What makes oncology phase I trials unique?

Most clinical trials use healthy participants. Research medication doses are adjusted according to toxic side effects. Then in phase II of the trials, the focus changes from toxicity to efficacy for specific diseases.

In oncology phase I trials, it is already known that cancer drugs are toxic. Based on the ethical principle of beneficence (do no harm) it is inherently unethical to administer this type of medication to a healthy person. Therefore, those eligible for these trials are either terminally ill cancer patients in whom standard therapy has failed, or cancer patients with no known therapy.

The Ethical Debate

Phase I research trials assess the potential toxicity of agents never before administered to humans. Two fundamental issues must be considered in the ethical debate. The first consideration is the risk-benefit ratio, with the second is informed consent.
PHASE I CLINICAL TRIALS

(Continued from page 1)

Risk-Benefit Ratio
Data measuring the risk-benefit ratio has been collected inconsistently for the past three decades. Available data dating back to 1991 shows that five percent of patients in a phase I clinical trial experienced tumor shrinkage with mortality of only 0.5 percent.1 In some cases, patients experienced long-term remission or cure.

According to the U.S. Food and Drug Administration, the risks and benefits of drugs in phase I trials are similar to drugs already offered for cancer therapy. There is no question these drugs are toxic. The patients are willing to take the risk of toxicity even when the known benefit is marginal. For example, patients with stage I breast cancer have a five year survival rate greater than 90 percent. These patients still choose to undergo two to three drug chemotherapy regimens for periods of four to six months in spite of side effects and additional survival benefit of only one to two percent.1

Some individual studies give a different picture than overall outcomes. For example, imatinib mesylate (Gleevec) was tested in a phase I trial for treating chronic myeloid leukemia. Although the goal of phase I is to evaluate toxicity and not efficacy, Gleevec administration demonstrated complete hematologic response rates of 98 percent with subsequent 96 percent response for one year.1

Clinical research can only be justified if potential risks to patients are minimized, potential benefits are maximized, and the potential benefits to both individuals and society either outweigh or are in proportion to the risks involved.

Autonomy and Informed Consent
In the Western liberal tradition of ethical and political thought, respect for a person’s autonomy means respect for his or her voluntary personal choices. Information is essential, and autonomy is exercised to the fullest only when one is making an informed decision.

Issues surrounding informed consent are central to the ethical debate.6 First, do physicians maximize the benefits and minimize the risks? Are clinical trials portrayed as a potential “cure”? Are the consent forms presented in such a manner that the patients understand what they are agreeing to? Physicians have an ethical duty to respect the autonomy of the patient. Regarding voluntary clinical trials, this requires full disclosure.

Do investigating physicians misinform the patients? Data is limited, however in one study of 272 oncology consent forms, 99 percent of the forms stated the study was specifically for research, and 92 percent listed toxicity testing as the only goal.1 The risks were described in 35 lines of the consent in contrast to only four lines used to describe possible benefits. Death was mentioned in 67 percent of all consents, and a mere five percent mentioned cure. Only one form stated that benefits could be expected. Deception destroys autonomy; therefore the results of this study are reassuring.

Studies have also analyzed the patient’s understanding and motivation. One study showed that 93 percent of the patients indicated that they understood the purpose of the clinical trial. However when asked to state the purpose, only 31 percent responded the purpose as dose finding.1

Lastly, are terminally ill patients too vulnerable to give informed consent? Many terminally ill patients understand there is little hope of physical benefit. The psychological benefit outweighs the risk when the patient becomes an active participant in the decision making process.

Invalid research is unethical if it is a

Requirements of Ethical Research
In addition to the risk benefit ratio and informed consent, the medical community has identified several other requirements for ethical research. These include value, scientific validity, fair subject selection, independent review, and respect for enrolled subjects.6 Societal response to research during the last 30 years has been the implementation of regulatory mechanisms that include detailed federal regulations. These mandates govern the research protocols and assure patients that the requirements are being met. Independent review boards are formed to examine and approve the scientific methodology. Invalid research is unethical if it is a
waste of resources, will not generate additional knowledge, cannot produce benefit, and cannot justify exposing people to burdens or risks.6

Clinical research relies on both patients and investigators. Patients offer their body, time, patience with testing, and tolerance of pain all with hope of a possible benefit. Physicians must maintain the integrity of the research by offering an ethically designed trial that will contribute scientific knowledge to improve the future of cancer patients.

