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International Cancer News

Compiled by Robert Short, News Editor, London

From the Globe

International Directory of Genetic Counsellors

A directory of genetic counsellors, physicians, geneticists and nurses who have expertise in counselling about familial risk for cancer and testing for genetic susceptibility is now available on CancerNetR (http://cancernet.nci.nih.gov). CancerNet is an on-line cancer information service developed and maintained by the National Cancer Institute's International Cancer Information Center (ICIC).

More than 200 health professionals are currently listed in The Family Cancer Risk Counselling and Genetic Testing Directory. "The directory will help health-care professionals who increasingly need to locate qualified cancer counselling and testing referral resources for their patients," said Susan Molloy Hubbard, ICIC director.

To be eligible for listing, applicants must be in an oncology or genetics profession; licensed, certified or eligible for board certification in their profession; a member of a recognised health profession organisation; and willing to accept referrals.

Initially four professional organisations asked their members to identify suitable candidates: the National Society of Genetic Counsellors; Canadian Association of Genetic Counsellors; Oncology Nursing Society; and the International Society of Nurses in Genetics.

The Directory is for use on behalf of people who have a family history of cancer or risk factors that may indicate heritable cancers. The directory is searchable by country, name, city, state, and type of cancer or cancer gene. The resources provides information on the degrees, institutional affiliation, professional licenses and certification of the counsellors. It also specifies the gene or disease sites for which the health-care professional provides counselling and gives the context in which service is provided. For example, it explains whether the counselling is designed to answer specific scientific questions in cancer genetics and whether there is a fee for clinical services.

The directory is found in the Health Professionals section of CancerNet, under Cancer Genetics.

Qualified health-care professionals who wish to be added to the directory may send an e-mail query to genetics@icic.nci.nih.gov, or fax a request to the Genetic Counselling Directory at +1 301 402 6728 *in the U.S.A.*

Definitive Evidence that Abnormal Moles Increase Risk for Melanoma

Abnormal moles *do* increase the risk of melanoma, the largest and most definitive study ever to examine this issue has found (1). Said Dr Margaret Tucker, lead author of the study and a researcher at the National Cancer Institute, "This study provides a basic profile of people who are at most risk of developing melanoma, opening the door for earlier prevention and detection strategies."

About half of the 738 people with melanoma in the study had numerous, clearly defined abnormal moles on their bodies. The investigators noted that the risk was greatest in people who also have extremely fair skin and heavy freckling, a sign of excessive sun exposure.

The scientists also report a strong risk of melanoma in people aged 50 years and older who had many abnormal moles on their bodies. Because people stop developing or lose moles by middle age, the investigators feel this finding suggests a possible profile of middle-aged and older people who are most likely to develop melanoma.

The researchers believe that the strong evidence they have, warrants doctors routinely evaluating the moles and freckling patterns of their patients, especially those with fair complexions. These people should limit their time in the sun and receive regular testing for skin cancer. The study involved nearly 1800 people — 738 people diagnosed with melanoma and 1030 people without the disease — who were examined primarily at the Melanoma Clinic of the University of California at San Francisco and the Pigmented Lesion Clinic of the University of Pennsylvania.

Clinicians agreed almost 9 out of 10 times on whether a mole was normal or dysplastic. (The study defined dysplastic naevi as being flat or partly flat, 5 millimetres or larger, and showing two or more of the following characteristics: variable pigmentation, asymmetric outline, and indistinct borders.)

The number and types of moles, both normal and abnormal, correlate with the risk of a person getting melanoma. For those with unusually high numbers of normal, but no abnormal moles, the researchers calculated a 2-fold increased risk for melanoma. For those with numerous small and large normal moles, the risk for melanoma was four times higher than normal.

The risk associated with clearly defined dysplastic moles was much higher. The scientists estimated that individuals with a single dysplastic mole on their bodies have a 2-fold risk of developing melanoma. The risk rises to 14-fold in those with 10 or more abnormal moles. "The fact that we could make this correlation strongly suggests that dysplastic naevi are precursor lesions that, with additional genetic damage, can trigger melanoma", said Dr Tucker.

