

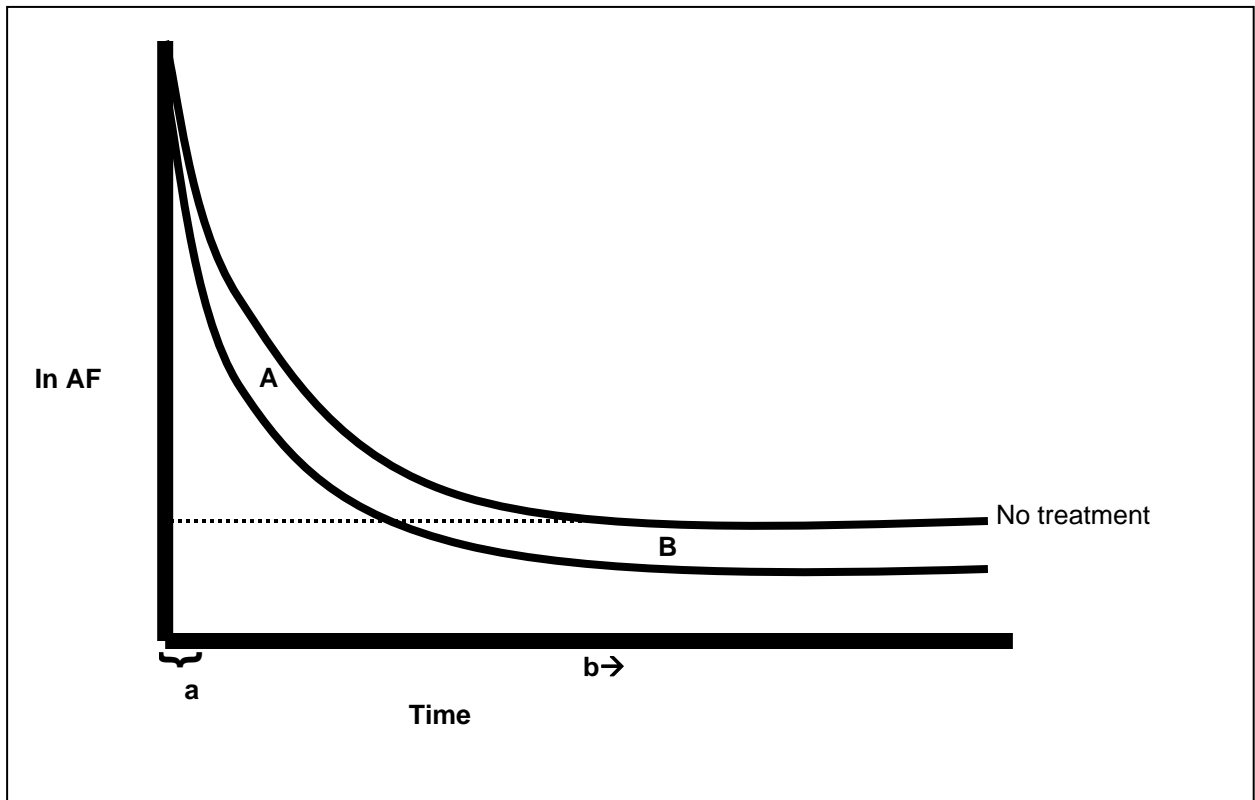
Questions



General
Considerations
Atrial Fibrillation
December 11, 2007

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Cardio-Renal Advisory Committee

The Advisory Committee is asked to opine on the appropriate role of two proposed new drugs to effect conversion of atrial fibrillation (AF) to normal sinus rhythm. The time dependencies make this determination challenging, as illustrated by the diagram below:



Any effective therapy reduces the risk of being in AF corresponding to region A. There may or may not be a region B representing risk reduction for patients who would never have converted spontaneously.

Using an effective therapy too early (period a) is of no utility because the spontaneous conversion rate is high, so the opportunity for benefit is small compared with the risks of treatment.

If region B exists, delaying treatment too long (period b) loses any opportunity to benefit patients who are at risk because of their AF for moderate periods of time.

If that were not complicated enough, one may have to consider that some of the risks associated with being in AF (e.g., for having an embolic stroke) are also likely to depend on time in AF.

1. Before considering drugs to effect conversion of AF (and AFL) to normal sinus rhythm, the AC is asked to consider:
 - How well characterized is the time course for spontaneous conversion?
 - How well characterized are the harms of being in AF??
 - How well characterized is the time course for successful electrical conversion?
2. What are the disadvantages to waiting for spontaneous conversion?
 - Symptoms?
 - Risk of being on anticoagulant therapy?
 - Reduction in the success rate for conversion?
 - Poorer hemodynamic outcome?
 - Shorter duration of normal sinus rhythm?
 - Other?
3. Can you describe the magnitude and durability of any of these disadvantages?
4. What is the right interval to integrate the success of spontaneous conversion? If someone were very likely to convert spontaneously within the next hour, would it make sense to consider treatment options? Within the next day? Within the next week?