Advantages of Participation in Phase I Research
Patients in phase I clinical trials have the opportunity to be treated with therapies that may not be readily available for years. If the treatment works, most patient are able to continue the therapy after the clinical trial ends.5 The clinical trial provides the patient with personal knowledge that the goal of the research is to help others and promote the advancement of scientific research for their disease.

By the time oncology therapy is offered in phase I trials, lab animal testing has already been completed. Investigators have a good estimate of the proper human doses and potential side effects. If the medication being tested has been used for other diseases, much information has already been gathered, reducing the risk to the patient.

Disadvantages of Participation in Phase I Research
The focus of the phase I trial is on toxicity, not efficacy. Potentially the medication is being used for the first time with humans and there may be serious side effects not yet demonstrated in animals. There is a chance the therapy will have no impact on the cancer being treated, or the estimated trial dose may be below a therapeutic level. Also, trials are usually offered at large research medical centers, so a patient may have to travel or relocate to participate.

Pediatric Research
Clinical trials are necessary for children to both improve the available therapies and find more effective ones. A phase I clinical trial for children may involve treatments never before applied to pediatric diseases. Biologically, children are not miniature adults. For this reason, findings based on adult studies cannot simply be applied to childhood cancer. Since children differ significantly from adults in drug reactions, it is wrong to subject a child to dosages derived from adult testing.

Without trials, it is impossible to know which treatment strategy will work the best with children. As with adults, investigators must always respect the balance between therapeutic benefit and side effects. Over the past three decades, the cure rate for childhood cancer has doubled, and today, 70 percent of children with cancer are cured, even when the disease is very advanced.6

Conclusion
Therapy considered standard of care for cancer today started with yesterday’s phase I clinical trials. In many cases these trials are considered the last hope for desperate patients who have failed standard therapy. As stated by George Zimmer, a English professor who participated in several phase I clinical oncology trials, “letting a patient choose the poisons (under professional guidance) adds something to the will to struggle…The enemy is not the pain or even death…the enemy is cancer, and we want it defeated and destroyed.” The crux of the issue in offering a clinical trial is beneficence, or “doing good”. The goal is to uncover information that will benefit society as a whole, and perhaps the patient. 8

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"Credentialing in Case Management: A Yardstick for Competency, Credibility, and Commitment"

by Sandra Lowery

History of Credentialing of Case Managers

For the past three decades, there has been significant growth of case management in both the private and public health care sectors. This has been attributed to the growing perception that case managers play a critical role in satisfying society’s need for quality, cost-effective health care services. However, as with all health care roles, purchasers and recipients of case management services are increasingly demanding a credible method of ensuring service consistency, some level of competency, and professionalism. There is the realization that there is more to knowledge than simply accessing information. The effective case manager uses information to critically analyze barriers to best outcomes and creatively use this information to achieve effective solutions. But how is this discerned? Credentialing appears to be an increasingly accepted method of achieving this.

The initial period of rapid and expansive case management occurred in the 1970s, however, it was in the early 1990s, during the second major period of expansion that case management leaders determined that some level of standardization and demonstration of competency was needed. A national consensus group of stakeholders decided in 1992 that the best method of achieving this would be an individual certification process. For the most part because case management was described as a specialty practice within an existing health professional role and not a free standing profession. The first certification developed was undertaken by the Foundation for Rehabilitation, Education, and Research and was entitled the Certified Case Manager (CCM). Since then, there have been several other national case management credentials. Additionally, an accreditation process was established for case management programs within an organization by URAC who reports that approximately 100 case management programs have been accredited to date.

Defining Credentialing

Credentialing is defined as the process of evaluating an individual’s knowledge and experience against a standard...
to determine if an individual is qualified to perform a role. The evaluation process takes into consideration: community standards, national standards, state practice acts, and liability. The components include a national definition, philosophy, job description, eligibility criteria, and a research based exam. The process is governed by independent bodies who define and set standards and administer the process.

