

Combinations of antibiotics effective against Extensively- and Pandrug Resistant *Acinetobacter baumannii* patient isolates

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Table S2: List of combinations screened by disc diffusion assay.

Antibiotic Combination	Synergy Observed
Amikacin x Eravacycline	Yes
Amikacin x Cefepime	Yes
Amikacin x Meropenem	No
Amikacin x Levofloxacin	Yes
Amikacin x Amp/Sul	No
Amikacin x TMP/SMX	No
Amikacin x Rifampin	No
Amikacin x Doxycycline	No
Eravacycline x Cefepime	No
Eravacycline x Meropenem	No
Eravacycline x Levofloxacin	Yes
Eravacycline x Amp/Sul	Yes
Eravacycline x TMP/SMX	No
Eravacycline x Rifampin	Yes
Omadacycline x Cefepime	No
Omadacycline x Meropenem	No
Omadacycline x Levofloxacin	Yes
Omadacycline x Amp/Sul	Yes
Omadacycline x TMP/SMX	No
Omadacycline x Rifampin	Yes
Cefepime x Meropenem	No
Cefepime x Levofloxacin	Yes
Cefepime x Amp/Sul	Yes
Cefepime x TMP/SMX	No
Cefepime x Rifampin	Yes
Cefepime x Doxycycline	No
Meropenem x Levofloxacin	No
Meropenem x Amp/Sul	No
Meropenem x TMP/SMX	No
Meropenem x Rifampin	No
Meropenem x Doxycycline	No
Levofloxacin x Amp/Sul	Yes
Levofloxacin x TMP/SMX	No
Levofloxacin x Rifampin	No
Levofloxacin x Doxycycline	No
Amp/Sul x TMP/SMX	No
Amp/Sul x Rifampin	No
Amp/Sul x Doxycycline	No
TMP/SMX x Rifampin	No
TMP/SMX x Doxycycline	No

		Concentration of Cefepime ($\mu\text{g/mL}$)									
		256	128	64	32	16	8	4	2	1	0
Concentration of Tobramycin ($\mu\text{g/mL}$)	128	0.099	0.099	0.091	0.098	0.131	0.102	0.097	0.09	0.076	0.096
	64	0.084	0.089	0.091	0.085	0.107	0.087	0.082	0.078	0.081	0.083
	32	0.086	0.084	0.092	0.088	0.086	0.087	0.09	0.081	0.083	0.084
	16	0.077	0.062	0.062	0.062	0.063	0.07	0.064	0.061	0.06	0.075
	8	0.067	0.064	0.068	0.068	0.067	0.067	0.069	0.072	0.068	0.079
	4	0.069	0.071	0.072	0.07	0.078	0.069	0.072	0.084	0.086	0.104
	2	0.075	0.07	0.078	0.075	0.082	0.081	0.091	0.09	0.253	0.596
	0	0.068	0.079	0.079	0.086	0.101	0.106	0.107	0.188	0.271	0.854
		Growth									
		No Growth									
		Additive									
		Synergistic									

		FIC Cefepime									
		8	4	2	1	0.5	0.25	0.125	0.063	0.031	0
FIC Tobramycin	16	24	20	18	17	16.5	16.25	16.13	16.06	16.03	-
	8	16	12	10	9	8.5	8.25	8.13	8.06	8.03	-
	4	12	8	6	5	4.5	4.25	4.13	4.06	4.03	-
	2	10	6	4	3	2.5	2.25	2.13	2.06	2.03	-
	1	9	5	3	2	1.5	1.25	1.13	1.06	1.03	-
	0.5	8.5	4.5	2.5	1.5	1	0.75	0.63	0.56	0.53	0
	0.25	8.25	4.25	2.25	1.25	0.75	0.5	0.37	0.31	0	0
	0	-	-	-	-	0	0	0	0	0	0

