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Pfizer Global Pharmaceuticals

August 28, 2007

Mr. Eddie Vos
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Dear Mr. Vos:

Your June 22nd email to Jeffrey Kindler, CEO, Pfizer Inc requesting certain Lipitor mortality data was forwarded to me for a response. Specifically, you requested data referenced in a peer reviewed publication entitled *Comparative Safety of Atorvastatin 80mg versus 10mg derived from analysis of 49 completed trials in 14,236 patients*' which was published in the *American Journal of Cardiology* in 2006.

The objective of this analysis was to compare the safety of atorvastatin 10 mg with the higher dosage of 80 mg, and placebo using data available as of Sept 15, 2004. Accordingly, 49 studies were pooled for this analysis.

In connection with your request, it is important to highlight certain limitations of the analysis, which were clearly outlined in the publication:

1. The majority of these 49 studies were short term and designed to evaluate efficacy with respect to lipid profiles (e.g., LDL-C lowering) and were not designed or powered to evaluate mortality.
2. Many of the studies were non-placebo controlled such that the comparator was not placebo but another dose, statin or a procedure. That explains why the number of subjects randomized to placebo was significantly lower than the number randomized to Atorvastatin.
3. The baseline LDL-C and total cholesterol levels and the duration on treatment was significantly less for the placebo arm as compared to the Atorvastatin 10 or 80 mg dosage arms and as you may be aware there is an association between lower mortality rates and lower LDL-cholesterol levels.
4. Three of the 49 studies were long term studies and included "mortality" as a pre-specified *efficacy* endpoint. As described in the publication, the mortality data from these three studies were not included as a *safety* endpoint in this publication. However, the data from these three studies have been published and the references are included in the above-referenced American Journal of Cardiology.

With respect to mortality, the publication states that "The incidence of death was low, <=0.4% in each of the treatment groups. None of the deaths were considered to be related to treatment." Keeping in mind the limitations noted in the publication and that we reiterate above, the specific information which you have requested for each arm reported in the publication is: 0.4% or 29/7258 for Atorvastatin 10mg, 0.35% or 17/4798 for Atorvastatin 80mg, 0.09% or 2/2180 for placebo.

Because of your apparent interest in the incidence of mortality with Atorvastatin usage, we wish to point out that Pfizer has, in conjunction with independent steering committees, designed and conducted numerous long term cardiovascular endpoint studies which have examined the effect of Atorvastatin on long term cardiovascular endpoints, including mortality. These studies have been presented at scientific congresses, published in various peer reviewed journals and are also posted publicly on the www.clinicalstudyresults.org website.

Although beyond the scope of your initial request, we have taken the liberty of including for you the mortality rates from many of these long term cardiovascular endpoint trials:

- The *ASCOT-LLA*[1] study, consisting of 10,305 patients with hypertension and additional risk factors, showed all cause mortality event rates as 3.6% (185/5168) on atorvastatin 10mg compared to 4.1% (212/5137) on placebo resulting in a hazard ratio of 0.87 (p-value = 0.166).
- The *CARDS*[2] study with 2838 diabetic patients who had no history of coronary heart disease showed all cause mortality event rates to be 4.3% (61/1428) on Atorvastatin 10mg compared to 5.8% (82/1410) on placebo resulting in a hazard ratio of 0.73 (p-value = 0.059).
- In a higher risk patient endpoint study, *ALLIANCE*[3] with 2442 patients with coronary heart disease, demonstrated all cause mortality event rates of 9.9% (121/1217) on Atorvastatin compared to 10.4% (127/1225) on usual care resulting in a hazard ratio of 0.92 (p-value =0.52).
- The *TNT*[4] study with 10,001 patients with clinically evident coronary heart disease showed all cause mortality event rates of 5.7% (284/4995) on Atorvastatin 80mg compared to 5.6% (282/5006) on Atorvastatin 10mg resulting in a hazard ratio of 1.01 (p-value = 0.92).
- The *IDEAL*[5] study with 8888 patients with coronary heart disease showed all cause mortality event rates of 8.2% (366/4439) on Atorvastatin 80mg compared to 8.4% (374/4449) on simvastatin 20-40mg resulting in a hazard ratio of 0.98 (p-value = 0.81).
- The MIRACL[6] study, although only 16 weeks, looked at high risk patients with Acute Coronary Syndrome; mortality event rates were 4.2% (64/1538) on Atorvastatin 80mg compared to 4.4% on placebo (68/1548) with a hazard ratio of 0.94.
- In the AVERT[7] study, following 341 patients with coronary artery disease for 18 months who had either received Atorvastatin 80mg or undergone angioplasty, there was only 1 death in each arm (0.6% in each arm).
- The *SPARCL*[8] study in 4731 patients with recent stroke or TIA showed that all cause mortality event rates were 9.1% (216/2365) on Atorvastatin 80mg compared to 8.9% (211/2366) on placebo with a hazard ratio of 1.03 (p-value = 0.77).

As is evident in each of these long-term cardiovascular endpoint trials, the incidences of deaths between treatment groups are similar.

We hope that this letter responds to your inquiry and we appreciate your interest in the safety of our product. Pfizer is committed to disclosing information about its medicines and actively pursues publication of its data in peer reviewed journals and continuously posts results from our completed clinical trials on public websites.

Sincerely,

H. S. Bander

Halit S. Bander, PhD
Senior Director, Global Medical Team Leader, Atorvastatin
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Cc: Jeffrey B. Kindler, CEO, Pfizer Inc.

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