Journal of Cancer Research and Therapeutics

January-March 2008 | Volume 4 | Issue 1

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Criteria for deciding cost-effectiveness for expensive new anti-cancer agents

Rajiv Sarin

Radiation Oncology and I/C Cancer Genetics Unit, Director, ACTREC, Tata Memorial Centre, Navi Mumbai - 410 210, India

For correspondence: Prof. Rajiv Sarin, Radiation Oncology and I/C Cancer Genetics Unit, Director, ACTREC, Tata Memorial Centre, Navi Mumbai - 410 210, India. E-mail: rsarin@actrec.gov.in

Containing the spiralling cost of modern cancer care with its repertoire of targeted anti-cancer biological agents and the technological breakthroughs has become a matter of great concern worldwide. Targeted therapies are hailed as breakthroughs in science and medicine, offer new hope for desperate cancer patients and also present huge commercial opportunities for the industry. However, there is a growing tussle between the beneficiaries of these breakthroughs (cancer patients and industry) and those who decide how public funds allocated for healthcare should be used in a judicious and equitable manner. The root cause of this tussle is the projected and perceived degree and duration of clinical benefit with newer agents and the economic implications for providing these treatments. At the two extremes of this tussle, the drug rationing authorities are projected as being slow and sometimes insensitive to the suffering of cancer victims while the industry is accused of being opportunistic or even unethical, as exemplified by the unfolding story of erythropoietin with sales of over 10 billion US$ annually.

Most new targeted biological therapies developed for cancer are required to be given for 6-12 months and sometimes longer until the response lasts. With the exception of certain biological agents where more economical generics are available in some countries like India, the cost of the entire course of these new drugs range from 10,000 to 100,000 US$. While a few of these new molecules can increase cure rates of some cancers, the most common use of these newer agents is in advanced disseminated cancers where the clinical benefit is either symptom relief or a very modest prolongation in life, often measured in months. It is therefore not surprising that several governments and health authorities around the world have evolved elaborate methods to critically evaluate the evidence for the clinical benefit of new molecules before recommending their provision using public funds. As expected, any form of drug rationing is detested by patients who feel that they are being denied their right to get free access to the latest medicines, and also by their doctors who feel handicapped by not being able to offer the latest and the best drug to their patients for some macro-economic reason.

Sir Michael Rawlins, Chairman of the UK National Institute for Health & Clinical Excellence (NICE), in his recent keynote comment in Lancet Oncology titled "Paying for Modern Cancer Care - A Global Perspective", examines this very complex issue of 'how the health care systems will judge affordability of these products in the face of finite resources and competing demands from other patients'. For cancer, NICE has published appraisals for 36 drug-clinical indication pairs. They used the notion of incremental cost-effectiveness ratio (ICER) as the additional cost for gaining one year of life. When quality of life data was available the parameter used was the quality of life-year gained. Thus, if the use of a new targeted therapy in a particular metastatic cancer increased the median survival by 3 months at an additional cost of 5,000 US$, the ICER would be 20,000 US$ per life-year gained. Sir Rawlins admits that there is no reliable empirical basis for deciding cost-effectiveness thresholds and that NICE uses the collective judgement of its health economics advisor. If NICE was to accept and recommend new treatments with ICER of above 48,600 US$ per quality-adjusted life-year gained, it would result in an opportunity cost, i.e. displacement of other more cost-effective healthcare programmes. Using these criteria, NICE considers use of Bevacizumab or Cetuximab for metastatic colorectal cancer and Fludarabine for CLL as cost-ineffective in the UK, implying that the manufacturers were asking too high a price for the benefits the products conferred.

The World Health Organization (WHO) has recommended that the per-capita Gross Domestic Product, adjusted for the purchase power parity of the country can be used for setting thresholds for cost-effectiveness in different countries. Thus, interventions for which the additional cost incurred to gain one quality-adjusted life year is less than the country's per-capita GDP are considered as very cost-effective, those between 1 and 3 times the per-capita GDP as cost-effective and those

with an additional cost of over three times per-capita GDP as cost-ineffective. Using this WHO criterion, Sir Rawlins has estimated that the vast majority of the 26 pairs of new drugs-clinical conditions in cancer would be considered as cost-ineffective for most countries in South Asia and Asia Pacific Region.

The per-capita GDP of India using the Purchase Power Parity figures of the World Bank is 3,800 US$. Using the present exchange rate of 40 Indian Rupees to a US Dollar, if the cost of gaining one quality-adjusted life year with a treatment is up to Rs. 1,50,000 it would be considered as very cost-effective, if it is between Rs. 1,50,000 and Rs. 4,50,000 it would still be considered as cost-effective, but if it is over Rs. 4,50,000 the intervention would be considered as cost-ineffective. In India, the Working Group on Drugs and Pharmaceuticals for the eleventh five-year plan (2007-12) in its report to the Planning Commission has highlighted the need for 'Provision for Price and availability of Cancer medicines Fund' as one of the seven important measures for the welfare of the common man.

The health authorities, government organizations and other reimbursing agencies in the developing world are yet to establish the elaborate machinery required to systematically evaluate the clinical benefit of any new expensive treatment and decide whether it would be cost-effective to provide them using the limited public funds. In the absence of any definitive guidelines from national agencies in the developing world, it is imperative that patient groups, ethicists, clinicians, industry representatives and health economists debate the pros and cons of rationing very expensive drugs when paid for through public funds. In my opinion, the WHO recommendations for judging cost-effectiveness as outlined above would be a good beginning. It is inevitable that several limitations of this approach would emerge when it is implemented, and with time a better and truly equitable system would emerge.

It was never easy for a clinician and the healthcare system to come up to the expectation of a person with advanced disseminated cancer, and such economic undercurrents could only make it worse for all concerned. As much as we hate rationing of drugs provided through public funds, it is a reality that cannot be escaped. The best and the most logical solution would be for the industry to realize that what it sells should be good value for money in a holistic societal context and for the life-saving drugs, the society should be in a position to make it affordable to the majority of people who would benefit from it. This may be rather optimistic, but at no cost we want the argument to be lost to either numbers or sentiments.