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Letter to the Editor

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Rifabutin-based 10-day and 14-day triple therapy as a third-line and fourth-line regimen for *Helicobacter pylori* eradication: how should rifabutin be managed in rescue regimens?

Giuseppe Losurdo, Andrea Iannone, Floriana Giorgio, Mariabeatrice Principi, Alfredo Di Leo and Enzo Ierardi

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We read with great interest the original article by Mori et al. about the use of rifabutin in rescue treatment for *Helicobacter pylori* infection.[1] The increasing incidences of antibiotic resistance are a clinical dilemma in this setting, with increasing failure rates of conventional eradication regimens.[2] Therefore, novel strategies are needed to achieve successful *H. pylori* eradication. Despite a culture-guided strategy being recommended by guidelines, this approach is difficult to perform extensively, since the culture of this organism is complex, even in expert hands.[3,4] For this reason, empirical rescue regimens are still warranted, and rifabutin is gaining increasing interest in this scenario.[5] However, current studies show success rates ranging from 60 to 80% in relation to drug dose and treatment duration and, therefore, there is not a full agreement with the results of the study of Mori et al.[1]

Moreover, it should be emphasized that the use of rifabutin needs to be managed in relation to several factors. First, this antibiotic is extensively recommended for tuberculosis (TB) treatment, in particular in patients suffering from HIV co-infection.[6] For this reason, before starting a rifabutin-based eradication regimen, TB status should be ascertained (i.e. QuantiFERON-TB Gold In-Tube test), since its use could imply the onset of antibiotic resistance, thus precluding its effectiveness against Koch's bacillus. Further, *H. pylori* resistance to rifabutin is low, as confirmed in the paper of Mori et al.[1] Indeed, genotypic resistance revealed by mutations in the *rpoB* gene (a factor of resistance to rifamycins) has been found only in 3 out of 29 patients, despite phenotypic resistance to rifabutin being observed only in one patient at culture. This disagreement suggests that, at the moment, a valid genotypic marker for rifabutin resistance may not be available yet. Further evidence in favor of this hypothesis is that all patients with *rpoB* mutation-positive strains showed successful eradication. Indeed, it has been shown that mycobacterial strains bearing this mutation are often rifabutin-susceptible and rifampicin-resistant.[7] This detail could cause difficulties in identifying a possible increase of resistant strains with the diffusion of its use in the near future. For this reason, the use of rifabutin should be recommended with caution and restricted to selected rescue treatments.

The use of rifabutin is linked to several side effects, some of which are harmful such as cytopenia or neuropathy. Similarly to experience in the TB setting, such side effects match with the duration of the treatment and the dose of the drug.[8,9] In this regard, Mori et al. showed that the 29% of patients in the 14-day and the 8.3% in the 10-day arm stopped the treatment due to adverse events.[1] In our experience,[10] the combination of a tetracycline (minocycline 100 mg b.i.d) with rifabutin at low dose (150 mg b.i.d) given for 10 days allowed a high per protocol eradication rate (84%) to be achieved, similar to what was found by Mori et al. (81.1%). Analogously, a similar side effect rate was

Gastroenterology Section, Department of Emergency and Organ Transplantation, University of Bari, Italy

Corresponding author:
Enzo Ierardi, Section of Gastroenterology, Department of Emergency and Organ Transplantation, University of Bari, Piazza Giulio Cesare, 70124 Bari, Italy.
Email: ierardi.enzo@gmail.com

observed (7.4% versus 8.3%), even if no patient stopped therapy in our series.

Finally, the ideal combination of antibiotics with rifabutin should be guided by the previous treatment failures. This detail has not been reported by Mori et al.,[1] even if they found that 16 strains (55%) were resistant to amoxicillin. This value is unexpectedly high compared to that reported worldwide.[2] Despite the authors having demonstrated that resistance to amoxicillin did not affect the outcome of the treatment, in agreement with current evidence,[11] it could be reasonable to avoid drugs that have been already used in previous unsuccessful regimens. This recommendation has been recently endorsed by the last Italian guidelines for *H. pylori* management.[12]

In conclusion, we believe that Mori et al. have provided useful information about the good performance of rifabutin in the treatment of multi-resistant *H. pylori*,[1] despite some warnings that could arise with the diffusion of this antibiotic administration. Therefore, the optimal patient and antibiotic association need to be linked to several factors.

Conflict of interest

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References

1. Mori H, Suzuki H, Matsuzaki J, et al. Rifabutin-based 10-day and 14-day triple therapy as a third-line and fourth-line regimen for *Helicobacter pylori* eradication: a pilot study. *United Eur Gastroenterol J*. Epub ahead of print 13 November 2015. DOI: 10.1177/2050640615618043.
2. Ierardi E, Giorgio F, Losurdo G, et al. How antibiotic resistances could change *Helicobacter pylori* treatment: a matter of geography? *World J Gastroenterol* 2013; 19: 8168–8180.
3. Malfertheiner P, Megraud F, O'Morain CA, et al. Management of *Helicobacter pylori* infection: the Maastricht IV/Florence Consensus Report. *Gut* 2012; 61: 646–664.
4. Cammarota G, Ianiro G, Bibbò S, et al. Culture-guided treatment approach for *Helicobacter pylori* infection: review of the literature. *World J Gastroenterol* 2014; 20: 5205–5211.
5. Gisbert JP and Calvet X. Review article: rifabutin in the treatment of refractory *Helicobacter pylori* infection. *Aliment Pharmacol Ther* 2012; 35: 209–221.
6. Rawson TM, Brima N, Almajid F, et al. Outcomes from treating tuberculosis with rifampicin or rifabutin in HIV-infected persons also receiving antiretroviral therapy. *J Acquir Immune Defic Syndr* 2015; 68: e84–e87.
7. El Maraachli W, Slater M, Berrada ZL, et al. Predicting differential rifamycin resistance in clinical *Mycobacterium tuberculosis* isolates by specific rpoB mutations. *Int J Tuberc Lung Dis* 2015; 19: 1222–1226.
8. Miehlke S, Hansky K, Schneider-Brachert W, et al. Randomized trial of rifabutin-based triple therapy and high-dose dual therapy for rescue treatment of *Helicobacter pylori* resistant to both metronidazole and clarithromycin. *Aliment Pharmacol Ther* 2006; 24: 395–403.
9. Griffith DE, Brown BA, Girard WM, et al. Adverse events associated with high-dose rifabutin in macrolide-containing regimens for the treatment of *Mycobacterium avium* complex lung disease. *Clin Infect Dis* 1995; 21: 594–598.
10. Ierardi E, Giangaspero A, Losurdo G, et al. Quadruple rescue therapy after first and second line failure for *Helicobacter pylori* treatment: comparison between two tetracycline-based regimens. *J Gastrointestin Liver Dis* 2014; 23: 367–370.
11. Mégraud F. Resistance of *Helicobacter pylori* to antibiotics and its impact on treatment options. *Drug Resist Update* 2001; 4: 178–186.
12. Zagari RM, Romano M, Ojetti V, et al. Guidelines for the management of *Helicobacter pylori* infection in Italy: the III Working Group Consensus Report 2015. *Dig Liver Dis* 2015; 47: 903–912.