Effective Health Care

Pharmacogenetic Testing for CYP2C19 Variants for Guiding Antiplatelet Treatment Nomination Summary Document

Results of Topic Selection Process & Next Steps

- Pharmacogenetic testing for CYP2C19 variants for guiding antiplatelet treatment will go forward for refinement as a systematic review. The scope of this topic, including populations, interventions, comparators, and outcomes, will be further developed in the refinement phase.

- When key questions have been drafted, they will be posted on the AHRQ Web site and open for public comment. To sign up for notification when this and other Effective Health Care (EHC) Program topics are posted for public comment, please go to http://effectivehealthcare.ahrq.gov/index.cfm/join-the-email-list1/.

Topic Description

Nominator: Government agency

Nomination Summary: The nominator is interested in evidence regarding the potential use of cytochrome P450 2C19 (CYP2C19) testing to predict response to clopidogrel in patients (1) with acute coronary syndromes, (2) who have suffered other cardiovascular disease-related events (e.g., ischemic stroke, symptomatic peripheral arterial disease), or (3) undergoing percutaneous coronary intervention. The nominator indicated interest in whether a genetic testing strategy could lead to improvements in health outcomes compared to a no-testing strategy, and in whether the genetic test results are useful in medical, personal, or public health decision making.

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Population(s): (1) Patients with acute coronary syndrome, (2) patients who have suffered other cardiovascular disease-related events (e.g., ischemic stroke, symptomatic peripheral arterial disease), or (3) patients undergoing percutaneous coronary intervention who are candidates for clopidogrel treatment. The nominator indicated that the prevalence of having one or two copies (corresponding to intermediate- and poor-metabolizer phenotypes, respectively) of reduced- or loss-of-function CYP2C19 variants is considered to be higher among Asians than African-Americans or Caucasians, suggesting that such subgroups of patients are of particular interest.
Intervention(s): Genetic testing for CYP2C19 variants to guide treatment selection. Because this is a comparison of testing strategies, there exist several treatment options that may be selected based on the test results (such as use of an alternative antiplatelet medication, or modification of the clopidogrel dosing regimen).
Comparator(s): A no-testing (for CYP2C19 variants) strategy or a strategy of testing for

intermediate phenotypes such as platelet reactivity. Note that a no-testing strategy implies treatment following the current guidelines (i.e., clopidogrel administration). **Outcome(s):** Recurrent ischemic events, stent thromboses, cardiovascular disease-related morbidity and mortality. Misclassification of drug metabolizer status, along with the possibility that it might result in excessive or inadequate dosing, and selection of alternate drug that proves to be less effective or to have more severe side effects (e.g., severe bleeding).

Key Questions from Nominator:

1. What is the evidence on the comparative effectiveness of genetic testing for CYP2C19 variants in patients who are candidates for clopidogrel treatment, compared to alternative testing strategies or a no-testing strategy?
   - What is the predictive value of CYP2C19 genetic testing for clinical outcomes among patients receiving clopidogrel treatment for the prevention of major adverse cardiovascular events?
   - What is the utility of CYP2C19 genetic testing for guiding treatment choice for patients who require antiplatelet therapy for the prevention of major adverse cardiovascular outcomes, compared to alternative testing strategies or a no-testing strategy?
2. Is the comparative effectiveness of testing for CYP2C19 variants modified by patient-level characteristics, including patient ethnicity or the co-administration of proton pump inhibitors?

Considerations

- The topic meets all EHC Program selection criteria. (For more information, see http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/.)

- While clopidogrel may decrease morbidity and mortality associated with several cardiovascular diseases, individual patient response to clopidogrel can vary substantially. Pharmacogenetic testing for CYP2C19 variants that could affect clopidogrel response is commercially available. An evidence-based review is needed, however, to determine whether and how these tests should be used in clinical practice to predict clopidogrel response in a way that could effectively improve health.