Survival following first line fluorouracil single agent therapy for advanced colorectal cancer in a cancer unit practice in the UK

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Introduction

In the UK a third of all colorectal cancer cases present with advanced disease. (1) Fluorouracil alone is recommended as first line treatment for patients with advanced colorectal cancer (ACRC). It has been shown to increase median survival, compared to best supportive care, from 5-9 months to between 7-14 months. (2)

Studies since 1998 have demonstrated survival advantage for irinotecan and oxaliplatin in first and second line use. (3,4,5)

In the UK, the regulatory body **NICE** (National institute for clinical excellence) was setup in 1998 to produce and disseminate clinical guidelines. It is an independent organisation responsible for providing national guidance for people using the NHS in England and Wales. It makes recommendations on treatments and care using the best available evidence. This evidence is usually from randomised controlled trials. Other forms of evidence carry less weight. Funding for drugs is absolutely dependent on **NICE** approval.

AIMS

The aim of our study was to assess the validity of the **NICE** recommendations in the context of a standard cancer unit practice.

Methods

A computerised database was used to identify patients treated between 1999 and 2004. Patients were eligible if they had histologically proven ACRC and had had no previous chemotherapy for advanced disease. They could be included if they had adjuvant treatment in the past.

104 patients, all of whom had 5FU single agent as 1st line therapy, were retrospectively studied. Further treatment regimes on progression of disease were also noted. All patients were assessed using CT scans and RECIST criteria.

Chemotherapy consisted of the modified de Gramont regime in all cases (Folinic acid 200mg/m2, 5FU bolus 400mg/m2 followed by 5FU 2400mg/m2 intravenously by 48hr infusion repeated every 2 weeks).

Patient Demographics

Total no. of patients = 104 Male n=54 (52%) Female n=50 (58%)

Performance Status:

Performance Status:	Number of patients (%)
0	28 (27)
1	38 (37)
2	11 (10)
3	10 (10)
No data	17 (16)

No. of cycles of Modified de Gramont administered:

Number of cycles	Number of patients (%)
1	6 (6)
2	5 (5)
3	4 (4)
4	5 (5)
5	10 (10)
6	11 (10)
7	4 (4)
8	7 (6)
9	6 (6)
10	6 (6)
11	3 (3)
12	36 (35)

Results

104 patients were evaluable. The response rate for first line fluorouracil was 13%.

Stable disease was achieved in 31%.

The disease progression rate was 56% with the median time to progression being 3 months (range 0-60 months).

Overall survival was 12.1 months (95% C.I. 9.92-14.2 months).

Second and third line treatment was received by 49 and 11% of patients respectively.

Discussion

Randomised control trials tend to exclude certain important groups of patients, such as the elderly and those with co-morbidities. In addition, there is bias towards reporting only results from successful trials. Within this context it is not surprising that our results are worse than those from randomised controlled trials. No patients were excluded from our study.

Our data suggests that the response rate, uptake of second and third line therapy as well as survival falls short of those from randomised controlled trials.

Study	No' of pts	Response rate %	Time to progression - months	Survival (months)
de Gramont 2000 **(4)**	**210**	**22.3**	**6.2**	**14.7**
Saltz 2000 **(6)**	**226**	**21**	**4.3**	**12.6**
Rougier 2000 **(8)**	**188**	**31**	**4.4**	**14.1**
Hoff 2001 **(9)**	**303**	**15.5**	**4.7**	**13.3**

Table showing reported response rates, TTP, overall survival of the 5FU single agent arms.

More than half of patients who received treatment progressed and are likely not to have benefited. We would propose that institutions such as NICE whose guidelines have significant influence on the funding of new therapies should take into account the "real world" data as well as those from RCTs.

References

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