Q/What’s the best secondary treatment for patients who fail initial triple therapy for *H pylori*?

Evidence-based answer

TREATING PATIENTS with *Helicobacter pylori* infection who have failed clarithromycin-based triple therapy (with amoxicillin and a proton pump inhibitor [PPI]) or a bismuth-based quadruple therapy produces cure rates of 75% to 81%. Ten-day regimens produce higher cure rates than 7-day regimens. Repeating the initial clarithromycin-based triple therapy cures fewer than half of patients (strength of recommendation [SOR]: A, meta-analyses of randomized controlled trials [RCTs]).

Treating with a metronidazole-based triple therapy (with amoxicillin and a PPI) also produces high (87%) cure rates (SOR: A, meta-analyses of RCTs in exclusively Japanese populations).

Selecting a secondary treatment regimen based on *H pylori* antibiotic susceptibility testing probably doesn’t improve cure rates over empiric antibiotic treatment (SOR: B, meta-analyses of RCTs with conflicting results). However, after 2 treatment failures it may be necessary (SOR: C, expert opinion-based guidelines).

Bismuth-based quadruple therapy has a more complex dosing regimen, and bismuth isn’t available in some countries. Rising rates of *H pylori* resistance to levofloxacin in certain areas could make levofloxacin-based triple therapy less effective in the future (SOR: C, expert opinion-based guidelines).

Evidence summary

A meta-analysis of RCTs evaluating levofloxacin-based triple therapy as a secondary treatment regimen for patients with *H pylori* infection who had failed initial clarithromycin-based triple therapy found cure rates averaging 76% (TABLE).¹ Most of the regimens comprised levofloxacin (500 mg), amoxicillin (1 g), and a PPI (40 mg), all twice daily for 7 to 10 days. Ten-day regimens produced better cure rates than 7-day regimens (84% vs 69%; comparison statistic not supplied).

The meta-analysis also included RCTs evaluating bismuth-based quadruple therapy as secondary treatment, which found cure rates averaging 78%.¹ The regimens varied, comprising bismuth salts (120-600 mg, 2-4 times daily), metronidazole (250-500 mg, 2-4 times daily), tetracycline (250-500 mg, 2-4 times daily), and a PPI (40 mg twice daily). Longer duration of therapy produced higher cure rates (7 days=76%; 95% confidence interval [CI], 0.72-0.80 in 29 RCTs with 2097 patients; 10 days=77%; 95% CI, 0.60-0.93 in 2 RCTs with 142 patients; 14 days=82%; 95% CI, 0.76-0.88 in 12 RCTs with 831 patients).

Repeating the original clarithromycin-based triple therapy (8 RCTs, 265 patients) produced low cure rates (46%).¹

Metronidazole-based therapy has high cure rate in a homogeneous population

A meta-analysis of 24 RCTs (1611 patients) that evaluated metronidazole-based triple therapy (mostly composed of amoxicillin 750 mg, metronidazole 250 mg, and any of
Two RCTs evaluating the use of a number of PPIs, all dosed at 40 mg) twice daily for 7 days found cure rates averaging 87% in an exclusively Japanese study population.1

**Comparable cure rates for levofloxacin- and bismuth-based therapy**

Six RCTs with a total of 1057 patients compared cure rates for levofloxacin-based triple therapy with bismuth-based quadruple therapy and found no difference.1

Two earlier meta-analyses not included in the previously described study, comprising 8 RCTs with a total of 613 patients, produced conflicting results. The larger study (15 RCTs, 1462 patients) found no difference in cure rates. The smaller study (7 RCTs, 787 patients) favored quadruple therapy.3

**Two secondary antibiotic regimens show similar cure rates**

A meta-analysis of 4 RCTs (total 460 patients) that compared susceptibility-guided antibiotic secondary treatment (SGT) with empiric antibiotic secondary treatment found no difference in cure rates, although the largest single RCT (172 patients) favored SGT.4

**Recommendations**

The Maastricht IV/Florence Consensus Report (a periodically updated European study group evaluating Helicobacter management) includes expert opinion-based guidelines for H pylori treatment that recommend using antibiotic susceptibility to select treatment regimens in the event of 2 treatment failures.2 The report also notes that bismuth-based quadruple therapy may not be available in all countries and has a more complex dosing regimen, and that local resistance to levofloxacin must be taken into account when prescribing levofloxacin-based triple therapy.4

**References**