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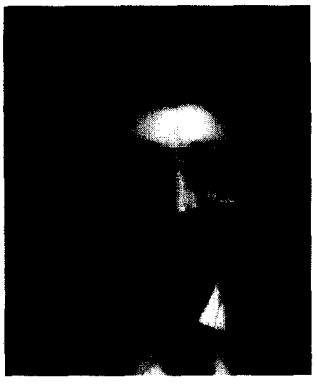
International Cancer News

From the Globe:

New Director Pledges to Give NCI "New Look and Feel"



Dr Richard Klausner New Director of the U.S. National Cancer Institute

Richard Klausner, director of the U.S. National Cancer Institute since 1 August, promises big changes in the structure as well as the climate of the NCI under his leadership.

In a meeting with NCI Extramural Program staff the day after he took office, Klausner outlined the Institute's realignment — the "new look" — which took effect on 1 October, and shared his vision of guiding principles — NCI's "new feel."

Structurally, most of the Institute's divisions will be broken up and their components put together differently. A major part of the strategy involves separating intramural and extramural functions more cleanly. Some senior officials have moved to new jobs, and others are being recruited from outside the NCI.

Klausner's deputy director is Alan Rabson, director of the Division of Cancer Biology, Diagnosis, and Centers. Rabson, whose division has been split up under the new system, is a veteran NCI scientist and administrator, having once served as acting director of the institute during an interregnum.

Klausner has said that all the new division leaders have been designated "acting directors" or "special consultant".

Two new divisions, responsible for basic and clinical sciences, will be strictly intramural. George Vande Woude, who heads the Basic Research Program for Advanced BioSciences Laboratories, Inc., a major contractor at NCI's Cancer Research and Development Center in Frederick, Maryland, takes charge of the Division of Basic Sciences. Pediatric AIDS researcher Philip Pizzo, NCI's Pediatric Branch chief, will lead the Division of Clinical Sciences.

Only two of NCI's existing divisions remain intact and their directors in place: the Division of Cancer Prevention and Control under Peter Greenwald and the Division of Extramural Activities under Marvin Kalt.

The newly created division of Cancer Epidemiology and Genetics will be led by Joseph Fraumeni, who was head of the Epidemiology and Biostatistics Program in the now dismantled Division of Cancer Etiology. He is joined by Alfred Knudson of the Fox-Chase Cancer Center in Philadelphia who will serve as a special advisor to the director for cancer genetics.

The new director expressed great respect for and confidence in his lieutenants, most of whom are widely known in the oncology and cancer research communities. He called Knudsen "the father of cancer genetics," and Fraumeni "an individual who has been there at, and [been] part of the creation of the field of molecular epidemiology."

At the time of going to press, no acting director had yet been named for the new Division of Cancer Biology, which includes part of Rabson's old division as well as the Frederick Center. However, Klausner said he is "currently in the process of negotiating with... some very wonderful cancer biologists from outside of the NCI."

Klausner is not a complete stranger to the NCI. He did a brief stint in the Institute's mathematical biology programme before moving to the National Institute of Child Health and Human Development in 1984. Much of his research has been on iron metabolism, and he was awarded the Damashek Prize in 1992 by the American Society of Hematology.

Probably Klausner's highest profile activities, however, have been outside the lab. He has long been an advocate for change at the National Institutes of Health, having chaired a committee that in 1992 studied intramural NIH science and recommended sweeping changes. In addition, Klausner led the National Academy of Sciences effort to develop nationwide standards for scientific literacy among students in 1994.

In describing the "feel" of the new NCI, Klausner referred to "an institution that has to get away from lurching from crisis to crisis... an institution that cannot be motivated by fears about what might go wrong, about what might be expected, but rather an institution that is thereby free to achieve things." "The administrative functions of the NCI must serve the science, full stop," he added.

Denouncing the rise of institutional "fiefdoms" vying for power and money, he said the NCI under his leadership will be a meritocracy, where support will be based on productivity and excellence, not prerogative. "I do not believe that there is any budget but the NCI's budget, and that means the resources will be distributed based upon an open and defensible process of scientific discussion across any structural lines..."

He stressed openness in other respects as well: "There must not be any sense that to speak, to give your ideas, violates

codes of ownership or control, and certainly that there would ever be any issue of retribution for... speaking the truth."

