



ILLUMINATE trial terminated

The ILLUMINATE trial was a Pfizer-funded study designed to test whether the experimental cholesteryl ester transfer protein (CETP) inhibitor drug, torcetrapib, reduces cardiovascular events. On Saturday December 2nd the Chairman of the Steering Committee of the ILLUMINATE study informed Pfizer that the Independent Data Safety Monitoring Board (DSMB) overseeing the study had reported an adverse imbalance of mortality and cardiovascular events in the torcetrapib arm. As a consequence, the Steering Committee recommended to Pfizer that the study be terminated.

In the interest of patient safety, Pfizer accepted this recommendation and terminated the ILLUMINATE study and all other trials with torcetrapib. They contacted all clinical investigators to request that they inform patient participants to stop taking study medication immediately. Pfizer has informed the FDA and other regulatory authorities of the outcome. No one in Pfizer had access to the data prior to December 2nd and as recently as one month before, the company had received an official communication from the Data Safety Monitoring Board that there was no reason to stop the study. Pfizer has announced that it will discontinue the development of torcetrapib.

Based on all the evidence available regarding torcetrapib and in the light of prior study results, this adverse outcome in the ILLUMINATE study was most unexpected and extremely disappointing.

The ILLUMINATE trial enrolled over 15,000 patients. The number of deaths was 82 in the torcetrapib/atorvastatin arm compared to 51 deaths in the atorvastatin arm. This difference was statistically significant. The event rate seen in the atorvastatin arm of the ILLUMINATE trial was consistent with the rate seen in other trials including those with similar populations.

It is not known at this time why there was an excess of deaths in the patients treated with torcetrapib. It is hoped that the explanation will emerge following further analyses of the results.

Question: **What do the safety issues in ILLUMINATE mean for the HDL hypothesis?**

Answer: There is nothing in the ILLUMINATE trial to invalidate the HDL hypothesis.

Question: What do the safety issues in ILLUMINATE mean for CETP inhibition as a strategy to reduce cardiovascular disease?

Answer: This question cannot be answered at this time. It is not yet known whether the excess of deaths in patients taking torcetrapib was a consequence of inhibiting CETP or whether it was due to some side effect of the drug that is unrelated to CETP inhibition. The answer to this question will have to await further analysis of the ILLUMINATE results.