rationing and rational health care resource allocation. Industry does not like the notion of rationing, but it supports identifying the best use of medicines in terms of the most appropriate patients for the treatment and the most appropriate time in their disease progression or treatment. There is a significant role for BDA in working toward the aim of using biologics and biomarkers in identifying most appropriate target populations and the optimal time for treatment. Another key concept in HTA is reducing uncertainty, which decreases as the number of clinical studies evaluating safety and efficacy increases. HTA has a significant impact on data requirements. Meeting the HTA hurdle requires strong epidemiological evidence (i.e. the potential number of suitable patients), as well as an evidence-based position for the new agent in therapy or clinical guidelines. Ideally data are also necessary that identify the subpopulations that receive the greatest clinical benefit. Investigation of the agent must be based on meaningful endpoints and economic models must be transparent. Clinical trials must demonstrate its clinical efficacy and safety. Real-world studies must identify its clinical effectiveness. Finally, analysis of economic effectiveness of the agent must demonstrate its budget impact, cost effectiveness, cost utility and address equitable use. All supporting studies must include an indication of evidence quality.

A ROLE FOR BIOMARKERS AND SURROGATE ENDPOINTS IN HTA: How do clinical trial endpoints based on biomarkers figure into the development and licensure scheme? Biomarkers are surrogate endpoints that have substantial value in both clinical and HTA evaluations of new products. Biomarkers can be used to identify likely responding patients who have an abnormal condition prior to treatment initiation. They can also be used to assess the extent of disease, monitor the safety of an intervention, and evaluate the desired response.[1]

There are, however, some problems associated with reliance on surrogate rather than clinical endpoints in trials of anticancer agents. First, one must understand under what circumstances a surrogate endpoint provides both a qualitative and quantitative prediction of the clinical endpoint. Second, surrogate endpoints provide little or no information about the risk–benefit profile of the product and scant quantitative evidence of the magnitude of any effects on utility. For example, demonstrating an anti-tumour agent's significant effect on complete or partial response rates may have little relationship to its effect on either longevity or quality of life. The ultimate goal is to work toward patient benefit and measuring outcomes that are meaningful to, and valued by, the patient. Ideally the focus should evolve from patient reported outcomes to patient relevant outcomes.

CONFLICT OF INTEREST STATEMENT: Mr. Chris Teale is an employee of AstraZeneca Ltd. and it can be confirmed that there is no conflict of interest involved in this paper, nor in his participation in this entire event.

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doi:10.1016/j.ejcsup.2007.09.035

THE BASIC ECONOMIC PROBLEM – INTERACTION OF ALL STAKEHOLDERS REQUIRED

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Demands are increasing on health care systems as the population ages and competition heats up among numerous branches. What data should serve as the basis for difficult decisions, and who should make them? Various financial barometers signal that burgeoning needs and shrinking resources will lead to scarcity (or perhaps, a perception of scarcity), and reimbursement is a central part of scarcity steering. To balance needs with available resources, we must establish priorities based on state, association and individual regulations.

Disease and scarcity are considered by people today to be unconquerable and omnipresent. The greater the knowledge people have of disease and its panoply of treatments, the greater is their awareness of the gap between demand and resources. Interestingly, the more society spends for disease management and meeting health-care needs, the larger the scarcity appears to be. Stated otherwise, being on the highest-ever level of material supply and per capita health-care spending for all ages in Europe, the topic of scarcity is being discussed more heatedly than at any other time.

For conventional cancer treatments for which response to treatment depends on the duration of treatment, the greatest value likely occurs near the beginning of treatment and decreases over time. The interest of payers is in reducing cost, and the interest of doctors and patients is in maximising treatment. Maximal medical care, of course, has higher costs. Optimal treatment, in an economic sense, occurs where the cost curve intersects the curve representing decreasing medical benefits over time. Payers, patients and doctors negotiate and compromise to arrive at the point of economically optimised medical care.

Predictive markers must be developed for molecularly targeted therapies to improve the benefit–cost relationship by only treating patients with a high expectation of response. For registration or licensure of new products, alternatives to randomised trials should be considered. Indirect comparisons might help facilitate patient access to new medicines. Also, it is important to keep in mind that molecularly targeted therapies mostly involve small populations. Randomised trials require a great deal of time, during which therapeutic options might change, thereby compromising the value of the trial's findings.

