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Capecitabine (Xeloda™) improves medical resource use compared with 5-fluorouracil plus leucovorin in a phase III trial conducted in patients with advanced colorectal carcinoma

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Abstract

Standard therapy for advanced or metastatic colorectal cancer consists of 5-fluorouracil plus leucovorin (5-FU/LV) administered intravenously (i.v.). Capecitabine (Xeloda®), an oral fluoropyrimidine carbamate which is preferentially activated by thymidine phosphorylase in tumour cells, mimics continuous 5-FU and is a recently developed alternative to i.v. 5-FU/LV. The choice of oral rather than intravenous treatment may affect medical resource use because the two regimens do not require the same intensity of medical intervention for drug administration, and have different toxicity profiles. Here we examine medical resource use in the first-line treatment of colorectal cancer patients with capecitabine compared with those receiving the Mayo Clinic regimen of 5-FU/LV. In a prospective, randomised phase III clinical trial, 602 patients with advanced or metastatic colorectal cancer recruited from 59 centres worldwide were randomised to treatment with either capecitabine or the Mayo regimen of 5-FU/LV. In addition to clinical efficacy and safety endpoints, data were collected on hospital visits required for drug administration, hospital admissions, and drugs and unscheduled consultations with physicians required for the treatment of adverse events. Capecitabine treatment in comparison to 5-FU/LV in advanced colorectal carcinoma resulted in superior response rates (26.6% versus 17.9%, $P=0.013$) and improved safety including less stomatitis and myelosuppression. Capecitabine patients required substantially fewer hospital visits for drug administration than 5-FU/LV patients. Medical resource use analysis showed that patients treated with capecitabine spent fewer days in hospital for the management of treatment related adverse events than did patients treated with 5-FU/LV. In addition, capecitabine reduced the requirement for expensive drugs, in particular antimicrobials fluconazole and 5-HT3-antagonists to manage adverse events. As anticipated with an oral home-based therapy patients receiving capecitabine needed more frequent unscheduled home, day care, office and telephone consultations with physicians. In the light of clinical results from the phase III trial demonstrating increased efficacy in terms of response rate, equivalent time to progression (TTP) and survival (OS), and a superior safety profile, the results from this medical resource assessment indicate that capecitabine treatment of colorectal cancer patients results in a substantial resource use saving relative to the Mayo Clinic regimen of 5-FU/LV. This benefit is derived principally from the avoidance of hospital visits for i.v. drug administration, less expensive drug therapy for the treatment of toxic side-effects, and fewer treatment-related hospitalisations required during the course of therapy for adverse drug reactions in comparison to patients treated with 5-FU/LV.

Keywords: Medical resource use; Capecitabine; Xeloda™; 5-FU/LV; Phase III trial; Colorectal cancer

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1. Introduction

Every year, approximately 780 000 people worldwide are diagnosed with colorectal cancer. Globally, colorectal cancer is the third most commonly diagnosed cancer and the fourth most common cause of death from cancer [1–3]. If detected in early stages, colorectal cancer can be cured by surgical resection. However, despite improvements in early detection and in treatment, e.g. with adjuvant chemotherapy, mortality from colorectal cancer has not changed appreciably in the industrialised world over the past 40 years [4].

The incidence rate for colorectal cancer differs considerably between countries, but is strongly correlated with age. Data from both the United States and United Kingdom demonstrate that the incidence of colorectal cancer rises 3-fold between the ages of 60 and 80 years. Improvements in health care have led to an increase in the proportion of elderly people in the general population. At present, in the industrialised nations a quarter of the population is over 70 years old and this proportion is expected to increase to one third over the next two decades [5,6]. Therefore, the number of people developing colorectal cancer and, consequently, the resources required to treat them will rise. In a climate where health managers need to reconcile increased demand with limited medical resources, optimisation of benefits and costs is an important feature in treatment selection. Therefore, drugs offering a high therapeutic index coupled with a reduced demand for medical resource use are to be welcomed.