"We need to create and support structures that allow us to communicate, to seek advice from the collective wisdom of the... community...we must be open to discussion, to advice, and to listening carefully what people have to say."

To ensure that the NCI leadership hears the opinions and concerns of the rank and file scientists, Klausner will create two new advisory boards representing intramural and extramural programme staff. He also stressed that authority will be delegated as much as possible: "The leadership of the new NCI needs to function as leaders and not as micromanagers."

Klausner promised intensified collaboration both inside and outside NIH: "Despite there being many parts to the biomedical enterprise, it is important that the NCI... be a seamless part of... the research community and the clinical community and it cannot be a separate entity, a sort of enemy, an antagonist. It must be part of the community that it works with and that it serves."

Tom Reynolds

Reach to Recovery International

Brief history

Initiated by the American Cancer Society (ACS) in 1974, the development of Reach to Recovery Programmes in Europe, and gradually worldwide, was promoted, structured, and supported by Mrs Francine Timothy during 20 years of pioneering work. Following Mrs Timothy's recent retirement, the ACS has requested UICC to oversee further development and support of Reach to Recovery International (RRI) and has provided funding for 3 years for this work. A UICC–RRI Advisory Committee, chaired by Mrs Gungerd Lemon (Sweden), has been established and now provides active support guidance and training to groups throughout the world.

Purpose

RRI is a non-medical Programme designed to assist women with breast cancer in their return to everyday life after treatment by providing practical and emotional person-to-person support. It is based on the premise that women who have experienced breast cancer themselves, and who are now physically and emotionally healthy, can relate in a unique and positive way to women newly diagnosed with breast cancer. This Programme, with its carefully selected, well-trained volunteers, is approved by medical professionals and is promoted by cancer societies worldwide.

Future trends

Changing needs of cancer patients and developments in medical technology and contemporary rehabilitative practices have been identified as challenges for RRI. To address these issues, a workshop will be held during the World Conference for Cancer Organisations in Melbourne, Australia, 3–7 March 1996, entitled "Diversity and Change: Challenges for the Read to Recovery Programme in the Third Millennium".

Key issues faced by RRI will be discussed and a set of recommendations for its International Advisory Committee will be formulated on how to adapt and position the programme to best meet the needs of women with breast cancer.

This half-day workshop would suit anyone with a professional or personal interest in breast cancer. The workshop will aim to incorporate the experience and understanding of participants into the discussion and the formulation of recommendations. This process will be assisted by various short presentations on the organisation of RRI, relevant psychosocial literature, and recent evaluations of the Programme.

Reach to Recovery International is a project under Patient Support and Rehabilitation of the UICC–COPES Programme.

From UICC News, September 1995

From Europe:

European Drug Agency Promises Quicker Approvals

A new London-based international agency aims to cut time, costs and red tape from the marketing approval process for new drugs and medical products in Europe.

The European Agency for the Evaluation of Medicinal Products (EMEA) officially opened on 26 January 1995. The inauguration followed years of political debate as well as official negotiations bringing the 15 countries of the European Union (EU) into accord on testing and other procedural requirements for product approvals.

"Consumers wanted a strong central system," said Fernand Sauer, EMEA's executive director. "Industry was divided, but since the decision was made [to create the agency], we have had full support from most sectors of industry, particularly research-based industry. For them, there was no doubt that the new system would create greater opportunities — in particular, to get their products on the market within 1 year."

Better access, profits

Quick access to the whole European market means bigger profits. Taken as a whole, the EU is the world's largest market for drugs, with 370 million consumers and $50 billion in annual sales. According to a report in the British *Financial Times*, one additional year of sales of a patented drug throughout Europe adds abut $150 million on average to the company's revenues.

Although the approval regulations have been standardised for all EU Countries since 1993, enforcement has been at the national level until this year. A company seeking to market a new drug across Europe had to apply separately to each of 15 national agencies. Because this process is so time consuming and because some countries have been slower than others to act on applications, drugs went on the market in some countries much earlier than others. The result of such discrepancies, Sauer said, was that "penetration of the European market could take 5 or 6 years." This situation frustrated physicians and patients waiting for access to promising new treatments, and also made for multiplication of effort among national drug agency staffs.

