REPORT EORTC OSTEOSARCOMA INTERGROUP MEETING
Amsterdam, October 26, 1988

Chairman : R.L. Souhami, London.

Statistical Report on Protocol 80831
A total of 297 patients has been entered in this study which was closed to patient entry in October 1986. The acute and chronic toxicity of the two regimens have been evaluated on the basis of 274 patients, while haematological toxicity is evaluable for 225 cases. When comparing the two drug regimens, more severe leucopenia and a higher rate of neurological side effects can be seen in arm 1 while there is a higher rate of liver toxicity in arm 2. A difference in response to therapy can be seen between metastatic patients and primary patients : 28% of metastatic patients responded to treatment 1 (CR+PR) while 58% responded to treatment 2 showing an apparent superiority of the HDMTX regimen in advanced disease. However, this conclusion must be considered tentative since it is based on a limited sample size. In primary patients no difference in response rate was found between the two treatment arms and this lack of difference should be verified with the histological evaluation which is not yet available.
When assessing the results of the randomized comparison of the two chemotherapy regimens in operable non-metastatic patients (more than 100 patients in each arm, median follow-up nearly 3 years), the study demonstrates the superiority of the ADM/DDP arm in survival and in disease free interval. However, this difference is not apparent in patients whose tumour was initially considered as not suitable for conservative surgery (bad risk patients).
In the (neo)adjuvant trial, overall disease free rates are estimated at 58% after 2 years and 46% after 4 years. The relapse rate is decreasing now after 2 years although a "plateau" has not yet been reached. The previous EORTC adjuvant study showed no relapse after 4 years and so it can be estimated that 75% to 80% of the relapses are recorded during the first 2 years.
A publication on the results of this study will be prepared for the Spring of 1989.

Pathology Review
The pathology panel, consisting of Pringle, Malcolm, Misdorp, Voisin, Roels and Martinez Tello has been meeting regularly to carry out quantitative response measurements according to the method they have developed. This method, which was presented to the EOI members in Madrid last year, has been presented also by Malcolm and Pringle in Vienna at the EMSOS and at the Pathological Society meeting in Newcastle, U.K.
Cases in protocol 80831 are proposing problems to the group : some data are missing in 174 cases in the U.K. However, quantitative assessments can already be made for 149 cases but some initial biopsies are missing. Biopsy material may be retrievable but resection specimens are not always available. There are 25 cases in the U.K. were no material is available at all. It will be necessary to retrieve these cases before the pathology publication can be completed. The pathologists should obtain material from primary and metastatic tumours concurrently. The Data Center will provide an updated list of patients (eligible and non-eligible) for the pathologists.

Administrative Report on Protocol 80861
One hundred and thirty-two patients have been randomized. Recruitment is very slow from continental Europe and this makes assessment of the multidrug arm difficult as too few patients are evaluable for toxicity. So far this is consistent with the previous trial.
The data should be brought up to date as soon as possible.
European participants should be encouraged to enter patients, and members were asked to publicize the protocol in an effort to raise accrual. Van Oosterom will present some preliminary data within the next 3 months and Bramwell will do her best to increase recruitment from Canada.
Patients refusing randomization may now be registered in protocol 80861 as this was approved by the Protocol Review Committee of the EORTC and the Cancer Therapy Committee of the MRC. Souhami will send all members a reminder of this in a newsletter.

Administrative Report on Protocol 80862
No renal toxicities have been reported in the study which has accrued 50 patients. A decision will be made on future work - either building on the PIA study or devising a new study for non-metastatic patients. A more aggressive chemotherapy regimen was discussed and also the combination of ifosfamide and platinum. A subcommittee was formed to select a general direction and present outlines for a future study. This committee, consisting of Van Oosterom, Lewis and De Kraker, will define the next step for metastatic and axial primary cases for the next meeting.

Protocol 80871 - Pilot study of ADM/DDP chemotherapy in patients with spindle cell sarcomas of bone other than osteosarcoma
One patient has been entered in this study which was opened for patient entry in September 1988.

Surgical Review of Protocol 80831
At the start of the protocol where there was a possibility of a choice between amputation or conservative surgery, amputations were done in 60% of patients, 40% having conservative surgery. There is now a striking difference, conservative surgery being twice as frequent as amputation. Surgical incisions are narrowing as more conservative procedures are adopted. This can influence the number of recurrences.

Next meetings
Saturday, March 11, 1989 in Amsterdam
Sunday, September 3, 1989 in London

REPORT EORTC RADIOTHERAPY COOPERATIVE GROUP
Besançon, October 28-29, 1988

President : W. van den Bogaert, Louvain

Administrative Data Center Report
Protocol 22844
Randomized trial on the dose response in radiation therapy of low grade cerebral gliomas. The so-called "believers" protocol.
Accrual : 214 patients from 23 institutions.
Off study : 33 patients, mostly because of progression.
There has been a good response to the Quality of Life questionnaire.

