These reports will appear on a monthly schedule whenever available. They are based on information provided by individuals or clinical and research groups pertinent to cancer research. More detailed information if needed may be obtained by writing to

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Guidelines for the preparation for publication of reports from EORTC Cooperative Groups

1. The chairman, convener or secretary of the Group is requested to mail the report to the office of the European Journal of Cancer & Clinical Oncology. The reports will be edited and published in the Journal within 6 to 8 weeks after reception in the office.
   Address : H.J. Tagnon, M.D.
   Editor, EUROPEAN JOURNAL OF CANCER & CLINICAL ONCOLOGY
   Institut Jules Bordet
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2. Please send the report typewritten on one side of page, double spaced with a 5 cm left margin. Brevity is essential. Tables and figures are difficult to print and should be replaced by an appropriate text.

3. Please consult the reports published in the March 1989 issue of the Journal and consider them as models to be adopted for all reports with possible exceptional adaptations.

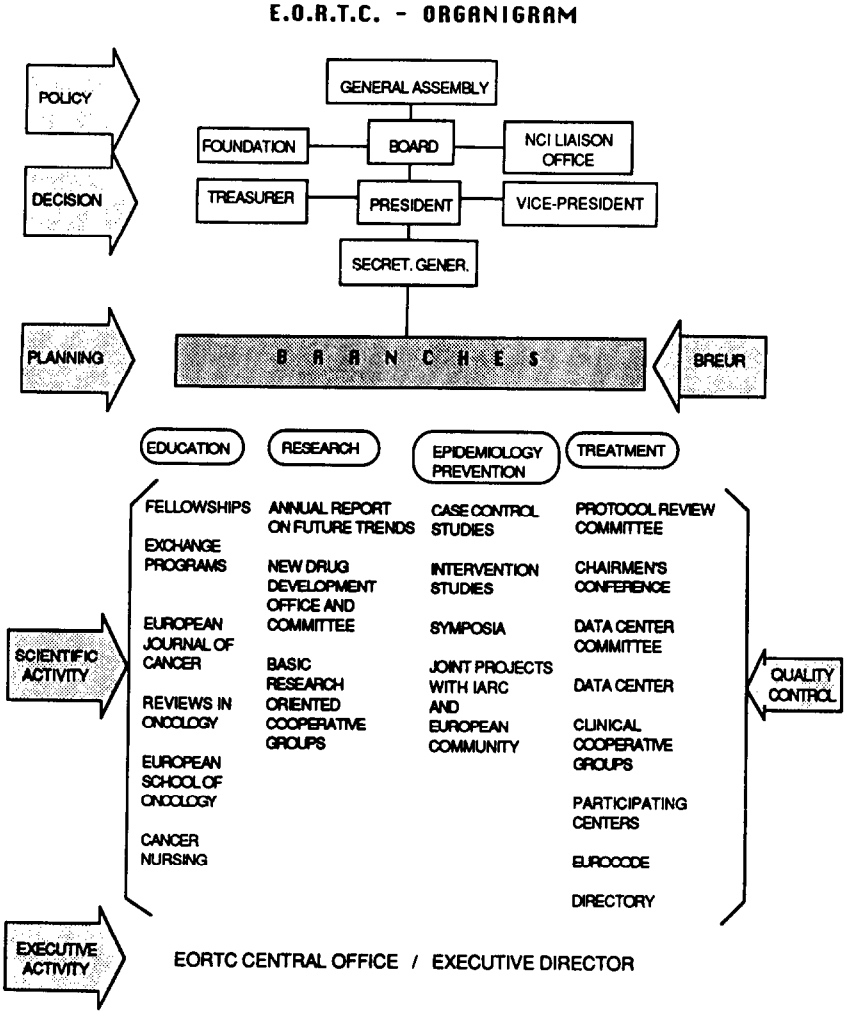
4. We request omission of list of names of attendants to the group meetings. Reports should be signed by either the chairman, convener, secretary of the group, or by all three ad libitum.

5. Please add as a conclusion to your report : "Additional information may be obtained by writing to the secretary of the group".

6. Protocols will be published at the request of the groups.

This office will be glad to receive your comments, criticism and suggestions on the edition and publication of your reports.

The Editor.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CONSTITUTION OF A STUDY COMMITTEE OF TUMORS IN OLD AGE - AN EORTC INITIATIVE

As an example to be offered to other EORTC groups a retrospective study on the treatment of elderly patients with non-Hodgkin's lymphomas has been already carried out in the EORTC Lymphoma Group. The results have been published in the Journal of Clinical Oncology in the November 1988 issue. A prospective randomized study comparing a specifically designed regimen tested against conventional chemotherapy has been recently activated by the same group.

Those who intend to participate to future EORTC studies in the domain of neoplasia of elderly may ask for further information to Silvio Monfardini, Chairman of the study group on neoplasias in elderly people (≥ 70 years).

Dr. Silvio Monfardini
Centro Di Riferimento Oncologico
Aviano 33081, Italy
Tel: 434/652512

REPORT EORTC BREUR COMMITTEE
Amsterdam, 23 March 1989

Chairman: S.B. Kaye, Glasgow, U.K.

APOLOGIES
Apologies were received from J.P. Armand, H.H. Hansen and E. van der Schueren

1.1 Minutes of meeting of 10 October 1988 were received and approved. They had been submitted to the Board at its meets on February 22, 1989.