"The EMEA will not replace national drug agencies, nor will it become a "European FDA" that conducts evaluations centrally", Sauer said, alluding to early critics of the proposed agency who involved the U.S. Food and Drug Administration's past reputation as a foot-dragging bureaucracy. Instead, EMEA will coordinate and in some cases allocate the work of the national agencies' staffs.

Two different procedures will be available to drug marketers at least until 2000, when the whole system will be reviewed. In the centralised procedure, applications are submitted directly to EMEA and the drug approval process is coordinated by EMEA scientific committees. The work itself is farmed out to

multinational, multidisciplinary teams of experts drawn from the ranks of national agency staffs and consultants. The agency has developed a network of about 1200 such experts for its human drugs unit and 400 for the veterinary unit.

"Biotechnology drugs must be approved through the centralised process, and companies are likely to use it for other innovative products as well", Sauer said. Concern over the potential economic impact of biotech-developed growth promoters for farm animals promoted the special rule on biotech products, he added.

The decentralised procedure resembles the old system in that companies apply to one national agency for marketing authorisation. The crucial difference is that the authorisation will now be extended to other EU countries without a separate review, so that products will go on the market simultaneously throughout the EU. Any disputes that cannot be settled between countries will be subject to binding arbitration by EMEA.

Three-year transition

During a 3 year transition period, companies have the option (for non-biotech drugs) of either using EMEA or using the national agencies as in the past. Essentially, national agencies will compete with EMEA for fee-paying customers. During that time, 12 to 15 biotech products are expected to come through the centralised system, while another 20 or 25 drugs will have the option of either route, Sauer said, adding that "it will be interesting to see how many choose the centralised system".

"There is still a big question mark" about whether the national authorities can work in close cooperation with EMEA while maintaining their separate existence, he said. "We have to demonstrate between now and next year that it can work."

For now, half of EMEA's $25 million annual budget will come from the European Community and half from user fees paid by drug companies, although Sauer said the agency is expected eventually to become "self-funding" through fees. The agency's riverside offices in London's Docklands area now house a staff of about 35, drawn from across Europe. That number will rise to 100 by the end of 1995 and to about 250 by 1999.

An oncology working group has recently been formed to advise the EMEA on issues related to cancer drugs. The group will be headed by Mary E. Teeling, M.D., deputy director of the National Drug Advisory Board in Dublin, Ireland.

The EMEA will enhance "pharmacovigilance," or postmarketing surveillance for adverse drug effects, in two ways, Sauer said. Work-sharing by national agency staffers under the new system will free more of their time for surveillance, and the new European agency will serve as a clearinghouse for adverse event reporting.

EMEA publications emphasise the "openness" and "transparency" of the agency's proceedings. Sauer said this reflects suspicions that some national agencies have historically been in the pockets of powerful pharmaceutical companies.

"In the past there have been cases of alleged corruption, so when we created the new European system, we had to make it clear that this would be totally out of the question," he said. "We have built into the system a variety of elements to achieve this," such as declarations of financial interest by committee members and experts working within the system, who could be excluded from decision-making if a conflict of interest arises.

Also, new for Europe will be the publication of a summary of the basis for approval for each drug that reaches the market. This document explains the critical parts of the evaluation and the motivations for the decision. While these are generally published 2 or 3 years after approval in the United States, Sauer said EMEA plans to publish them on the day of approval.

Parallel to the discussions that led to EMEA's creation, the International Conference on Harmonisation has brought together officials from Europe, the United States, and Japan to develop common guidelines for ensuring the quality, safety, and efficacy of drugs. The ICH as already produced 12 guidelines on issues such as good clinical practice, reproductive toxicity testing, and stability testing, and a further set will emerge from the next ICH meeting in November.

"The idea is by 1996 to allow companies to present an identical dossier in the three regions, which represent 95% of the pharmaceutical research in the world," Sauer said. If this accord is reached, "we could achieve de facto international harmonisation."

