Question 3 – Week of November 23

In which study populations were the COX-2 selective inhibitors celecoxib and rofecoxib shown to have a significantly increased risk of cardiovascular events compared to placebo?

A. Rheumatoid arthritis subjects.
B. Osteoarthritis subjects.
C. Subjects with prior colorectal neoplasms.
D. Subjects with recent myocardial infarctions.

Answer: C

To assess whether these agents increased the risk of cardiovascular events vs. placebo would require large studies of long duration. This is not practical in the standard studies of NSAIDs because these studies are conducted in arthritis subjects who cannot remain on placebo for long periods. The fact that NSAIDs may decrease the development of colorectal neoplasm led to large, long-term trials of coxibs vs. placebo in subjects with prior colorectal neoplasms to determine if coxibs would decrease recurrences with relative safety. These trials allowed assessment of CV events as well and documented a significant increase (RR: 1.9-3.4) with rofecoxib and celecoxib (the latter was dose related with the larger increase with 400 mg bid). Another group in which a COX-2 selective inhibitor was shown to be worse than placebo, but over a matter of days rather than years, was the very high-risk post-CABG population (valdecoxib was used in this case).

References:

1. Solomon SD, McMurray John JV, Pfeffer MC, et al. Cardiovascular risk associated with celecoxib in a clinical trial for colorectal adenoma prevention. N Engl J Med 2005;352:1071-1080.

2. Bresalier RS, Sandler RS, Quan H, et al. Cardiovascular events associated with rofecoxib in a colorectal adenoma chemoprevention trial. N Engl J Med 2005;352:1092-1102.