Survival of patients with colorectal cancer is related to the stage of the disease at diagnosis. Approximately 50% of patients with colorectal cancer have metastatic or non-operable disease at the time of diagnosis, or will develop metastases or a local recurrence following surgery [7]. Response rates to chemotherapy are low in patients with advanced colorectal cancer. The standard treatment regimens for these patients are based on 5-fluorouracil (5-FU) [8]. However, the activity of 5-FU is limited by its rapid metabolism, the S-phase dependence of its action, and the characteristically slow doubling time of colorectal cancer tumour cells. Therefore, attempts to improve 5-FU-based treatment efficacy have focused on the need to prolong exposure of tumour cells to therapeutically relevant cytotoxic doses of the drug. The addition of biomodulators such as leucovorin (LV) to 5-FU monotherapy allows the stabilisation of therapeutically active ternary complexes between fluorodeoxyuracil monophosphate (FdUMP) and thymidylate synthase within the cell. This enhances tumour response rates to 20–30%, without a major impact on overall survival [9]. An alternative approach is to administer 5-FU by continuous infusion rather than bolus intravenous (i.v.) infusion [10]. This allows an increase in drug dose intensity and reduces myelosuppression [11]. The majority of phase III trials confirm increased tumour response rate with continuous infusion compared with bolus 5-FU alone [12,13]. Moreover, the therapeutic advantages observed with continuous infusion regimens are offset by their inconvenience due to the required use of portable i.v. infusional pumps, cost to administer, and their association with significant morbidity [14].

The recent development of a new generation of rationally designed and orally administered fluoropyrimidines promises considerable advances in the management of colorectal cancer. Orally administered drugs permit convenient dosage flexibility and prolonged drug exposure while avoiding complications associated with indwelling catheters required for continuous infusion. One of the most interesting of these drugs is capecitabine (Xeloda™) because its tumour selective activation leads to high intratumoral levels of active 5-FU anabolites resulting in potentially maximum antitumour activity and low systemic 5-FU exposure [15–17].

A recent prospective randomised open-label phase III clinical trial compared oral capecitabine with a standard i.v. 5-FU/LV (Mayo Clinic) regimen in patients with advanced or metastatic colorectal cancer (data not shown). Capecitabine achieved a significantly higher objective response rate and equivalent median time to disease progression and median overall survival compared with 5-FU/LV. Clinically important toxicities, in particular grade 3 or 4 neutropenia or stomatitis were less common with capecitabine. Patients treated with capecitabine had a higher incidence of hand foot syndrome (HFS), but this cutaneous side-effect, affecting the palms and soles only, was easily managed by dose interruption and adjustment where necessary. These differences in the mode of administration and patterns of toxicity may have a significant impact on medical resource utilisation.

This paper describes medical resource use in patients with advanced or metastatic colorectal cancer using orally administered capecitabine or i.v. 5-FU/LV collected during a randomised phase III clinical trial (data not shown) Information was collected on the number of hospital visits (inpatient and outpatient) required to administer each regimen, the incidence of hospitalisation, unscheduled consultations, and medication required to treat adverse events.

2. Patients and methods

2.1. Patients

Patient eligibility for this phase III trial is described in detail elsewhere (data not shown). In brief, patients with advanced or metastatic colorectal cancer who had not received any prior chemotherapy for advanced or metastatic colorectal cancer, and who had not completed adjuvant chemotherapy during the preceding 6

months were enrolled in the trial. Histological or cytological confirmation of colorectal adenocarcinoma and one or more bidimensionally measurable indicator lesion not treated with radiation therapy were required. Patients were at least 18 years of age, ambulatory (Karnofsky performance status $\geqslant 70\%$) with a life expectancy of at least 3 months, and must have given written informed consent. Patients were excluded if they had previous severe reactions to fluoropyrimidines or other serious medical conditions such as myocardial infarction within the previous 12 months.