1.2 Kaye and the Committee extended their thanks to E.H. Cooper for his work as Chairman over the years.

2. MATTERS ARISING

2.1 The Role of the Breur Committee:
Following the discussion of the role of the Breur Committee in its meeting of 20.10.88 (item 1.3 -1.5) further discussions of the role of the Breur Committee had taken place in Lugano (29.10.88) and at the EORTC Board meeting (22.2.89). Kaye and Cleton informed the Committee that the feeling within the Board of the EORTC was that the Breur Committee should perform a general reviewing function, not only of the clinical cooperative groups but also of other branches of the EORTC including the Education, Research and Epidemiology/Prevention branches. The President of the EORTC had produced an outline organigram indicating the relationship of the Breur Committee and other committees with the Board and branches. Although further detailed work was in progress this outline had been accepted.
In order to fulfill a general reviewing function it was felt that the membership of the Breur Committee should consist in part of members with little or no involvement in other EORTC activities; representatives of the European Community countries should continue to be present but there was no exclusion of non EC members. After further discussion of the recommendations, it was AGREED that the Breur Committee should meet twice a year with a programme to review part of each of the four branches of the EORTC. The Breur Committee will comment on the overall quality of their activity, their interaction with other EORTC components and their levels of funding. In reviewing the cooperative groups, the general principles and standards of trial organisation and analysis would be considered carefully but detailed consideration of patient accrual and quality control would fall within the remit of the Protocol Review Committee and the Quality Control Committee.
The Breur Committee reports in an advisory capacity to the President and Board of the EORTC. All present expressed their concern that reports of the Breur Committee should be considered and an appropriate response should come from the President and Board. The Committee RECOMMENDED that the minutes of the Board of the EORTC should be routinely available to the Breur Committee.

2.2 Membership:
S. Kaye commented that the Committee should consist of 9 people. He reminded Committee members that it was a general rule of the EORTC that members serve for 3 years and this period could be renewed once only. Members therefore serve for a maximum of 6 years continuously. The Committee felt that there was a need to retain experienced members with knowledge of the EORTC and national and international stature.
It was felt that it may be appropriate to co-opt members to the Breur Committee for particular purposes.

Armand, Cleton, Hansen, Fossa, van der Schueren and Staquet indicated their willingness to stand down as members of the Breur Committee at this time. Boyle, Cooper, Hossfeld, Kaye, Marsoni, Senn and Selby will continue as members and the Chairman will approach.
- G. Gahrton, Sweden
- M.J. Moriarty, Eire

3. Overview of Study Groups and Project Groups (S. Kaye)

Kaye reviewed the existing clinical cooperative groups and project and study groups of the EORTC. In discussion it was noted that the Lung Cancer and Breast Cancer National Working Parties are now closed. Further enquiries about the status of the Gnotobiotic Project Group and the Thyroid Cancer Group will be made by the secretary who will report to the Committee at the next meeting.

4. Review of Pharmacokinetics and Metabolism Group (Chairman: Paul Workman)

The discussion was led by D.K. Hossfeld.
P. Workman drew attention to the differences between the Pharmacology and Metabolism Group and the Clinical Cooperative Groups. Within the PAM Group a flexible approach was taken drawing on individual expertise as needed for specific purposes and these purposes usually involved laboratory research independently or in support of a clinical research programme. The role of the Clinical Cooperative Groups in drawing patient accrual from their membership was quite different. The PAM Group had close working relationships with a number of research organisations within and outside the EORTC. Within the EORTC the most important relationships lay to the New Drug Development Office, the Early Clinical Trials Group and the Screening and Pharmacology Group. Outside, the relationship with the National Cancer Institute of the USA and the Cancer Research Campaign New Drug Trials Committee in the UK were important to the PAM Group. A committee representing the EORTC New Drug Development Office, the National Cancer Institute of the USA and the UK CRC existed in order to coordinate and steer research activity and avoid overlapping programmes. The New Drug Development Committee of the EORTC represented the main European coordination committee and the Chairman of the PAM Group sits on this.
P. Workman recorded the current objectives of the PAM Group as:
1- Provision of expertise in mechanism of action, biochemistry, molecular pharmacology, analytical methodology, synthesis, formulation, preclinical and clinical pharmacokinetics and metabolism.
2- Application of the above to the rational identification and progression of new drugs within EORTC.

3- Initiation and evaluation of new developments in cancer pharmacology.
4- Provision of a unique forum for collaboration and exchange of technical expertise and new ideas.
Particular problems that have been encountered by the group were related only to inadequate funding. The group is rich in technical expertise, new ideas and enthusiasm but the application of these may be restricted by the availability of resources.