Academia, industry, regulators as well as patient advocacy groups and economists will have to act in concert, and scientific associations, such as the BDA will have to take active roles. Of para-

mount importance is the requirement to keep public health care at the highest scientific level, based on evidence and medical competence.

CONFLICT OF INTEREST STATEMENT: Professor Max E. Scheulen is an employee of the University of Essen and it can be confirmed that there is no conflict of interest involved in this paper, nor in his participation in this entire event.

doi:10.1016/j.ejcsup.2007.09.036

SHOULD REGULATORS BE CONCERNED WITH PHARMACOECONOMIC ISSUES?

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Risk–benefit analysis should be the only basis for approval or registration of a new agent. However in addition to this, in Sweden, for example, there is an obligation to promote cost-effective use of drugs based on written information or workshops that include subscribers. The National Institute of Clinical Excellence (NICE), a special health authority of the British National Health Service, deals with issues of cost and reimbursement. Regulators may think of considering cost effectiveness when they request data to substantiate efficacy of new anticancer agents as long as patients are provided with best possible treatment. If, however, society is not prepared to pay for new products, then they should not be developed.

The goal of regulators is to limit unnecessary queries because they needlessly increase the price of new drugs. A tradeoff exists between quality of data and cost and data quality cannot be lowered below some point. Industry dislikes segmented pricing, but, particularly in the case of drug combinations, costs are prohibitive for many countries. Differential pricing, based on the region where a drug is being marketed, is one way to maximise income. Regulatory authorities should take this factor into account as they consider registering or licensing new anticancer therapies.

Oncology involves a very special group of drugs. Is a new drug development model for oncology drugs required to get them to the market more quickly? Is conditional or accelerated approval the best means to do so? In theory, conditional approval should work although it is a relatively new process. Linking conditional approval to conditional reimbursement, however, needs to be very carefully evaluated as it should be possible to reassess the cost–benefit of a conditionally approved therapy and take it off the market if the cost–benefit analysis is not favourable (although it would be a very difficult situation).

CONFLICT OF INTEREST STATEMENT : Professor Jan Liliemark is an employee of The Medical Products Agency in Sweden and it can be confirmed that there is no conflict of interest involved in this paper, nor in his participation in this entire event.

doi:10.1016/j.ejcsup.2007.09.037

THE ETHICS OF PHARMACOECONOMICS FROM THE PATIENT'S PERSPECTIVE

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This discussion on pharmacoeconomics involves not only industry and academia, but also real people who have cancer. Some people are treated and cured, but many have to live with the disease. Results of a keypad voting survey[1] regarding the patient access to anticancer therapy of 104 cancer advocates in May 2005 are shown in Table 1.

Interestingly, 100% of respondents from France indicated they knew of no one who had been refused access to a cancer treatment because of cost, whereas 100% of those from Poland responded that they did. Clearly, cost is a factor, and the ability to access new anticancer therapies varies greatly across Europe. Patients do not think like consumers, though, because they do not care about price; they just want the best treatment.

Therefore the question is that if a significant number of people in Europe are not able to access technologies, what is the point of developing or testing them? To ensure that real people can benefit from new drugs means eliminating barriers to access, which include the high price tag of the drugs and the time it takes for registration or licensure. Clinical trials, regulatory agency review and health technology assessments (HTAs) all take time, but patients with life-threatening disease often do not have that luxury.

The goals of new-drug development should be to provide patients everywhere with timely access to safe and effective therapies and to ensure that patients are not put at undue risk by taking innovative medicines. Thanks to the informed consent process, patients understand risk and many are willing to accept it by participating in clinical trials, even if they might not benefit directly. Nevertheless, placebo-controlled trials present challenges because patients generally desire the opportunity to take a potentially effective drug. Patients are likely to benefit from the regular monitoring provided during clinical trials, but their

Table 1 – Results of a keypad voting survey of cancer advocates, 2005

Survey item	Response (%)
Are you aware of any cancer drugs that are not available in your country but are available in others?	
Yes	54
No	46
If yes, why is the drug not available?	
The drug(s) are not licensed in my country	39
The public health authority will not reimburse the drug(s)	56
Physicians will not prescribe the drug	0
Do not know	5
Do you know of anyone who has been refused access to a cancer treatment, because it was considered too expensive?	
Yes	51
No	49