2.2. Study design and treatment

This was an open-label, randomised, parallel-group study in which patients were randomly allocated to treatment with either oral capecitabine or the i.v. 5-FU/LV (Mayo Clinic) regimen. Capecitabine was administered orally twice daily as an intermittent 3 week regimen at a dose of 2500 mg/m^2/day for 2 weeks followed by 1 week's rest. The Mayo Clinic regimen comprised 5-FU/LV (20 mg/m^2 of LV as a rapid i.v. injection followed by 425 mg/m^2 of 5-FU as an i.v. bolus) given daily for 5 days, every 4 weeks. Treatment in both arms was continued for 30 weeks or until the development of progressive disease or unacceptable toxicity. Treatment interruption or dose reduction only occurred in cases of grade 2 toxicity or worse (National Cancer Institute of Canada Common Toxicity Criteria (NCIC CTC)). In the capecitabine arm, sequential dose reduction to 75 and 50% of the original dose were made for given toxicities re-occurring at grade 2 or 3. Treatment was usually discontinued if a given toxicity either occurred at grade 4 or recurred at grades 2 or 3 despite a dose reduction to 50% of the original dose. In the 5-FU/LV arm, sequential dose reduction to 80 or 70% of the original dose were made depending on the nature and severity of the toxicity.

2.3. Evaluation of patients

Safety evaluations made during treatment and at 4 weeks after the end of therapy included assessment of clinical adverse reactions (classified according to the NCIC CTC grading system) and laboratory parameters. Tumour sites and dimensions, measured clinically and on computer tomography (CT) scans, X-rays and by magnetic resonance imaging, were assessed at the start of treatment and then at predetermined times during therapy up to and including week 48. Tumour responses were classified as complete response (CR), partial response (PR), progressive disease (PD) or stable disease (SD) using standard World Health Organization (WHO) criteria. Investigator assessment of tumour response was reviewed by an Independent Review Committee (IRC) composed of radiologists, with an oncologist as required. Patients were followed up every 3 months after the end of treatment and the dates of disease progression and survival recorded.

2.4. Medical resource use

During the trial, medical resource use data were collected prospectively at all participating centres on study case report forms. Table 1 summarises the data collected and the definitions of medical resource use employed for this study. The data collected were analysed using standard descriptive statistical techniques. Information was collected on the number and duration of visits required for scheduled i.v. drug administration. Adverse event reports noted nature, duration, intensity, treatment and outcome of these events; hospitalisations, drug treatment and unscheduled patient visits to health care professionals were also recorded. No information is available on resource utilisation outside the treating centre apart from unscheduled visits.

Table 1
Medical resource use variables

Resource use component	Description
Treatment related	
Clinic visits	Number of scheduled visits made to a hospital, clinic or office for a course of cancer therapy
Duration of visit	The difference between start time and end time of a scheduled visit for a course of cancer therapy. A duration of 16 h or more was interpreted as an overnight stay
Chemotherapy agents	Name, dose route, schedule and total number of doses of chemotherapy agents administered
Related to adverse event management	
Consultations	Number of unplanned day care unit, office and home visits plus telephone consultations with general practitioners or specialist physicians
Hospitalisation days	Hospital admission and discharge dates for treatment of adverse events were collected and used to calculate the duration of stay in hospital
Treatments for management of adverse effects	Drug name and treatment duration for each treatment episode for any drug given for any adverse event

2.5. Statistics

A one-sided chi-square test was used at an alpha level of 2.5% to compare response data in the two patient groups. This is based on the confidence interval according to Hauck-Anderson.

3. Results

3.1. Patients and treatment

The trial enrolled 602 patients, 301 in each arm, from 59 centres in eight European Union countries, Russia, Israel, Australia, New Zealand and Taiwan during a 17 month period from October 1996 to February 1998. A total of 6 patients (4 in the capecitabine group and 2 in the 5-FU/LV group) did not receive treatment after randomisation, and are not included in the analyses of resource utilisation presented here (Fig. 1).

Table 2 summarises the main demographic and baseline disease characteristics for all enrolled patients. The two groups were well matched for all evaluated characteristics.

