Clinical trial	Study regimen[a]	No. of patients randomized (no. clinically evaluable)	Percentage of patients with clinical response[b]	Percentage of patients with microbiologic response[b]	Differences in toxicity
Feld *et al.* (2000)	MER 1 g every 8 h vs. CFZ 2 g every 8 h	411	54, 44 (p = 0.033)	45,[f] 51	NS
Cometta *et al.* (1996)	MER 1 g every 8 h if > 50 kg or 20 mg/kg every 8 h if < 50 kg vs. CFZ 2 g every 8 h for adults and 35 mg/kg every 8 h for children plus AMK 20 mg/kg/d once daily	1034 (958)	56, 52	43,[f]32	NS

[a]All antibiotics were administered intravenously.
[b]A *p*-value is provided only when statistical significance was achieved.
[c]The first, second, and third percentage relate to pancreatic or peripancreatic infection, mortality, and surgical intervention, respectively.
[d]The first and second percentage relate to cure with no sequelae and survival with sequelae, respectively, both at 5–7 weeks followup.
[e]Complete response to first-line antimicrobial therapy.
[f]Complete response rates to documented infection were similar among groups (p = NS).
Abbreviations: MER: meropenem; IMI: imipenem; NA: not available; NS: nonsignificant; CLD: clindamycin; TOB: tobramycin; CTX: cefotaxime; MTZ: metronidazole; CTZ/TZB: ceftolozane–tazobactam; CFZ: ceftazidime; CFZ/AVI: ceftazidime–avibactam; DAPTO: daptomycin; GTM: gentamicin; AMK: amikacin; TAZ: piperacillin/tazobactam; AE: adverse effect.

meropenem is a potential therapeutic option as an adjunct to complete surgical débridement, especially in patients with polymicrobial disease. Clinical trial data are lacking, however. The 2014 IDSA guidelines for the diagnosis and management of skin and soft tissue infections, include meropenem (with and without vancomycin) as an option for therapy in severe infections in immunocompromised hosts, empirical therapy for necrotizing fasciitis and for polymicrobial surgical site infections (Stevens *et al.*, 2014).

7b. Intraabdominal infection

Several randomized, controlled trials show that meropenem has excellent efficacy for intraabdominal infections (see Table 38.10). Meropenem is now frequently used in phase III trials as the standard of care comparator for newly developed antibacterial agents such as ceftolozane–tazobactam (Solomkin *et al.*, 2015) and ceftazidime–avibactam (Mazuski *et al.*, 2016) for the treatment of complicated intraabdominal infections (see Table 38.10). Meropenem has been compared with imipenem (Brismar *et al.*, 1995; Colardyn and Faulkner, 1996; Basoli *et al.*, 1997; Zanetti *et al.*, 1999), clindamycin and tobramycin (Wilson, 1997), and cefotaxime and metronidazole (Mehtar *et al.*, 1997), with similar efficacy reported. In patients with advanced appendicitis (gangrenous or perforated), meropenem showed small yet significant benefits compared with tobramycin and clindamycin, including reduced postoperative fever, duration of antibiotics, and hospital stay (Berne *et al.*, 1996). Given the higher likelihood of drug-resistant pathogens in healthcare-associated intraabdominal infections (most often postoperative), meropenem constitutes an excellent single agent to cover against Gram-negative aerobic and anaerobic organisms. Meropenem has no activity toward methicillin-resistant *S. aureus*, many enterococci, and, obviously, *Candida* species, which are all possible causative organisms (Solomkin *et al.*, 2010). As seen with other infections in critically ill patients, the adequacy of empirical therapy for postoperative intraabdominal infection may influence patient outcome (Montravers *et al.*, 1996). The current IDSA guidelines for the management of complicated intraabdominal infections lists meropenem as an appropriate empiric agent, but not for mild to moderate community-acquired infections in adults in whom the risk of resistant organisms is low; when used it should also be limited to 4–7 days (provided source control has been achieved) and tailored to reflect susceptibility testing of identified microorganisms (Solomkin *et al.*, 2010). In an open-label study of critically unwell infants with complicated intraabdominal infections, meropenem was effective and well-tolerated (Cohen-Wolkowiez *et al.*, 2012).

Piano *et al.* (2015) conducted a randomized controlled trial of meropenem plus daptomycin versus ceftazidime on 31 patients in Italy with nosocomial spontaneous bacterial peritonitis. A significant difference was seen in cure rates (86.7% vs. 25%; $p < 0.001$) between the meropenem–daptomycin arm and those given ceftazidime, largely explained by the high prevalence of organisms (80%) with resistance to ceftazidime (Piano *et al.*, 2015). Although there were no significant differences in mortality, the trial was stopped early due to poor efficacy of the comparator arm, so was underpowered to detect mortality differences. Furthermore, it is not clear that such a study is applicable to circumstances with lower background prevalence of multiresistant organisms or to what extent efficacy can be attributed to the addition of daptomycin.

7c. Acute pancreatitis

The use of carbapenems for the prophylaxis of infection in patients with acute necrotizing pancreatitis has been controversial. A Cochrane review performed in 2006 concluded