P. Workman commented on the relationship of the PAM Group and the Research Branch. The PAM feels strongly that, like the other basic research groups, it provides not only a reserve of expertise which can be tapped in relation to clinical studies, but also the basis for the development of new treatments for the future. The Group supports the proposal to relocate at the Research Branch providing that steps are taken to ensure:
1- The level of funding for basic research is increased.
2- The opportunity for intra and inter branch collaboration is not diminished.
3- The basic research groups have representation on the Board as applies now for the clinical groups.
Details of studies in preparation were given including pharmacokinetically guided dose escalation for Phase I clinical trials, the development of new analytical techniques for drug levels, the analysis of membrane targets for cancer chemotherapy and critical assessment of therapeutic and toxicological monitoring in the individualisation of drug dosage. In principle, P. Workman felt that the thrust of the research effort was moving away from analytical methodology towards new targets for cancer chemotherapy.
A list of EORTC publications was given including 4 full peer review papers in major cancer research journals. Discussion then centred on the nature of additional funding requirements into the PAM group. P. Workman felt that such requirements should not be met by shifting funds from other EORTC enterprises but rather by the provision of new funding particularly to strengthen the number of personnel working within the New Drug Development Office. Two more full time professional staff within the NDDO could generate a great deal of additional research. The need for additional administrative support for the Group perhaps in the form of a half time administrative assistant to the Chairman was identified.
In discussion of possible amalgamation between the PAM Group and other drug development groups, P. Workman commented that an effective overall and integrated new drug development effort does exist and any new structure would seem unnecessary unless new funding was available. There maybe savings by amalgamation but the present very small administrative costs suggest that these might be trivial and at present duplication of effort was avoided by a careful consultative process.
As a result of the review of the Pharmacology and Metabolism Group, the Breur Committe OBSERVED that the Group was undertaking research to a high standard with very limited resources. It was the general feeling of the Committee that the Pharmacokinetics and Metabolism Group should be complimented on their work and that they should continue to be supported actively.
It is RECOMMENDED that careful consideration should be given to:
1- Further financial support for administrative assistance and professional staff within the New Drug Development Office.
2- Moves to restructure or amalgamate the existing drug development efforts of the EORTC should be undertaken cautiously with careful consultation with the existing workers and that no changes should be made unless they can be shown to be required.

5a. Genito-Urinary Cancer Cooperative Group (Chairman: D. Newling)
The discussion was led by F.J. Cleton. D. Newling described a large and carefully organised group with the current objectives:
1- To coordinate clinical research in urological cancer by formulating and performing clinical trials involving new and established therapies.
2- To support scientific research into urological cancer.
3- To broadcast information thus acquired at biannual meetings and by publication in suitable scientific journals, monographs and a newsletter.
Clinical studies which are in progress or completed were listed and included 12 in the treatment of bladder cancer, 8 in the treatment of prostatic cancer, 7 in the treatment of testicular cancer and 3 in the treatment of renal cancer. With reformation of the infrastructure of the group there has been a pause in the introduction of new studies in superficial bladder cancer, advanced prostate cancer and testicular cancer at the present time. This reformation has coincided with a time when the group feels that it must reappraise the results of earlier studies and design new studies to take into account information on prognostic factors in urological tumours and careful analysis of quality of life and response criteria in advanced disease.
In discussion it was concluded that the groups clinical trials have been of high standard with great efforts being made to maintain high quality data collection.
Discussion then centred on a number of problems identified by D. Newling:
A- Group membership. This had now become stricter so that full members must contribute 10 patients per year to group studies, 85% of which must be valid. This had resulted in an improvement of active members and a small reduction in the total membership.
B- Data management. The group provides funding for 2 data managers and a statistician and recently 2 half time positions. Outstanding work still involves study analysis rather than data accrual but this should be resolved by maintaining the present level of staffing. D. Newling highlighted the problems of making use of advanced information technology; for instance Eurocode in many district general hospitals who contribute patients to the Cooperative Urology Group. He emphasised that in future studies standardised forms and data collection, strict financial rules and very careful consideration of rate of patient accrual and data analysis and publication would be important within his group.
C- Quality control. The quality control group of the Cooperative Urological Research Group was systematically visiting the major centres contributing patients, but it was impractical to visit all centres contributing only a small number of patients. In the light of current assessments, the best way of maintaining quality control for small centres would be considered.
D- Reference pathology. Each tumour orientated working group now has a reference pathologist who provides external review for all slides and this approach is still being developed.
In summary D. Newling commented that the Urological Cancer Cooperative Clinical Group was a happy and successful organisation. Moderate changes in internal organisation and more site orientation with detailed quality control should continue to improve the quality of the groups' work. No current major financial problems were identified although as new studies became less frequent during the next year or two the availability of funding from industrial resources might be reduced. It was noted that at present the Group is able to provide substantial secretarial help for its own officers from its own funds.

In subsequent discussion the Breur Committee concluded that the Genito-Urinary Clinical Cooperative Group was highly successful and contributed considerably to the profile of the EORTC as a clinical research organisation. Members of the group should be complimented on their previous success and their commitment to high standards in future. In particular, their caution in avoiding too many small contributing centres and too large a group was appropriate. In reviewing the Group's publication record the Committee notes the large number of papers in meetings proceedings and abstracts, but a paucity of papers in peer-reviewed journals. The Committee RECOMMENDED that this aspect of the Group's output shall be carefully considered in the future.

5b. The Role of the Chairmen's Committee (Chairman D. Newling)

D. Newling attended to report on the activities of the Genito-Urinary Cooperative Group. However, the Breur Committee felt that it was an appropriate opportunity to discuss with him the Chairmen's Committee of the Treatment Branch, the chair of which he has held for 3 weeks. In response to S. Kaye's questions about the relationship of the Chairmen's Committee to the Protocol Review Committee, the Quality Control Committee, Data Centre Committee and EORTC, D. Newling responded that he saw the role of the Chairman of the Chairmen's Committee to act as a spokesman for the cooperative groups in general terms to the Data Centre, PRC and QCG. He seen this role involving the collection and dissemination of views and information rather than a directive or executive role.

