United States Senate
Committee on Finance

Sen. Chuck Grassley · Iowa
Ranking Member

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M E M O R A N D U M

TO: Reporters and Editors
FR: Jill Kozeny, 202/224-1308
for U.S. Sen. Chuck Grassley of Iowa
RE: Questions about statements regarding drug trial
DA: Friday, January 25, 2009

Sen. Chuck Grassley made the comment below about the American College of Cardiology clarifying its position today on ezetimibe (Zetia). In an email from CEO Jack Lewin, the College stated, "The benefits of statins have been proven in large studies, while the effect of ezetimibe is unproven." The text of the email appears below Sen. Grassley's quote. The College's January 15 statement is below today's email message, along with a statement made yesterday by Sen. Grassley about the ENHANCE study.

"I'm glad to see that the ACC is putting doctors and patients first. I can only wonder what took them so long. I look forward to their continued cooperation with my investigation," said Sen. Chuck Grassley of Iowa, Ranking Member of the Committee on Finance.

ACC Email on ENHANCE, released on January 25, 2008.
From: Jack Lewin [mailto:jlewin@acc.org]
Sent: Friday, January 25, 2008 10:55 AM
To: Board of Governors
Subject: ACC Response to ENHANCE

Dear BOG:

By now you may have heard through media reports or word-of-mouth that the ACC is receiving inquiries from Congress and others regarding the release of a January 15 public statement regarding the ENHANCE trial. The College's intent in issuing this statement was to advise our physician members looking for guidance in light of the ENHANCE trial data release. A long delay in the release of the data and highly focused media attention led to questions and concerns from our members and their patients. Our statement was designed to minimize undue panic and guide our physicians in communicating with patients about the new data.

The following statement further clarifies our position in light of recent inquiries and news reports:

"The American College of Cardiology (ACC) is concerned that recent news reports and advertisements for ezetimibe (zetia) and ezetimibe/simvastatin (vytorin) could be misinterpreted by patients as an ACC endorsement of ezetimibe for first-line treatment for high LDL (bad cholesterol) or to reduce further risks of coronary heart disease.

The ACC and American Heart Association have published guidelines which recommend that a statin be given as first-line treatment and that alternatives be used only when statins fail to be effective or are associated with significant side effects. The benefits of statins have been proven in large studies, while the effect of ezetimibe is unproven.

Nonetheless, if patients taking medications have questions about their treatment, they should discuss concerns with their physician before making any changes.

The ACC has provided guidance to all our members regarding the recent findings."

The ACC will of course cooperate fully with all congressional requests for information related to the January 15 statement, including sharing our commitment to patient-centered quality and a high standard of professional ethics.

Thank you for your attention to this important matter.

Jack

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ACC Statement on ENHANCE Trial

January 15, 2008

The ENHANCE (Effect of Combination Ezetimibe and High-Dose Simvastatin vs. Simvastatin Alone on the Atherosclerotic Process in Patients with Heterozygous Familial Hypercholesterolemia) trial results were released by Merck and Schering-Plough Pharmaceuticals on January 14, 2008. The results of the trial show no benefit from the combination of ezetimibe (Zetia) and simvastatin (sold together as Vytorin) over simvastatin alone in terms of affecting the rate of atherosclerosis progression.

The study involved 720 patients with heterozygous familial hypercholesterolemia and showed no significant difference in the primary endpoint between patients treated with ezetimibe and simvastatin versus patients treated with simvastatin alone over a two-year period. The study was designed to prove that Vytorin could slow the growth of plaque in carotid arteries supplying the brain more than simvastatin alone. Media reports indicate that the results of the trial show no benefit from the combination of ezetimibe (Zetia) and simvastatin (sold together as Vytorin) over

simvastatin alone.

The American College of Cardiology recommends that major clinical decisions not be made on the basis of the ENHANCE study alone.

According to the American College of Cardiology (ACC), this study deserves serious thought and follow-up. The overall incidence rates of cardiac events were nearly identical between both treatment groups, and both medicines were generally well tolerated. There should no be reason for patients to panic. The difference in IMT changes between the simvastatin group and the Vytorin group was 0.006 mm vs. 0.011 mm.

Health care professionals should speak to their concerned patients using this drug. The ACC is also releasing a public statement explaining that this is not an urgent situation and patients should never stop taking any prescribed medications without first discussing the issue with their health care professional. Further research will be needed in this area to provide conclusive evidence about which lipid lowering strategy is preferred (statin alone vs. statin plus ezetimibe).

Furthermore, the ACC notes that this trial is an imaging study and not a clinical-outcome study. Conclusions should not be made until the three large clinical-outcome trials are presented within the next two to three years. The ACC recommends that Zetia remain a reasonable option for patients who are currently on a high dose statin but have not reached their goal. The ACC also notes that Zetia is a reasonable option for patients who cannot tolerate statins or can only tolerate a low dose statin.

Reports also indicate that the ENHANCE trial has been submitted as an abstract to be presented at the upcoming American College of Cardiology Scientific Session in March, 2008. The late-breaking clinical trial selections by the meeting co-chairs are scheduled to occur in late January.

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M E M O R A N D U M

TO: Reporters and Editors
FR: Jill Kozeny, 202/224-1308
for U.S. Senator Chuck Grassley
RE: Controversy over delayed release of drug trial on Vytorin
DA: Thursday, January 24, 2008

Senator Chuck Grassley, Ranking Member of the Committee on Finance, is asking drug makers Schering-Plough and Merck to explain when the companies first unblinded ENHANCE trial results and to account for sales and payments made for the cholesterol drug Vytorin to Medicaid. Senator Grassley has also written to the Securities and Exchange Commission, the American Heart Association and the American College of Cardiology regarding this matter. Copies of all four letters are posted with this statement at http://finance.senate.gov.

Background information:

Schering-Plough and Merck recently released the results of the ENHANCE trial which studied whether Vytorin performed as well as a generic statin to lower cholesterol levels. Vytorin is a combination pill of ezetimibe and a generic statin. The ENHANCE trial results found that Vytorin performed just as well as a much cheaper statin. The professional associations issued statements at the time the ENHANCE study was released, so Sen. Grassley is asking for more information about contributions to this statement. For the past three years, Senator Grassley has conducted oversight of various federal agencies and companies to ensure that peer reviewed science forms the basis for decisions in healthcare and healthcare payments.

Senator Grassley's comment:

"In Iowa City, generic simvastatin costs $54.54 for a month's supply while Vytorin costs $112.46. It's fair to assume the public would have benefitted from knowing that a less expensive drug works just as well. Instead, people in Iowa and elsewhere paid more for nearly two years while industry leaders sat on a scientific study that would have revealed this information."