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Figure 2. Univariate and multivariate regression analysis for risk factors associated with 28-day recurrence. Legend: ICU= Intensive care unit.

Regression analysis for 28-day recurrence		
	Univariate analysis (OR–CI 95%)	Multivariate analysis (OR–CI 95%)
Age	1.00 (0.97–1.03)	1.01 (0.97-1.04)
Major surgery in past 90 days	0.23 (0.05–1.08)	0.34 (0.06-1.86)
Respiratory tract infection	**3.11 (1.01–9.61)**	2.27 (0.61-8.39)
ICU	2.34 (0.76–7.23)	1.23 (0.28-5.47)
Septic shock	**6.00 (1.36–26.45)**	2.91 (0.48-17.63)
Sepsis	1.24 (0.34–4.61)	0.73 (0.16-3.34)
Dialysis	**6.67 (1.68–26.51)**	3.80 (0.80-18.03)
Combination therapy	0.46 (0.14–1.54)	0.57 (0.14-2.32)

References
1. doi:10.1016/S1473-3099(20)30796-9 2. doi:10.1016/S1473-3099(25)00469-4

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Antibiotic strategies in difficult-to-treat *Pseudomonas aeruginosa* infections: monotherapy vs combination therapy in the italian SUSANA multi-centre study

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Background
Evidence comparing monotherapy versus combination strategies with novel beta-lactam/beta-lactamase inhibitors (BL/BLI) for difficult-to-treat resistant (DTR) *Pseudomonas aeruginosa* infections is limited. Combination therapy is widely used, but factors guiding its use and its impact on outcomes remain unclear. We aimed to identify predictors of monotherapy versus combination therapy and variables associated with 28-day mortality.

Methods
We performed a retrospective analysis of patients with pneumonia or bloodstream infection caused by DTR *P. aeruginosa* treated with a novel BL/BLI [ceftolozane/tazobactam (C/T), ceftazidime/avibactam (C/A), cefiderocol, imipenem/relebactam, or meropenem/vaborbactam], either as monotherapy or combination therapy (BL/BLI plus aminoglycoside, fluoroquinolone, colistin, or fosfomycin). Data were obtained from the multicenter SUSANA cohort, which collects demographic, clinical, and microbiological information. Outcomes were assessed up to 28 days after therapy initiation. Kaplan–Meier curves evaluated crude survival; uni- and multivariable regression analyses identified factors associated with 28-day mortality.

Results
A total of 172 patients were included in the study (123 monotherapy, 49 combination therapy). Demographic and clinical characteristics are summarized in Table 1. Patients on combination therapy were younger, with fewer comorbidities and less chronic kidney disease (CKD). C/A was more frequent in combination regimens, whereas C/T and cefiderocol were primarily prescribed as monotherapy. Overall, 28-day mortality was 23.8%. In multivariable Cox regression adjusted for age, sex, CVD, CKD and treatment strategy, the presence of sepsis or septic shock was independently associated with mortality [adjusted hazard ratio (aHR) 4.30, 95% confidence interval (CI) 1.30–14.21]. Treatment strategy did not significantly affect survival (aHR for combination vs monotherapy 0.74, 95% CI 0.31–1.74). Prescribing decisions appeared driven by baseline patient characteristics rather than infection severity.

Conclusions
In this multicentre cohort, the choice of novel BL/BLI agents was primarily driven by patient-related factors, such as age, comorbidity burden and renal function. Sepsis or septic shock emerged as the strongest predictor of 28-day mortality, with monotherapy and combination therapy yielding comparable adjusted outcomes. Controlled studies are needed to determine the most effective treatment strategies for DTR *P. aeruginosa* infections and to improve patient stratification in comparative effectiveness research.

