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The costs of managing advanced colorectal cancer: a broad perspective

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Cancer care is expensive, consuming between 5 and 10% of health-care resources in industrialized countries. Therefore increasing emphasis is being placed on the value of treatment interventions. Colorectal cancer is the second most common cancer in the Western world and nearly two-thirds of patients will require palliative treatment. Only limited data are available on the cost of palliative chemotherapy for patients with advanced disease. The profile of raltitrexed ('Tomudex', formerly ZD1694) suggests that it may reduce costs associated with the administration of chemotherapy. Recent studies demonstrate that the total monthly cost of raltitrexed is lower or about the same as a variety of commonly used 5-fluorouracil-based regimens and offers potential savings for hospitals in terms of demand on specialist facilities, physician, nursing and pharmacy time, and overnight bed occupancy. The personal cost borne by patients and their carers for travelling and time off work is reduced with raltitrexed compared with the widely used Mayo regimen. However, there may be disincentives within certain national health-care systems to the introduction of a more resource-efficient drug such as raltitrexed. Physicians will need information on both the benefits and costs of drug treatments to be able to make informed decisions on the provision of high quality, cost-effective patient care, and it is likely that health economic assessment will be incorporated into increasing numbers of clinical trials.

Keywords: Advanced colorectal cancer, cost, 5-fluorouracil, regimens, raltitrexed, 'Tomudex'

Introduction

In their 1985 summary of the economic burden of cancer in the United States, Rice *et al.* estimated that the cost of medical care for cancer comprised almost 5% of total personal health spending [1]. Of the estimated $18.1 billion spent on cancer care, hospital care accounted for 67% and physician services accounted for a further 22.5%, while drugs accounted for just 3.6%. Comparable figures have been reported from estimates in the Netherlands, West Germany and Sweden, where the total costs of treatment for malignant cancer were 4.8, 4 and 5.1% of total health-care costs, respectively [2], and in the United Kingdom, where cancer therapy accounts for around 7% of health service spending [3]. The cost of cancer care in the United States increased by 60% between 1985 and 1990 [4] and recent reports suggest that cancer now accounts for 10% of total health-care costs, with direct medical expenditure estimated at $40 billion [5]. Factors contributing to this escalation of costs include advances in prevention, diagnosis and treatment, management of costly medical complications and the requirement for specialized facilities for delivery of care. Although these factors increase the survival and quality of life of cancer patients, budgets are becoming increasingly constrained and budget holders are faced with decisions on how best to allocate a limited resource in order to maximize the health gain.

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Colorectal cancer

Colorectal cancer is the second most common cancer in the Western world and as such is an important disease in terms of impact on society and on health-care services. The effects of patient education about risk factors and of mass population screening in reducing the impact of colorectal cancer remain to be elucidated. About two-thirds of colorectal cancer patients will die from their disease; therefore, palliative care is an important part of overall treatment provision. Different approaches have been taken to assess the cost of caring for patients with this type of cancer, including assessment of the initial, continuing and terminal phases of the disease, assessment by Dukes' stage and assessment by age. Such studies have their limitations as different methodologies are used, which may obscure variation in costs within a category. This issue appears to be of real importance, as a recent study [6], which estimated resource use in eight European hospitals for management of patients with advanced colorectal cancer, concluded that only 54% of patients received chemotherapy and that there was considerable variation between hospitals in associated resource use, both within and between countries. This suggests, therefore, that efficiency could be improved.

5-Fluorouracil given alone or modulated, most usually with leucovorin, has been the treatment of choice for colorectal cancer for nearly 40 years. The survival advantage following chemotherapy in advanced disease

