A Prospective Trial in Saudi Arabia Comparing the 14-day Standard Triple Therapy with the 10-day Sequential Therapy for Treatment of *Helicobacter pylori* Infection: A Further Confirmation of "Geographic Weight"

Sir,

We read with interest the paper by Alsohaibani *et al*.[1] The problem of an adequate choice of firstline regimen for *Helicobacter pylori* eradication represents a hot topic. Ten-day sequential (S10) and 14-day prolonged triple (T14) therapies are the most used regimens. Authors demonstrated that success rates of S10 and T14 were 50.4% versus 59% in the intention-to-treat and 62.4% versus 67.6% in the per-protocol analysis, respectively, demonstrating an equivalent poor efficacy in their geographic area. These results are in agreement with a recent meta-analysis from our group,[2] which confirmed that S10 and T14 may have a comparable effectiveness in a global perspective, although the analysis was influenced by regional antibiotic resistances. Indeed, we demonstrated that S10 was better than T14 in areas with high resistance to clarithromycin. In the paper by Alsohaibani *et al*., the authors found that 23.3% of strains were resistant to clarithromycin (conventionally considered as high value: >20%). However, they found that the resistance to this antibiotic reduced more deeply the success of S10 (70.1% vs 10%) than T14 (74.1% vs 33.3%). This finding seems to contradict our previous experience.[3] Possible explanations for this disagreement could be as follows: (1) The low number (only 10) of patients with clarithromycin resistance receiving S10, (2) the lack of genotypic resistance evaluation. Indeed, a dozen 23SrRNA mutations may confer resistance to clarithromycin, even if they differently affect eradication rate, since A2143G mutation impacts on therapeutic outcome more than others.[4]

The relevance of geographic weight may be argued by another study recently performed in Taiwan[5] on a large sample. Antibiotic resistance rate was about 10% to clarithromycin and 25% to metronidazole by phenotypic analysis; thus, this country could be considered as a low resistance area for both drugs. This experience reported that success rates of S10 and T14 were 87.2% versus 85.7% in the intention-to-treat and 91.6% versus 91.0% in the per-protocol analysis, respectively, showing a very satisfactory outcome. In agreement with geographic power hypothesis, our above-mentioned meta-analysis[2] found that, in areas with low clarithromycin and high metronidazole resistance, S10 and T14 regimens had a similar outcome, whereas S10 was superior to T14 in areas with high resistance to clarithromycin, as pointed out here.

Therefore, we highlight that the choice of the most suitable regimen should be guided by the "geographic matter," that is, related to epidemiologic studies investigating the prevalence of antibiotic resistance.[6]

A final consideration is that the comparison between S10 and T14 has been reported in several trials, even if most of them have been performed in Asia, including Saudi Arabia and Taiwan. Conversely, similar studies are lacking in Europe or Northern America, thus limiting a worldwide conscious choice of the best firstline regimen. Thus, we feel that further studies comparing T14 and S10 from Western countries are warranted to overcome this geographic boundary. On these bases, we would like to underline that firstline *H. pylori* treatment should be advised country by country.

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Conflicts of interest
There are no conflicts of interest.

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