HIV-infected and identified association of the infection with known risk factors.

Results. Of 570 patients, 491 HIV-uninfected patients with DMAC were studied. Underlying structural pulmonary diseases were COPD and bronchiectasis (51% and 47%, respectively). Two hundred ten patients had concomitant malignancy of which lung cancer was the most frequent (43%). Seventy-nine percent were receiving corticosteroids and 10 patients (2%) were on TNF inhibitors (2%).

Conclusion. In this study, majority of patients with DMAC are HIV-uninfected. Larger studies should focus on identifying the prevalence and risk factors of DMAC in the post-AIDS era.

Table: Distribution of the Sample According to Associated Conditions

	N = 490 (%)
Age, years	
Senior (>65)	330 (67%)
Adult (18–65)	160 (33%)
Female	310 (63)
Smoking history	420 (86)
Bronchiectasis	230 (47)
Previous pulmonary tuberculosis	40 (8)
COPD	250 (51)
HTN	310 (63)
Diabetes mellitus	130 (27)
Chronic kidney disease	110 (22)
Interstitial lung disease	90 (18)
Inflammatory bowel disease	20 (4)
Concomitant malignancy	210 (43)
Lung	60 (28)
GI	50 (23)
Head and neck	40 (19)
Hematological	40 (19)
Renal	30 (14)
Chronic oral corticosteroid treatment	390 (79)
Tumor necrosis factor alpha inhibitor therapy	10 (2)

COPD; chronic obstructive pulmonary disease, HTN; hypertension, GI gastrointestinal.

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785. Treatment of *Mycobacterium immunogenum* Skin and Soft-Tissue Infections: A Case in a Peritoneal Dialysis Patient

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Background. *Mycobacterium immunogenum* is a somewhat recently identified species of rapidly growing nontuberculous mycobacteria, genetically related to *M. abscessus* and *M. chelonae*. Resistance patterns of rapidly growing nontuberculous mycobacterium species can make them difficult to treat. This is particularly true of *M. immunogenum*, in part due to the infrequency of reported cases of human infection and limited data to guide therapy.

Methods. We present here a case of *M. immunogenum* skin and soft-tissue infection at the site of insertion of a peritoneal dialysis catheter in a patient with end-stage renal disease. He initially presented with nodular subcutaneous lesions around his catheter site that progressed through oral antibiotics. This led to sampling which confirmed the diagnosis of *M. immunogenum*. We conducted a review of the literature to identify previously reported cases of *M. immunogenum*, including skin and soft-tissue infections, and used these data to guide management.

Results. We reviewed 11 reports (cases and case series) of *Mycobacterium immunogenum* in the literature. Susceptibilities often take weeks to return, and so empiric therapy is based on case series, and then later adjusted based on susceptibilities. Patients received combined antimicrobial regimens with durations of 2 weeks to 12 months, with variable outcomes. Several required surgical debridement, as was the case with our patient. His PD catheter was removed and he was treated empirically with amikacin, azithromycin, and tigecycline intravenous induction. His ultimate long-term regimen was later switched to azithromycin, clofazimine, and tedizolid due to side effects and the eventually available susceptibility profile.

Conclusion. The treatment of *M. immunogenum* remains a challenge due to the relative scarcity of data to guide treatment, and consequent lack of systemic approach to therapy. Most reported cases involve the use of a macrolide, often in combination with an aminoglycoside or a fluoroquinolone. Several started with intravenous induction, followed by transition to oral therapy on the order of weeks to months. Others also require surgical debridement. More data are required to develop a standardized approach to the treatment of *M. immunogenum*.

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

786. Ceftaroline and Avibactam? Is This a Potential Combination for *Mycobacterium abscessus* Infection?

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Background. *Mycobacterium abscessus* harbors a β-lactamase enzyme, Bla_{Mab}, able to hydrolyze penicillins, most cephalosporins and carbapenems. As of today, management of *M. abscessus* with β-lactams does not include combination of β-lactamase inhibitors. The potential benefit of combinations of several β-lactams with new diazabicyclooctane (DBO) inhibitors, such as relebactam and avibactam, has not been well studied. Based upon the ability to inhibit BlaMab by highly potent DBO inhibitors, our goal herein was to investigate the efficacy of a novel combination, ceftaroline (CEF) and avibactam (AVI), to restore susceptibility to β-lactam antibiotics and inhibit growth.