1. Tucker, MA, Halpern A, Holly EA, Hartge P, Elder DE, Sagebiel RW, DuPont Guerry IV, Clark WH. Clinically Recognised Dysplastic Nevi: a central risk factor for cutaneous melanoma. JAMA 1997 277: 1439–1444.

Special report
33rd Annual Meeting of the American Society of Clinical Oncology, Denver, Colorado, USA

Over 14,000 cancer physicians and researchers from around the world came to the American Society of Clinical Oncology (ASCO), this year. This makes it the largest professional cancer meeting of the year. Participants came to hear and see the programme of 2,000 scientific abstracts, 23 oral sessions and 15 poster discussion sessions.

Said Dr James O Armitage, president of ASCO, "As scientists gain increased understanding of the mechanics of cancer, the field of oncology is moving toward more targeted approaches–turning off specific cellular activity to control and prevent cancerous growth." He added, "The research presented at this year's Annual Meeting provides further evidence that we are slowly but surely gaining ground in the fight against cancer."

This news report presents a selection of some of the most striking presentations at ASCO.

Her-2 Predicts Survival of Breast Cancer Patents

A study of 280 women with metastatic breast cancer from the Eastern Co-operative Oncology Group showed that those patients who had a moderate to high level of Her-2 did less well than patients with minimal or undetectable levels. Her-2 is a protein produced by a specific gene found in some breast cancer cells.

Patients who were Her-2 negative lived an average of 30.2 months. Those with positive Her-2 levels survived 17.7 months. Also, women who are hormone sensitive (oestrogen receptor positive) and Her-2 negative have prolonged survival. Hormone sensitive patients with positive Her-2 levels did no better than oestrogen receptor negative women. Thus, Her-2 expression may explain why not all hormone sensitive patients do as well as expected. "The results of this study suggest that a simple blood test may predict patients who may be candidates for biological therapy such as antibody treatments instead of chemotherapy," said Dr GW Sledge Jr, Indianapolis. No association was found between the presence of Her-2 in the blood and response to either Taxol or Adriamycin.

GOG-111 Results Confirmed by Inter-group Ovarian Cancer Trial

Patients with advanced ovarian cancer who receive first-line treatment with a combination of paclitaxel (Taxol) and cisplatin, survive longer before their disease progresses than patients who receive a cisplatin-cyclophosphamide combination, a trial conducted by several major groups, including the EORTC, NOCOVA, NCI-C and the Scottish Gynaecological Cancer Study Group.

Dr Martine Piccart, co-ordinator of the Inter-Group Study, Belgium presented the results. This 680-patient study (which still has a short period of follow-up to run) showed that patients with advanced ovarian cancer who receive first-line treatment with Taxol/cisplatin, had a progression-free period of 16.6 months compared with 12 months for those receiving cisplatin plus cyclophosphamide. The objective clinical response rate was also significantly quicker for Taxol/cisplatin than for Cisplatin-cyclophosphamide.

Dr Martine Piccart says, "We now have an unequivocal body of evidence—provided by one american trial ane one very large multicentre international trial involving 100 hospitals —demonstrating the critical role of Taxol-based treatment regimens in ovarian cancer." She added, "The efficacy of a three-hour infusion schedule means a much more convenient dosing regimen for both patients and physicians, but it does lead to more severe neurotoxicity than the 24 hour schedule."

In discussing the results, Dr James Tate Thigpen, University of Mississippi Medical Center, U.S.A. said that the Inter-Group study differed in two particular respects from US Gynecologic Oncology Group trial 111: firstly in that the infusion time was shortened to 3 hours and secondly, small-volume residual disease in stage 2 patients were included in the population. Nevertheless, the results replicated the GOG study. "This nails down the fact that combination chemotherapy with Taxol/cisplatin is the treatment of choice for advanced ovarian cancer", he said. But he noted the neurotoxicity was worse in this trial: "24% grade 3 neurotoxicity with the short Taxol infusion, as oppose to only 4% grade 3 in GOG-111 with a 24 hour infusion. What this means to me is that 3-hour Taxol plus cisplatin is an unacceptable combination in the treatment of ovarian cancer, because of the accelerated development of neurotoxicity."

