Main treatment regimens for the Clostridioides difficile-associated infection

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| Clinical manifestations | S. Johnson et al, 2021 | |  | C.R. Kelly et al, 2021 | |  | J. van Prehn et al, 2021 | |  | Yu.A. Shelygin et al, 2018 | |
| Recommended and alternative treatment regimens | Comment |  | Recommended and alternative treatment regimens | Comment |  | Recommended and alternative treatment regimens | Comment |  | Recommended and alternative treatment regimens | Comment |
| First episode CDI | Preferred: fidaxomycin 200 mg twice daily for 10 days | Depending on the resource availability |  | Oral fidaxomycin 200 mg twice daily for 10 days | Strong recommendation, moderate quality of evidence |  | Oral fidaxomycin 200 mg twice daily for 10 days | High relapse risk: fidaxomycin 200 mg twice daily day 1 to 5, then 200 mg every 48 hours for 7 to 25 days. Combine with bezlotoxumab if necessary |  | Oral metronidazole 500 mg 3 times daily for 10 days. If clinically non-effective at 5 to 7 days, switch to vancomycin | Grade of recommendations B (level of evidence II) |
| Alternative: oral vancomycin 125 mg 4 times daily for 10 days | Vancomycin remains an acceptable alternative |  | Oral vancomycin 125 mg 4 times daily for 10 days | Strong recommendation, low quality of evidence |  | Oral vancomycin 125 mg 4 times daily for 10 days | Combine with bezlotoxumab if necessary |  | Oral vancomycin 125 mg 4 times daily for 10 days | Grade of recommendations B (level of evidence II) |
| Alternative for non-severe CDI, if the above listed agents are unavailable: oral metronidazole 500 mg 3 times daily for 10 to 14 days | Non-severe CDI is confirmed by the following laboratory parameters: white blood cell counts below 15 × 109/L and serum creatinine < 1.5 mg/dL |  | Oral metronidazole 500 mg 3 times daily for 10 days | Strong recommendation, moderate quality of evidence |  | Oral metronidazole 500 mg 3 times daily for 10 to 14 days | If not feasible, fidaxomycin and vancomycin |  | – | – |
| First CDI relapse | Preferred: fidaxomycin 200 mg twice daily for 10 days or twice daily for 5 days, then once daily every other day for 20 days | – |  | – | – |  | Preferred: oral fidaxomycin 200 mg twice daily for 10 days combined with bezlotoxumab |  |  | Oral vancomycin 500 mg 4 times daily for 10 days | Grade of recommendations C (level of evidence III) |
| Alternative: oral vancomycin in tapered and pulse regimens | Example of the tapered/pulse regimens of vancomycin: 125 mg 4 times daily for 10–14 days, twice daily for 7 days, once daily for 7 days, then every 2 to 3 days for 2 to 8 weeks |  | – | – |  | Alternative: fidaxomycin 200 mg twice daily from day 1 to 5, then 200 mg every 48 hours for 7 to 25 days | After vancomycin failure |  | – | – |
| Alternative: oral vancomycin 125 mg 4 times daily for 10 days | Standard course of vancomycin, if metronidazole has been used for the 1st episode |  | – | – |  | Alternative: oral vancomycin 125 mg 4 times daily for 10 days | If not feasible, fidaxomycin and bezlotoxumab |  | – | – |
| Additional treatment: bezlotoxumab 10 mg/kg intravenously once during administration of a standard antibiotic protocol | Data on the combination with fidaxomycin are limited. To be used with caution in patients with congestive heart failure |  | – | – |  | Alternative: vancomycin 125 mg 4 times daily for 10 to 14 days, twice daily for 7 days, once daily for 7 days, then every 2 to 3 days for 2 to 8 weeks | If not feasible, fidaxomycin and bezlotoxumab |  | – | – |
| 2nd and subsequent relapses of CDI | Fidaxomycin 200 mg twice daily for 10 days or twice daily for 5 days, then once daily every other day for 20 days | – |  | – | – |  | Fecal microbiota transplantation is preferred |  |  | – | – |
| Oral vancomycin in the tapered and pulse regimens | – |  | – | – |  | Alternative: fidaxomycin 200 mg twice daily for 10 days in combination with bezlotoxumab | – |  | – | – |
| Oral vancomycin 125 mg 4 times daily for 10 days, then rifaximin 400 mg 3 times daily for 20 days | – |  | – | – |  | Alternative: oral vancomycin | If no other treatment alternatives are available |  | – | – |
| Fecal microbiota transplantation | Before the fecal microbiota transplantation is considered, an antibiotic course should be tried, at least in the case of 2 relapses (i.e., 3 episodes in total) of CDI |  | – | – |  | – | – |  | – | – |
| Additional treatment: bezlotoxumab 10 mg/kg intravenously once during administration of a standard antibiotic protocol | Data on the combination with fidaxomycin are limited. To be used with caution in patients with congestive heart failure |  | – | – |  | – | – |  | – | – |
| Severe CDI | – | – |  | Oral vancomycin 125 mg 4 times daily for 10 days | Strong recommendation, low quality of evidence |  | Vancomycin or fidaxomycin | If oral administration is not feasible, administer by enema in combination with intravenous metronidazole or tigecycline |  | Oral vancomycin 125 mg 4 times daily for 10 days | Grade of recommendations B (level of evidence II) |
| – | – |  | Oral fidaxomycin 200 mg twice daily for 10 days | Consensus recommendation, very low quality of evidence |  | – | – |  | Tigecycline at starting dose for adults of 100 mg as a 30–60 minutes intravenous infusion, then 50 mg every 12 hours. Average duration of treatment 5 to 14 days | Grade of recommendations C (level of evidence III) |
| Fulminant CDI | Oral vancomycin 500 mg 4 times daily or via a nasogastral tube | Fulminant CDI is confirmed by presence of hypotension, or shock, or ileus/megacolon |  | Oral vancomycin 500 mg every 6 hours during the first 48 to 72 hours | Strong recommendation, very low quality of evidence |  | – | – |  | Oral vancomycin 500 mg 4 times daily in combination with metronidazole 500 mg 3 times daily intravenously | Grade of recommendations B (level of evidence II) |
| In the case of ileus, rectal instillation of vancomycin should be considered. Intravenous metronidazole (500 mg every 8 hours) should be administered in combination with oral or rectal vancomycin, especially if ileus is present | – |  | Combination with parenteral metronidazole 500 mg every 8 hours can be considered | Consensus recommendation, very low quality of evidence |  | – | – |  | If oral administration is not feasible, vancomycin is administered rectally. 500 mg of the agent are diluted in 500 mL 0.9% saline and administered as enema 4 times daily | Grade of recommendations B (level of evidence II) |
| – | – |  | For patients with ileus, vancomycin enemas could be useful (500 mg every 6 hours) | Consensus recommendation, very low quality of evidence |  | – | – |  | – | – |

CDI, Clostridioides difficile-associated infection