D. Newling emphasised the need for clear lines of communication between the different supervisory committees and clear areas of responsibility for each.

6. Quality of Life Study Group (Chairman S. Ahmedzai)

The discussion was led by S. Fossa. S. Ahmedzai reported that the Quality of Life Study Group had in the past saw itself as functioning as a think tank on quality of life measurement issues rather than providing a service to aid in the application of quality of life measurements in existing cancer clinical trials of the site related EORTC groups.

The current objectives of the group are:

1- To develop and validate improved methods for measuring quality of life in cancer patients.

2- To develop and conduct clinical trials in palliative oncology.

3- To improve knowledge about the state of psychosocial oncology and its practitioners in Europe.

4- To liaise with other European and international organisations concerned with quality of life research and psychosocial oncology.

Recent changes had involved the focusing of group activities on practical (clinical) studies, rather than on 'concepts' of quality of life and psychosocial oncology. Also, the membership now consists of a relatively greater number of clinicians, compared to the previous dominance of psychologists and sociologists.

Among the problems identified by S. Ahmedzai were included:

1- Diverse professional backgrounds of members i.e. from medical oncology, radiotherapy, internal medicine, palliative medicine, psychology, psychotherapy, sociology, social work, and nursing. This heterogeneity has frequently led to misunderstandings between disciplines, and sometimes to a dilemma of priorities. On the other hand, it has also provided a very rich and fertile source of ideas and critical review.

2- Designation as a 'study group' has tended to encourage members in the past to think of themselves as an 'ideas group' rather than as an 'active research' group. This occasionally has led to resistance from some members in pursuing 'clinical' studies. However, with the successful implementation of Protocol 15861, this has become less of a problem as all members have seen the group's ability to work in the field.

He proposed that the group feels that it is now time for it to be granted the status of 'Clinical Cooperative Group' within the Treatment Branch EORTC. Acknowledging that the Group would continue to be fundamentally different from other existing cooperative groups, by virtue of its multidisciplinary membership; and because of its very broad objectives, which embrace educational as well as therapeutic aims.

He felt the benefits of a change of status would be:

a- to confirm the EORTC's commitment of 'quality of life' research as a valid scientific endeavour, rather than as a theoretical possibility

b- to regularise the Group's financial position with regard to EORTC and EC grants

c- to allow the members to take more 'clinical' projects, in cooperation with other EORTC groups and with oncological organisations elsewhere.

In discussion, S. Kaye pointed out that the Quality of Life Study Group had in fact just been awarded a grant for the first time, and therefore there was no advantage to a change in status from the financial view point. It was also pointed out that the recent reorganisation of the Research Branch lent itself to retaining groups such as the Quality of Life subgroup within its structure.

Detailed discussion for the method of measuring quality of life being studied by S. Aaronson within the Quality of Life Study Group ensued. It was noted that the initial phase of development of the questionnaire had been based upon the idea of groups of questions related to general quality of life issues and separate groups of questions related to the specific problems of individual cancers. The development involved testing the internal consistency of the data generated in a large group of patients who have now been accrued. Future studies involved comparison of the questionnaire to external measurements such as the Sickness Impact Profile or Psychological Indicators. At present, the method being developed was felt to have some application but its use should be restricted to a research setting.

Finally S. Ahmedzai indicated that he felt that the move within the group should be towards more clinically applied work and that consideration was being given to dividing the group into a quality of life study group and a palliative care study group.

The publications were reviewed and included 4 items, but it was noted that none of these had yet appeared in peer review journals.

S. Ahmedzai withdrew and in subsequent discussion the committee felt that there were a number of major problems with the functioning of the Quality of Life Study Group:

1- Slow and insubstantial progress in the development of the method for measuring quality of life. A number of years had been spent with no peer review publications of the method and no completed evaluation of it. Complete analysis of the existing data was urgently needed to assess the way forward with this measurement method. It remains unclear whether the method will represent a significant advance.

2- The relationships between the quality of life study group and the clinical cooperative groups have not yet been adequately developed. The Quality of Life Study Group does not at present provide useful advice or act as a valuable resource for clinical cooperative groups in this difficult area of research methodology.

3- The failure to obtain peer review publication of its methodological work was seen as a serious failing in a group of this kind.

The Breur Committee RECOMMENDED -
1- That the Quality of Life Study Group should be reviewed again in 18 months.
2- That there was no necessity to grant it the status of a clinical cooperative group at present.
3- Publication of methodological work in a peer review journal should be expected within 2 years.
4- Continued support in terms of the annual grant would depend on evidence that satisfactory progress had been made.
5- Urgent consideration within the Quality of Life Study Group should be given to forming links with the existing clinical cooperative groups to assist them with their research.