Total Androgen Blockade Questioned in Prostate Cancer

A comparison of bilateral orchiectomy with or without flutamide in stage D2 prostate cancer in a study of 1 387 patients has shown that flutamide in combination with surgical castration does not result in improvement in progression-free survival or overall survival when compared with patients given a placebo with orchiectomy.

The study was presented by Dr Mario Eisenberger of The Johns Hopkins Oncology Center on behalf of the Southeast Oncology Group and collaborating centers.

Overall progression-free survival was 20 months for the study group, 19 months for the control, while overall survival was 32 months for the study group and 30 months for the control. Despite no significant difference in survival rates, there was a significant difference in the reduction of PSA blood levels between the group receiving flutamide (80% reduction) and those who did not receive this drug (68% reduction).

A major fall in PSA levels has traditionally been regarded as an indication of successful treatment, and this new discrepancy suggests that this may not always be true.

Ovarian and Breast Cancer Histories and BRACA1 Gene

The most comprehensive study to date on the prevalence of BRCA1 among women with breast or ovarian cancer and the extent to which age of diagnosis and family history raises a woman's chance of carrying a mutation was presented at ASCO.

The study of was presented by Dr Tom S Frank, medical director of Myriad Genetic Laboratories, Inc.

He said that about one in six women diagnosed with breast cancer under the age of 40 carry a mutation and that the presence of ovarian cancer in the family greatly increases the likelihood of having a BRACA1 mutation. The study authors anticipate that their data may help to define which women would benefit most from BRACA 1 testing.

The study analysed data from sequencing the BRACA1 gene in 830 women with breast cancer, ovarian cancer or both and compared the results to family history and age of onset. Overall, 161 women in the study (19%) were found to carry abnormalities in the BRACA1 gene, of which 117 mutations (14% of the total, or 73% of those with any alterations) were known to contribute to the development of cancer.

Dr Frank said the study showed that a single case of ovarian cancer in the family of a woman under 50 with breast cancer greatly increases the likelihood that her disease is due to a mutation in BRCA1 and, therefore, hereditary. "ASCO recommended that testing should be considered if the chance of a positive test was at least 10%," says Dr Frank. "Our data indicate that families where at least two women have breast cancer before age 50 meet this 10% threshold and if a relative has ovarian cancer the likelihood of a BRCA1 mutation is about 30%.

New EORTC Benchmark for Advanced Lung Cancer: Paclitaxel and Cisplatin

Patients with advanced non-small cell lung cancer (NSCLC) who were treated with a combination of paclitaxel and cisplatin, responded better to treatment, had fewer side-effects and an improved quality of life, compared with those who received a standard combination of teniposide and cisplatin.

A Phase III pan-European trial involving 332 patients showed that 40% of patients receiving Taxol combined with cisplatin respond to treatment, as compared with only 28% of patients receiving teniposide combined with cisplatin. This study confirmed the Eastern Co-operative Oncology Group (ECOG) study results which involved 599 patients.

No survival advantage was seen in the EORTC study, but palliation of the disease was achieved by reduction of the tumour size, and the Taxol combination was better tolerated. "Based on the results of this trial, the EORTC will use this combination as the benchmark against which all future therapies will be measured in its NSCLC clinical trials programme," commented Dr Giaccone, EORTC Lung Cancer Group, The Netherlands.

Haematological toxicities were more frequent and more profound in the teniposide-cisplatin arm. Severe haematological toxicities in the teniposide-cisplatin arm were associated with more infections, dose reductions and treatment delays. With the exception of myalgia and peripheral neurotoxicity, all non-haematological toxicities were similar for both treatment groups. Patients who participated in the study's quality of life self-assessment, gave themselves better scores for emotional, cognitive and social functioning in the Taxol combination arm than in the teniposide-cisplatin arm.

From Europe

EORTC Chronotherapy Study Group

The first strategic meeting of the EORTC Chronotherapy Study Group (CTSG) resulted in strategy for gastrointestinal cancers and breast cancers as well as for the development of new chronomodulated schedules.

