RAG Risk Assessment Group

PRIMARY RISK ASSESSMENT

Helicobacter pylori

Date of the signal	Date of the RA	Signal provider	Experts consultation	Method
16/11/2017	**12/12/2017**	**NRC Helicobacter**	Dr Sophie Quoilin, Dr Daniel Reynders, Dr. Valeska Laisnez, Dr Carole Schirvel, Dr Romain Mahieu, Mme Mireille Thomas Persons consulted: Gaetan Muyldermans, Dr Stéphanie Jacquinet	**eMail**
Date of update	**Closing date**			

RAG persons of contact: Dr Sophie Quoilin (Sophie.quoilin@wiv-isp.be, 02/642.54.04), Dr Tinne Lernout (tinne.lernout@wiv-isp.be), Ms Javiera Rebolledo (Javiera.rebolledo@wiv-isp.be)

PRIMARY RISK ASSESSMENT OF POTENTIAL PUBLIC HEALTH EVENT

RAG Risk Assessment Group

Signal	Early in 2017, the NRC compared over a 2-month period the performance of a new commercial multiplex RT PCR assay to H. pylori culture plus antimicrobial susceptibility testing to clarithromycin. Their results strongly suggest treatment failure despite the negative culture results. The NRC has therefor requested an emerging budget of the NRC to have additional financial support in order to realise a study. The procedure to benefit from this budget includes that the emergency will be assessed by the RAG.

Description			**Description / arguments**
Public health impact			
A	Public health impact in Belgium (Low/Medium/high)		We do not consider that a RA is required because we do not assess this finding as an emergency. We nevertheless consider that it is important to describe the impact of this finding in order to possibly improve the treatment for patient.
B	Recommendations (surveillance, control, communication)		This request does not match the criteria for an emerging public health threat but well for a need of further study. The RAG recommends that 1. Such a study will be included in the surveillance plan to be developed for/by the NRC in order to submit a financial request to MTAO (e.g.: one shot study or to be repeated on a regular base, how many samples, from how many centres, …) for the next call (foreseen in 2019). 2. In the meanwhile the MTAO will evaluate if a mechanism to finance specific or unexpected study having public health importance can be made available and for instance - if a study is necessary each X years, the budget for such an activity could be included in the yearly budget and the yearly part for the study 'transferred' to year X when the study is performed - a specific reserve for study such as for emergency 3. Considering that the role of the NRCs is indeed to have gold standard for the tests and that this finding is of importance for the treatment of patient, this study can be financed beforehand to have the position from the MTAO **IF** the financial balance of budget 2017 allows it **AFTER** having supported the already introduced requests on emerging budget.

REFERENCE DOCUMENT FROM THE NRC

FACTS

- **Testing for clarithromycin-resistance in *H. pylori* is essential** (before or after treatment failure) because this antimicrobial drug is a cornerstone drug in most anti-*H. pylori* regimens.
- **Primary clarithromycin-resistance in *H. pylori* is a strong predictor of treatment failure** and the **current prevalence is estimated as +/- 20% in Belgium**.
- **The proportion of secondary resistance to clarithromycin is increasing** over the recent years
- **The number of gastric biopsy specimens submitted "post-eradication therapy"** (ie: for monitoring the efficacy of anti-*H.pylori* drug regimens) **amounts 30% of all received specimens** and it has doubled over the last 5 years and in 2016-2017.

WHAT WE HAVE DONE AT THE NRC FOR H.PYLORI

Early in 2017, we evaluated over a 2-month period the performance of a new commercial multiplex RT PCR assay (*Helicobacter pylori* test Amplidiag® *H. pylori+ClariR*) comparatively to *H. pylori* culture plus antimicrobial susceptibility testing to clarithromycin.

Of a total of 160 patients (originating from 10 different endoscopy units) we found that **9% of the biopsies were positive for Hp by PCR while being negative by culture (**PCR+/culture -). The majority of the patients in this subgroup had received previous eradication therapies and detection of *H.pylori* nucleic acid was present in these cases in association with ARN23S alleles displaying point mutations that are known to be associated in with clarithromycin resistance, thus strongly suggesting treatment failure despite the negative culture results*.

*NB; the patients were not submitted to further follow-up for their *H.pylori* status

WHAT WE WOULD BE WILLING TO DO

Our aim is to evaluate **this test on a larger scale (over a 6 month period) all consecutive biopsies (estimated number =1000 to 1500 patients)** received at our reference center activity and also **to evaluate its clinical impact on a subset of patients that would be followed before and after eradication therapy**. The *H. pylori+ClariR* RT PCR assay will be performed in parallel to culture and to antimicrobial susceptibility testing. **Additional costs** for this test represent **€10/sample** and an **extra-budget of 15.000 € would be required** to cover the expenses and allow completing our evaluation.

PROSPECTS

This molecular RT-PCR assay is performed in less than 2 hours and is easy to implement in a clinical laboratory with facilities for molecular diagnostics. Further, this new assay could allow clinical laboratories to have access to H.pylori and clarithromycin-resistance status without practising culture which is quite demanding and cumbersome because of pre-analytical constraints and analytical requirements.