with st PNET is unsatisfactory, and intensification of therapy is needed. In ependymomas the predominant site of failure is the primary tumour site. The irradiation of neuraxis did not improve survival. For ependymomas intensified local therapy is warrantable.

721 ORAL

Risk of second primary cancer in hereditary and non-hereditary retinoblastoma: results from a population based study with more than 40 years follow-up

J. Alsner[1], J.H. Olsen[2], N. Ehlers[3], J. Overgaard[1]. [1] *Aarhus University Hospital, Department of Experimental Clinical Oncology, Aarhus, Denmark;* [2] *Danish Cancer Society, Institute of Cancer Epidemiology, Copenhagen, Denmark;* [3] *Aarhus University Hospital, Department of Ophthalmology, Aarhus, Denmark*

Purpose: To determine the risk of second primary cancer in retinoblastoma survivors, we have identified and followed the 240 patients diagnosed with the disease in Denmark between 1943 and 1995.

Methods: Data on treatment, heredity, mortality and observed/expected numbers of second primary cancers have been extracted from the Danish Cancer Registry, primary records from the clinical departments, the Danish Population Registry, and church records. Data on heredity are based on family history and genetic analysis. Median follow-up of the 210 retinoblastoma survivors is 25.2 years of age.

Results: At 40 years of age, the cumulative incidence (3%) and mortality (3%) of second primary cancer in the non-hereditary group (144 patients) is similar to the population at large. In contrast, the corresponding values for the hereditary group (96 patients) is significantly higher at 19% and 11%, respectively. Among the hereditary patients, the increased risk is the same for patients treated with or without radiation therapy for their primary disease. None of the patients have received chemotherapy. Except for a higher incidence (particularly of malignant melanomas), the second primary cancers are of the same type as the time- and age-specific cancers observed in the population.

Conclusions: Associated with hereditary retinoblastoma is an increased risk for second primary cancer. This is not linked to the use of radiation therapy but strictly to the genetic status of the patient

722 ORAL

Detection of relapse in childhood solid tumours

L. Howell[1], A. Mensah[2], B. Brennan[1], T. Eden[1,2], A. Will[1], R. Stevens[1], G. Makin[1,2]. [1] *Royal Manchester Children's Hospital, Dept of Paediatric Oncology, Manchester, United Kingdom;* [2] *University of Manchester, Medical School, Manchester, United Kingdom*

Aims: Frequent follow-up, often with regular investigation, is a routine part of Paediatric Oncology. Many treatment protocols specify both the type and frequency of the investigations to be performed. There is however, little evidence as to the value of such surveillance in the detection of relapse. We thus conducted a retrospective study of relapse detection in a patient cohort.

Methods: A cohort of 316 children diagnosed with solid tumours between 1992 and 1996 was identified. This patient group had a minimum follow up period of 5 years from the end of treatment. Case notes were reviewed and numbers of clinic visits and surveillance investigations recorded. For any relapse that occurred the method of relapse detection was noted.

Results: The average age of the cohort was 5.4 years, and the mean period of follow-up was 5.9 years. 76 patients were excluded because they never achieved remission, or were lost to follow-up. 3417 routine clinic visits were made by this cohort. The frequency of clinic attendance varied from 11 visits/ patient/yr for those with bone tumours, to 6/yr per brain tumour patient in the first year after finishing treatment, although there was less variation in subsequent years. 1860 radiological investigations were performed on this patient group over this period. 60% of these were chest radiographs, 14% were ultrasounds, and 12% were MRI scans. Wilm's tumour patients had on average 11 radiological investigations/yr during this period of follow up, whilst brain tumour patients had only 3/yr. 37 relapses were detected in this cohort. 53% were detected symptomatically, 13% at routine clinic visits, and 27.5% on routine investigation. 81% of relapses occurred >1 year from the end of treatment. We calculated that routine MRI scan detected 1 unsuspected relapse for each 42 scans performed. Routine CT scan detected 1 relapse for every 129 scans performed, whilst routine chest radiography detected only 1 relapse for every 257 films. The low incidence of relapse detection by routine surveillance in this cohort raises questions as to the usefulness of such follow-up in children with solid tumours.