REPORT EORTC MINUTES OF THE GASTRO-INTESTINAL TRACT MEETING Brussels, March 3-4, 1989

Chairman: Harry Bleiberg

40855: Randomized Phase II trial of cisplatin, 5 fluorouracil (5FU) and cisplatin (DDP) alone in advanced oesophageal cancer.
Patients were randomized to receive DDP 100 mg/m2 i.v. daily, 5FU 1gr/m2 i.v. continuous perfusion day 1-5 or DDP 100 mg/m2 i.v. day 1. Cycles were repeated on day 22. A total of 89 patients have been randomized, 3 are not evaluable. 49 are still on study. The most prominent feature of the patient's characteristics is that about two thirds of the patients had a weight loss of less than 10%. The nadir of the leucocytes and the thrombocytes was 3.3 (1.2-6.8) and 122.000 (32.000-325.000) respectively for the DDP/5FU arm, 4.4 (3.6-6.6) and 167.000 (66-274.000) respectively for the DDP arm. The mean number of courses were similar (3.5) in both arms, dose reductions were comparable but treatment was more often delayed in the DDP/5FU arm. Neurological toxicity occurred in 25% of the patients receiving DDP/5FU, compared to 13% for those receiving DDP alone. One patient died from a cerebral stroke that might be treatment related. Response rate is 42% and 14% respectively for DDP/5FU and DDP alone. One year survival rate is 40% in the DDP/5FU arm and 15% in the DDP arm. This difference is not statistically significant.
The study will continue as a Phase III comparative trial in view to confirm the one year survival rate that has been observed.

40831: Phase III trial comparing split course radiotherapy with or without cisplatin for the treatment of patients with inoperable oesophageal cancer.
Patients less than 70 years old with proven squamous cell carcinoma of the oesophagus were randomi zed to receive split course radiotherapy 20 Gy in 5 fractions with a free interval of 2 weeks, without or with DDP 100 mg/m2, given 3 to 5 days before each radiotherapy course and then every 4 weeks. Until now, 124 patients have been evaluated, one-third had a weight loss of more than 10%. Toxicity due to radiotherapy and cisplatinum was moderate, 3% had severe mucositis.
One year survival rate was 24% for radiotherapy alone and 48% for radiotherapy plus DDP (p =.27).

40813: Phase III trial of adjuvant chemotherapy (5FU/adriamycin/mitomycin C) versus no further treatment in resectable gastric cancer.
This protocol on adjuvant chemotherapy for gastric cancer was started in 1982. Patients with stage II and III gastric cancer, who had undergone curative surgery were randomized to receive chemotherapy (FAM) or no treatment.
Up to now, 313 patients have been registered from 28 institutions in 10 European countries. The latest evaluation regarding disease stage, toxicity and prognostic factors, was made in March 1988 on 291 patients.
A new analysis will be presented at the next meeting in Strasbourg, November 1989.
At this meeting an analysis of the surgical aspects of the protocol were presented. Lymphadenectomies performed in 231 patients were evaluated by comparing surgical and pathological reports. Lymphadenectomy was defined adequate for cure when a tier of non-involved lymphnodes was removed beyond those containing secondary deposits. On the basis of this definition, lymphadenectomies were classified as adequate in 81 cases, possible adequate in 111 cases and inadequate in 47 cases. In 37/231 patients, a lymphadenectomy less than R1 (limited to the perigastric nodes) was performed.

40851: Phase III study of sequential high dose MTX and 5-FU combined with adriamycin (FAMTX) versus FAM in advanced gastric cancer.
The EORTC GI Group has demonstrated activity of the FAMTX regimen (MTX, 1500 mg/m2,i.v. followed after 1 hour by FU(F), 1500 mg/m2, i.v., day 1, with leucovorin rescue starting after 24 hours, 15 mg/m2, orally, every 6 hours for 48 hours, and adriamycin (A), 30 mg/m2, i.v. day 15, every 4 weeks) in advanced gastric cancer (J Clin Oncol 4, 1077, 1986). This protocol has been further assessed in a randomized way by comparing FAMTX with FAM (F, 600 mg/m2, i.v., day 1,8,28,35; A, 30 mg/m2, i.v. day 1 + 28; mitomycin-C(M) 10 mg/m2, i.v. day 1, every 8 weeks). Stratification was made for measurable, evaluable and non-measurable disease. From November 1985 until February 1989, 183 patients were randomized. One hundred and twenty three are now fully evaluable. All responses are currently being extramurally reviewed. Six patients underwent a "second look" laparotomy with the aim of removing residual tumor, which was achieved in three of them. The toxicity of FAMTX in this study was acceptable and fully comparable to that of FAM. There was 1 toxic death in both arms; one other patient in the FAM arm died of hemolytic uremic syndrome and in two other patients in the FAMTX arm, it could not be excluded that toxicity contributed to death. There was a cumulative hematological toxicity in the FAM arm, while this was not the case in the patients treated with FAMTX. The median survival of all eligible patients so far is now around 9 months. To demonstrate a potential survival difference of 50%, a total of 200 evaluable patients must be accrued. This accrual is foreseen within the next few months.

40862: Phase II study of ifosfamide and epirubicin in advanced pancreatic cancer.
In this trial ifosfamide, 5 g/m2, 24 hours infusion, with MESNA protection, combined with epirubicin, 90mg/m2, day 1, i.v., every 4 weeks was assessed. Thirty-two patients were registered and all were evaluable. Patients characteristics were not different from our previous studies. Patients received a median of 2 courses (range 1-8). There were 4 partial responses documented by CT scan for a response rate of 12.5% (95% confidence interval 4 - 24%). The median duration of response was 7 months. The median survival of all patients was 5 months. These results fall within the confidence intervals of our previous trials. The toxicity of this regimen was severe. Forty-three percent of the patients experienced grade IV hematological toxicity and 23% grade 3-4 nausea/vomiting. This resulted in dose reductions in 50% of the patients who received at least 2 courses.

