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Position Paper

EORTC Scientific Strategy Meeting 25–26 March 1999

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INTRODUCTION

THE EUROPEAN Organization for Research and Treatment of Cancer organised a Scientific Strategy Meeting (ESSM) in Brussels on 25–26 March 1999. During the past three decades, the EORTC has taken a leading role in conducting high quality and comprehensive cancer research programmes. Currently there are more than 300 institutions and more than 2000 specialists collaborating on a voluntary basis to establish state-of-the-art treatment for all cancer patients in Europe. An average of 7000 patients per year are entered in EORTC trials.

The art and science of clinical trials require interdisciplinary exchange and constant adjustment to new diagnostic modalities and innovative agents' discoveries. Moreover, the legal framework of international clinical research has become a real challenge due to the current lack of harmonisation of national laws regarding clinical trials despite the existing guidelines produced by the European Commission and the International Conference on Harmonisation (ICH) procedures for studies conducted in North America, Europe and Japan, but currently only applied in Europe.

Therefore, EORTC strategies must take into consideration these issues for promoting more effective international cancer research into the next millennium.

The transfer of laboratory discoveries into practice may take several years (usually approximately 8 to 10 years). This time must be reduced as much as possible in order to pass on these benefits to the patients more quickly and to prevent discoveries from becoming obsolete by the time they are put into practice.

The aim of the ESSM meeting was for the EORTC to undertake a critical review of past and present research and to establish its future strategies.

There is presently a considerable acceleration in the development of new families of drugs and therapies based upon progress in our knowledge of molecular mechanisms involved in cancerous cells.

All major partners involved in high quality clinical research were invited, including other international and national research organisations such as the US NCI, ECOG, SWOG, NCI-Canada and all European research partners as well as regional groups, the European Commission, the pharmaceutical industry, health authorities and cancer leagues. Current challenges of pan-European cancer research and major priorities to be addressed in the coming years were therefore discussed, with the contribution of major North American and European EORTC partners. Overall, there were 500 participants from 28 countries.

On the first day, the EORTC General Assembly and members of the various EORTC groups steering committee discussed four topics in a closed brainstorming meeting: drug development and cooperation with the pharmaceutical industry, translational research, quality assurance programmes, intergroup collaboration and improvement of accrual in clinical trials.

The same day, two parallel educational sessions, open to all participants, were organised concomitantly. An introduction to cancer research and EORTC activities was presented to those willing to have an overview of the EORTC. The second session was on methodology of research including new developments of cancer clinical research addressing specific topics such as clinical trial design, tumour response criteria, new imaging techniques, quality of life issues, the challenges of genetic testing as well as management of cancer in the elderly.

During the second day, open to all participants, chairmen of EORTC groups presented a selection of important achievements and innovative strategies. Last, the chairmen of the four workshops provided a summary of the first day's discussion and an overview of statements and conclusions to be considered by the EORTC Board.

SELECTION OF ACHIEVEMENTS AND STRATEGIES OF THE EORTC

Ten EORTC groups were selected to present their achievements and strategies.

The EORTC PAMM group:

Research activities of preclinical groups were presented, including the objectives of the Pharmacology and Molecular Mechanisms group mainly involved in pharmacology and pharmacokinetics. Close interaction between basic scientists and clinicians was successfully established. Several joint projects are ongoing including the development of laboratory standards and standard operating procedures equivalent to

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good laboratory practice. A BIOMED II project supported by the DGXII of the European Commission on population pharmacokinetics—dynamic analysis of anticancer drug treatment, conducted in cooperation with the EORTC Early Clinical Studies Group was also presented. In addition, close cooperation with other groups belonging to the EORTC Research Division is achieved by the set-up of joint meetings on a regular basis with the aim to promote translational research projects.

The EORTC leukaemia group:

The major strength of the EORTC Leukaemia Group lies in its ability for conducting clinical trials on adult leukaemia in Europe involving more than 600 patients on a yearly basis. This is achieved by close intergroup cooperation in such cases with the GIMEMA (Gruppo Italiano Malattie Ematologiche Maligne dell' Adulto, Italy) but also HOVON (Hemato-Oncologie Volwassenen Nederland), EBMT (European Bone Marrow Transplantation), etc.