Methods. Minimum inhibitory concentrations (MICs) of CEF with or without AVI were examined using the microdilution method.

Results. MIC_{50} and MIC_{90} of CEF is 8 mg/L; in the presence of 4 μg/mL of AVI, the MICs of CEF decreased to ≤4 mg/L in 31 of 35 cases (table).

Conclusion. Our results add to the growing evidence of using β-lactams as agents effective against Mycobacterial infections. Inhibition of the hydrolytic activity of (BlaMab) using DBOs such as AVI suggest that this combination should be evaluated in animal and clinical models.

Table 1: MICs of M. abscessus Strains (mg/L).

Avibactam (AV), Ceftaroline (CEF)					
	CEF	CEF+AVI		CEF	CEF+AVI
M. ab 15-103	8	0.25	*M. ab* (ATCC)	16	0.25
M. ab 15-442	8	1	*M. ab* IDR1400012185	32	0.25
M. ab 137-10561	8	0.5	*M. ab* IDR1400011191	8	<0.25
M. ab 15-305	16	2	*M. ab* IDR130008519	16	2
M. ab (bolletti) 15-148	16	1	*M. ab* 138-4796	2	0.25
M. ab 16-49	2	1	16-49	16	1
M. ab (ATCC)	32	<2	15-228	16	1
M. ab 16-21	8	0.5	15-235	8	0.5
M. ab 15-228	8	0.5	137-1061	>128	8
M. ab 15-206	128	1	*M. ab* 15-206	32	<0.25
M. ab 15-235	8	0.5	*M. ab* 15-86	64	0.5
M. ab 138-4796	32	<2	15-305	16	1
M. ab IDR130008519	16	16	*M. ab* 16-21	2	0.5
M. ab IDR1400012185	16	4	*M. ab* 15-103	4	0.5
M. ab 15-86	16	2	*M. ab* 15-148	8	1
M. ab 132-10561	4	1	15-442	32	1
M. ab #3	4	1	*M. ab* 132-10561	4	0.5
M. ab N1	4	0.5	*M. ab* #1	4	0.5
M. ab 60-2016	32	32	*M. ab* #2	8	2
M. ab IDR1400011191	16	16	*M. ab* #3	4	0.5
M. ab #14	16	1	*M. ab* #4	16	2
M. ab W2	8	1	*M. ab* #5	>128	4
M. ab #12	0.5	<0.125	*M. ab* #6	64	4
M. ab #13	32	2	*M. ab* #7	4	0.5
M. ab #11	16	0.5	*M. ab* #8	8	1
M. ab #10	32	2	*M. ab* #9	64	8
M. ab #7	4	1	*M. ab* #10	64	8
M. ab #1	16	0.5	*M. ab* #11	4	0.5
M. ab #8	18	0.25	*M. ab* #12	4	0.5
M. ab #9	32	4	*M. ab* #13	4	0.5
M. ab #6	32	1	*M. ab* #14	8	1
M. ab #4	8	0.5	*M. ab* 60-2016	32	32
M. ab #2	4	0.5	*M. ab* W2	8	0.5
M. ab #5	>64	4	*M. ab* N1	4	0.5

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

787. The Addition of Avibactam Augments the Activity of Piperacillin Against *Mycobacterium abscessus in vitro*, and Is Effective in Treating *M. abscessus* Infection in a *Galleria mellonella in vivo* Model

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Background. *Mycobacterium abscessus* is an emerging multi-drug-resistant pathogen, harboring the β-lactamse Bla_{MAB}. Avibactam is a non-β-lactam, β-lactamase

inhibitor shown to inhibit Bla_{MAB} and improve the efficacy of ampicillin for *M. abscessus* infections in *in vitro* and *in vivo* models. Whether the addition of avibactam to piperacillin enables use of the latter against *M. abscessus* is unknown

Methods. We used a recombinant, luminescent *M. abscessus* to measure the reduction of MIC to meropenem, ampicillin, and piperacillin induced by avibactam. We then used our previously established *G. mellonella* infection model (Figure 1)[1] to evaluate the effect of antimicrobial treatments *in vivo*.

