Pharmacogenomics-based treatment of helicobacter pylori infection
BlueCross BlueShield Association

Record Status
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Authors' objectives
To determine whether a pharmacogenomics-based treatment regimen is superior to a standard treatment regimen for the eradication of H. pylori, and whether the use of a pharmacogenomics-based treatment regimen improves health outcomes compared to standard treatment.

Authors' conclusions
This study demonstrates how pharmacogenomics can be used to individualize medication regimens, and how a clinical trial can be constructed to evaluate the impact of a pharmacogenomics-based treatment approach. This study is also notable in that it addresses a common, real-life clinical problem, and uses commercially available technology for pharmacogenomics-based decision-making. The optimal clinical trial for evaluating the utility of a pharmacogenomics-based H. pylori treatment regimen would isolate the impact of treatment changes made as a result of genetic status. Ideally, such a trial would be done in the U.S. in a population with rates of CYP2C19 polymorphisms approximating that of the general U.S. population. Also, the ideal trial would use an approach to diagnosing H. pylori that reflects usual care in the U.S. and would use a standard treatment regimen recommended for U.S. patients.

While the single available randomized, controlled trial reports an increased rate of H. pylori eradication in the pharmacogenomics strategy compared with a standard approach, this study does not meet the parameters for an optimal trial. The protocol for this trial includes changes in treatment regimen that are unrelated to genetic status, particularly regarding clarithromycin resistance. In addition, the study was performed in a Japanese population and did not employ a diagnostic approach or a treatment regimen that is standard care in the U.S.

The numerous variations in treatment regimen within the experimental group make it difficult to isolate the impact of genetic status on outcome, apart from other modifications in the treatment regimen, that may have led to benefit. In particular, it appears that clarithromycin resistance is an important factor in treatment success, and that there may be an interaction between clarithromycin resistance and CYP2C19 status. From the data reported in the study, it is not possible to separate the potential impact of clarithromycin resistance on eradication rates from the impact of tailored PPI dosage schedules.

In addition to the limitations on internal validity, the clinical relevance of the study is also limited for several reasons. The treatment approach used was relatively intensive, including genetic testing for CYP2C19, EGD with biopsy for all patients, and testing of H. pylori isolates for clarithromycin resistance. This treatment approach is much more intensive than generally used in the U.S., where the diagnosis of H. pylori is usually made by noninvasive methods and initial empiric treatment is instituted without isolating H. pylori or testing for resistance. Furthermore, the patient population was from Japan, limiting the generalizability of the results, especially given the higher prevalence of CYP2C19 polymorphisms in the Asian population compared to that in Caucasian populations.

Alternative treatment strategies exist for eradicating H. pylori that address some of the issues raised by CYP2C19 variability but do not rely on testing for CYP2C19 status. For example, empiric treatment with higher-dose PPI for all patients might be reasonable, particularly for non-Asian populations in which CYP2C19 mutation rates are lower. This approach may be as effective as regimens tailored by pharmacogenomics, with little additional risk. The use of a PPI that is less susceptible to CYP2C19 status, such as rabeprazole, might also be justified given that there is no reason to suspect that the use of omeprazole or lansoprazole offer other advantages. Ideally, a future clinical trial will evaluate...
whether a tailored pharmacogenomics approach is superior to other empiric approaches such as these.

Based on the available evidence, the Blue Cross and Blue Shield Association Medical Advisory Panel made the following judgments about whether the use of a pharmacogenomics-based treatment regimen for H. pylori meets the Blue Cross and Blue Shield Association's Technology Evaluation Center (TEC) criteria.

1. The technology must have final approval from the appropriate governmental regulatory bodies.

   At least one commercially available genetic test, the Roche AmpliChip® CYP450 test, has been cleared for diagnostic use by the U.S. Food and Drug Administration (FDA). This test examines polymorphisms in CYP2D6 and CYP2C19 isoenzymes of the cytochrome P450 enzyme system. Clearance for this device was originally granted in December 2004 as an aid in determining treatment choice and individualizing treatment dose for therapeutics that are metabolized primarily by the CYP2D6 enzyme. Subsequent clearance for CYP2C19 testing was granted in January 2005.

2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.

   The scientific evidence does not permit conclusions on whether the use of a pharmacogenomics-based treatment regimen for H. pylori improves eradication rates. In the single randomized, controlled trial comparing a pharmacogenomics-based treatment regimen with a standard regimen, eradication rates after first-line treatment were higher for the pharmacogenomics group compared with the standard treatment group. However, because of numerous variations in treatment protocol within the pharmacogenomics group, it is not possible to determine whether the improvement resulted from the tailored PPI dosages according to CYP2C19 genetic status, or was due to other variations in the treatment protocol unrelated to CYP2C19 status. It is possible that other clinical factors, such as clarithromycin resistance, or other treatment factors, such as length of antibiotic treatment, may have influenced eradication rates.

3. The technology must improve the net health outcome; and

4. The technology must be as beneficial as any established alternatives.

   It cannot be determined whether pharmacogenomics-based treatment of H. pylori improves the net health outcome, nor whether pharmacogenomics-based treatment of H. pylori is as beneficial as any established alternatives, since the evidence is not sufficient to permit conclusions on its effect on health outcomes.

5. The improvement must be attainable outside the investigational settings.

   It cannot be determined whether improvement is attainable outside the investigational setting since the evidence is not sufficient to permit conclusions on the effect of pharmacogenomics-based treatment for H. pylori on health outcomes.

For the above reasons, the use of a pharmacogenomics-based treatment regimen for H. pylori does not meet the TEC criteria.

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