Table 1. Mean treatment costs per month (£) excluding pharmacy costs

Regimen	Dose	Chemo-therapy	Other drugs	Tests	Consum-ables	Fluids	Opera-tions	Out-patient	In-patient	Help-line	Total cost
De Gramont	5-FU 400 + LV 200 (2 h), then 5-FU 400 (22 h) for 2 days every 14 days	393.38	71.27	195.03	25.92	22.97	108.90	177.41	1027.14	6.50	2028.52
Raltitrexed	3 (15 min) every 21 days	456.52	32.77	226.41	0.00	20.62	0.00	137.51	244.02	0.00	1117.85
Continuous infusion	5-FU 300 per day	93.22	17.30	301.95	45.69	9.16	138.45	117.57	471.57	12.71	1207.62
Mayo	5-FU 425 + LV 20 for 5 days every 4–5 weeks	74.16	50.66	188.04	0.00	7.46	10.85	329.96	292.91	0.00	954.04

5-FU, 5-fluorouracil; LV, leucovorin. All drugs were given intravenously. Doses are given in mg/m².

compared with best supportive care alone has now been established [7], along with indicators of improved patient well-being such as performance status and weight gain [8]. However, the doses and the intensity of schedules have a variable impact on patients and hospital resources and it is currently not possible to define the optimal schedule of administration, although it is recognized that the drug costs of these regimens vary enormously [9].

Costing palliative care in colorectal cancer

When assessing the total cost of medical interventions there is general agreement [10] that relevant costs include direct medical costs (e.g. hospital costs for labour, drugs and equipment) and direct non-medical costs (e.g. costs incurred by the patient and his family such as travel costs). For some interventions, it may also be relevant to consider indirect costs (e.g. time off work leading to a loss of production).

A small number of studies have addressed the hospital cost of palliative care in colorectal cancer. Glimelius *et al.* [11] prospectively assessed the cost-effectiveness of primary chemotherapy versus best supportive care with rescue chemotherapy (if supportive measures did not result in palliation) in 61 patients with inoperable gastrointestinal cancer. They concluded that primary chemotherapy improved survival and quality of life and was cost-effective for gastric cancer and colorectal cancer patients, compared with the accepted costs for a number of other well-established treatment interventions (e.g. lowering of cholesterol). While the overall conclusion supports other work regarding the benefits of chemotherapy for palliation of disease, the combination of different gastrointestinal cancers and the lack of detail on the doses of chemotherapy regimens present limitations for physicians in the application of cost-effective care. In a separate study, hospital notes for 92 advanced colorectal patients were reviewed over a 2-year period [12]. Patients were grouped according to whether they were treated with 5-fluorouracil alone or modulated in three different ways (with methotrexate and leucovorin, leucovorin alone or leucovorin plus mitomycin). The authors [12] concluded that efficacy was similar in the two groups (5-fluorouracil alone or modulated regimens) and that cost savings could therefore be made by using 5-fluorouracil alone. As in the previous study, the absence of detail on doses and the amalgamation of the three modulated 5-fluorouracil regimens into a single grouping limits the usefulness of these data.

In a large multicentre phase III trial, 'Tomudex' (raltitrexed) at a dose of 3 mg/m² intravenously once every 3 weeks has been shown to be as clinically active as the Mayo regimen (5-fluorouracil at 425 mg/m², modulated by low-dose leucovorin at 20 mg/m², administered intravenously for five consecutive days once every 4–5 weeks) but with a more convenient administration schedule and a different toxicity profile, which may permit easier patient management. This profile suggests that raltitrexed may reduce costs associated with the administration of chemotherapy [13] and this point has been further explored in a number of economic studies.

Hospital costs

In a retrospective audit of patient notes undertaken at the Royal Marsden Hospital, United Kingdom [14], the monthly cost of treating advanced colorectal cancer patients with raltitrexed was compared with that of a number of 5-fluorouracil-based regimens. As shown in Table 1, when all the hospital components of treatment (excluding pharmacy resource) were costed, the cost of raltitrexed was lower than the De Gramont regimen and was similar

Table 2. Pharmacy charges and median disposable and time costs per cycle (£)

Regimen		Disposable cost	Time cost	Pharmacy charge
Raltitrexed	3 mg/m² (15 min) every 21 days	0.62	2.87	12.50
Continuous infusion	5-FU 200 mg/m² daily	30.46	5.24	94.00
De Gramont	5-FU 400 mg/m² plus LV 200 mg/m² (2 h) 5-FU 400 mg/m² (22 h) for 2 days every 14 days	4.58	8.17	75.00
Mayo	5-FU 425 mg/m² plus LV 20 mg/m² for 5 days every 4–5 weeks	7.08	8.02	75.00
Machover	5-FU 400 mg/m² plus LV 200 mg/m² for 5 days every 4 weeks	8.02	13.16	75.00