Tom Reynolds
JNCI, Vol. 87, No. 14
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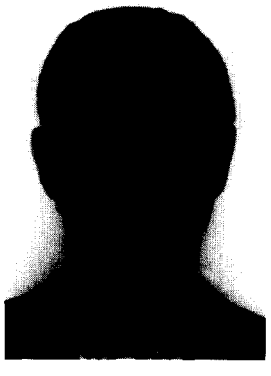
Awards

Professor Herbert Pinedo and Dr Hans Acha-Orba receive the Josef Steiner Cancer Award

Congratulations to Professor Herbert Pinedo, Chairman of the Department of Oncology at the Free University Hospital in Amsterdam and to Dr Hans Acha-Orbea, Research Associate at the Swiss Institute of Experimental Cancer Research in Lausanne who have been chosen to receive the highly prestigious "Josef Steiner Cancer Award" for 1995.

The award was presented during a ceremony on November 3, 1995 at the University Hospital, Bern. Professor Pinedo

Professor Herbert Pinedo



Dr Hans Acha-Orbea

addressed an audience, including the Royal Dutch Ambassador to Switzerland and the minister of Health of the Canton of Bern, with his award lecture on "Bridging the Gap between Basic and Clinical Oncology", following a series of scientific workshops at the annual meeting of the Swiss Society for Oncology, 2–3 November 1995. Hans Acha-Orbea, who received a "Young Investigator's Award", newly created on the occasion of this 10th anniversary of the Steiner Prize, gave a lecture about his research on "Mouse-Mammary-Tumour-Virus: A Retrovirus, employing Immune Response". The decision to award these prizes was made by the foundation Council of the "Josef Steiner Krebsstiftung", a Swiss committee consisting of basic researchers and clinical specialists.

The Josef Steiner Krebspreis is considered equivalent to the Nobel Prize amoung cancer research awards worldwide, offering a regular annual prize of 400,000 Swiss Francs and now, also the newly created prize of 100,000 Swiss Francs for the Young Investigator's Award.

The prize has evolved from a legacy which was left to the University Hospital in Bern 10 years ago by a pharmacist from Biel. Worth several million Swiss Francs, this money was dedicated as a substantial annual award to promote scientific research in cancer.

H.-J. Senn

EORTC Data Centre Receives Grants under the EU's 4th Framework RTD Program (BIOMED 2) for Meta-Analysis and Health Economic Studies

Meta-analysis for the improved treatment of cancer

With support from the European Commission, the EORTC Data Centre established a Meta-analysis Coordination Unit in May 1994. This has provided the EORTC with the scientific means and expertise required to identify, process and analyse the individual patient data from trials to be included in meta-analyses which are conducted by the unit and to coordinate meta-analysis activities with other centres such as the MRC Clinical Trials Services Unit (CTSU), Oxford, U.K., and the MRC Cancer Trials Office, Cambridge, U.K., with whom joint projects exist.

A permanent staff was selected consisting of the head of the unit, Richard Sylvester; a statistician, Luc Bijnens; a computer analyst/statistician, Albert Ivanov; and a secretary/data manager, Jacqueline Roche. Development has already started on the design of an integrated meta-analysis system and was presented at the 1995 meeting of the Society for Clinical Trials.

Status of meta-analyses

Superficial bladder cancer. A protocol defining the meta-analysis was written. Ten EORTC and MRC trials to be included were identified. Quality control verifications and site visits to update the data were carried out. The statistical analysis was carried out and a prognostic factor analysis was performed. Manuscripts are being prepared for publication.

Bone marrow transplantation in adult leukaemia. The definitions of the data to be transferred and analysed were made and the first draft of a protocol was written in conjunction with the other participants. The collection, quality control and computerisation of the individual patient data has been initiated and a database set up. An interim analysis was presented at the investigators meeting in Oxford in January 1995.

Perioperative chemotherapy in early breast cancer. The quality control, statistical analysis and preparation of a report was finalised. The results have been discussed in a meeting held at the EORTC Data Centre with the coordinators of the individual studies. An abstract was published in the 1995 ASCO proceedings and a manuscript was sent to the *Journal of Clinical Oncology.*

Future perspectives. The success of the work already accomplished ensures the continuation of the ongoing meta-analysis projects in order to allow for their updating, an essential requirement to ensure conclusive results. Planning of new projects in malignant melanoma, soft tissue sarcoma, locally advanced head and neck cancer, and locally advanced cervical cancer has already started.