Says Dr Frances Lévi, chairman of the group, "A clear goal was defined for randomised Phase III studies to demonstrate survival and/or quality of life advantages of chronotherapy. A new clinical trial methodology needs to be developed in Phase I or II trials to validate the chronotherapy schedules extrapolated from animal studies."

The Chronotherapy Study Group (CTSG) was formed in 1996. In their first strategic meeting last year, 50 oncologists and scientists from eight European countries, Canada and the U.S.A. debated the strategy the group would develop over the next few years. This report is based on the full minutes of the meeting which are available from Dr Lévi.

Circadian rhythms (24-hour rhythms) are endogenous and are co-ordinated by a biological clock in the hypothalamus, the suprachiasmatic nucleus (SCN). This biological clock is reset by light perception through the retina and by darkness through the secretion of melatonin by the pineal gland. Metabolic and proliferative cellular rhythms also follow a circadian timescale, both in laboratory rodents and in human beings. This explains the chronopharmacology of anticancer agents. Preclinical and clinical studies have shown that the adaptation of chemotherapy to biological rhythms could have clinical benefits.

There are small portable devices that allow a non-invasive monitoring of wrist activity (actigraphy) or body temperature. Cancer patients entering chronotherapy trials should undergo such circadian rhythm studies. Summarising the group's conclusions, Dr Lévi says, "At the present time, 'actigraphy' represents the only method which appears to be reliable and is non-invasive. Such investigations should confirm the relevance of circadian system function for patients outcome. Furthermore, cancer-associated clock disturbances may be amenable to specific therapy."

Dr R Smaaland (Bergen, N) summarised tumour rhythm studies in patients with ovarian cancer or non-Hodgkin's lymphoma. At a group level, the proportion of cells in S-phase of the cell cycle differed by 8 hours or more in cancer and in healthy tissues, a finding which helps define an optimal time window of therapy. In addition, the 24-hour changes in S-phase tumour cells could also vary largely among cancer patients, especially in those with advanced or aneuploid tumours. Intersubject differences in the circadian rhythm of plasma cortisol were shown in patients with advanced ovarian cancer or metastatic breast cancer by Dr Y Touitou (Paris, F), despite this these groups of patients did exhibit a significant 24-hour rhythm. E Haus has documented the major abnormality in the cortisol rhythm of cancer patents being an earlier rise at night: cortisol concentrations between 1900 hours and 0400 hours were higher in cancer patients than in healthy subjects. Using wrist actigraphy, C Mormont (Villejuif, F) reported that the strength of the 24-hour rhythmic component was correlated with the overall Quality of Life Score from the EORTC QLQ 30 (v 2.0) questionnaire in 109 patients with metastatic colorectal cancer. She suggested that an appropriate circadian functioning constitutes an important component of the quality of life in cancer patients, a hypothesis which is now being tested.

New anticancer chronotherapy schedules

F Lévi reported large differences in mice in the toxicity of vinorelbine, docetaxel and CPTII according to their circadian dosing time. Giving vinorelbine or docetaxel at their least toxic time allowed a safe increase in their tolerable dose by 30% or more and resulted in a large and significant survival prolongation in tumour-bearing mice. Such results warrant the clinical development of chronotherapy schedules for these agents. The pharmacodynamic effects of cytokines and haemopoietic growth factors (namely G-CSF, GM-CSF and IL-3) also vary by 50% or more along the circadian time scale in mice. O Laerum (Bergen, N) emphasised that haemopoietic regulators such as goralatide or pentapeptide HP5 could reduce CFU-GM count in a narrow temporal window, near the transition from darkness to light.

Considering the implications of such findings, B Hecquet (Lille, F) indicated that a drug with a long half-life and a profound rhythm in its elimination rate would benefit from being given 6 hours before its anticipated time of maximal pharmacodynamic effect. Conversely, if drug distribution is the main parameter modified with a change in dosing time, optimisation can be expected from drug delivery at the expected maximum of the initial distribution rhythm.