Several EORTC studies on leukaemia were summarised including the testing of the value of allogeneic bone marrow transplantation, the in-depth analysis of prognostic factors, the salvage treatment and the use of colony stimulating factors highlighting the significant contribution of this group in the management of adult acute myelogenous leukaemia [1–7] Studies on acute myelogenous leukaemia evaluating the use of recombinant granulocyte-macrophage colony stimulating factors and an assessment of prognostic factors in the elderly have also been conducted [8, 9]. A network of cytogenetic and molecular immunological laboratories was established and is currently conducting translational research within the BIOMED programme of the DGXII of the European Commission.

The EORTC genito-urinary group:

The EORTC Genito-Urinary Group is also entering a large number of patients (more than 900 on a yearly basis) thanks to an outstanding network of European urologists and medical oncologists, and to the cooperation of other disciplines such as radiation oncologists, pathologists, and other specialists. Some of these studies are joint clinical trials with the Medical Research Council (MRC, U.K.).

This group has conducted a series of high quality trials in superficial bladder cancer in the last decade, testing BCG, as well as in advanced bladder cancer, testing the value of neo-adjuvant chemotherapy [10, 11]. In non-metastatic and metastatic prostate cancer studies in cooperation with the EORTC Radiotherapy Group are being carried out to evaluate the role of irradiation after surgery, duration of hormonal therapy and the role of combination radiotherapy and hormonal therapy [12–15]. The EORTC Genito-Urinary group also has an outstanding track record in conducting studies in testicular cancer to assess the value of treatment intensification in the patients with poor prognosis and treatment reduction in the good prognosis patients [16–18]. A recent joint study with the MRC shows a significant survival improvement for patients with poor prognosis treated in more experienced institutions [19, 20]. The group also conducts important studies in renal cancer [21].

The EORTC breast cancer cooperative group

The EORTC Breast Cancer Cooperative Group has contributed to EORTC clinical trials with more than 15 000 women with breast cancer.

The third edition of the 'Manual for clinical research in breast cancer' has been produced by the EORTC Breast Cancer Cooperative group [22] and is also available on CD-ROM.

Among other studies this group conducted a phase III trial which demonstrates that hormonal therapy extends survival in irradiated locally advanced breast cancer [23].

Quality of life of early breast cancer patients treated with mastectomy or breast conserving procedures has also been investigated [24].

The EORTC Breast Cancer Cooperative Group was also a major partner in the first European Breast Cancer Conference organised in Florence in 1998, which was attended by approximately 5000 delegates. The second European Breast Cancer Conference is scheduled from 26–30 September 2000 in Brussels and is likely to be the largest world conference on that topic.

Among new activities, one should mention the development of studies on hereditary breast cancer, implementation of a surgical task force, integration of prognostic factors in treatment studies and development of a tumour bank in close cooperation with the EORTC pathology group as well as joint projects with the EORTC Biomarker and Receptor Group. The EORTC Breast Cancer Cooperative Group also works closely in cooperation with the EORTC Radiotherapy Group and other national and international groups within the framework of the Breast International Group (BIG).

The EORTC quality of life group

Major achievements in the field of quality of life evaluation were reported, including an extensive description of the conceptual approach to quality of life assessment leading to a reference tool (the EORTC QLQ-C30), which has been developed, tested and validated in 33 languages. The instrument is currently in use in more than 1000 studies worldwide. The EORTC QLQ-C30 is a copyright instrument whose distribution is subject to user agreement via the Quality of Life Unit based at the EORTC Data Center in Brussels [25]. However, the use of this instrument is free for academic research.

The EORTC Quality of Life group developed procedural guidelines for analysis of Quality of Life in 13 specific cancers. The quality of life group has also developed a series of supporting documents including a scoring manual, reference values (also available on CD-ROM), translational procedures, etc. [26, 27].

Training in methodology of quality of life assessment will also be performed during a course scheduled in 28–29 October 1999, in Brussels ('Quality of Life Evaluation in Cancer Clinical Trials').

The EORTC early clinical studies group

The goal of the ECSG is to develop and improve comprehensive new drug development in Europe and to face the challenges of new end points for innovative agents.

The EORTC ECSG is now involved in early clinical trials with 48 member institutions distributed in 14 countries.