Protocol 22845
Randomized trial on the efficacy of radiation therapy of low grade cerebral gliomas. The "non-believers" protocol.
Accrual : 51 patients.
Off study : 3 patients, due to recurrence or progression.

Since most of the centers participating are non-Radiotherapy Group members quality control (as performed in the Radiotherapy Group) is important.

Protocol 22851
Randomized trial on accelerated fractionation of radiotherapy in advanced head and neck cancer.
Accrual : 205 patients by 16 institutions.
In the parallel cell kinetics study (present accrual : 29 patients) at least 100 patients are needed.
Members are urged to enter patients and may contact Adrian Begg at the Netherlands Cancer Institute for further information.

Protocol 22861
Randomized phase II trial of radiotherapy-alone and radiotherapy with concomitant chemotherapy in the treatment of anal carcinoma.
Accrual : 20 patients by 11 institutions. This accrual is disappointingly slow.
Since the MRC is doing a very similar study the study coordinator will be urged to try to combine both studies.

Protocol 22863
Controlled clinical trial in high metastatic risk carcinoma of the prostate comparing pelvic radiotherapy-alone with pelvic radiotherapy plus LHRH analogue.
Accrual : 38 patients.
The treatment is well tolerated and compliance to the hormone treatment is good.
Not everybody was aware of the fact that a 4-field box technique was acceptable in this study.

Protocol 08844
Randomized phase III study in inoperable non-small cell bronchogenic cancer.
Accrual : 294 patients.
The majority of patients in this joint study of the Radiotherapy and Lung Groups have been randomized for the Radiotherapy Group or both groups.

Protocol 08861
Randomized phase III study of adjuvant therapy in completely resected non-small cell bronchogenic cancer.
Accrual : 54 patients by 13 centers.

Protocol 10853
Randomized phase III trial of external radiotherapy versus no treatment for in-situ ductal carcinoma of the breast treated by wide excision.
Accrual 100 patients by 20 centers.

New protocols
On conservative treatment of breast cancer
The 4th draft of this new joint protocol (a randomized study in the conservative management of breast carcinoma - assessment of the role of a booster dose of radiotherapy) of the Breast Group and the Radiotherapy Group was not accepted by the PRC for a number of reasons :
1. The PRC objected to the inclusion of T3 cases. Our Group proposes to agree with the suggestion of the PRC.
2. The PRC read in the draft that macroscopically resected patients were to be included. However microscopically resected patients were meant.
3. The PRC felt that the small differences in local control in the different treatment arms will be obscured when the adjuvant treatment is not uniform.
The protocol committee proposed a uniform schedule for the treatment of the axilla and the adjuvant therapy of premenopausal as well as postmenopausal women.
These proposals will be discussed with the Breast Group and resubmitted to the PRC thereafter.

Quality control of individual patient data
This pilot study was carried out by the Amsterdam Group on 5 patients from each of the main participating centers in the rectum trial (22831). A scoring system was developed for each item reviewed such as simulation and treatment data, radiotherapy charts and eligibility criteria. A short overview was presented by Hamers. In fact mainly small deviations were found. The feasibility of checking of individual patient data has been proved and although the financial implications have not been solved, it is hoped that this work can be extended in a prospective setting.

Miscellaneous
Intestinal damage from postoperative radiotherapy for rectal cancer and measurement of small bowel volume in patients treated in rectum protocol 22831
J. LETSCHERT and J.C. HORIOT
Letschert of the Netherlands Cancer Institute described a method for measuring how much small bowel is irradiated. Her CT method correlated well with Gallagher's method. However she found a volume exponent of 0.5 which is greater than reported in the literature. It was proposed to continue this work in order to :
- confirm the 0.5 factor
- study the correlation of the complication rate resulting from irradiated small bowel
- study the influence of the type of surgery on the occurrence of complications.
Centres interested are Amsterdam (AMC), Antwerp, Besançon, Dijon, Florence and Tours.

Reflections on a new trial in B2-C rectal cancer
J.F. BOSSET and J.C. HORIOT
As trial 22831 will be completed within 12 months it is time to consider programs for further study of rectal carcinoma. Bosset gave a comprehensive overview of the literature and included also (as yet unpublished) information gained on a recent trip in the United States. Horiot discussed various possibilities for new studies. Amsterdam (AMC and VU), Besançon, Florence, Grenoble and Pisa were centers interested in participating. All members will get a copy of the presented review to be discussed within their departments.

Bile duct cancer
D.G. GONZALEZ
Gonzalez gathered information on the treatment of a series of 81 patients with bile duct carcinoma and presented details of patient characteristics.

Limited small cell lung cancer
An outline of this randomized phase II study in alternating versus sequential radio-chemotherapy in limited small cell lung cancer (protocol 08877) was presented by Gonzalez. Eventually this study may run into a joint phase III study of the Lung Group and the Radiotherapy Group.

Bladder
N'Guyen gave details of the state of affairs with this pilot study of external irradiation with etanidazole (SR 2508) radiosensitizer in advanced bladder cancer. The provision of the drug remains a problem in several countries. Necessary accrual : 30 patients in 6 months.