As discussed elsewhere in greater detail (data not shown), both treatment groups adhered well to their planned regimen. In both groups, disease progression was the most common reason for stopping therapy.

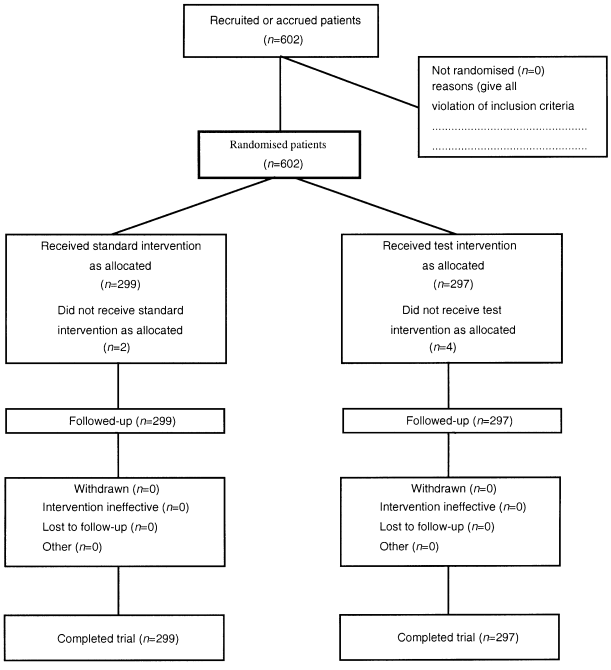

Fig. 1. Flow chart of the progress of patients through the trial (adapted from Begg C, Cho M, Eastwood S, *et al.* Improving the quality of reporting of randomized controlled trials: the CONSORT statement. *JAMA* 1996, **276**, 637–639).

3.2. Efficacy

Table 3 summarises the efficacy of treatment for all enrolled patients in each group. The overall response rate was significantly higher for patients treated with capecitabine than those receiving 5-FU/LV (26.6% versus 17.9%, respectively, $P=0.013$, Chi-square test). Median progression-free survival and overall survival in the capecitabine group were equivalent to the group treated with 5-FU/LV.

3.3. Medical resources use

3.3.1. Drug administration

Table 4 illustrates the number of visits planned and the number actually required for the administration of 5-FU/LV or the prescription of capecitabine. Because the administration of 5-FU/LV required five successive visits for office/hospital-based i.v. treatment, the total number of scheduled visits needed for administration of a complete course of 5-FU/LV was greater than the number of visits required to provide patients with capecitabine and to assess the safety of the treatment.

The mean number of cycles administered during the course of this study was 7.1 for capecitabine (3-week cycles) and 5.1 for 5-FU/LV (4-week cycles). Because some patients did not receive the full planned course of therapy, the actual number of visits required for drug administration was less than that planned in both treatment groups. Nevertheless, far fewer visits (2109 versus 7625) were required in the capecitabine group than for patients treated with 5-FU/LV.

Both capecitabine and 5-FU/LV are suited for outpatient treatment, and the majority of administration visits (87.8%) were for 2 h or less. However, for patients in the 5-FU/LV group, approximately 5.5% of administration visits included overnight hospitalisation. The requirement for overnight hospitalisation varied markedly between countries; the incidence in Germany (40.6%) was higher than in other countries (0–3.2%). For patients who received capecitabine, no hospitalisation was required for physical examinations, laboratory tests and providing treatment at the beginning of each cycle.

