completeness, but also give comprehensive overviews of the trial endpoints for all concerned. Copies of such a flowsheet are now available from the EORTC Chemotherapy Quality Control subcommittee.

Apart from general data that was missing, the data managers reported that in two of the trials reviewed the surgery form and the radiotherapy form respectively required details that had to be supplied specifically by the surgeon and radiotherapist. This is a perfectly acceptable situation, although in such cases it is advisable to discuss these forms with the doctors involved before the trial starts so that they can ensure that the data required is retrievable.

Data managers reported that in some studies there were items of "unusual" data, such as "sediment cells", "weight loss in the 3 months prior to study", "size of metastases at progression" and "time of headache", which had not been documented in patient charts. These problems indicate that there is still room for intensification of the contact between the physician/oncologist and the data manager. If the CRFs are discussed prior to the start of the study special attention can then be paid to documentation of these unusual items.

A number of comments (7%) could only be categorised as "lack of data management experience" and it was particularly disturbing to see that even experienced data managers were still having problems with determining certain study endpoints, for example "best/overall response", "data onset response" and "reason off study". Although this is data that can be checked and corrected by the Data Centre, these are fundamental concepts which a data manager should learn early in his/her career. It is obvious from this that data management training is essential and these topics have therefore been given extensive coverage in the recent EORTC–ESO Data Management Course.

Another point which was apparently not clear, and which was therefore emphasised during the Data Management Course, is the difference in endpoints between phase II and phase III trials. For phase II the CRFs must collect precise and extensive details on drug dosage, concomitant medication, toxicity and response assessment, whereas for phase III trials this degree of detail is superfluous since the emphasis should be on the harder endpoint of survival. The organisation of data collection must take these differences into account: entailing close monitoring of patients during the treatment period for phase II and paying careful attention to prestudy prognostic factors and regular patient follow-up for phase III.

In conclusion, the difficulty of understanding the questions on the CRFs is in the order of 5% and can be reduced, if not eliminated, by more explicit wording of the questions on the forms. In any case it does not warrant the production of specific handbooks, as was originally supposed. The Cooperative Groups, the study coordinators and the EORTC Form Review Committee should be aware of the types of problems of interpretation that the data managers have highlighted and the EORTC FRC, with support from the EORTC Study Group on Data Management, now has an important role to play in the supervision of all new EORTC forms.

From the reports of missing data in the patient chart, it became obvious that improvements need to be made in hospital file management. We strongly recommend the use of standard flowsheets to ensure that all general items are documented and that responsible physicians and data managers cooperate more closely in order to arrange ahead of time that *all* the required data is collected.

During this exercise on quality control of trial data and study forms it came to light that there is a need for ongoing data management training and a number of topics have been highlighted to receive special attention in the EORTC–ESO course.

1. Franklin HR, Kerr M, Tarayre M, Bierhorst FJ, Van Glabbeke M. Quality Control of Case Report Forms: A collection of data managers' comments. Report to the EORTC Quality Control Committee, March 1991.
2. Vantongelen K, Steward W, Blackledge G, Verweij J, van Oosterom A. EORTC Joint Ventures in Quality Control: Treatment-related Variables and Data Acquisition in Chemotherapy trials. *Eur J Cancer* 1991, 27, 201–207.

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High-dose Folinic Acid, 5-Fluorouracil Bolus and Continuous Infusion in Metastatic Colorectal Cancer: a 3-day/3-week Schedule

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5-FLUOROURACIL (5FU) modulated by folinic acid is a standard treatment for metastatic colorectal cancer. Various combinations of the two drugs have been studied for an overall response rate of 30–50% and median survival of 10–15 months [1, 2]. We previously reported a 2-day schedule at 2-week intervals of high dose folinic acid, 5FU bolus and continuous infusion (LV5FU2, protocol C85) which obtained a 54% response and 18 months median survival at particularly low toxicity [3]. We had added a 5FU continuous infusion to a bolus at 2-day/2-week schedule in

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Table 1. High-dose folinic acid, 5-fluorouracil bolus and continuous infusion in metastatic colorectal cancer: results and tolerance of a 2-day/2-week (LV5FU2) and a 3-day/3-week (LV5FU3) regimen

Regimen	N	Response (%)	Grade 2+ toxicity (%)	Mucositis (%)	Reference
LV5FU2	37	54.1	2.7	0	3
LV5FU2	42	37.0	0	8.0	4
LV5FU3	37	42.9	5.4	13.5	present study

order to maximise the 5FU dose and to avoid the cumulative toxicity of consecutive 5 day regimens. This present study was performed to investigate whether a less demanding regimen (3-day/3-week schedule, LV5FU3), would obtain similar results.

