Reviewer's report:

Title: Genetic risk for atrial fibrillation could motivate patient adherence to warfarin therapy: a cost effectiveness analysis

Authors:
Dov Shiffman (dov.shiffman@celera.com)
Marco V. Perez (mvperez@stanford.edu)
Lance A. Bare (lance.bare@celera.com)
Judy Z. Louie (judy.louie@celera.com)
Andre R. Arellano (andre.arellano@celera.com)
James J. Devlin (james.devlin@celera.com)

Version: 1 Date: 25 March, 2015
Reviewer: Devender Dhanda

Level of interest: An article whose findings are important to those with closely related research interests

The authors have conceived and modeled an innovative approach to deal with the adherence issues prevalent with the warfarin therapy.

Major Compulsory Revisions:

1. In the methods section, the authors need to adequately describe and clarify the intervention and the two strategies compared in this study. It was unclear what the two arms were at the decision node. In the first few sentences of the methods section, the authors mentioned the first strategy was genetic testing and the second strategy was aspirin therapy (standard of care). In the last few sentences, the authors mentioned that they calculated the incremental cost effectiveness ratios (ICERs), “by dividing the difference in the costs of two strategies (warfarin adherence motivated by positive genetic test and warfarin non-adherence without genetic test”. The authors are advised to explicitly define the two strategies being compared and how were the ICERs calculated. In addition, a clear definition of study population would also be helpful.

2. Similar changes regarding the clear definition of comparators as mentioned above would be helpful in the methods section of the abstract.
3. A simple decision tree before the patient enters the Markov states would be helpful for the reader to understand the model structure. Since, the authors have developed a novel approach to improve adherence to warfarin therapy, the impact of study should not be lost in the complexity of the decision model structure.

Minor Essential Revisions:

1. In the methods section, the authors mentioned that the annual rate of conversion to warfarin for test-positive patients would be twice that of test-negative patients. Did the authors keep this two-fold rate constant throughout the life of the patient after entering the markov cycle, or the rate varied as the patients moved along the life markov states?

2. It would help the readers to better interpret and comprehend the results of the study if the authors can provide a table of comparative costs and outcomes (mentioned in the methods section), from the two strategies compared at different adherence levels assumed by the authors.

3. The authors are advised to clearly mention the cycle length between the markov states in the methods section

4. The year of the costs incorporated to estimate the ICERs should be mentioned in the methods section.

Discretionary revisions:

1. Under the sensitivity analyses section (methods), the authors referred to “multivariate analysis using Monte Carlo simulations...”. The authors may use the term “probabilistic sensitivity analysis”, consistent with the economic evaluation literature. If the authors already ran 10,000 simulations to perform PSA, reporting of the cost and outcomes with 95% credible ranges would enhance the impact of the estimates of the study.

2. The authors may use the term the genetic testing “dominated” standard of care rather than reporting negative ICERs, wherever possible.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.