Figure S1: Representative checkerboard assay with cefepime and tobramycin against strain M13. Top: OD₆₀₀ measurements following 16 hours of static growth at 37°C. The MIC values for each drug alone are highlighted in gray. The pink boxes indicate wells in which no bacterial growth occurred (OD₆₀₀ < 0.1), and green boxes indicate wells in which bacterial growth did occur. The box in the bottom right corner contains no drug and serves as a growth control. Bottom: Fractional inhibitory concentrations (FICs) were calculated for each drug (concentration/MIC) and added together for all wells where no growth was observed. The yellow boxes indicate additive interactions (FICI between 0.5-1.0), and blue boxes indicate synergistic interactions (FICI ≤ 0.5).

Concentration of Eravacycline (µg/mL)
Concentration of Amikacin (µg/mL)

	Growth
	No Growth
	Additive
	Synergistic

	128	64	32	16	8	4	2	1	0.5	0
32	0.044	0.042	0.042	0.042	0.045	0.044	0.049	0.05	0.047	0.053
16	0.044	0.042	0.045	0.043	0.045	0.047	0.047	0.049	0.049	0.049
8	0.048	0.042	0.045	0.046	0.047	0.047	0.045	0.05	0.052	0.073
4	0.051	0.045	0.043	0.046	0.046	0.048	0.048	0.057	0.078	0.129
2	0.048	0.045	0.044	0.046	0.047	0.047	0.058	0.088	0.16	0.217
1	0.045	0.043	0.045	0.044	0.046	0.046	0.055	0.198	0.201	0.283
0.5	0.046	0.045	0.044	0.044	0.045	0.045	0.046	0.19	0.219	0.353
0	0.045	0.045	0.046	0.047	0.05	0.051	0.168	0.312	0.557	0.757

	FIC Amikacin									
	32	16	8	4	2	1	0.5	0.25	0.125	0
4	36	20	12	8	6	5	4.5	4.25	4.13	-
2	34	18	10	6	4	3	2.5	2.25	2.13	-
1	33	17	9	5	3	2	1.5	1.25	1.13	-
0.5	32.5	16.5	8.5	4.5	2.5	1.5	1	0.75	0.63	
0.25	32.25	16.25	8.25	4.25	2.25	1.25	0.75	0.5		
0.125	32.13	16.13	8.13	4.13	2.13	1.13	0.51			
0.063	32.06	16.06	8.06	4.06	2.06	1.06	0.56			
0	-	-	-	-	-	-				

Figure S2: Representative checkerboard assay with amikacin and eravacycline against strain M2. Top: OD₆₀₀ measurements following 16 hours of static growth at 37°C. The MIC values for each drug alone are highlighted in gray. The pink boxes indicate wells in which no bacterial growth occurred (OD₆₀₀ < 0.1), and green boxes indicate wells in which bacterial growth did occur. The box in the bottom right corner contains no drug and serves as a growth control. Bottom: Fractional inhibitory concentrations (FICs) were calculated for each drug (concentration/MIC) and added together for all wells where no growth was observed. The yellow boxes indicate additive interactions (FICI between 0.5-1.0).

		Concentration of Eravacycline ($\mu\text{g/mL}$)										
		4	2	1	0.5	0.25	0.125	0.0625	0.03125	0.01563	0	Growth
32	0.044	0.045	0.045	0.044	0.044	0.044	0.047	0.047	0.045	0.044	0.06	No Growth
16	0.047	0.047	0.051	0.054	0.055	0.06	0.058	0.064	0.063	0.061		Additive
8	0.051	0.052	0.056	0.083	0.143	0.117	0.116	0.135	0.125	0.129		Synergistic
4	0.046	0.053	0.096	0.158	0.149	0.192	0.155	0.185	0.165	0.211		
2	0.055	0.063	0.321	0.394	0.405	0.423	0.429	0.454	0.377	0.424		
1	0.047	0.25	0.363	0.451	0.389	0.321	0.394	0.509	0.387	0.458		
0.5	0.048	0.258	0.452	0.524	0.395	0.504	0.532	0.586	0.547	0.59		
0	0.068	0.66	0.702	0.696	0.665	0.726	0.795	0.907	0.805	0.948		