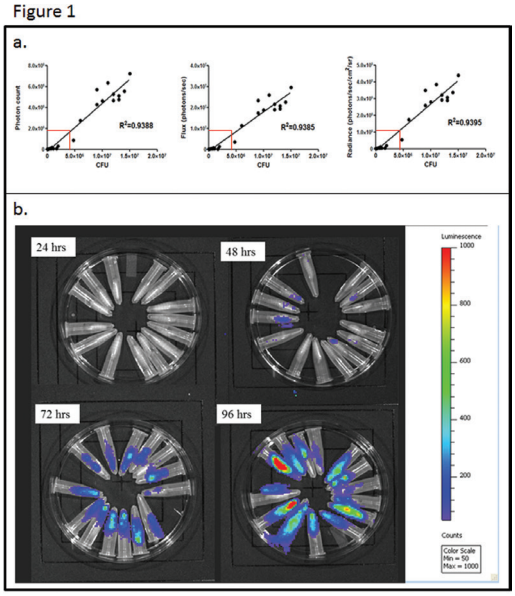
Results. Addition of avibactam (4 μg/mL) consistently decreased MIC of ampicillin and piperacillin by 16 and 16–32-fold, respectively, but as expected had no significant effect on meropenem MIC (Figure 2). We inoculated 60 *G. mellonella* larvae with luminescent *M. abscessus* on day 0, and treated larvae with meropenem, piperacillin, avibactam alone, or piperacillin combined with avibactam on days 2 and 3. Using IVIS® imaging, we measured infection progression in live infected larvae on day 4. Larvae treated with meropenem and piperacillin–avibactam had significantly lower infection burden compared with untreated controls ($P < 0.0001$ and $P = 0.004$, respectively). Piperacillin and avibactam alone had no significant inhibitory effect (Figure 3).

Conclusion. Our findings suggest that the piperacillin–avibactam combination is effective against *M. abscessus* infections. This novel combination may hold a great promise for patients with cystic fibrosis suffering from *M. abscessus*, *Pseudomonas aeruginosa*, and/or *Staphylococcus aureus* co-infections. The *G. mellonella* infection model may be used in future studies to assess the efficacy of various antimicrobials and antimicrobial combinations on *M. abscessus*, *P. aeruginosa*, and *S. aureus* co-infections.

Reference

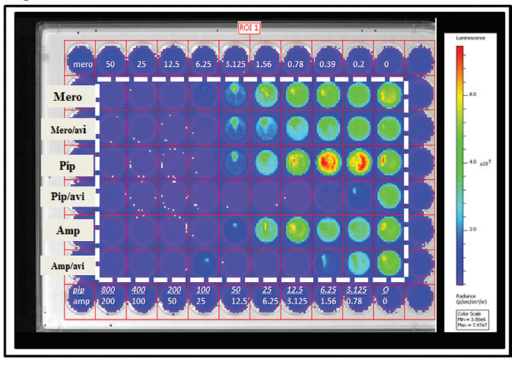
1. Meir M *et al. Antimicrob Agents Chemother*. 2018.

Figure 1



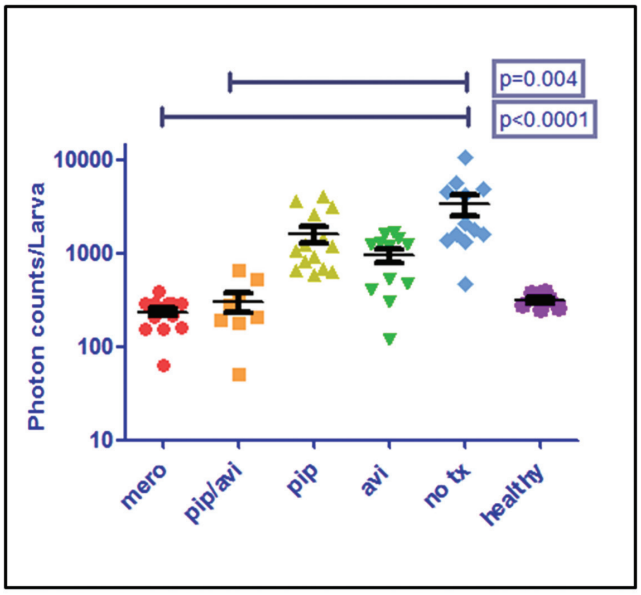
Luminescence is proportional to, and representative of bacterial counts. **a)** 25 Larvae were injected with serial dilutions of luminescent *M. abscessus* mutant (mDB158), imaged using IVIS, and immediately sacrificed and plated for CFU. Photon counts (left), photon flux (photons/sec) (center) and radiance (photons/sec/cm^2/sr) (right) were compared to CFU counts. **b)** Live imaging of luminescent *M. abscessus* infection. 14 Larvae injected with 5*10^4 CFU of mDB158 were imaged. Images shown were taken 24 hrs , 48 hrs, 72 hrs, and 96 hrs post infection.