40873: Phase II clinical trial of epirubicin and cisplatin (EP) in combination with a spit course radiotherapy plus 5-fluorouracil in locally advanced unresectable pancreatic cancer.
The treatment consists of 3 cycles of EP followed by a split course radiotherapy 20 Gy in 5 fractions with a free interval of two weeks.

On the first 3 days of each radiotherapy treatment 5-fluorouracil 500mg/m2 i.v., is given. If after the first 3 cycles of EP the disease has not progressed, another 3 cycles of EP is given after radiotherapy.

At the time of evaluation, 19 patients have been entered. Nine patients were too early for evaluation. After the first 3 cycles of EP, 4 out of 10 patients achieved a partial response (PR), 2 no change and 2 patients had progression of their disease. There was 1 toxic death and 1 patient refused further treatment. Five patients have completed the treatment. Two patients who had a PR after 3 cycles achieved a complete response.

40891: Radiotherapy and 5FU treatment after curative resection for cancer of pancreas and periampullary region. A Phase II clinical trial.
The proposal of this trial is to study in a prospective randomized trial the value of adjuvant treatment with post-operative radiotherapy (2 times 20 Gy) and 5FU after potentially radical resection in patients with cancer of pancreas in the periampullary region.
After surgery the patients are randomized in two groups, one receiving adjuvant treatment and the other without any further treatment. Recurrence of disease and survival will be the main end-points of this study.

40861: Double-blind clinical trial of an anti androgen therapy versus a placebo in unresectable hepatocellular carcinoma.
The objective of the study is to test the activity of an anti-androgen therapy in patients with unresectable, measurable, hepatocellular carcinoma and to assess the impact of this treatment upon survival.

-This is a two by two factorial design trial. Every patient receives two drugs:
  -Anandron, a pure anti-androgen, or the corresponding placebo.
  -and Zoladex or Decapeptyl, which are LH-RH agonists, or the corresponding placebo.
-This study is accruing exceptionally well: 14 institutions are participating and the inclusion rate is 60 to 90 patients a year. The number of patients to be included has been increased from 60 to 240. No major toxic problem has been observed. No intermediate analysis has been performed so far.

40863: Pilot study on the regional treatment of colorectal liver metastases by intermittent arterial ischaemia with degradable starch microspheres and arterial and portal infusion with mitomycin C plus 5FU.
From February 1987 to August 1988, forty patients were entered in the study by seven institutions. Eleven patients were never treated mainly because of early catheter-related problems. Later technical problems prevented administration of more than two cycles in eight other patients. This pilot study indicates that the simultaneous administration of chemotherapy by the inter-arterial and the inter-portal route is not feasible in a multicentric study. Nevertheless out of twenty-three evaluable patients, 4 complete responses and 6 partial responses were observed.
On this basis a phase II trial of locoregional administration of MMC and 5FU by the hepatic artery alone will start very soon.

REPORT EORTC MELANOMA COOPERATIVE GROUP Valencia, April 20-22, 1989

Chairman, F. Lejeune

Participants:
E. Aniz/VALENCIA, J. Banuls/VALENCIA, P. Boyle/LYON, E. Bröcker/MÜNSTER, D. Byrne/GLASGOW, J. Calap/CADIZ, S. Carrel/EPALINGES, N. Cascinelli/MILANO, B.Cava/VALENCIA, A. Cervantes/VALENCIA, J.P. Césarini/PARIS, C. Chartier/STRASBOURG, B. Czarnetzki/BASEL, J.F. Doré/LYON, K.T. Drzewiecki/COPENHAGEN, E. Engel/HAMBURG, A. Galli/FIRENZE, W. Gatzemeier/GÖTTINGEN, B. Gerard/ROTTERDAM, S. Henzen-Logmans/ROTTERDAM, P. Israels/AMSTERDAM, U.R. Kleeberg/HAMBURG, K. Kölmel/GÖTTINGEN, F. Lejeune/BRUXELLES, H. Luther/GOCHUM, E. Macher/MÜNSTER, R. MacKie/GLASGOW, D. Mamoun/VALENCIA, D. Ruiter/NIJMEGEN, H. Schraffordt-Koops/GRONINGEN, D. Thomas/BRUXELLES, P. Torres/VALENCIA, F. Trautinger/WIEN, M. Vaglini/MILANO, F. Weiss/MANNHEIM, A. Zayas/VALENCIA, C. Zechel/GIESSEN

Workshop on melanoma epidemiology
- K.P. Gallagher (Western Canada Melanoma Group, Vancouver, Canada) Lecture: "Overview on recent trends in Melanoma Epidemiology"
- P. Boyle (International Agency for Research on Cancer, Lyon, France) Surveillance on environmental aspects related to cancer in humans" (Search). Collaborative Study of Malignant Melanoma: Study design
- D. Ruiter (Chairman Pathology Group EORTC-MCG and Scottish Melanoma Group, Glasgow): "Clinical and histopathological criteria for identifying dysplastic naevi"
- S. Carrel (Chairman Immunology Subgroup EORTC-MCG, Lausanne, Switzerland) Discussant: E.B. Bröcker (Münster, Germany) "Immunological and genetic markers of dysplastic naevi and of UV damaged skin"
This workshop and the following discussion helped to establish a joined research initiative of the International Agency for Research on Cancer (IARC) and its "**search programme**" of the WHO and the EORTC-MCG as well as various national epidemiology projects to prospectively study various aspects of melanoma epidemiology.
Scientists interested in this important programme are invited to contact Dr. F. Lejeune, chairman MCG, Brussels, who together with J.P. Césarini (Paris) and J.F. Doré (Lyon) have been elected as project-coordinators.

