To: Nies, Alan S.; Gertz, Barry J.
From: Reicin, Alise S.
Cc Ehrich, Elliot W.; Daniels, Brian F.; Scolnick, Edward M.; Slater, Eve; Blois, David W.
Bcc:
Date: 2000-03-28 19:54:40
Subject: FW: Carlo Patrono on VIGOR

I have attached a message from Martino re his discussions with Carlo Petrono. I think it would be worth walking through the data with Carlo. Do you think we should try and set up a teleconference?
Alise

From: Laurenzi, Martino
Sent: Tuesday, March 28, 2000 2:10 PM
To: Daniels, Brian F.; Ehrich, Elliot W.; Reicin, Alise S.
Cc: Chakhov, Iouri; de Jesus, Daniel G.; Guerra, Jorge G.; Hormbrey, Janet; Kylish, Gregory S.; McKinney, Errol S.; Moan, Andreas; Ruef, Tim; Salib, Atif; Schwartz, Jules; Yrivarren, Juan Luis
Subject: Carlo Patrono on VIGOR

Guys,

I met with Carlo Patrono last Saturday in Rome. He had already been informed by other sources about the results of VIGOR, and we had an interesting chat about it.

He said that he does not think that the CV effect that we observed can be attributed to naproxen for a couple of good reasons. First there is a weak pharmacological basis and no epidemiological evidence (Garcia Rodriguez & Patrono, Epidemiology, in press) for CV protection associated with conventional NSAIDs. Additionally the magnitude of the effect would not be plausible even if the comparator had been aspirin itself. In fact, in at least three different trials, aspirin has shown no effect on the primary prevention of stroke, while we have seen a 50% lower incidence of stroke in the naproxen arm of VIGOR; additionally, we have an overall reduction of the risk of CV events of 47% with naproxen, while aspirin has shown a reduction of cumulative CV risk of a magnitude between 15 and 18%. Aspirin data come from a primary prevention setting (similar to VIGOR) and include the Physicians Health Study, the Thrombosis Prevention Trial (Lancet 1998) and the Hypertension Optimal Treatment Trial (Lancet 1998).
Carlo also does not think that the CV effect can be explained by the inhibition of prostacyclin given that VIOXX inhibits only the COX-2 component of prostacyclin secretion, and he has conceptual difficulties in explaining how this could translate in an increase of the CV risk of the magnitude that we observed. His conclusion is that what we saw in VIGOR is to be attributed to a large extent to chance. He is curious about the 95% confidence interval around the 47% reduction in CV risk. He also pointed out that in CV disease DVT (deep venous thrombosis) is considered as a soft end-point which usually is not included in this type of analysis. He suggested that we carry out an analysis limited to nonfatal MI, nonfatal stroke and vascular death, i.e. the cluster typically used in the studies on platelet aggregation.

Food for thought, coming from the world's most respected and knowledgeable gourmet.

Best regards,

Martino Laurenzi
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