3.3.2. Management of adverse events

In this phase III trial, 11.8% of the patients in the capecitabine group and 15.7% of patients in the 5-FU/LV group were hospitalised for adverse events that were designated related to study treatment as classified by investigator assessment on the adverse event form. Table 5 summarises the numbers of patients and hospitalisations, and the numbers of days of hospitalisation required for each adverse event. Capecitabine led to markedly fewer hospitalisations, and fewer days in hospital with infection, neutropenia and stomatitis than treatment with 5-FU/LV. Hospitalisation for dehydration was

Table 2
Patient demographics and disease characteristics at baseline

Parameter	Capecitabine ($n=301$)	5-FU/LV ($n=301$)
Male/female *n* (%)	172 (57)/129 (43)	173 (57)/128 (43)
Age (years): median (range)	62 (29–84)	63.5 (36–86)
Race: caucasian *n* (%)/others *n* (%)	283 (94)/18 (6)	288 (96)/13 (4)
Body weight (kg): median (range)	68.9 (38–120)	68 (37–122)
Body surface area (m^2): median (range)	1.78 (1.25–2.36)	1.76 (1.24–2.49)
Karnofsky performance status (%): median (range)	90 (70–100)	90 (70–100)
Colon/rectal cancer *n* (%)	199 (66)/101 (34)	196 (65)/105 (35)
Liver/lung metastases *n* (%)	230 (76)/89 (30)	238 (79)/89 (30)
Previous treatment		
Surgery *n* (%)	265 (88)	268 (89)
Radiotherapy *n* (%)	42 (14)	42 (14)
5-FU adjuvant treatment *n* (%)	56 (19)	41 (14)

5-FU, 5-fluorouracil; LV, leucovorin.

Table 3
Response rates

Status	Capecitabine ($n=301$)[a]		5-FU/LV ($n=301$)[a]	
	n (%)	Confidence interval	*n* (%)	Confidence interval
Objective response (PR or CR)	80 (26.6[b])	21.6–31.6	54 (17.9[b])	13.6–22.23
Complete response (CR)	7 (2.3)	0.6–4.0	7 (2.3)	0.6–4.0
Partial response (PR)	73 (24.3)	19.5–29.2	47 (15.6)	11.5–19.7
Time to progression (TTP) median (months)	5.2	4.4–5.5	4.7	4.0–5.5
Overall survival (OS) median (months)	13.2	12.0–14.8	12.1	11.1–14.1

5-FU, 5-fluorouracil; LV, leucovorin.
[a] Population of all randomised patients.
[b] $P=0.013$.

more frequent in the capecitabine group, while hospitalisation for diarrhoea was similar in the two groups. Overall, the number of days spent in hospital for the treatment of adverse reactions was 30% higher in the 5-FU/LV group than in the capecitabine group.

Table 6 summarises the numbers of unscheduled medical consultations, excluding hospitalisations, which were required for treatment or management of adverse events during therapy. Unscheduled consultations comprised office or clinic visits, telephone contacts and visits to the patient's home by a treating physician. In order of occurrence, office visits were the most common followed by day care unit visits, phone consultations and home visits. Overall, patients treated with capecitabine were more likely to visit a day care unit or office, or to require telephone contacts, than were patients treated with 5-FU/LV. Home visits were required for fewer than 10% of patients, and were similar in number between the two groups. The numbers of unscheduled visits or consultations required for each patient were higher in the capecitabine group, although the differences were not large (<0.6 visits per patient overall).

Drug use for the management of adverse events was analysed with emphasis on expensive drugs that are likely to be economically important. Table 7 summarises the use of antimicrobials, antiemetics, and granulocyte-

Table 4
Hospital visits required for administration of drug regimen

	Capecitabine ($n=297$)		5-FU/LV ($n=299$)	
	Planned	Observed (mean)	Planned	Observed (mean)
No. of visits/cycle	1	1	5	5
No. of cycles/30 weeks	10	7.1	8[a]	5.1
Total scheduled visits per patient	10	7.1	40	25.5
Total scheduled visits	2970	2109	11 960	7625

[a] The 5-day treatment period for cycle 8 would be complete by week 29.