In conclusion, the animal models clearly illustrate the need to deliver the highest tolerable dose of cytostatics at the least toxic time in order to maximise the survival advantage which can result from chronotherapy. This strategy will be followed in those clinical trials with survival as an ultimate endpoint. Chronomodulated drug-delivery patterns will be first constructed under the assumption of the need for a sinusoidal infusion and a fixed relationship between the rest–activity cycle and toxicity rhythm. However, these patterns will be improved through iterative drug pharmacokinetic determinations in the early stages of chronotherapy testing. Randomised Phase I trials may be needed for better defining an appropriate chronomodulated schedule. Thus, the determination of the maximum tolerable dose of a chronotherapy schedule will be an essential step for the subsequent Phase III clinical trials. While chronopharmacology clearly also applies to cytokines of chemokines, the clinical experience of chronotherapy with these agents is scarce and exploratory studies are needed.

B Perpoint (Saint-Etienne, F) and J Bernhard advised that a subcommittee of both the CTSG and the Quality of Life EORTC study groups should be constituted in order to propose specific quality of life assessment methods for psychological status, toxicity and symptom-free survival.

Chronotherapy trials on gastrointestinal cancers or breast cancers

An overview of the protocols led by the EORTC Gastro-Intestinal Cancer Cooperative Group was presented by H Bleiberg (Brussels, B). Through his presentation and the discussions which followed on other studies, several areas were identified where chronotherapy could be developed: oesophageal cancer for which the reference treatment combines 5-FU and CDDP, gastric cancer, for which standard regimens are FAMTX, FU-CDDP or ECF, pancreatic cancer with gemcitabine, 5-FU with or without FA and/or CDDP as standard modalities and anal canal for which standard treatment usually combines continuous 5-FU with RT. Chronotherapy could be readily tested against locally advanced or advanced metastatic disease in oesophageal, gastric or pancreatic cancer and both. Of course, chronotherapy should be further assessed against colorectal cancer, both in adjuvant situation and at a metastatic stage.

JL Misset (Villejiif, F) reviewed the recent therapeutic developments in breast cancer to help define the strategy of the group in this disease. He stressed that the probability of recurrences at 5 years after primary breast cancer was relevant to the natural history of the disease and was prognostic for response. He could foresee three areas of possible development of chronotherapy in breast cancer:

- an optimisation of available therapies such as 5-FU or doxorubicin,
- an improvement of therapeutic index of new drugs such as vinorelbine, taxanes or topo-I inhibitors,
- a reversal of the resistance phenotype. As a follow-up to lively discussions, a chronotherapy protocol with vinorelbine-5-FU will be developed in 2nd or 3rd line chemotherapy. Docetaxel chronotherapy will be developed as first-line treatment for metastatic disease.

The full minutes of the meeting can be obtained from Dr Francis Lévi, Chairman CTSG, Centre de Chronotherapie, FMSIT, Hopital Paul Brousse, 14 Avenue PV Couturier, 94800 Villejuif, France. Tel: +33 1 45 59 35 14/38 55
Fax: +33 1 45 59 36 02.

Taxotere Response Rate Better Than Adriamycin in Metastatic Breast Cancer

A Phase III study shows a response rate to Taxotere that is superior to standard treatment, Adriamycin, in metastatic breast cancer. This study of 326 patients by Dr Stephen Chan, Nottingham City Hospital NHS Trust, U.K., shows "Taxotere is the first drug shown in a clinical study to be more effective than doxorubicin in the treatment of metastatic breast cancer." The patients receiving Taxotere showed a 50% better overall response rate when compared with the doxorubicin patients (47.2% for Taxotere and 31.5% for doxorubicin). Of the 161 Taxotere patients, 39.1% had a partial response and 8.1% a complete response. Of the 165 Adriamycin patients, 27.3% had a partial response and 4.2% had a complete response.

Dr Chan said, "13 patients receiving doxorubicin dropped out of the study due to cardiac toxicity. We observed 3 dropouts in the Taxotere group due to fluid retention. Both drug groups exhibited a similar incidence of neutropenia, infection and asthenia. Although side effects were observed in both groups, Taxotere showed a lower incidence of diarrhoea."