Richard Sylvester

Rapid assessment of cost-effectiveness through training in the cancer field

Cost-effectiveness studies, often used by health care insurers or pharmaceutical companies to assess potential profitability is now being included in selected EORTC cancer clinical trials whenever relevant. The EORTC Health Economics Unit, directed by Koen Torfs, has received a grant from the European Commission, DG XII, to add this approach to EORTC cancer clinical trials. A previous European Commission grant allowed for the establishment of this unit in 1993 and this second grant will allow for health economics studies to be built into selected EORTC cancer clinical trials. Along with evaluations of new drugs or treatment regimens, economic information will be collected. The field of health economics is relatively new and in many cases, the standard costs of treatments need to be established. Scientists will need to ascertain the cost of treatments and consequently training for clinical researchers will be built into this EORTC research.

Such approaches will be of great value as new, often expensive, treatments are developed and health care financing becomes more restricted. The EORTC Data Centre has also included quality of life studies in its clinical trials whenever relevant.

Health economic evaluations can compare the cost of treatment against measures of the long-term value of a number of treatment approaches, including mainly overall survival, as well as measures of the patient's quality of life. Evaluating the patient's quality of life is not simply a humane measure as there is a huge market in drugs manufactured to address the adverse effects of cancer chemotherapy. As a result a less toxic treatment might bring cost savings. In some cases, a very expensive treatment such as use of new biologically engineered immune or growth factors or bone marrow transplantation is compared to a less expensive treatment, thus providing valuable information not only for clinicians, but also for agencies involved in planning for and financing health care.

Koen Torfs

EORTC Leukaemia Group Receives a Grant Under the EU's 4th Framework RTD Programme (BIOMED 2) for the Project Clonal Remission after Intensive Antileukaemic Therapy (CRIANT)

Before introducing new treatment modalities for MDS and s-AML in the European health care system, extensive

assessment of the treatment and its underlying molecular mechanisms is necessary, as well as the implementation, standardisation and quality control of the innovative laboratory techniques involved.

Knowing the fundamental mechanisms, a more well-founded medical decision will become possible concerning the appropriate treatment strategy.

Aims

The main aims of CRIANT are:

- To study on a molecular level the cytogenetic and clonal remission during and after Intensive Antileukaemic Therapy (chemotherapy and autologous stem cell transplantation).
- To determine the prognostic impact of cytogenetic and/or clonal remission on the duration of remission and the prognosis of the patients. Analysis of the nature of remission (cytogenetic, monoclonal versus polyclonal) and monitoring of residual disease is essential for rational application of the expensive myelotoxic treatment.
- To encourage cooperation between laboratories concerning new techniques not yet being implemented in routine clinical care by mutual training, quality control and personnel exchange (PCR and FISH).
- To promote vital links between basic research and clinical studies.

The partners will assess the efficacy of intensive chemotherapy, whether or not followed by autologous stem cell transplantation for patients with MDS in terms of cytogenetic and clonal remission, clinical response, survival and costs. At the same time a very important prerequisite has to be met concerning the inter- and intralaboratory comparability of molecular determinations in different member states. For that goal, during the project the quality of *in situ* hybridisation techniques, and the quality of PCR determinations in four reference laboratories, will be assessed.

European dimension

The proposed project is closely related to an already running clinical trial, which is carried out by the EORTC/EBMT. In this study, 22 institutes from 10 different European countries are participating. The major aim of this trial is to assess the efficacy and toxicity of a more intensive remission-induction chemotherapy, containing the new anthracycline Idarubicin (Pharmacia), in bad prognosis and transformed MDS in terms of partial and complete response rate, duration of hypoplasia and death rate during hypoplasia.

The objectives of this study are:

- To assess the quality of remission marrow achieved by intensified remission-induction therapy by means of cytogenetic analysis and *in situ* hybridisation.
- To assess the feasibility of autologous stem cell transplantation in prolonging remission of those patients who have achieved a cytogenetic remission.
- To assess disease-free survival of overall survival.

Whereas the European trial focuses on the clinical feasibility of the intensive antileukaemic treatment modality, the CRIANT project deals with an in-depth analysis of the underlying molecular mechanisms.

Within the CRIANT project the same basic treatment protocol will be used as in the clinical trials. Overall, 28 clinical and/or research institutes from 10 European countries are participating. By using the existing organization of the ongoing European clinical study, a number of organizational issues can be avoided, thus focusing on the scientific value of the research.