Table 5
Number of study treatment-related adverse events requiring hospitalisation

Adverse event	Capecitabine ($n=297$)			5-FU/LV ($n=299$)		
	Patients[a]	Admissions	Total days in hospital	Patients[a]	Admissions	Total days in hospital
All events	35	40	368	47	49	477
Dehydration	5	5	50	0	0	0
Diarrhoea	13	13	112	14	14	106
Hand foot syndrome	2	2	3	0	0	0
Infection/sepsis	1	1	11	10	10	106
Neutropenia	1	1	5	2	2	19
Stomatitis	1	1	32	11	11	129
Vomiting	1	1	4	1	1	5
Other	14	16	151	11	11	112

[a] Patients may be hospitalised one or more times.

colony stimulating factor (G-CSF) in the treatment of adverse reactions used either whilst the patients were in hospital or prescribed as outpatients.

As a result of the lower incidences of stomatitis and neutropenia, a smaller proportion of patients treated with capecitabine required treatment with antimicrobials of any sort compared with those receiving 5-FU/LV. Markedly fewer patients required treatment with fluconazole. Similarly, although their overall use was limited, G-CSF and octreotide were prescribed less often for patients in the capecitabine group than those in the 5-FU/LV group.

Indeed, no patients treated with capecitabine required octreotide. Patients treated with capecitabine were also less likely to require 5 HT-3-antagonist antiemetics.

Table 6
Unscheduled consultations with specialist or general physicians for the treatment of adverse events

Type of consultation and visit	Capecitabine ($n=297$) n (%)	5-FU/LV ($n=299$) n (%)
Home visits (range)	(0–11)	(0–13)
No. patients with visits	28 (9)	26 (9)
No. of visits	94	76
Mean/median visits per patient	3.36/2.0	2.92/2.0
Phone consultations (range)	(0–23)	(0–10)
No. patients with consultations	53 (18)	42 (14)
No. of consultations	164	129
Mean/median consultations per patient	3.09/2.0	3.07/3.0
Office visits (range)	(0–20)	(0–31)
No. patients with visits	91 (31)	65 (22)
No. of visits	253	179
Mean/median visits per patient	2.78/2.0	2.75/2.0
Day care unit visits (range)	(0–18)	(0–48)
No. patients with visits	75 (25)	57 (19)
No. of visits	261	214
Mean/median visits per patient	3.48/2.0	3.75/2.0

4. Discussion

The medical resource use data reported here were collected as part of a randomised phase III trial in patients with advanced colorectal cancer comparing orally administered capecitabine with a standard i.v. 5-FU/LV regimen. The emphasis was on the medical resources relevant to standard clinical practice and focused on the medical care required for drug administration and treatment of drug-induced adverse reactions. The most important finding was that, in comparison with 5-FU/LV, capecitabine led to a marked reduction in medical resource use.

Examination of patient demographics, disease baseline characteristics and previous medical history showed that the two arms of the trial were well balanced. The patient population was consistent with those described for other comparable clinical studies of colorectal cancer patients treated with 5-FU-based chemotherapy regimen [9–12] and, therefore, should accurately reflect medical resources required for the treatment of this group of patients. The clinical results of this trial

Table 7
Drugs required for the treatment of adverse events

Drug	Capecitabine ($n=297$)		5-FU/LV ($n=299$)	
	No. treatment episodes	Total treatment (days)	No. treatment episodes	Total treatment (days)
Antimicrobials	10	308	70	1087
Cephalosporins	21	166	29	181
Fluoroquinolones	23	203	28	182
Fluconazole	7	99	33	300
5-HT-3 antagonists	9	123	27	203
Octreotide	0	0	8	90
G-CSF	3	11	7	27

G-CSF, granulocyte-colony stimulating factor.

indicated that capecitabine was more active than 5-FU/LV in terms of tumour responses, and that progression-free and overall survival were equivalent for the two treatments [16]. An additional advantage of capecitabine was its substantially improved safety profile compared with 5-FU/LV. This was reflected in the substantial reductions in the medical resources employed for the management of these patients.