Workshop on experimental models of melanoma - E.B. Bröcker, "Progression markers, PAMA's"
- B. Muel (Institut Curie, Orsay, France), "Photophysics and photobiology of environmental UV. Relation with melanoma"
- F.X. Real and T. Thompson (I. Municipal Investigacion Medica, Barcelona, Spain), "In vitro models of Human Malignant Melanoma"
- Ch. Zechel (Genetisches Institut, J.-Liebig University, Giessen, Germany), "In vivo experimental models in vertebrates"
- J.-F. Doré (EORTC-MCG, Unité INSERM 328, Lyon, France), "In vivo models in laboratory animals"
- F. Solano (Bioquimica, University of Murcia, Spain), "Biochemistry of normal and abnormal pigmentation"

With this workshop the EORTC-MCG established a most interesting collection of the present state in experimental models for research about etiology, induction, promotion and proliferation of melanoma.
The papers presented will be published to serve scientists as an important information for melanoma related research.

Clinical trials - Interim report
(18831): Phase II-study of tamoxifen in post-menopausal women with advanced melanoma (Ph. Rümke, study coordinator)
113 patients entered, 101 so far evaluable. One complete and four partial remissions, confirmed by the extramural review committee. This trial is now closed to patient entry.

(18852): Pilot Phase II study on recombinant Interferon Alpha2 in advanced melanoma, (F. Lejeune, M. Prade, S. Carrel study coordinators)
37 patients entered with one complete, one partial remission and 8 no change, confirmed by the extramural review committee.
In October 1988 it has been decided to increase the Interferon Alpha2 dosage (10 M IU/m2 s.c. x 3/w), to match the latest experience.
The immunological side studies disclosed most interesting alterations of the tumor cell-phenotypes due to Ifn Alpha2 treatment. These results will be published during the 2nd International Melanoma Conference in Venice (E. Bröcker et al.).

(18881): Phase II study of Fotemustine in patients with advanced melanoma (U.R. Kleeberg, S.P. Israels study coordinators)
97 patients have been entered with 56 evaluable up to now: one complete and 7 partial responses, 16 no change, confirmed by the extramural review committee.

The drug is considered as being active against melanoma and suitable for various systemic and regional combination treatments.

(18832): A randomized trial on prophylactic isolation perfusion for stage I high risk melanoma of the limbs, (M. Vaglini, F. Lejeune, E. Krementz: study coordinators)
450 patients have been entered, 425 still being followed. Quality control and site visits have markedly improved on the surgical techniques of the 15 participating institutions.
Pharmacokinetic side studies have led to interesting new observations, to be published shortly.

(18871/DK 80-1): Adjuvant trial in melanoma comparing Ifn Alpha2 to Gamma, to a control group after surgical removal of either high risk primary (>3 mm) or curative resection of lymphnode metastases (stage IIb) (Additional protocol testing Iscador M as promoted by the German Cancer Society (DK 80-1)).
(U.R. Kleeberg study coordinator)
113 patients have been randomized by 22 institutions. Side studies concerning psycho-social factors as well as following immunological parameters are considered to be of major importance for this trial in particular, as well as the effect of adjuvant treatments in general.

New trials
(18891): Phase II study of Toremifene in patients with advanced melanoma (U.R. Kleeberg: study coordinator)

This trial, testing a new antiestrogen and its effect on cytokines both in vivo and in vitro, supplemented by immunological side studies as to the tumor cell-phenotype is about to be activated. Interested clinicians as well as basic scientists are invited to contact the secretary.

Quality control
A panel of surgical oncologists, chaired by H. Schraffordt-Koops (Groningen) as well as pathologists, chaired by D. Ruiter (Nijmegen) and clinicians, chaired by U.R. Kleeberg (Hamburg), are following both Phase II as well as III studies to improve on clinical technology, histologic as well as immunocytochemical and clinical diagnosis and treatment, also including pharmacokinetics and bioavailability of the drugs tested and validation of the results obtained.
The work of these extramural review committees is considered to be of great importance for the quality of the clinical research.