723 ORAL

CPMP guidance in paediatric oncology

F. Rotblat[1], Ö. Anak[2], G. Apolone[3], E. Baumelou[4], J. Boos[5], H.N. Caron[6], J. Ersbøll[7], M. Gårdmark[8], U. Hermes[9], A. Mathieu-Boué[10], B. Morland[11], J. Otten[12], I. Papadouli[13], F. Pignatti[13], M.T. San Miguel[14], G. Vassal[15]. [1] *Medicines Control Agency, Department of Health, London, United Kingdom;* [2] *EORTC Data Centre, Brussels, Belgium;* [3] *Istituto di Ricerche Farmacologiche Mario Negri, Laboratory of Clinical Research in Oncology, Milano, Italy;* [4] *CHRU Lille, Délégation à la Recherche, France;* [5] *Westfälische Wilhelms-Universität, Department of Paediatric Haematology and Oncology, Münster, Germany;* [6] *Emma Kinderziekenhuis AMC, Amsterdam, The Netherlands;* [7] *Danish Medicines Agency, København, Denmark;* [8] *Medical Products Agency, Uppsala, Sweden;* [9] *Bundesinstitut für Arzneimittel und Medizinprodukte, Bonn, Germany;* [10] *Agence Française de Sécurité Sanitaire des Produits de Santé, Paris, France;* [11] *Birmingham Children's Hospital, Department of Paediatric Oncology, Birmingham, United Kingdom;* [12] *Akademisch Ziekenhuis VUB, Brussels, Belgium;* [13] *The European Agency for the Evaluation of Medicinal Products (EMEA), London, United Kingdom;* [14] *Agencia Española del Medicamento, División de Farmacología y Evaluación Clínica, Madrid, Spain;* [15] *Department of Paediatric Oncology, Institut Gustave-Roussy, Villejuif, France*

Background: Since 1990, the Committee for Proprietary Medicinal Products (CPMP) anticancer guideline has provided advice on the clinical investigation of anticancer agents, in particular of cytotoxic/cytostatic agents (Note for Guidance on Evaluation of Anticancer Medicinal Products in Man, CPMP/EWP/205/95). Recently, the CPMP has been working together with European paediatric oncology research groups, including the EORTC Children's Leukaemia Group, the Société Française d'Oncologie Pédiatrique (SFOP), the United Kingdom Children's Cancer Study Group (UKCCSG), the German Society of Paediatric Oncology and Haematology (GPOH), and experts from other European institutions, to produce specific guidance on paediatric oncology, with recommendations for regulatory submission, and phase I trial methodology.

Results: Promising new agents should be studied or made available to researchers, so as to avoid unnecessary delays in paediatric development. Prioritisation of agents for evaluation in children is critical. Factors to be considered include evidence of activity in pre-clinical models, mechanism of action, drug-resistance profile and activity observed in adults. It is recommended that a marketing authorisation application for anticancer agents for adult use should contain information on any past, ongoing or planned paediatric oncology development. A comprehensive overview of any pre-clinical testing in model systems of paediatric tumours should be provided. Data requirements and the timing of paediatric development should be discussed with the regulatory authorities. Sponsors should seek the advice of established international paediatric oncology co-operative groups, and regulatory authorities, early enough during the development so that agreed priorities can be followed, avoiding unnecessary delays. The existing consensus on the design of phase I trials (Smith, M., M. Bernstein, et al., (1998) "Conduct of Phase I trials in Children With Cancer." J Clin Oncol 16(3): 966-78) has also been reflected in the guideline.

Conclusions: Co-operation between the pharmaceutical industry, research groups, and health authorities worldwide can ensure a coherent approach to paediatric drug development in oncology. The paediatric addendum to the CPMP anticancer guideline can be consulted on the EMEA website (htpp://www.emea.eu.int). Finalisation is expected before the end of 2003.

724 ORAL

Caring for survivors of childhood cancers: the size of the problem

J.R. Mann, H.L. Curry, S.E. Parkes, J.E. Powell. *Birmingham Children's Hospital, Oncology, Birmingham, United Kingdom*

Background: Survival for children with cancer has improved greatly, although many survivors have significant health problems from their illness or treatment, requiring long-term medical care. This study utilises survival and clinical data to estimate current and future numbers of long-term survivors and their disabilities, and considers how their care might be provided.

Materials & Methods: The West Midlands Regional Children's Tumour Registry provided data on 5,016 children aged 0-14 years diagnosed with cancer (or benign brain/CNS tumours) between 1960 and 1999. Future numbers of long-term survivors were estimated from actuarial survival rates. Treatment and late effects data were collected from their medical casenotes