



## Q/What is the optimal duration of PPI therapy for healing a gastric or duodenal ulcer?

### EVIDENCE-BASED ANSWER

**A** | IT DEPENDS on the type of ulcer. For *Helicobacter pylori*-associated peptic ulcers, 7-day treatment with a proton pump inhibitor (PPI) plus 2 antibiotics heals more than 90% of ulcers and is as effective as the same regimen followed by 2 to 4 additional weeks of PPI therapy (strength of recommendation [SOR]: A, meta-analysis of randomized controlled trials [RCTs]).

For peptic ulcers associated with non-steroidal anti-inflammatory drugs (NSAIDs), 8 weeks of PPI treatment is better than 4 weeks in the case of gastric ulcers, but no more effective than 4 weeks for duodenal ulcers. (SOR: A, meta-analysis of RCTs).

For gastric ulcers resulting from endoscopic submucosal dissection, 4 weeks of PPI therapy is as effective as 8 weeks, but both regimens leave nearly a third of ulcers unhealed (SOR: B, single RCT).

#### For *H pylori* ulcers, 7 days of therapy does the trick

A 2005 meta-analysis of 6 RCTs with 862 patients compared 7 days of triple therapy with a PPI and 2 antibiotics with the same regimen followed by 2 to 4 additional weeks of PPI therapy.<sup>1</sup> One RCT studied both duodenal and gastric ulcers; the remaining 5 assessed only duodenal ulcers. Investigators included only studies that clearly identified both *H pylori* eradication and ulcer healing as treatment goals and specified the number of patients treated, the number who experienced successful healing, endoscopic ulcer confirmation, and no concurrent NSAID use.

Triple therapy regimens comprised ei-

ther omeprazole or esomeprazole 20 mg twice daily plus clarithromycin and either metronidazole, amoxicillin, or tinidazole for 7 days. In all studies, patients randomly assigned to receive an additional 2 to 4 weeks of PPI treatment were given omeprazole 20 mg/d.

Mean ulcer healing rates were 91% (95% confidence interval [CI], 87%-95%) for 7 days of PPI triple therapy compared with 92% (95% CI, 89%-96%) when PPI treatment was extended for an additional 2 to 4 weeks (odds ratio=1.1; 95% CI, 0.71-1.7).

#### Longer PPI therapy works better for NSAID-associated gastric ulcers

A 1998 meta-analysis examined 2 large RCTs that evaluated healing rates of NSAID-associated ulcers at 4 weeks and 8 weeks in 656 patients with gastric or duodenal ulcers who were treated with omeprazole 20 mg/d or 40 mg/d.<sup>2</sup> Patients had ulcers 3 mm or larger or more than 10 erosions in the stomach or duodenum. Gastric ulcers outnumbered duodenal ulcers 2 to 1. Patients had taken continuous therapeutic doses of NSAIDs for at least 5 days per week during 2 weeks in the month preceding PPI therapy; about half were *H pylori*-positive.

For gastric ulcers, treatment success at 8 weeks was significantly higher at both PPI doses than at 4 weeks. The 208 patients taking the 20-mg dose showed 67% treatment success at 4 weeks and 83% at 8 weeks ( $P=.001$ ). The 212 patients taking 40 mg had 67% treatment success at 4 weeks and 82% at 8 weeks ( $P=.002$ ).

Duodenal ulcers showed no difference

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in healing at 4 and 8 weeks at either PPI dose. The 20-mg dose (116 patients) produced 84% treatment success at 4 weeks compared with 93% at 8 weeks ( $P=.2$ ), and the 40-mg dose (120 patients) showed 86% treatment success at 4 weeks compared with 88% at 8 weeks ( $P=.8$ ).

### Procedure-induced ulcers respond similarly to 4- and 8-week regimens

A 2014 RCT assessed the effect of 4 and 8 weeks of PPI treatment on healing of gastric ulcers resulting from endoscopic submucosal dissection (ESD), a procedure used to treat early gastric cancer or adenoma that leaves a large ulcer at the site.<sup>3</sup> The study randomly assigned 84 patients to treatment with lansoprazole 30 mg/d for 4 or 8 weeks after undergoing ESD. Exclusion criteria included NSAID use or ingestion of mucosal protective agents within 4 weeks of the procedure, illness that might influence PPI effects, history of gastric surgery, and pregnancy or breast-feeding.

All patients underwent endoscopy the day after ESD and again at 8 weeks. Ulcer dimension ( $\text{mm}^2$ ) was determined by multiplying the longest diameter by the diameter perpendicular to the longest diameter. The ulcer reduction ratio, an assessment of healing, was determined by dividing the ulcer dimension at 8 weeks after ESD by the initial ulcer dimension.

No significant difference was observed in the 4-week and 8-week groups in terms of ulcer healing (68% vs 69%, respectively;  $P=.93$ ) or the ulcer reduction ratio (0.0081 vs 0.0037, respectively;  $P=.15$ ). **JFP**

#### References

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2. Yeomans ND. New data on healing of nonsteroidal anti-inflammatory drug-associated ulcers and erosions. Omeprazole NSAID Steering Committee. *Am J Med.* 1998;104:56S-61S.
3. Park JH, Baek EK, Choi CH, et al. Comparison of the efficacy of 4- and 8-week lansoprazole treatment for ESD-induced gastric ulcers: a randomized, prospective, controlled study. *Surg Endosc.* 2014;28:235-241.

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