Current research communications
The presentation of current results, particularly of those with immediate interest for the ongoing trials has grown to become an important part of the MCG workshops.
In particular young active members have been encouraged to report on their studies and presentations have been honored by travel grants.
The following topics have been touched upon:
- Retrospective evaluation of elective lymphnode dissection, Trautinger F., Kokoschka E.M., Kokoschka R. (Vienna)
- Transcutaneous oxygen tension - an indicator of effective circulation during isolated limb perfusion for melanoma, Byrne D.S., McKay A.J., Scott R.N., Hughes J., Burnside G., Blackie R., MacKie R.M. (Glasgow)
- Drug leakage measurement in hyperthermic isolation perfusion in patients with melanoma of the extremities, Rauschecker H.F., Gatzemeier W., Voth H., Michaelis H.C., Horst F., Kahl G.F. (Göttingen)
- Phenotypic alterations of melanoma cells in vitro following cytostatic exposure, Engel E., Kleeberg U.R., Dietel M. (Hamburg)
- Chemosensitivity of melanoma cells in vitro, Kleeberg U.R., Dietel M., Engel E. (Hamburg)
- Isolated limb perfusion with TNF, Lejeune F. et al. (Brussels)
- DNCB-immunisation as prognostic factor in melanoma, Calap J. (Cadiz)
- DNA flow cytometry in melanoma, Guillen C., Aliaga A. (Valencia)

Epilog
The members of the Melanoma Cooperative Group gratefully acknowledge the nice welcome in Valencia by A. Castells-Rodellas, A. Masmani and their staff for three days of excellent scientific exchange and charming social recreation, honoring the 20th anniversary of the MCG.

Future meetings
20/21 October 1989 in Verona, c/o Accolla
Immediately following the 2nd International Melanoma Conference in Venice (16/19.10.89).
27/28 April 1990 in Copenhagen, c/o K.T. Drzewiecki
16 August 1990 in Hamburg, c/o U.R. Kleeberg
Immediately preceding the UICC International Cancer Congress (17/22.08.1990).

Members interested in participating in the Verona and Hamburg meetings are urgently requested to inform the secretary for advanced hotel booking.
U.R. Kleeberg (secretary)

MOLECULAR BIOLOGY IN PHARMACOLOGY

Milan, Italy, February 7-9, 1990

A Course organized by the Steering Committee for the Federation of the European Pharmacological Societies.

Information:
Ida Ceserani
"Molecular Biology in Pharmacology"
Institute of Pharmacological Sciences
Via Balzaretti 9
20133 Milan, Italy
tel: (02) 29404672
fax: (02) 29404961

5TH HEAD AND NECK SURGERY WORKSHOP

Atlanta, Georgia, U.S.A., October 14-15, 1989

Information:
Society of Head and Neck Surgeons
13 Elm Street
Manchester, MA 01944, U.S.A.
tel: (508) 526-8330

SECOND INTERNATIONAL SYMPOSIUM ON "HORMONAL MANIPULATION OF CANCER: PEPTIDES, GROWTH FACTORS AND NEW (ANTI) STEROIDAL AGENTS"

Rotterdam, The Netherlands, April 9-10-11, 1990

Information:
Congress Secretariat/Dept. of Medical Oncology
Second Int. Symposium, "Hormonal Manipulation of Cancer"
The Dr Daniel den Hoed Cancer Center
P.O. Box 5201
3008 AE Rotterdam
The Netherlands

INTERNATIONAL CONFERENCE ON BLOOD CELL GROWTH FACTORS: THEIR BIOLOGY AND CLINICAL APPLICATIONS

Capri, Italy, Ocotober 8-12, 1990

Information:
Ann Murphy
Conference Coordinator
4100 South Kettering Boulevard
Dayton, Ohio 45439-2092
U.S.A.
tel: 513-293-8508
fax: 513-293-7652

FIRST INTERNATIONAL WORKSHOP AND SYMPOSIUM ON NEW UROLOGICAL TECHNOLOGY

Leuven, Belgium, September 6-9, 1989

Information:
Congress Secretary
Mrs. M. Peeters
University Hospital St Pieter
Department of Urology
Brusselsestraat, 69
B-3000 Leuven, Belgium
tel: 016/21 75 39

FOURTH INTERNATIONAL MEETING ON BIOLOGICAL REACTIVE INTERMEDIATES

Tucson, Arizona, U.S.A., January 14-17, 1990

Information:
I. Glenn Sipes, Ph.D.
Department of Pharmacology and Toxicology
College of Pharmacy
University of Arizona
Tucson, Arizona 85721
U.S.A.

FORTY-SECOND ANNUAL SYMPOSIUM ON FUNDAMENTAL CANCER RESEARCH

Houston, Texas, U.S.A., October 24-27, 1989

Cellular and Molecular Targets of Cancer Therapy

Information:
1989 Research Symposium
Conference Services-HMB 131
U.T. M.D. Anderson Cancer Center
1515 Holcombe Boulevard
Houston, Texas 77030, U.S.A.
tel: (713) 792-2222

WORKSHOP ON NEW APPROACHES TO PROBLEMS IN RADIATION ONCOLOGY: APPLICATIONS OF MOLECULAR BIOLOGY

Tucson, Arizona, U.S.A., November 12-15, 1989

AND

SIXTH INTERNATIONAL CONFERENCE ON THE ADJUVANT THERAPY OF CANCER

Tucson, Arizona, U.S.A., March 7-10, 1990

Information:
Mary Humphrey, Conference Coordinator
Arizona Cancer Center
University of Arizona College of Medicine
1501 N. Campbell Avenue
Tucson, Arizona 85724, U.S.A.
tel: (602) 626-2276
fax: (602) 626-2284

PSYCHO-SOCIAL ONCOLOGY

London, U.K., September 1-2, 1989

Information:
M. Watson
CRC Psychological Medicine Group
The Royal Marsden Hospital
Downs Road
Sutton, Surrey SM2 5PT
U.K.
tel: (01) 642 6011 ext. 3009