The ECSG is also contributing actively to support networking within the EORTC together with other national/regional organisations involved in drug development, including the Cancer Research Campaign (CRC), the SENDO (Southern Europe New Drugs Organization) and other groups as appropriate. The ECSG is also integrating population

pharmacokinetics into early clinical trials and is promoting translational research in order to provide proofs of principle in drug development studies; the group is also aiming to increase the cooperation with tumour type-oriented development and the various EORTC disease-oriented groups.

The ECSG has been successfully involved in the development of several new compounds, which have achieved market approval. These compounds include docetaxel, CPT-11 and Topotecan. The merge between the EORTC Early Clinical Trials Group and the EORTC Clinical Screening Group in 1996 to form the Early Clinical Studies group brought a further milestone in the setting up of a drug development network in Europe providing 20 centres available to perform high quality phase I studies.

The creation of the EORTC New Drug Development Program in Brussels has already proved to work well and provides an excellent forum for comprehensive European drug development programmes from phase I to phase III trials. Such a structure also features promising new opportunities for vertical drug development within the EORTC. Partnerships with the preclinical groups of the EORTC will also be promoted as well as cooperation with other research groups, outside the EORTC, in order to aim at a more effective intercontinental network for drug development.

The EORTC biological therapeutic development group

The aim of the EORTC BTDG is to combine preclinical and clinical research with biologically active agents by also conducting phase I and early phase II trials with these agents.

The EORTC BTDG organised a consensus meeting thanks to the support of a BIOMED grant (DGXII) to discuss *ex vivo* research methodology and based these recommendations on surrogate endpoints. A series of clinical trials have been launched by the EORTC BTDG and combined with *ex vivo* research. One of the clinical studies is the first European multicentre clinical trial with a genetically modified organism (recombinant vaccinia virus) in patients with cervical cancer.

Before the initiation of this trial, considerable logistic difficulties based on the various regulatory restrictions in the European countries had to be solved. Several ongoing trials are investigating immunomodulators, humanised monoclonal antibodies (MAbs) and vaccines. All of these trials include a comprehensive translational research programme to define the optimal biologically active dose of these new compounds.

In addition, standardised methodologies for *in vitro*, *in vivo* and *ex vivo* testing are being elaborated.

Every 2 years, the EORTC BTDG organises an open meeting (Biological Therapy of Cancer: from basic research to clinical application in cooperation with the US NCI and the Cancer Research Campaign (U.K.). The fifth edition of the meeting is scheduled on 27–30 October 1999 in Munich.

The EORTC radiotherapy group

Radiation oncology remains a major tool in the curative treatment of most cancers. The EORTC Radiotherapy Group has been a leading research group for the past 20 years. Progress has been achieved in biologically improved radiotherapy schemes, dose–effect studies, and the combination of radiotherapy with newly developed drugs and innovative therapies. The most sophisticated treatment techniques are also being investigated, including stereotactic radiotherapy, 3-D conformal radiotherapy and brachytherapy.

Numerous studies were conducted in cooperation with several EORTC disease-oriented groups (Breast, Gastrointestinal, Head and Neck, Brain, Genito-urinary, Lung and others).

The EORTC Radiotherapy Group was the first to document the benefits of local control and survival improvements with hyperfractionated radiotherapy in oropharyngeal carcinoma and local control improvements with accelerated radiotherapy in head and neck cancers [28, 29].

Concomitant radio-chemotherapy was shown to be superior to radiotherapy alone, achieving better and colostomy free survival in locally advanced anal carcinoma [30].

A multicentre study conducted on 297 patients jointly with the EORTC Gastrointestinal Tract Cancer Cooperative Group and the Fondation Française de Cancérologie Digestive showed that preoperative chemoradiotherapy prolongs disease-free survival and survival free of local disease compared with surgery alone in squamous cell cancer of the oesophagus [31].

Pelvic irradiation combined with a three year LHRH analogue resulted in improved survival and local control of patients with high metastatic risk carcinoma of the prostate [15]. This treatment became a standard and is now compared to radiotherapy with a 6-month hormonal treatment.

The largest trial ever performed in conservative treatment of breast cancer was conducted in cooperation with the EORTC Breast Cancer Cooperative Group. 5500 women with breast cancer were accrued to evaluate the role of a boost dose of radiotherapy in the conservative management of breast cancer, following tumorectomy and irradiation. Loco-regional control, survival and cosmetic results are the main end points of this study, which will be analysed within a year. It is clear that this type of trial will never be undertaken anywhere else, and will provide answers of major interest regarding optimal cancer management on the most frequent cancers in women, but also on relevant health economics issues.

