Stanford De-escalation Guide for Gram-negative Bacteremia Rapid Antimicrobial Susceptibility (average turnaround time 9 hrs after organisms is identified)

Antibiotic Selection

<table>
<tr><th>Pathogens</th><th>Preferred therapeutic options IF SUSCEPTIBLE
Switch to PO when clinically stable, able to take orals, no concern for absorption issues</th></tr>
<tr><td rowspan="2">E.coli, Klebsiella spp., Proteus spp, Citrobacter koseri</td><td>Cefazolin 2g IV q8h – please call micro lab to add on susceptibility testing
Ceftriaxone 2g IV q24h
Ciprofloxacin 500 PO BID
Levofloxacin 500-750mg* PO daily
2nd line oral alternatives: Case by case basis. Consult ASP or ID if unsure. May consider if ALL conditions met*:
<table><tr><td>• source-controlled
• uncomplicated
• received ≥ 3 days of active IV therapy
• data strongest in urinary and biliary sources</td><td>• TMP-SMX* 2DS PO BID or 8-10mg TMP/kg/day PO divided in 2 or 3 doses
• Amoxicillin* 1g PO q8h if MIC ≤ 2
• Amoxicillin/clavulanate* 875/125mg PO q8h or 2g XR BID (if covered by insurance) if MIC ≤ 2
• Call ASP or ID if cephalosporins are needed</td></tr></table>* In recent published data, stepdown to oral β-lactams and TMP/SMX appeared to result in similar clinical outcomes vs FQ after ~3 days of effective IV therapy.[1,4] However, recurrence of infection may be higher with non-FQs when used at typical doses. Higher than usual doses may decrease the chance of infection recurrence, but may still not achieve PK/PD targets.</td></tr>
<tr><td><u>ESBL-producers (often ceftriaxone resistant, cefoxitin susceptible. See Micro comments)</u>
Ertapenem 1g IV q24h
Ciprofloxacin 500-750mg* PO BID
Levofloxacin 500-750mg* PO daily
TMP-SMX 8-10mg/kg/day PO divided in 2 or 3 doses
Note: Avoid Zosyn, Augmentin, most beta-lactams. May report as susceptible, but treatment failure may occur. MERINO trial: higher mortality in those treated with Zosyn vs meropenem.</td></tr>
<tr><td>Enterobacter spp, Serratia spp. Citrobacter spp. (not koseri)</td><td>Cefepime 1-2g* IV q8h extended infusion if CTX and ceftazidime susceptible. Otherwise call lab to add on cefepime testing.
Pip-tazo 3.375g IV q8h extended infusion
Ertapenem 1g IV q24h
Ciprofloxacin 500-750mg* PO BID
Levofloxacin 500-750mg* PO daily
TMP-SMX 8-10mg/kg/day PO divided in 2 or 3 doses
Caution with ceftriaxone, ceftazidime, even if reported as susceptible. Prolonged use may select for resistant AmpC mutants. AmpC producers are often CTX resistant, cefoxitin resistant</td></tr>
<tr><td>Pseudomonas aeruginosa</td><td>Cefepime 2g IV q8h extended infusion
Ceftazidime 2g IV q8h
Ciprofloxacin 750mg PO BID
Levofloxacin 750mg PO daily
Consider ID consult</td></tr>
<tr><td>Stenotrophomonas</td><td>TMP-SMX 8-10mg/kg/day IV/PO divided in 2 or 3 doses
Levofloxacin 750mg IV/PO daily
ID consult recommended</td></tr>
<tr><td>Acinetobacter baumanii</td><td>ID consult recommended. Commonly resistant to many antibiotics. Unasyn is usually active.</td></tr>
</table>

* Lower doses listed are for typical 70kg, normal renal function, tailored for the organism causing bacteremia. Higher dose may be considered for deep seated infections, obese (BMI ≥ 30), high CrCl > 100 ml/min. Use clinical judgement.

Duration

Source of bacteremia	Duration of therapy	Notes
General: urine, biliary, intraabdominal, skin/soft tissue, respiratory, surgical site, ENT	7 days[2, 7, 8] 10 days if *P.aeruginosa*[3]	• Must have clinically improved rapidly • Must not be neutropenic • Must have source control • Rule out infections involving long term catheters, ports, or hardware: longer treatment may be warranted if prosthesis/foreign materials are infected. Consult ID or ASP if unsure • Data strongest in urinary (including pyelonephritis) and biliary infection sources • Day 1 = 1st day of active ABX if source controlled and clinically improved (no need for clearance on repeat BCx. See below)†
	7-14 days in hematopoietic stem cell transplant or solid organ transplant patients	• Consider source of infection (e.g. 7 days for urinary source), source control, clinical improvement. • Repeat BCx may be considered in those with no clinical response and/or neutropenic and concern of uncontrolled source
Line (CVC, PICC, port, etc)	7 days[2] Uncomplicated + line removed (no abscess, endovascular, or metastatic infection) 10-14 days in some circumstances	• Day 1 = 1st negative BCx • Remove infected catheters if possible. Consider pathogen, clinical status, clearance of BCx, metastatic infection – see IDSA guidelines. If unable to remove infected line or port, some cases may require longer treatment, e.g. ≥10-14 days, ± ABX lock therapy. Consult ID or ASP. • If no clinical response, repeat BCx and consult ID
Endovascular (e.g. infective endocarditis, ICD/pacemaker, VAD) Osteomyelitis Complicated abdominal Meningitis/ventriculitis	Varies depending on source control and other co-morbid conditions	Consult ID
†Repeat blood cultures are generally not necessary to confirm clearance of uncomplicated gram negative bacteremias and are not necessary to determine day 1 of treatment.[10, 12] For clinically improved patients with source control, count day 1 from the 1st day of active therapy. Consult ID or ASP if unsure.		

References:

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2. Yahav et al, CID 2018 PMID: 30535100
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