Table 1. Demographic and clinical characteristics of study patients

Characteristics	Overall (n = 172)	Monotherapy (n = 123)	Combination therapy (n = 49)	p-value
Demographic				
Age, years, median (IQR)	67 [54–72.5]	68 [59–74]	59 [45–70]	**0.004**
Gender male	120 (69.8 %)	83 (67.5 %)	37 (75.5 %)	0.30
Comorbidities, n (%)				
Diabetes mellitus	39 (22.9 %)	28 (22.8 %)	9 (18.4 %)	0.74
Liver disease	12 (7.0 %)	9 (7.3 %)	3 (6.1 %)	0.89
Cardiovascular disease[a]	47 (27.3%)	38 (30.9%)	9 (18.3%)	0.096
Solid tumour	31 (18.0 %)	20 (16.5 %)	11 (22.4 %)	0.35
Leukaemia/lymphoma	6 (3.5%)	4 (3.3%)	2 (4.1%)	1.00
COPD	35 (20.3 %)	27 (22.0 %)	8 (16.3 %)	0.39
Chronic kidney disease[b]	46 (26.7%)	39 (31.7%)	7 (14.3%)	**0.02**
Charlson Comorbidity Index, median (IQR)	4 [2–6]	4 [3–6]	3 [2–5]	0.07
Immunosuppression conditions[c]	31 (18%)	23 (18.7%)	8 (16.3%)	0.34
Site of infection				
Pneumonia	127 (73.8%)	86 (67.7%)	41 (32.3%)	0.25
Bacteremia	23 (13.4%)	19 (82.6%)	4 (17.4%)	0.06
Both	22 (12.8%)	18 (81.8%)	4 (18.2%)	
Severity of illness				
Intensive care unit at infection onset	43 (25.0%)	28 (22.8%)	15 (30.6%)	0.31
Duration of therapy in days	11 [7–16]	10 [7–14]	15 [9–18]	**0.001**
Outcome				
Mortality at day 28	41 (23.8%)	7 (14.3%)	34 (27.6%)	0.0635

a heart failure. prior myocardial infarction, peripheral vascular disease, stroke.
b moderate–severe chronic kidney disease or dialysis.
c immunosuppressive conditions (steroids, pre-transplant induction chemo, post-transplant maintenance therapy, chemotherapy for solid tumors/hematologic malignancies, immunotherapy, monoclonal antibodies, neutropenia, AIDS).

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Delafloxacin beyond the label: early clinical experience against fluoroquinolone-resistant infections

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Background
Delafloxacin is a broad-spectrum fluoroquinolone active against Gram-positive bacteria, including methicillin-resistant Staphylococcus aureus, and Gram-negative organisms such as Pseudomonas aeruginosa. It is approved for acute bacterial skin and skin-structure infections (ABSSSIs) and community-acquired pneumonia. A distinguishing feature of delafloxacin is its enhanced stability and antimicrobial activity in acidic micro-environments, which may offer therapeutic advantages in chronic, deep-seated, or intracellular infections such as bone and joint infections. However, clinical MIC breakpoints are currently defined only for S. aureus, and real-world data on its use against fluoroquinolone-resistant pathogens remain limited.

This study aimed to describe the clinical characteristics of patients treated with delafloxacin in a tertiary-care setting, to identify the criteria that supported its selection, and to describe clinical outcomes along with microbiological susceptibility profiles.

Methods
We conducted a prospective observational single-centre study at Luigi Sacco Hospital. Eligible adults had bone, joint, or soft-tissue infections with documented resistance to ciprofloxacin and/or levofloxacin and were not suitable for OPAT. Isolates from the deep infectious focus were tested for delafloxacin susceptibility in a reference laboratory. Consecutive patients meeting these criteria and subsequently treated with delafloxacin were included. Clinical and microbiological data—demographics, comorbidities, infection type, treatment duration, outcomes, adverse events, MICs—were collected during outpatient visits or hospitalization. Descriptive statistics were used due to the small sample size.

Results
Five patients were included. Three had bone and joint infections due to P. aeruginosa, and two had polymicrobial ABSSSIs. Delafloxacin was prescribed as targeted therapy after ≥2 previous treatment failures. Median treatment duration was 50 days. Among bone and joint infections, one patient relapsed at three months (MIC 0,190 µg/mL), one achieved remission (MIC 0,125 µg/mL), and one remains on therapy (MIC 0,250 µg/mL). Among ABSSSI cases, one discontinued treatment due to non-severe adverse events (MIC 0,750 µg/mL), and one achieved partial remission (MIC 0,250 µg/mL). [Table 1][Table 2].

Conclusions
Delafloxacin retained in-vitro activity against isolates resistant to conventional fluoroquinolones and showed variable yet encouraging outcomes in complex infections. Larger studies are needed to establish MIC breakpoints and clarify its optimal clinical role.