The EORTC Radiotherapy Group has pioneered the establishment of European Quality assurance programmes as well as the development of telematic tools to improve quality of irradiation all over Europe [32, 33].

EORTC Soft tissue and bone sarcoma group

Rare tumours in soft tissue and bone sarcoma constitute one of the major incentives for cooperative international research. The EORTC SBSG conducted 33 consecutive clinical trials in rare diseases recruiting an average of more than 200 patients per year.

The database of the EORTC Soft Tissue and Bone Sarcoma Group now consists of more than 2500 patients. Strict quality assurance programmes are implemented for all trials, including central review pathology and external review of response in advance disease.

The inclusion of a systematic therapy checklist in the patients file has been pioneered and investigated within the EORTC Soft Tissue and Bone Sarcoma Group and has shown tremendous benefits in the quality of the data.

Through this unique network of investigators, one can now consider a worldwide uniform approach for soft tissue sarcoma [34, 35].

The EORTC melanoma cooperative group

Impressive progress has also been made in the management of melanoma during the last 30 years. The EORTC

Melanoma Group research includes studies in the field of epidemiology, pathology, surgery, immunotherapy, translational research as well as large clinical trials [36, 37]. BIOMED (DGXII of the European Commission) and Europe against Cancer (DGV of the European Commission) grants have supported studies on numbers of naevi as well as on the pitfalls of sunbeds and sunscreen use [38, 39].

Several large clinical trials are currently testing adjuvant therapy and immunotherapy within a comprehensive melanoma research programme, involving intergroup studies.

A large trial of the EORTC Melanoma group has shown that prophylactic isolated limb perfusion for high risk primary melanoma must be abandoned, which is also a major contribution to clinical practice, having no effect on distant metastasis, nor on survival [40].

OVERVIEW OF THE FOUR WORKSHOPS

Drug development and cooperation with the pharmaceutical industry

As a result of major progress in the understanding of cellular and molecular mechanisms of cancer growth and drug resistance, the last decade witnessed the emergence of a much larger number of potentially active new drugs and novel therapies than the previous three decades. Hence, every year, new anticancer compounds with a variety of new molecular targets are available for their first human investigation in phase I studies.

Patients are also increasingly informed about potential innovative agents in the pipeline and pharmaceutical industries are under increasing pressure to get results early and rapid drug registration.

New drug developments should, therefore, take into account the need for rapid accrual while maintaining high quality data and high scientific standards. Overall, clinicians and basic scientists largely underestimate the financial investment necessary for drug development.

The EORTC multidisciplinary network offers the ideal partnership to the pharmaceutical industry and to other academic research organisations established on a national or regional basis. A unique pan-European co-ordinating structure is being set up to optimise available resources, increase speed while maintaining quality. Industry and non-industry driven studies can then be carried out with the same level of scientific independence.

Rapid high quality drug development is one of the first EORTC priorities for the next decade. EORTC's major involvement in promoting pivotal (registration) trials conducted in Europe is also consistent with its unmatched multidisciplinary structure which offers opportunities in conducting comprehensive drug evaluations from phase I to phase III trials, from the laboratory to standard practice.

The main strategy to achieve effective new drug development includes the need to promote vertical drug development but also to benefit from existing resources within the various disease-oriented groups of the EORTC and thereby to promote horizontal (intergroup) approaches for the EORTC investigators.

The recently created EORTC New Treatment Committee (NTC) is playing a major role in promoting both horizontal and vertical approaches of drug development within the EORTC, as well as in making the appropriate recommendations about the need for translational research projects within early clinical trials. For phase I studies suggestions for cooperation will be made by NTC/PRC. For phase III studies, intergroup studies (within the EORTC) should always be considered in order to develop a more horizontal structure.

Administrative support for the EORTC NTC and Protocol Review Committee (PRC) is co-ordinated at the EORTC Data Center in Brussels with a single mailing address (PRC-NTC Secretariat, EORTC Data Center, avenue E. Mounier 83, B-1200 Brussels, tel: +32 2 774 16 74/43; fax: +32 2 772 61 97; e-mail: ntc-prc@eortc.be). The average time for a review of the NTC was calculated last year; on about 40 submissions, a response to the investigator was provided within 26 days (range: 7–39 days).