Within this project several networks are built making the techniques mutually available. Moreover, an interlaboratory quality control will be established.

Expected results

The main expected benefit is improvement of MDS care throughout Europe. In malignant haematology, a remarkable progress has been achieved in the knowledge and expertise concerning the molecular biology of the pathogenesis of malignant hematopoiesis. However, this knowledge is limited to a few countries and a few sophisticated expert laboratories, mainly in the framework of specialized research projects. The urgent and important next step implies application of the available expertise to large scale clinical practice. This means creating access to these sophisticated molecular techniques for centres and countries that lack these facilities. As a consequence, clinical and cytogenetic data can be linked to molecular studies, thus providing better funded medical decisions. An additional advantage will be the education and training of physicians and biologists in this knowledge and these techniques. In order to make them available to an increasing number of clinical centres throughout Europe, a high standard quality control of the laboratory assessments is a necessary requirement as well as the promotion of high standards for routine practice.

Theo de Witte

European Day Against Leukaemia and Lymphoma

For many years "United Europe" has been a matter of discussion and great expectations, yet practical results have so far been rather disappointing. On 21 June 1996 — with the beginning of the summer — we will witness a further positive achievement: Europe united in the fight against leukaemia and lymphoma.

This is the initiative launched by Prof. Franco Mandelli (Department of Haematology, University "La Sapienza", Rome) which has attracted the attention of many voluntary associations which act in support of European haematological institutions.

The "Old Continent" united toward new humanitarian frontiers will certainly bring renewed enthusiasm and energy into the battle against blood malignancies. Despite the important progresses achieved during the last decades in the field of haematological diseases, patients still die of leukaemia and lymphoma. Much is still to be done, both in terms of research and of the diagnostic–therapeutic assistance to our patients.

All associations of volunteers operating in Europe are enthusiastically invited to join and support this European Day by contacting AIL (Associazione Italiana contro le Leucemie), 15 via Lancisi, 00161 Roma, Italy. Tel: +39 6 4403763 / 4403795, Fax: +39 6 4404038.

We hope to be part of a large crowd on June 21, 1996 to plan and encourage initiatives within the "European Day for the Fight against Leukaemia and Lymphoma".

Franco Mandelli

Merge of the EORTC Early Clinical Trials Group and the EORTC Clinical Screening Group into the Newly Created EORTC Early Clinical Studies Group

On 1st January 1996, the Early Clinical Trials Group and the Clinical Screening Group of the European Organization for Research and Treatment of Cancer (EORTC) will formally merge.

Clearly, this merger will complete the recent reorganization within the EORTC Research Division and will coincide with the reorganization of EORTC–NDDO. By the extension of the membership and the more extensive involvement of France in the activities, the merger will enable studies to be performed very rapidly which is of increasing importance in drug development.

The fact that the new group will perform largely along the lines previously set by the EORTC–NDDO, CSG and ECTG, ensures that the generated data will be of high quality. The three most important topics in recent drug development are speed, quality of data, and optimal communication. Concerning the latter, the EORTC Research Division with the EORTC–NDDO in its core has also proven recently to be able to guarantee optimal and rapid communication even in complex studies. Moreover, the extension of the membership of the newly formed group will enable the EORTC to be attractive towards pharmaceutical companies, to involve the vast majority of European countries and to take into account specific national regulatory requirements without hampering the necessary speed of studies.

The newly formed group will restrict itself to the performance of phase I studies and early phase II studies. Once human toxicology of a new drug has been appropriately defined and early hints of activity in several tumour types are obtained, further studying of new drugs can be performed through the mechanism of the EORTC Treatment Division with the EORTC Data Centre in Brussels in its core. The potential success of the formula necessitated an enlargement of the facilities for performing early clinical trials within the EORTC. This merger also fits into that perspective.

The newly formed group will complete ongoing studies of ECTG and CSG. Further phase II studies will be initiated with the new cytotoxic compound Carzelesin and the phase I portfolio will comprise of studies involving ET 743, CG 48664, LU79553 and Fostriecin. The first three of the latter drugs will also be studied in phase II studies later in 1996.

Bernard Chevallier / Jaap Verweij