5-FU, 5-fluorouracil; LV, leucovorin. All drugs were given intravenously.

to both the Mayo regimen and continuous ambulatory 5-fluorouracil. The pattern of costs varied between the regimens, particularly with respect to drug costs (which were highest for raltitrexed and the De Gramont regimens), inpatient costs (which were highest for the De Gramont and continuous infusion regimens) and outpatient costs (which were highest for the Mayo regimen). The combined in- and outpatient costs of raltitrexed were lower than any of the other regimens.

As shown in Table 2, the time and disposable costs associated with pharmacy preparation of raltitrexed and a number of 5-fluorouracil-based regimens were assessed in a separate time and motion study. Raltitrexed was significantly quicker and less costly to prepare than any of the other regimens [15], resulting in a significantly lower pharmacy charge for raltitrexed.

In a further study, data from a cohort of 62 United Kingdom patients recruited into the raltitrexed phase III trial were used to assess the drug costs associated with management of chemotherapy-related toxicity [16]. The mean total drug cost for toxicity management was 50% less with raltitrexed (£64) than with the Mayo regimen (£139), with the costs of managing infection, nausea and vomiting, pain or abdominal pain and mucositis all being lower in the raltitrexed group.

Thus raltitrexed reduces cancer chemotherapy costs by offering potential savings in physician, nursing and pharmacy time, overnight bed occupancy and associated costs. Potentially, the same number of patients could be treated using less resource than at present or an increased number could be treated using the same level of resource.

Patient impact and patient costs

In the phase III trial, administration of raltitrexed to an average patient required six outpatient visits compared with 22 visits for the Mayo regimen. Thus, in this study, raltitrexed required, on average, 16 fewer treatment days for a similar overall survival (median of 10.3 months in both treatment groups). An increase in treatment-free days also reduces the personal costs borne by patients and their carers in travelling and in time off work. These are important considerations in a health service committed to patient-centred treatment [17]: 87% of United Kingdom patients with colorectal cancer ($n=45$) who took part in a recent survey at St Luke's Hospital indicated a strong preference for the convenience of the raltitrexed schedule compared to the Mayo, De Gramont or continuous 5-fluorouracil regimens (C. Topham, personal communication, 1996).

Practical problems in the application of cost-effective care

Despite the potential benefits of raltitrexed, and an ongoing debate about how to improve value for money by maximizing health gains, there may be considerable disincentives within the health-care service to the introduction of a new drug such as raltitrexed. Economists define an efficient outcome as one that maximizes the benefit that can be obtained from the available allocation of resources. However, current rather crude contractual funding arrangements in the United Kingdom are sometimes linked to inpatient and outpatient activity levels, which would result in decreased income for a hospital using a more efficient product. It was to avoid such perverse incentives that the Diagnosis-Related Groups (DRG) system was introduced in the United States; by prospectively fixing the rate of payment for a service, health-care providers become motivated to reduce their costs below the fixed rate. Consequently, reductions in the length of hospital stay and a shift from inpatient to outpatient treatment were observed.

In other settings, a focus on cost containment through drug budgets alone will ignore savings that can be made in other aspects of the hospital budget. With such a focus, the potential to increase capacity (and hence treat more patients) with a more efficient product can be viewed negatively as overall costs may also be increased. Alternatively, with increasing demands being placed on

oncology services, the use of a more efficient drug may prove to be a more timely and less costly solution than recruitment and training of additional professional staff. Moreover, global hospital budgeting is likely to allow a broader assessment of the value of new drugs.

Conclusion

Physicians need to evaluate the economic implications of new drugs as well as conventional clinical endpoints if they are to achieve high-quality cost-effective patient care. In addition, a re-examination of the existing systems for funding treatment is necessary to ensure that available resources are used optimally.

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