Colon
The Steering Committee provided Karim with its comments on this phase II feasibility study on postoperative radiotherapy in caecum and ascending colon carcinoma. The main objections were on items such as feasibility, patient accrual and the rather heavy work up and follow up.

T3 larynx
Van den Bogaert presented on behalf of the writing committee this proposal for a joint study (by the Head and Neck Group and the Radiotherapy Group) of radiotherapy versus "upfront" chemotherapy followed by radiotherapy in the treatment of T3 laryngeal carcinoma. The Steering Committee was not in favour of going ahead with this study.

Quality Control Project
Site visits
In 1988 three Italian radiotherapy departments have been visited by the physicists and radiotherapists. Five other centers will be visited in the near future. A total of 28 centres have been visited up to now and there has been a 71% increase in participation in the last two years. If financially possible this program will be pursued.

Mailed TLD program
This program runs smoothly. Seventeen centers have participated in the in water calibrations and 8 in the in-vivo measurements. The results were excellent (90% of the dosimeters agreed within 4%).

Quality control workshop
This workshop is planned for April 13, 1989 in Louvain prior to the next group meeting. A physicist and a radiotherapist from each of the centers participating in the Quality Control Project will be invited to present reports and make proposals for discussion.

Pilot study on alternative methods of fractionation in the treatment of gliomas (an update)
D.G. GONZALEZ and E. van der SCHUEREN
Up to now it has been possible to deliver high doses in a short period of time (60 Gy in 12 days) in three fractions per day. With a good technique the reactions are only mild.

Information and follow up on experimental work on new bioreductive drugs
J.C. HORIOT
Horiot gave further details on the work of Adams on the newest bioreductive drugs. They seem to be less toxic and considerably more radiosensitizing. Clinical experience might be started early at the phase I level.

Next meetings
The Spring meeting will be held in Louvain, April 14 and 15, 1989.
The Autumn meeting will most probably take place in Pisa.

REPORT EORTC LUNG CANCER WORKING PARTY (Belgium) MEETING. Brussels, November 19, 1988

Chairman : J. Klastersky (Brussels)

Review of ongoing studies
NSCLC (EORTC 07861) : phase II randomized study comparing cisplatin + etoposide versus carboplatin + etoposide combination. 124 patients have been evaluated. Final results expected for early 1989.

SCLC (EORTC 07871) : phase III randomized study comparing an intensive multiple drug chemotherapy versus standard combination : 97 patients registered so far.

Biomarkers in lung cancer (EORTC 07851) : 327 patients so far entered into this study, 182 with non-small cell lung cancer and 145 with small cell lung cancer.

Pilot studies
NSCLC : phase II study of cisplatin + vindesine + 5-fluorouracil + mitomycin C in advanced disease : 34 patients have been registered.

Second-line treatment for SCLC : patients relapsing after treatment in the 07853 protocol (CEV vs EV) are now treated with a cyclophosphamide + adriamycin + vincristine combination (CAVi) potentiated by ampholiposomes. Thirteen have been included. In 11 evaluable patients, 6 partial responses have been obtained.

Ifosfamide + ACNU as salvage therapy for patients with SCLC and failing in protocol 07871 : this phase II study is now open. Patients will be evaluated separately according to their randomization in the first-line study. ACNU is given in a dose of 75 mg/m^2 in one day and ifosfamide at 4 g/m^2 (24 h infusion + mesna) on the same day.

Biomarkers in lung cancer
Body showed results obtained in both SCLC and NSCLC, where squamous cell carcinoma (SCC), lipid-associated scialic acid (LSA), calcitonine, CEA and neurone specific enolase (NSE) were measured.

New studies
Protoadjuvant chemotherapy in inoperable non metastatic NSCLC : the Group has agreed to write a protocol where all patients will receive 3 courses of combination chemotherapy (three drugs regimen). Responders and patients with no change will be randomized between chest irradiation and 3 further courses of chemotherapy. However, patients whose tumor will become resectable should be subjected to surgery. The protocol will be written by Sculier and Donnadieu (chemotherapy), Van Houtte (radiotherapy) and Monteau and Rocmans (surgery).

New SCLC study : a weekly schedule of combination chemotherapy including GM-CSF in supportive management will be studied.

Adjuvant immunotherapy in completely resected lung cancer : a phase II trial of CGP 19 835 A Lipid (MTP-PE in liposomes) will be started at Institut J. Bordet in patients with advanced NSCLC, in order to evaluate the tolerance to the drug and to determine antitumoral activity and macrophage activation.

Closed study
EORTC protocol 07853 (phase III randomized study comparing etoposide + vindesine versus cisplatin + etoposide + vindesine in SCLC) is undergoing final analysis. Part of the results were presented.

New plenary session
The next plenary session is scheduled in Brussels on March 11, 1989.

J.P. SCULIER, M.D.
Secretary