The recently created new drug development program (EORTC NDDP) within the EORTC Data Center based in Brussels allows facing the challenge of more effective drug development with confidence.

The main objective is to provide an adequate structural, scientific and administrative support to the EORTC Research Division as well as to establish a partnership with other national-regional research organisations with the final aim to set up and participate in a European Drug Development Network (EDDN), which would lead to an effective co-ordination of early clinical trials in anticancer drugs in Europe. Such a research network would provide a single voice towards the European Commission, Regulatory Authorities and the industry.

The EORTC New Drug Development Program (NDDP) consists of a preclinical team as well as a clinical research team benefiting from the logistic support already existing at the EORTC Data Center and which has been recently expanded, particularly in relation to the Regulatory and Safety Desk, the Monitoring Unit.

Specific standard operating procedures (SOP) have been developed for the EORTC NDDP and scientific support will also be provided to the (non-clinical) research groups.

Translational research

The EORTC is already involved in and will expand its preclinical studies to validate and exploit novel therapeutic targets or diagnostic procedures, as well as early clinical trials to evaluate new, preventive, diagnostic or therapeutic agents. The EORTC is also aiming at taking advantage of conducting laboratory studies on existing clinical material from patients included in EORTC clinical trials conducted by the disease-oriented groups.

The EORTC, however, stresses the need to obtain adequate funding, including from the European Commission, for such translational research conducted at pan-European level. Funding should also be sought from national cancer leagues, as they are usually able to fund basic research conducted in important laboratories from their respective countries.

It was agreed that all EORTC trials should consider the need to include a translational research component. Such translational research could be a driving force in remodeling and harmonising EORTC preclinical and clinical activities.

In addition to pathologists, the steering committee of disease-oriented groups also includes a molecular biologist or a pharmacologist or an immunologist to further enhance intergroup/interdivision activities within the EORTC. A joint workshop involving the Pathology Group, the Pharmacology and Molecular Mechanisms Group as well as the Receptor and Biomarker Group will be organised to investigate the integration of common technologies. In addition, ethical and

legal issues related to the creation of a virtual tumour bank linking tumour samples with the clinical database of all patients entered in EORTC clinical trials is regarded as a high priority. The role of the EORTC New Treatment Committee (NTC) to implement in a timely manner these translational research projects is paramount.

Quality assurance programmes

There are numerous justifications to adopt extensive quality assurance programmes in cancer research. Among them, the fact that narrow margins exist in oncology between treatment benefit and unacceptable toxicity, i.e. significant side-effects. Another reason is that large phase III clinical trials involve testing small treatment differences in a complex strategy. Furthermore, all legal aspects and guidelines on good clinical practice have to be implemented. Quality assurance also deals with prevention of fraud and misconduct.

The EORTC has been the European pioneer in the field of cancer research quality assurance in particular for radiation therapy and surgery, medical oncology and data management.

The EORTC workshop dealing with quality assurance has focused on quality assurance systems for cancer clinical research, from the planning of the study and set-up of the protocol to the collection of the data, analysis and reporting the results.

Quality control procedures should be implemented at all steps from patients selection, treatment prescription as well as treatment execution (involving surgery, irradiation, chemotherapy, as well as supportive care). It was acknowledged that an improvement in treatment quality immediately leads to an improvement in treatment outcome.

Quality assurance programmes are indeed involved in the improvement in the overall quality of cancer care. Tools developed and tested within the EORTC are now used for routine management in many European hospitals specialised in cancer care.

One should not wait 10 years for the results of molecular biology and immunology research to witness improvements in cancer care. The implementation of research results is also crucial in improving the management of all cancer patients, including those treated in institutions that are less oriented towards clinical research.

For example, appropriate quality assurance programmes for surgical procedures have been shown to be effective in decreasing the variation per institution in local recurrence for early breast cancer and for rectal cancer.

As a consequence, the implementation in Europe of quality assurance in surgery is likely to improve the outcome of uncommonly observed cancers. This issue will remain a high priority for EORTC. These aspects are closely related to the quality of pathology. The optimal strategy includes appropriate communication links between local pathologists and local surgeons. The role of infrastructure and cooperation of the various departments in dealing with cancer patients is also paramount for healthcare authorities to decrease the heterogeneity of treatment outcome.