Navigating the Field of Case Management Credentials

The undisputed leader among the array of case management credentials is the CCM, both in wide recognition as well as in sheer numbers. There are currently 26,000 CCMs today and more than 2,000 applications each year. The others, listed in Table 1 on pages 6 and 7, relate to specific areas of practice. In a 2001 national survey conducted by this author through the auspices of the Case Management Society of America and American Health Consultants, 69 percent of the respondents reported having the CCM credential whereas no other credential came close to approaching this level. The popularity of the CCM credential may be because it was the first developed or that it has the broadest scope.

The following issues should be considered when evaluating the various credentials:

- The certification is voluntary
- There is a professional code of conduct with disciplinary rules and procedures
- Certification examinations are free of bias and non-discriminatory
- The governing board is comprised of individuals who are certified by the body and represent the spectrum of individuals served as well as practitioners
- There is an ongoing research-based validity process for eligibility criteria and exam content
- The accreditation body is accredited by the National Commission for Certifying Agencies

As mentioned earlier, an accreditation process has been developed which evaluates case management programs. The only organization at this point in time that administers this is URAC who uses national standards for case management programs’ components, processes, and staff qualifications. The latter includes criteria for individual certification.

An Analysis of Credentialing in Case Management

In essence, certifying case managers provides a public service in that it:

- protects consumers by encouraging adherence to standards and a code of ethics
- is evidence of a certificant’s performance against an established standard
- serves as a recognized benchmark for purchasers who hire case managers
- allows a process for misconduct
- provides a standardized knowledge base

There are several advantages of certification for case management practitioners. These include:

- Possibly lead to an increase in salary and/or position within an organization
- Increasingly required for employment
- Indicates a commitment to professionalism and accountability
- Defines one as a member of a group with distinct preparation and capability

For employers of certified case managers there are several advantages in addition to those identified for the public, including:

- Meets the criteria for case management program accreditation
- May be required by state law
- Often provides an edge in marketing and/or in submitting proposals for contracts

The down side of case management certification certainly includes cost as most exams charge a fee of approximately $300. Some employers support their case managers by providing or funding certification preparation courses or materials, which is an additional cost. Increasingly, employers reimburse case managers for the exam fee if they pass the exam which is a great benefit though it places pressure on the applicant. Additional pressure is felt if the employer requires the case manager to be certified within a certain time period.

The Future of Case Management Credentialing

As with anything in health care, it is difficult to predict the future. The current trend is for private sector insurers, managed care organizations, and pendent case management providers to prefer case management certification, citing the CCM generally if they specify the credential. A growing trend is for the organization to require application for the CCM within a certain designated time frame. Sometimes this is part of their per-
formance criteria. The expectation is rarely seen in public sector case management and is just beginning to be desired by acute care hospitals.

Interestingly, as we have seen with the national case management publications, there has been a decrease in some credentials and a substantial increase in the more popular ones, i.e. the CCM and CMC. The latter may be due to the eligibility criteria that allows those who are non-health professionals to become eligible for the exam through experience alone. Another trend of interest has been in the field of workers’ compensation case management where the CDMS credential that was historically preferred is quickly changing to the CCM.

As we gaze into the future, an effort such as certification, will attempt to create order out of uncertainty as society seeks to codify and standardize definitions of quality as they appear to be worthy. As certification in case management identifies a common denominator of expertise and serves to verify the decision to trust advice and service, it is likely to be increasingly important as long as case management continues to survive. Though there will always be those who do not feel driven by an external stamp of approval, the purchasers of their services may demand otherwise in this era of increased accountability. One can only hope that the additional costs to our health care system from such measures will be offset by quality service.

One predictable benefit from the credentialing in case management, coupled with the national standards of practice, will be the increased standardization and identity of case management. From this, the pathway to evaluating the practice and its outcomes will be facilitated.

On the other hand, with standardization and credentialing, we are likely to see an increase in the filing of allegations of breaches in conduct as the public becomes aware of this possibility. Though this can lead to an increased ability to discipline the field it may cause more anxiety for case managers and their organizations.

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RSV Season preparation

Have you begun preparations for the upcoming RSV season? Are you in the process of identifying eligible babies from last season and your high-risk newborns? If you’re uncertain about either of these issues, or have questions of your own about the 2004 – 2005 RSV season including the best treatment options for your members, then ING Re may have a solution for you.

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