Chemotherapy Plus Tamoxifen Benefits All Women

Chemotherapy and tamoxifen is more effective than tamoxifen alone among patients not previously thought to benefit from combination: breast cancer patients whose tumours are hormone-receptor positive, but whose cancer has not spread to the lymph nodes.

In NSABP B-20 in which 2,363 patient study divided patients into three treatment groups: 788 received tamoxifen alone, 786 received tamoxifen and 6 cycles of methotrexate and 5-FU followed by leucovorin and 789 received tamoxifen and CMF chemotherapy (cyclophosphamide, methotrexate, and 5-FU). The study showed that women who received either regimen of chemotherapy in combination with tamoxifen were significantly more likely to be disease free after 5 years of follow-up — 90%, compared with 85% of women treated with tamoxifen alone. Initial results also suggest a survival benefit — 97%, compared to 94% at five years.

Dr Bernard Fisher, Pittsburgh, PA, U.S.A., who is Scientific Director of the National Surgical Adjuvant Breast and Bowel Project, says the study has huge implications for clinical practice, as it means that there is no group of women who do not benefit from chemotherapy–whether oestrogen positive or negative, node positive or negative, premenopausal or postmenopausal. Thus it is not necessary to know the nodal status of patients before treating them.

EORTC Affiliated Institutions and Departments 1997

The EORTC has established a list of institutions participating actively in EORTC Clinical Trials.
The enclosed lists show institutions which have been recognised in 1997 as EORTC affiliated institutions on account of their partcipation in EORTC studies over the last 3 years (1994—1996). The criteria used to merit that recognition are:

1. Recruitment of 75 patients during a period of 3 years (1994—1996) with a minimum of 15 patients per year;
2. Participation in more than 2 groups; institutions participating in less than 3 groups and fulfilling the other criteria are "EORTC Affiliated Departments."

The success of EORTC, as the most representative group of multidisciplinary cancer research in Europe, is based upon the corporate spirit of its dedicated members.
This list will be updated yearly.

EORTC AFFILIATED INSTITUTIONS 1997
(REVIEW 1994—1996)

Institution	Number of Groups	Recruitment 1994–1996
1. Universitair Ziekenhuis — Leuven, Belgium	12	786
2. Universitair Ziekenhuis — Rotterdam, The Netherlands	15	666
3. St. Radboud University Hospital — Nijmegen, The Netherlands	14	639
4. Antoni Van Leeuwenhoekhuis — Amsterdam, The Netherlands	11	504
5. Dr. Bernard Verbeeten Instituut — Tilburg, The Netherlands	3	490
6. Institut Jules Bordet — Brussels, Belgium	16	444
7. Academisch Ziekenhuis — Utrecht, The Netherlands	11	411
8. Academisch Ziekenhuis — Leiden, The Netherlands	10	341
9. Universitair Ziekenhuis Antwerpen — Edegem, Belgium	14	266
10. CLCC Georges-Francois-Leclerc — Dijon, France	4	252
11. Academisch Ziekenhuis Der Vrije Universiteit — Amsterdam, The Netherlands	7	245
12. Maria Sklodowska-Curie Cancer Centre — Warsaw, Poland	8	231
13. Academisch Medisch Centrum — Amsterdam, The Netherlands	8	227
14. CLCC Institut Gustave Roussy — Villejuif, France	12	205
15. CLCC Institut Bergonie — Bordeaux, France	4	203
16. Centro Di Riferimento Oncologico — Aviano, Italy	7	198
17. Institut Curie/Hôpital Necker — Paris, France	4	191
18. Medical University — Gdansk, Poland	4	183
19. Centre Hospitalier Universitaire — Besançon, France	6	178
20. CLCC Henri Becquerel — Rouen, France	5	178
21. CLCC Léon Berard — Lyon, France	9	172
22. Centre Hospitalier Universitaire Edouard Herriot — Lyon, France	5	167
23. Hôpital Cantonal Universitaire — Genéve, Switzerland	4	167