Extensive programmes of quality assurance in radiotherapy have been undertaken during the last decade by the EORTC, using various techniques, including Dummy Run (treatment of a patient by several centres participating in the same protocol, followed by a comparison), equipment checks and dosimetry, on-site review, immediate review of first randomised patients in recently opened clinical trials and follow-up review for major deviation.

An Emmanuel van der Schueren fellowship has been created, specifically dedicated to a quality assurance programme in radiotherapy and will be launched in 1999.

Concerning quality assurance in chemotherapy, the EORTC has developed and demonstrated the benefit of the use of the systemic therapy checklist, including a re-evaluation of centres which were visited in 1991 and 1995, and showing a significant improvement in the quality of the data. Quality assurance in chemotherapy is indeed aiming at decreasing mistakes that are repetitive-systematic errors and not accidental errors.

The environment where chemotherapy is prepared in all participating institutions is also important to guarantee high standards. EORTC is and will remain concerned with the way research results are published in peer-reviewed journals, sometimes lacking information on quality assurance procedures used for studies submitted to publication.

As one of its priorities, the EORTC will keep designing, developing and disseminating the use of template pro-formats of cancer management quality assurance programmes. Such programmes will undoubtedly constitute an important part of the criteria used for the accreditation of cancer care teams and institutions.

Intergroup collaboration-improvement of accrual in clinical trials

Significant progress in cancer management will mainly be achieved through high quality clinical trials. The optimal accrual of clinical studies is a critical factor, both for new drug development and for strategy trials, dedicated to the establishment of state-of-the-art treatment. Improved communication within EORTC groups but also with other national/international research groups is also important to improve the quality of science to allow translational research as well as to provide rapid accrual in clinical trials conducted throughout Europe.

Knowing the cost of effective drug development and the need for a minimum of 10 years of research between drug discovery and drug registration, the EORTC acknowledges the numerous barriers currently restraining all clinical investigators. Such difficulties also exist in North America and the US NCI, ECOG, SWOG, NCI-Canada, among other international groups, share these concerns.

Among the actions to be undertaken, the EORTC proposes improved information for patients and physicians, particularly in Europe where patients and physicians still lack awareness of the benefit of participating in high quality clinical trials. In Europe, less than 5% of cancer patients actually contribute to cancer clinical trials.

In the last few years, the EORTC has identified 'EORTC affiliated institutions' which are the hospitals accruing at least 75 patients (over 3 years) and participate in three or more EORTC groups. The list of EORTC affiliated institutions is updated on an annual basis and should allow the promotion of patient accrual in EORTC studies (as well as their inclusion in phase I studies whenever relevant).

EORTC, like other research groups, share the need to consider the simplification of trial designs and protocols, simplification as well as standardisation of data collection (including the amount of data used for final analysis), specifically when it is well known that only 50% of data collected are used for the final analysis and report. A minimal set of

data for each tumour type should be developed, particularly for non-registration trials and additional items should only be added if critical to the trial's endpoints.

New telematics tools recently developed will change the current workload of the clinical investigators as well as that of the local data managers. Those tools which are currently validated including the Multimedia Application for Clinical Research in Oncology (MACRO) developed by the EORTC with the support of the DGXIII of the European Commission are certainly major improvements which will provide their first results in the year 2000.

Indeed, MACRO has also been designed to improve accrual in EORTC clinical trials. This will provide an electronic access to protocols, and basic checks at randomisation. This system will generate electronic queries from the EORTC Data Center and will also have direct access to local databases in participating institutions. There is great hope that MACRO will improve patient accrual while maintaining, if not improving, the quality of the data. MACRO should also permit 'on-time' quality assurance of data entry, diagnostic criteria (telepathology, teledialogues) as well as treatment parameters (control of radiotherapy treatment planning, surgical specimens and biological samples, etc.).

The EORTC has been active in other European telematics initiatives including Europath, Cantor, Retransplant and Conquest which are briefly described hereunder:

EORTC is a main partner of EUROPATH (European Pathology Assisted by Telematics for Health). The project has involved the main worldwide manufacturers and the committed end-users in a major international effort. The project has provided opportunities for pathologists, in EORTC and elsewhere, to test various technologies and methodologies for sharing images and associated data. The feasibility of multimedia communication between pathologists, known as telepathology, has already been demonstrated, but a significant standardisation effort has been made by EUROPATH. EORTC has been the principal force within EUROPATH for the international validation of the results of the project. EUROPATH has given a major impetus to the setting up of the EORTC Pathology Study Group. EUROPATH started in 1996 and has been extended to summer 1999. Further information can be obtained from the EUROPATH Web site: http://europath.imag.fr/EUROPATH/Path_index.html

EORTC is a main partner in CANTOR (Converging Agreement by Networking Telematics for Object Recognition). Members of the EORTC Pathology Study Group participate in this project. CANTOR is developing software tools to facilitate collaboration in consensus formation and standardisation of classifications for objects in images. These tools will help pathologists to describe and explain their diagnosis and also to analyse the variation among pathologists in the interpretation of images. CANTOR is a 2-year project which started in May 1998.