		FIC Eravacycline										
		1	0.5	0.25	0.125	0.063	0.031	0.016	0.008	0.004	0	
2	3	2.5	2.25	2.13	2.06	2.03	2.02	2.01	2.004	-		
1	2	1.5	1.25	1.13	1.06	1.03	1.02	1.01	1.004	-		
0.5	1.5	1	0.75	0.63								
0.25	1.25	0.75	0.5									
0.125	1.13	0.63										
0.063	1.06											
0.031	1.03											
0	-											

Figure S3: Representative checkerboard assay with eravacycline and rifampin against strain M22. Top: OD₆₀₀ measurements following 16 hours of static growth at 37°C. The MIC values for each drug alone are highlighted in gray. The pink boxes indicate wells in which no bacterial growth occurred (OD₆₀₀ < 0.1), and green boxes indicate wells in which bacterial growth did occur. The box in the bottom right corner contains no drug and serves as a growth control. Bottom: Fractional inhibitory concentrations (FICs) were calculated for each drug (concentration/MIC) and added together for all wells where no growth was observed. The yellow boxes indicate additive interactions (FICI between 0.5-1.0), and blue boxes indicate synergistic interactions (FICI ≤ 0.5).

		Concentration of Levofloxacin ($\mu\text{g/mL}$)									
		64	32	16	8	4	2	1	0.5	0.25	0
Concentration of Omadacycline ($\mu\text{g/mL}$)	128	0.064	0.066	0.06	0.058	0.084	0.094	0.094	0.062	0.062	0.064
	64	0.065	0.056	0.059	0.058	0.061	0.059	0.061	0.062	0.062	0.064
	32	0.058	0.051	0.055	0.057	0.062	0.058	0.056	0.055	0.053	0.053
	16	0.051	0.049	0.054	0.055	0.119	0.084	0.089	0.078	0.074	0.068
	8	0.048	0.049	0.056	0.057	0.132	0.138	0.13	0.122	0.119	0.127
	4	0.05	0.049	0.056	0.065	0.07	0.242	0.267	0.253	0.233	0.219
	2	0.051	0.048	0.057	0.187	0.086	0.327	0.257	0.24	0.272	0.279
	0	0.054	0.048	0.062	0.319	0.487	0.349	0.695	0.674	0.697	0.706

FIC Levofloxacin										
FIC Omadacycline	4	2	1	0.5	0.25	0.125	0.063	0.031	0.016	0
8	12	10	9	8.5	8.25	8.13	8.06	8.03	8.02	-
4	8	6	5	4.5	4.25	4.13	4.06	4.03	4.02	-
2	6	4	3	2.5	2.25	2.13	2.06	2.03	2.02	-
2	5	3	2	1.5	1.25	1.13	1.06	1.03	1.02	-
0.5	4.5	2.5	1.5	1						
0.25	4.25	2.25	1.25	0.75	0.5					
0.125	4.13	2.13	1.13		0.38					
0	-	-	-							

Figure S4: Representative checkerboard assay with omadacycline and levofloxacin against strain M17. Top: OD₆₀₀ measurements following 16 hours of static growth at 37°C. The MIC values for each drug alone are highlighted in gray. The pink boxes indicate wells in which no bacterial growth occurred (OD₆₀₀ < 0.1), and green boxes indicate wells in which bacterial growth did occur. The box in the bottom right corner contains no drug and serves as a growth control. Bottom: Fractional inhibitory concentrations (FICs) were calculated for each drug (concentration/MIC) and added together for all wells where no growth was observed. The yellow boxes indicate additive interactions (FICI between 0.5-1.0), and blue boxes indicate synergistic interactions (FICI ≤ 0.5).