Comparative Effectiveness Research — Watch and Worry or Weigh In and Leverage?

Dr. Ramana Yalamanchili
Senior VP, Chief Clinical Strategist, HLS, part of Ogilvy CommonHealth

Mary Anderson
President, HLS, part of Ogilvy CommonHealth

Michael Zilligen
President, ProCom, part of Ogilvy CommonHealth

As CER takes root and grows in the United States, global medical education organizations will be well positioned to bring experience and insights from other regions to assist U.S. pharmaceutical and device manufacturers in positioning their products effectively and in educating health care stakeholders in the appropriate use of comparative data.

A little-publicized provision of the American Recovery and Reinvestment Act of 2009 is likely to have at least as big, if not a bigger, long-term impact on the pharmaceutical and medical device business as the recently passed Affordable Care Act. This provision allocated $1.1 billion for comparative effectiveness research (CER) — a mode of research that has been in place in many other countries for the past several decades. The stated goal of the CER program is to improve health outcomes based on evidence-based information. Other considerations include addressing the needs of populations traditionally underrepresented in clinical research and development of personalized medicine. CER studies are expected to be sufficiently powered to meet these needs. At the present time, the allocated funds are to be used for laying the foundation for such research, including the development of human and scientific capital, provision of data infrastructure, and dissemination of findings. Historically, the National Institutes of Health, the U.S. Department of Veterans Affairs, various state collaboratives, and payer organizations have funded public and private research projects that fit under the broader CER umbrella. Pharmaceutical and device manufacturers also fund some of this research.

Role in Regulator and Payer Decisions

The United States is a latecomer to CER. European countries have established CER systems over the past 2 to 3 decades to systematically assess the relative value of new products and technologies. In addition to policy makers, CER has a broad spectrum of stakeholders including physicians, pharmacists, health economists, insurance and industry representa-

tives, and patients. Some organizations, such as the National Institute for Health and Clinical Excellence in the United Kingdom, have a citizen council to provide the patient point of view on important social and ethical issues relating to the use of CER. Of note is the fact that the role of pharmaceutical manufacturers in many countries is limited to submission of dossiers.

The most important criterion determining coverage in many European countries is the relative therapeutic benefit of the drug (ie, mortality, morbidity, quality of life), followed by cost-effectiveness measured in cost per quality-adjusted life year. In most cases, randomized controlled trial data are preferred, while health economic information is required or recommended. Most agencies specify the type of comparator required for the analysis and may include one or more of the following: current best alternative, routine treatment, most frequently used alternative, cheapest alternative, nonmedical intervention, no treatment, and alternative most recently added to the positive list.

Following the review, most countries provide coverage for all approved drugs, but usually with restrictions on indications or patient populations, especially for me-too drugs. Thus, a certain level of innovation (eg, ease of use) or incremental therapeutic benefit is required for good reimbursement. In the case of expensive drugs and/or severe conditions with significant patient advocacy, some countries are instituting risk-sharing arrangements such that coverage is based on meeting prespecified targets of cost-effectiveness or collection of postmarketing evidence and reevaluation.

A combination of a drug's therapeutic benefit and the disease severity is used in some countries to determine the level of cost-sharing (copayment by patients). This strategy, which is somewhat similar to the tiered coverage in the United States, assumes that consumers are willing to share a higher proportion of the cost for certain more expensive medications offering additional benefits. However, most patients may not be equipped to determine the relative value of a medication. In such scenarios, manufacturers may have to educate consumers regarding the CER information supporting their products.

Implications for U.S. Pharmaceutical and Medical Device Industries

As CER becomes more established and gains acceptance in the United States, the data may eventually be used to make regulatory or coverage decisions in the public or private sector, as is the current practice in many other countries. If this were the case, the already astronomical cost of drug development is likely to continue increasing due to the need for ever larger studies with potentially longer duration to demonstrate superiority in end points. Barriers to entry of follow-on compounds may increase, or defense of a leadership position may become difficult, depending on how the coverage environment develops.

In the absence of rigorous standards, low-grade evidence may be used to deny coverage, reduce reimbursement, or restrict products to specific uses or patient populations. The Pharmaceutical Research and Manufacturers of America and the Advanced Medical Technology Association now have an opportunity to lead the CER process in the United States by providing guidance, using evidence-based medicine (EBM) principles, to the industry regarding standards for conduct and dissemination of CER.

In addition, manufacturers may also collaborate with decision makers to ensure transparency in the use of CER data early in the process of making regulatory, coverage, and reimbursement decisions. Transparency and access to data will allow professional societies and independent groups to continuously update clinical practice guidelines and decision tools to effectively and efficiently deliver individualized care.

In a world dominated by CER, the use of placebo controls, as is common in clinical trials, may be inadequate. Novel trial designs using active controls and ongoing refinements to incorporate novel end points, such as cost considerations, may be required to demonstrate value for initial approval as well as continued use. Pharmaceutical and device manufacturers have a significant opportunity to demonstrate innovation and support rational public health policies. In the process, CER may open up opportunities for enhanced coverage or reimbursement for innovative products demonstrating superior results compared with existing options or satisfying unmet needs, especially in severe conditions or diseases with high patient advocacy. Due to its very nature, CER may allow superiority claims and make direct-to-consumer campaigns more effective. Collaboration of commercialization and clinical teams early in clinical development may maximize such opportunities.

Opportunities for Medical Education

As stated in the 2009 Annual Report to the President and the Congress, justification for health care choices should include effectiveness, safety, and convenience for an individual patient, in addition to cost. Medical education groups will have a great opportunity to partner with pharmaceutical and device manufacturers to educate the decision makers and the general public about the nuanced value of CER. As CER takes root and grows in the United States, global medical education organizations will be well positioned to bring experience and insights from other regions to assist U.S. pharmaceutical and device manufacturers in positioning their products effectively and in educating health care stakeholders in the appropriate use of comparative data.

Organizations that are able to integrate the disciplines focused on managed access with expertise in EBM, clinical platform development, and insightful assessment of data will transform the value of medical education in the era of CER. Pharmaceutical and medical device manufacturers will benefit from partners offering broad global expertise in clinical trial designs, biostatistics, health economics, and sophisticated regional communication strategies throughout the product life cycle. ■

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