Although biomarkers that are not surrogate end points cannot be used as proof of efficacy, they can be used to increase the efficacy of clinical trials. A biomarker that is present only in certain patient populations, such as patients with HER2/neu-positive breast cancer, could be used as an entry criterion into a clinical trial designed to measure the clinical benefits of a candidate compound that modulates the target. Restricting the patient population in this manner increases the likelihood of success (assuming a positive result is possible), and decrease the risk to patients by preventing patient that could not benefit from the treatment (in this case, HER2/neu-*negative* breast cancer patients) from being exposed unnecessarily to candidate compounds that is unlikely to help them. Herceptin® (Trastuzumab), a monoclonal antibody for the treatment of HER2/neu-positive breast cancer, was brought to market using data based in part on this strategy.[27]

Safety-related biomarkers can also be very effective tools in clinical trials, as they can provide an early warning that a candidate compound has a potential problem. Consider, for example, a candidate compound under investigation for the treatment of osteoarthritis. Phase III clinical trials designed to determine the efficacy of a candidate compound for this condition would require a substantial number of people and long-term monitoring. Safety-related biomarkers that can be examined early in the trial could provide rational for ending a trial early if there is an indication that there may be problems with the candidate compound. If the candidate compound raised cholesterol concentrations in the blood or increased blood pressure in a subset of the patient population, it would be useful to know this early in the trial. If the risks are high enough, the trial might be ended early, or enrollment requirements may be altered so that patient at risk would not be allowed to enter the trial. In either case, the risk to patients is minimized and the overall cost of clinical trials is lowered as less time is required to terminate trials based on safety risks.

IMAGING TECHNOLOGIES

Although biochemical, physicochemical, and pharmacological biomarkers can be very useful, they are, at the end of the day, an indirect indication of what is truly occurring in the body. Elevated blood pressure and high cholesterol are certainly linked to an increased risk of cardiovascular disease, but recording changes in these biomarkers does not provide direct information on the condition of the cardiovascular system itself. Frequent measurements of blood pressure cannot on their own provide direct insight into the condition of the heart itself or indicate where blockages may be occurring. Similarly, human chorionic gonadotropin (hCG) can serve as a biomarker to indicate whether or not a woman is pregnant (e.g., at-home pregnancy tests via detection of hCG in the urine), but it provides no information on the overall progress of fetal development no matter how many times the test is administered.