Between October 1987 and January 1989, 37 previously untreated patients with measurable metastatic colorectal cancer received a 2 h intravenous infusion of high-dose folinic acid (200 mg/m^2), followed by a 5FU 400 mg/m^2 intravenous bolus and 400 mg/m^2 in an intravenous 22 h continuous infusion on day 1, and repeated on days 2 and 3 every 3 weeks. Mean age was 61.5 years (S.D.: 10 years, range 40–80), M/F ratio 21:16. Performance status (WHO) was 0–1 in 30 patients, 2–3 in 7. Primary localisation was the colon in 31 patients and rectum in 6 patients. 26 showed liver metastases, 10 peritoneal carcinomatosis and 7 lung metastases. The largest tumours were < 2cm in 5 patients, 2–5 cm in 19, 5–10 cm in 9 and > 10 cm in 4 (computed tomography scan). Median follow-up time was 36.8 months in July 1991. We observed four complete responses (WHO definition), 11 partial responses, stable and progressive disease in 15 and 5 patients, respectively. 2 patients were not evaluable. Median duration of response was 12 months (range 5–41+). Median survival was 17 months; 34% patients were alive at 2 years and 19.5% at 3 years. Median survival in responders was 33 months and one complete responder remained disease-free at 41+ months. Grade 1–2 mucositis was observed in 5 patients (13.5%), grade 1–2 nausea/vomiting occurred in 4 patients (10.8%), grade 2 diarrhoea in 3 patients (8.1%) and grade 1–2 alopecia in 4 (10.8%). 1 patient experienced grade 1 hand–foot syndrome and another grade 3 (5.4%). One patient presented grade 3 neutropenia (2.8%).

With 43% response and 17 months median survival, the LV5FU3 regimen is active against metastatic colorectal cancer with low toxicity. However, LV5FU3 obtains results and tolerance which are not superior to LV5FU2 (Table 1). In our opinion, the LV5FU2 schedule should be preferred. A multicentre randomised phase III study is in progress to compare LV5FU2 with the 5-day/4-week bolus of 5FU and low dose bolus folinic acid regimen reported by Poon *et al.* [1].

1. Poon MA, O'Connell MJ, Moertel CG, *et al.* Biochemical modulation of fluorouracil: evidence of significant improvement of survival and quality of life in patients with advanced colorectal carcinoma. *J Clin Oncol* 1989, 7, 1407–1418.
2. Petrelli N, Douglass HO, Herrera L, *et al.* The modulation of fluorouracil with leucovorin in metastatic colorectal carcinoma: a prospective randomized phase III study. *J Clin Oncol* 1989, 7, 1419–1426.
3. de Gramont A, Krulik M, Cady J, *et al.* High-dose folinic acid and 5-fluorouracil bolus and continuous infusion in advanced colorectal cancer. *Eur J Cancer Clin Oncol* 1988, **24**, 1499–1503.
4. Seymour MT, Johnson PW, Wrigley PF, and Slevin ML. 5-Fluorouracil, leukovorin and alpha-interferon: a new regimen suitable for randomized trial. *Proc Am Soc Clin Oncol* 1991, **10**, 160.

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Intra-arterial Cisplatin in Advanced Squamous Cell Carcinoma of the Bladder

M. Wishahi

PREOPERATIVE INTRA-ARTERIAL chemotherapy for locally advanced urinary bladder carcinoma has been reported to show encouraging clinical and pathological responses in pure transitional cell carcinoma (TCC) [1–3].

Intra-arterial cisplatin prior to cystectomy has been carried out in 6 patients with locally advanced (T3, T4) squamous cell carcinoma (SCC) of the urinary bladder. Patient characteristics are shown in Table 1. The entry criteria were: T3 or T4 (WHO), no previous chemotherapy or radiotherapy, no previous or concurrent malignancies, adequate haematological parameters and normal liver and renal function. Informed consent was obtained.

Patients were evaluated by bimanual examination under anaesthesia, intravenous urography, abdominopelvic ultrasonography, computed tomography (CT) scan and histopathological examination of tumour biopsy.

The intra-arterial chemotherapy was administered through a percutaneous catheter placed in the hypogastric artery, in the site where the tumour was most florid. Cisplatin was administered (75 mg/m^2) over 30 min, and a second course was given 2 weeks later. Patients were evaluated 2 weeks after the second course.

All cases underwent radical cystoprostatectomy and urinary diversion. The surgical specimen was subjected to histopathological examination. Clinical assessment after the two courses of intra-arterial chemotherapy showed that none of the 6 patients had responded; in 4 patients there was upstaging of the disease. Operative assessment and histopathology confirmed the absence of response. In all the patients the tumour was solid, bulky and low vascularity.

Table 1. Patient characteristics, response and survival period (months)

Patient (age, sex)	Stage: Clinical	Stage: Pathological	Pathological response*	Survival
1 (36, F)	$T_3N_xM_0$	$T_3N_0M_0$	No change	25
2 (40, M)	$T_4N_1M_0$	$T_4N_1M_0$	No change	12
3 (45, M)	$T_4N_1M_0$	$T_4N_1M_0$	Upstaged	15
4 (55, M)	$T_3N_xM_0$	$T_4N_1M_0$	Upstaged	13
5 (36, M)	$T_4N_1M_0$	$T_4N_2M_0$	Upstaged	8
6 (60, M)	$T_3N_xM_0$	$T_4N_1M_0$	Upstaged	10

*No patient had a clinical response.

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