

Mobidiag proposes a test that revolutionizes management of *Helicobacter pylori* infection

Professor Christophe BURUCOA, PUPH, Head of Laboratory Bacteriology and Hygiene Department, Poitiers Hospital, presents the results of the multicentric prospective study carried out in the framework of the Hepystool Hospital Clinical Research Project.

Framework and objective of the Hepystool project

The Bacteriology and Hygiene Department of Poitiers University Hospital piloted a multicentric prospective study with support from the CHU Department of Hepatology Gastroenterology, CH de Montmorillon, CH de Thouars and CH de Parthenay, including 1,200 patients [University Hospital: CHU, Hospital: CH]. This is a PHRC (Hospital Clinical Research Program), called Hepystool, financed by Mobidiag and whose promoter is the University Hospital of Poitiers. The set convention specifies that the principal investigator is free to design the study and present the results. The purpose of this study was to establish a direct comparison between a non-invasive molecular diagnostics test for the detection of the *Helicobacter pylori* (Hp) bacteria and its resistance to clarithromycin from stools, and classical methods with culture and PCR on biopsy. We have thus evaluated the multiplex qPCR test Amplidiag® *H. pylori*+ClariR on stools (also validated on gastric biopsies) manufactured and distributed by Mobidiag.

Recommendations concerning treatment of *H. pylori* infection

For a long time we implemented probabilistic processing, that is blindly, with several antibiotics, as soon as the infection was confirmed. This strategy has led to the development of resistances which are today the cause of many therapeutic failures. The Haute Autorité de Santé (HAS) [French High Health Authority] piloted a meeting of experts and published last year its latest recommendations for treatment of *H. pylori* infection. It now recommends an oriented treatment, with an antibiogram to test sensitivity to clarithromycin. In case of sensitivity, we set up 10 days of tritherapy (PPI + amoxicilin + clarithromycin). In case of resistance, we test levofloxacin, which replaces clarithromycin in triple therapy. In case of resistance to levofloxacin, we then use metronidazole for tritherapy. In all cases, it is necessary to control the effectiveness of the treatment because if the bacteria is not eradicated, the patient can develop a stomach cancer. Clarithromycin sensitivity test plays a key role in this process. Until this day, an endoscopy with gastric biopsies was mandatory to perform this test.

A revolutionary test for patient care management

A non-invasive test that would detect *H. pylori* infection and resistance to clarithromycin would revolutionize the care of infected patients. A test released in the 1990s offered contrasting performances, often unacceptable, whose studies were carried out a small number of samples with confidence intervals too wide. The Amplidiag® *H. pylori*+ClariR proposed by Mobidiag is a multiplexed real-time PCR test. It identifies simultaneously *H. pylori*, resistance markers and sensitivity to clarithromycin, directly from DNA extracted from stool, in one reaction.



Pr. Burucoa and E. Pithon, referral technician in the laboratory

The Hepystool protocol

To evaluate the performance of the Amplidiag® *H. pylori*+ClariR test on stool, we compared it to the following reference methods: culture and / or real-time PCR that targets a specific gene of *H. pylori* on biopsies and an E-test and / or a quadriplex PCR which detects mutations associated with resistance to clarithromycin. We conducted a prospective multicentric study on patients naïve from eradication treatment. We did an antral biopsy and a fundic biopsy on which we used our reference method and we gave them a sampling kit for stools. This includes a disposable device to be placed on the toilet seat, an eNAT™ tube along with a swab and a stamped envelope for sending to the laboratory. We have wished to include many patients, 1200, to have very low standard deviations to obtain results precise in terms of sensitivity and specificity. As of today, 1214

patients were included. Of these, only 114 patients were excluded for post-inclusion refusal reasons (20), loss of contact (36), no sample reception (51) or antibiotic intake (7). The majority of patients are women (57%), 75% are born in Europe and 25% are from other continents.

Results of the study

The results of this study relate to 1056 analysed patients. They are excellent. They are above 95% for the sensitivity and specificity of detection of the DNA of *H. pylori*, at very low confidence intervals. The fairly low prevalence of 15.3% corresponds to the situation observed for many years in our territory. For resistance to clarithromycin, the results are also very good. The sensitivity is 97% and the specificity at 99.2% with a slightly lower resistance at 20% on our population. This rate had reached 24% three years ago, but has shown a decrease in several studies currently conducted in France. This observation is linked to a decrease of the consumption of macrolides which include clarithromycin. In view of these results, the Amplidiag® *H. pylori*+ClariR test appears excellent. Without performing any biopsy, simply recovering the stool, we get the expected results, which completely changes the patient care management with *Helicobacter pylori*. Although we recruited as part of this study people already informed of their diagnosis, we have very good compliance patients, with a stool delivery rate of 90%.

• Detection of <i>H. pylori</i> DNA			
Culture and/or PCR <i>glmM</i>			
	Positive	Negative	Total
Amplidiag®	155	10	165
	6	885	891
Total	161	895	1056

Sensitivity: 96.3% (IC 92-98)
Specificity: 98.9% (IC 98-99)
Prevalence Hp: 15.3%

• Detection of clarithromycin resistance			
E-test and/or Scorpion PCR			
	R	S	Total
Amplidiag®	29	1	29
	1	124	126
Total	30	125	155

Sensitivity: 97% (IC 83-99)
Specificity: 99.2% (IC 96-100)
Prevalence clar: 19.3%

Amplidiag® *H. pylori*+ClariR performances on stool: preliminary results in 1056 patients

Conditions of realization of the Amplidiag® *H. pylori*+ClariR test

In the laboratory, the Amplidiag® *H. pylori*+ ClariR test requires 5 minutes of technician time to perform the extraction that lasts an hour on the instrument and 10 minutes of preparation for 2h20 of PCR. The time to result is not an issue for patients but the workflow at the lab is easily manageable with these conditions of realization.

Conclusions of the study

The results of this study allow us to see the excellent performance of the Amplidiag® *H. pylori*+ClariR test for detection of *Helicobacter pylori* infection and resistance to clarithromycin detection. The test is

very easy to perform in the laboratory and its cost between 20 and 30 euros is very affordable. The Amplidiag® *H. pylori*+ ClariR test will revolutionize the treatment of infections to *H. pylori*. In patients younger than 40 with a positive Hp serology, the orientation of the treatment would be possible for a much better efficiency. Patients with positive anatomical analysis and no bacteriology would not need a new fibroscopy to achieve oriented treatment. In case of probabilistic treatment failure, with an anapath already performed, PCR will be very appropriate. Therefore we are now going to sit with gastroenterologists to define the correct indications of the test Amplidiag® *H. pylori*+ ClariR and how to use it at CHU de Poitiers. We can already confirm the great interest of general practitioners for this test and, in collaboration with gastroenterologists, simplifying the decision in charge of the patients concerned.

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Mobidiag in brief

Mobidiag develops innovative molecular solutions for the diagnosis of infectious diseases and antibiotic resistance. With its wide range of tests and instruments based on well-established PCR technology, Mobidiag enables rapid and economical detection of the most common bacteria, parasites, viruses and antibiotic resistance to meet the requirements of microbiology laboratories. Mobidiag is headquartered in Espoo, Finland, with subsidiaries in France, Sweden and the United Kingdom. For more information www.mobidiag.com