An important economic and practical advantage of capecitabine is the reduced number of drug administration visits required for each treatment cycle. In this study, capecitabine-treated patients had 72% less scheduled visits than those treated with 5-FU/LV. Cost analysis has not been undertaken because of the variability in treatment patterns and unit costs between countries. However, it can be estimated that this factor alone saves between €2300 and 5000 per patient (depending on the country). Savings may be particularly high in Germany, where patients were hospitalised for approximately 40% of 5-FU/LV drug administrations. The high hospitalisation rates seen at German centres in this study may be due to national reimbursement practices for certain treatment procedures.

Both treatments were generally administered in an outpatient setting (except for Germany, as described above). From the point of view of the health care provider these data indicate that the medical resources savings associated with the use of capecitabine could allow increased patient through-put and more efficient use of trained personnel. There should also be important savings in pharmacy costs associated with the use of oral capecitabine rather than i.v. 5-FU/LV.

This study shows how important differences in the adverse events profiles of capecitabine and 5-FU/LV affect medical resource requirements in the management of drug toxicity. Overall, 34.3% more 5-FU/LV patients were hospitalized for the management of treatment-related adverse events. Additionally, patients treated with 5-FU/LV spent more days in hospital and tended to experience more serious complications including stomatitis, sepsis, neutropenia and infections, which often required treatment with expensive drugs. Comparison between the two arms of the trial showed that capecitabine treatment resulted in a substantial reduction in the use of costly medications. For example, 39% less 5-HT-3 antagonists, 67% less fluconazole and 72% less of other antimicrobials were required by the patients treated with capecitabine. There was also a considerable reduction in the use of G-CSF with capecitabine treatment and no octreotide was used. Cephalosporins and fluoroquinolones were used in similar amounts in both arms.

Although capecitabine was associated with a higher incidence of HFS, treatments for this condition were principally emollients, creams and vitamin preparations, in particular vitamin B6. These did not represent important cost items and were therefore not included in this resource use analysis. Likewise, HFS rarely required hospital admission, further indicating that the occurrence of this event did not have a major clinical or economic impact in patients treated with capecitabine.

An interesting finding of this study was that the number of unscheduled contacts with health care professionals for the treatment of adverse event was slightly (<0.6 visits per patient), but consistently greater with capecitabine than 5-FU/LV. There are two possible reasons for this difference. Firstly, because the capecitabine patients had fewer scheduled visits for drug administration than the 5-FU/LV group, they had less routine contact with health professionals. Consequently, whereas management of adverse drug reactions or other problems arising during treatment may take place during scheduled visits for 5-FU/LV patients, unscheduled *ad hoc* support was required more often for those in the capecitabine group. Secondly, the increased frequency of unscheduled visits in the capecitabine group may be associated with greater anxiety engendered in patients taking a novel or experimental treatment regimen rather than a therapy described to them as standard. Whatever the reason, this small increase in unscheduled visits is more than outweighed by the substantial reduction in visits for drug administration in patients receiving capecitabine.

Various 5-FU-based regimens are used in the treatment of colorectal cancer, including the 5 day bolus Mayo Clinic regimen studied in this trial [19], the 48 h infusion De Gramont regimen [20], the weekly 24 h infusion regimen, and continuous infusion [11]. In general, the De Gramont and continuous infusion regimens either require a more intensive hospital-based administration or the use and maintenance of ambulatory pumps and indwelling catheters. A comparison of medical resource use and associated costs of these regimens indicates that the Mayo regimen is the least expensive of these alternatives [21]. Since there is no evidence that any of these 5-FU regimens is superior to the others in terms of survival, the choice of regimen may be substantially influenced by the medical resource requirements and patient convenience. Accordingly, the finding that capecitabine requires less medical resource use than the Mayo regimen of 5-FU/LV offers significant support for its use in this indication.

This trial shows that capecitabine in comparison to the Mayo regimen of 5-FU/LV leads to a substantial reduction in medical resource use, as well as an improved response rate and tolerability. Patients also gain the additional benefit from the convenience of taking capecitabine at home with the presumed reduction in the disruption of normal life [22,23]. In conclusion, these data support capecitabine as the preferred fluoropyrimidine-based regimen for the treatment of patients with advanced colorectal cancer.

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