

BACKGROUND ON THE IMPROVE-IT TRIAL

ABOUT THE IMPROVE-IT TRIAL

The IMPROVE-IT trial is an event-driven cardiovascular clinical outcomes study. The purpose of the trial is to determine whether VYTORIN 10/40 mg provides incremental reductions in cardiovascular events in patients recovering from acute coronary syndrome in comparison to simvastatin 40 mg alone. The trial is also designed to determine whether this benefit can be seen in patients whose LDL cholesterol levels have been reduced to a lower absolute LDL cholesterol range than has been achieved in previous major outcomes studies.

IMPROVE-IT TRIAL ENROLLMENT INCREASED TO UP TO 18,000

The academic leadership of the IMPROVE-IT trial -- Dr. Eugene Braunwald from TIMI (trial chairman) or Dr. Robert Califf from Duke (co-chairman) -- have recommended increasing the size of the patient population to up to 18,000 to enable the accrual of the needed number of clinical events in the most timely manner. Merck/Schering-Plough Pharmaceuticals, sponsor of the study, agreed with the recommendation.

The trial will continue until a minimum of approximately 5,250 events (cardiovascular death, major coronary event, stroke) have occurred and until each patient is followed for a minimum of 2.5 years.

The recommendation from the academic leadership was based on recent analyses of the blinded, aggregate event rates in the IMPROVE-IT trial and published data on the relationship between lowering LDL cholesterol and clinical benefit that have emerged since the original protocol was prepared.

COMPLETION OF IMPROVE-IT TRIAL

It is not possible to determine with precision an exact date that the trial will end. IMPROVE-IT is an "event driven" trial and therefore the end of the study is determined when the target number of events is reached and the last patient enrolled has been followed for a minimum of 2.5 years. The actual date of completion is highly dependent on the observed event rates during the follow-up phase of the trial and the rate of enrollment. With the increase in enrollment, the current estimate for the completion of the trial is 2012.