EORTC is an associate partner in RETRANSPLANT (Regional and International Integrated Telemedicine Network for Medical Assistance in End Stage Diseases and Organ TRANSPLANT). RETRANSPLANT will implement a regional and international network to link national transplant systems, giving online access to European transplant co-ordinators, donor centres and diagnostic specialists. The EORTC will provide results from the MACRO project, including network-based multimedia data collection tools for clinical trials and a format for clinical data exchange. RETRANSPLANT is a 2.5 year project that began in October 1998.

CONQUEST (Clinical Oncology Network for Quality in European Standards of Treatment) has been developing and validating quality assurance tools, particularly in relation to the use of radiology imaging technologies. EORTC has been the associate partner in this programme. The intention was to reinforce the link with the MACRO project and to act as a user community for validation of the results of CONQUEST. CONQUEST was a 3-year project ending in December 1998. For further information, see the CONQUEST Website: http://www.nethotel.dk/conquest/public/cqpub.htm

Finally, several examples of successful collaboration within EORTC and other research groups such as GIMEMA, NCI-Canada, PETACC (pan-European Trials in Adjuvant Colon Cancer), etc. are very promising and will make the history of future intergroup collaboration in Europe but also worldwide. EORTC, as other research groups, will also face problems linked to the current requirements of too many protocol approvals prior to activation during intergroup collaboration. There is also the major challenge of harmonising the different rules existing within the various research groups throughout Europe and North America.

Moreover, health authorities should also realise that there are wide variations in the need for covering the cost of health care including patients entering clinical trials, in the various participating countries.

Competition between research groups should definitely be avoided and group chairs should address in an emergency the issue of cumbersome bureaucracy when intergroup collaboration is considered, whether at the European or at a transatlantic level.

Overall, the EORTC proposes considering intergroup collaboration at the stage of protocol submission to the EORTC NTC and/or PRC and discuss with the Director of the EORTC Data Center and the chairman of the EORTC group involved. Extension to non-EORTC members will be considered as well, provided that EORTC standards of conduct are guaranteed. Acceptance of intergroup studies should rely on past experience in the conducting of clinical trials with centralised co-ordination and adequate quality assurance programme. It was agreed that intergroup collaboration could be run in different ways but the only efficient way is that each group functions as a mail box, i.e. that the data collected on the Case Report Forms are provided to the various data centres but sent without any prior correction to the co-ordinating group for intergroup collaboration. It also seems important to set up a steering committee involving representatives of each participating group to guarantee optimal co-ordination.

CONCLUSION AND FUTURE PERSPECTIVES

Cancer cure rates have been steadily improving during the past 20 years as a result of cancer research. Tremendous progress has been made as regards paediatric tumours, lymphoma and Hodgkin's disease as well as testicular tumours. Significant improvements have been reached in many other sites such as breast, head and neck, colon and rectum, soft tissue and bone sarcomas and genito-urinary tumours. The next decade is likely to witness an acceleration in this progress thanks to the increasing number of new treatment modalities and to the widespread dissemination of quality assurance methods in standard practice.

The ESSM meeting created an ideal forum for the EORTC to discuss more effective European oncology, both from the academic and the pharmaceutical industry point of view. In order to insure optimal continuation of the EORTCs research effort, new strategic approaches to overcome changing healthcare systems, cutbacks in public funding and the lack of harmonisation in legal and administrative requirements for conducting clinical trials at the international level have to be addressed. The EORTC is now confident that EORTC scientific strategy meetings (these meetings will be organised on a 3-yearly basis) will provide a unique forum to promote pan-European cancer research, and transatlantic cooperation, as well as accessing progress achieved over that period, and to ensure that research strategies and priorities are adjusted accordingly.

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