Institution	Number of Groups	Recruitment 1994-1996
24. Centre Hospitalier Universitaire Vaudois — Lausanne, Switzerland	10	165
25. Cliniques Universitaires St. Luc — Brussels, Belgium	9	162
26. Royal Marsden Hospital — London/Sutton, United Kingdom	6	161
27. Algemeen Ziekenhuis Middelheim — Antwerpen, Belgium	8	148
28. Ospedale Di Circolo E Fundazione Macchi — Varese, Italy	5	142
29. Groot Ziekengasthuis — 'S Hertogenbosch, The Netherlands	4	137
30. I.P.O. — Porto, Portugal	3	132
31. National Cancer Institute — Bratislavia, Slovakia	3	131
32. Onze Lieve Vrouw Gasthuis — Amsterdam, The Netherlands	7	130
33. Clinique Sainte Elisabeth — Namur, Belgium	3	129
34. Centre Hospitalier Universitaire de Grenoble— La Tronche, France	3	129
35. Ospedale Molinette — Torino, Italy	4	127
36. Western General Hospital — Edinburgh, United Kingdom	4	124
37. Righospitalet — Copenhagen, Denmark	8	123
38. Weston Park Hospital — Sheffield, United Kingdom	3	121
39. Academisch Ziekenhuis — Maastricht, The Netherlands	9	120
40. Western Infirmary — Glasgow, United Kingdom	6	119
41. Universitair Ziekenhuis — Gent, Belgium	5	114
42. St. James Hospital — Leeds, United Kingdom	3	114
43. Instituto Nazionale per lo Studio e la Cura dei Tumori — Milano, Italy	7	111
44. Inselpital — Bern, Switzerland	8	107
45. General Hospital & City Hospital — Nottingham, United Kingdom	4	107
46. Institute of Oncology & Radiology — Belgrade, F.R. Yugoslavia	3	102
47. Centre Hospitalier Universitaire Hôtel-Dieu — Paris, France	5	95
48. Academisch Ziekenhuis — Groningen, The Netherlands	10	93
49. Centre Hospitalier Universitaire Saint-Louis — Paris, France	4	84
50. The Institute of Oncology — Ljubljana, Slovenia	4	84
51. Centre Hospitalier Universitaire — Angers, France	3	83
52. Newcastle General Hospital — Newcastle Upon Tyne, United Kingdom	5	83
53. Academisch Ziekenhuis St. Jan — Brugge, Belgium	4	82
54. Centre Hospitalier Universitaire Pitié-Salpetriére — Paris, France	5	81
55. Hôpital Universitaire Erasme — Brussels, Belgium	8	80

Institution	Number of Groups	Recruitment 1994-1996
57. CLCC René Huguenin — Saint-Cloud, France	4	80
58. Centre Hospitalier Régional — Lille, France	5	79
59. Hospital Universitario 12 de Octubre — Madrid, Spain	6	77
60. CLCC Oscar Lambret — Lille, France	5	77
61. Akademisch Ziekenhuis VUB — Brussels, Belgium	4	77
62. Universita Degli Studi-Policlin. Di Careggi — Firenze, Italy	3	77

EORTC AFFILIATED DEPARTMENTS
(REVIEW 1994—1996)

Institution	Group Particpation	Total accrual (No of patients)
1. Norwegian Radium Hospital — Oslo, Norway	2	178
2. Hospital De Navarra — Pamplona, Spain	2	130
3. Hôpital Debrousse — Lyon, France	1	121
4. Policlinico Umberto Primo — University La Sapienza - Roma, Italy	1	110
5. Institute of Oncology — Medical Academy - Lodz, Poland	1	107
6. CLCC Val d'Aurelle — Montpellier, France	2	93
7. St. Laurentius Ziekenhuis — Roermond, The Netherlands	1	93
8. Ospedale B. Ramazzini — Carpi, Italy	11	90
9. Freeman Hospital — Newcastle-Upon-Tyne, United Kingdom	2	89
10. Hôpital Robert Debré — Paris, France	2	80
11. Clinical Hospital Rebro — Zagreb, Croatia	2	76
12. Kaiser Franz Josef Spital — Vienna, Austria	2	75
13. Thoraxklinik Rohrbach — Heidelberg, Germany	2	75

EORTC AFFILIATED INSTITUTIONS PER COUNTRY / 1997 (review 1994 - 1996)