Figure 2



Avibactam lowers MIC of piperacillin for *M. abscessus*. A broth dilution assay was performed using 5*10^3 CFU luminescent *M. abscessus* mutant with serial 1:2 dilutions of meropenem (50 to 0 μg/ml), piperacillin (800 to 0 μg/ml) and ampicillin (200 to 0 μg/ml) alone or with the addition of 4 μg/ml of avibactam. Image showing luminescence demonstrated by IVIS® following 65 hrs of incubation. Avibactam significantly decreased the MIC of ampicillin and piperacillin. Avibactam had no effect on meropenem MIC, as β-lactamases do not play a significant role in meropenem resistance. Mero – meropenem, pip – piperacillin, amp – ampicillin, avi – avibactam. Dotted white line showing test area. White numbers showing mero/pip/amp μg/ml concentrations in wells, accordingly.

Figure 3



Piperacillin/avibactam is as effective as meropenem in treating *Mycobacterium abscessus* in a *Galleria mellonella* infection model We inoculated 60 *G. mellonella* larvae with luminescent *M. abscessus* on day 0, and treated larvae with 2 daily doses of meropenem, piperacillin, avibactam alone, or piperacillin combined with avibactam on days 2 and 3. Using IVIS® imaging, we measured infection progression in live infected larvae on day 4. Larvae treated with meropenem and piperacillin-avibactam had significantly lower infection burden compared to untreated controls (p<0.0001 and p=0.004 respectively). Piperacillin and avibactam alone had no significant inhibitory effect

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788. Therapeutic Drug Monitoring for Pyrazinamide During Tuberculosis Treatment: What Is the Diagnostic Accuracy?

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Background. Pyrazinamide (PZA) is a key drug for both drug-sensitive and drug-resistant tuberculosis (TB). Patients co-infected with TB and human immunodeficiency virus (HIV) are more likely to have low blood levels of PZA, associated with inferior outcomes. Therapeutic drug monitoring (TDM) with sparse blood sampling is recommended for high-risk groups, including HIV/TB patients, but the accuracy is uncertain. We performed a pharmacokinetic (PK) simulation study to estimate the diagnostic accuracy of TDM for PZA among HIV/TB patients.

Methods. We recently performed a population PK study among HIV/TB patients in Botswana, identifying a 1-compartment model with first-order elimination. In the current work, we performed an intensive PK simulation (n = 10,000 patients) to determine the accuracy of sparse blood sampling in identifying HIV/TB patients with low PZA blood levels, as defined by the AUC in a dosing interval ($AUC_{0\text{-}24}$) predictive of successful outcome (363 mg*hr/L). PZA dosing followed WHO guidelines with weight-based dosing bands. In secondary analysis, we examined the peak concentration (Cma_x) target predictive of 2-month sputum conversion (58 mg/L). To determine the accuracy of sparse sampling (2- and 6-hours), we performed receiver-operating-characteristic (ROC) analysis, with bootstrapping (n = 1,000) for 95% confidence intervals (CI), and defined accuracy as the area under the ROC curve.

Results. In this simulation PK study of PZA among HIV/TB patients, the PZA $AUC_{0\text{-}24}$ fell below the target in 29% of patients, while in 71% of patients the PZA C_{max} was below the target. For the $AUC_{0\text{-}24}$ target, the area under the ROC curve was 0.69 (95% CI 0.68–0.70) for a single 2-hour sample, increasing to 0.75 (95% CI 0.74–0.76) for 2- and 6-hour samples. For the C_{max} target, diagnostic accuracy was similar for a 2-hour sample (0.87, 95% CI 0.86–0.87) and 2- and 6-hour samples (0.88, 95% CI 0.88–0.89).

Conclusion. We observed modest diagnostic accuracy of TDM for identifying in silico HIV/TB patients with low PZA $AUC_{0\text{-}24}$, and higher accuracy for low C_{max}. By identifying diagnostic performance characteristics of sparse sampling strategies, including optimal cut-offs, the ROC framework can support wider implementation of TDM in high-risk TB populations.