ded tissues stained with HE, and for FN expression on cryostat sections. We used the MoAb antiFN from Boehringer-Mannheim. SBC (Boehringer-Mannheim) was used for immunohistochemical staining. Hematoxilin was used for nuclear staining.

**Results:** The expression of fibronectin is heterogenous at both benign and malignant lesions. We evaluated as negative, positive and strong positive the staining for fibronectin.

**Conclusion:** These results bring the fibronectin expression at a new level-that of malignancy marker. It also have the quality to reveal the perivascular metastatic capacity. We consider that the fibronectin through it's receptor property in cell adhesion can become an useful indicator for metastatic potential of the tumor and also for the tumoral evolution.

393 PUBLICATION

### Dominant properties for the suppression of development of preneoplastic foci in the liver of carcinogen resistant inbred DRH strain rats

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**Purpose:** The post-initiation stage of hepato-carcinogenesis was investigated in carcinogen resistant inbred DRH rats and the parental Donryu rats.

**Methods:** Male rats (5 W) were treated with DEN followed by 3'-methyl-DAB and partial hepatectomy. At 8 weeks after the start of treatment, the number and size of glutathione S-transferase (GST-P) positive lesions were determined.

**Results:** The mean area occupied by GST-P positive lesions was 30% in Donryu rats but less than 4% in DRH rats despite of the presence of comparable numbers of foci in livers of both strains. This genetic property was dominantly inherited in the F1 rats by crosses of DRH and carcinogen sensitive inbred F344 rats.

## Cancer in children

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### The standards, options and recommendations (SOR) project for the management of childhood cancer

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**Objectives:** The "Standards, Options and Recommendations" (SOR) project, was started in 1993, and is a collaboration between the Federation of the French Cancer Centres (FNCLCC), the 20 French Cancer Centres end specialists from French Public Universities, General Hospitals and Private Clinics. For pediatic cancer, this project is a collaboration between the FNCLCC end the French Society of Pediatric Oncology (SFOP). The main objective is the development of clinical practice guidelines to improve the quality of health care and outcomes for cancer patients. The methodology is based on literature review and critical appraisal by a multidisciplinary group of experts, with feedback from specialists in cancer care delivery.

**Methods:** Data have been Identified by literature search using Medline and personal references lists. The main criteria considered were incidence, risk factors, prognostic factors and efficacy of cancer treatment. Once the guideline, was defined, the documents were submitted for review to national and International Independent reviewers, and to the medical committees of the French Cancer Centres which have expertise in pediatric cancer management, for agreement.

**Results:** To date, SOR documents have been produced for neuroblastoma, rhabdomyosarcoma, medulloblastoma, osteosarcoma and pain management in children. These recommend standard diagnostic and therapeutic approaches on the basis of file strength of published evidence. The SOR guidelines for rhabdomyosarcoma in which imaging, pathological studies, surgery, radiotherapy and chemotherapy strategies are critically reviewed, the details of SOR methodology and the planned methods of dissemination will be presented.

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### Prognostic value of blasts on day 15 in bone marrow and of molecular evaluation of remission in children with acute lymphoblastic leukemia

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Childhood acute lymphoblastic leukemia is curable in approximately 70% of all patients with current treatment protocols. Risk-directed protocol strategies using multiagent chemotherapy have resulted in complete remission rates of 98% after induction therapy. Despite these achievements, still 25 to 30% of these children will subsequently relapse. With conventional prognostic factors at diagnosis and prednisone poor response one third of patients, who will suffer a relapse can be detected. In vivo response to multiple agent therapy appears to be an independent predictor of outcome. In this study we have evaluated the prognostic significance of early response to induction therapy, as measured by the percentage of lymphoblasts in the day 15 bone marrow aspirate and by the detection of MRD by molecular methods using clone-specific immunoglobulin and T cell receptor gene rearrangements in 75 children with ALL treated according to current BFM protocols. All children achieved morphological remission after induction chemotherapy. After a median observation time of 4.5 years (range 1–7 years) 14 children relapsed. Results of blasts on day 15: M1: 47 patients, M2: 18 children, and M3: 10 children. Five, 4, and 5 relapses occurred in the M1, M2, and M3 group, respectively. Results of MRD analysis (combined evaluation after induction and consolidation treatment): MRD low risk group 38 children, no relapse; MRD medium risk group 31 patients with 10 relapses; MRD high risk group 6 patients with 4 relapses. Log rank test showed significant differences for event free survival (RFS) between BFM risk groups ($p = 0.0039$), for M1, M2 and M3 on day 15 ($p = 0.0014$) and for MRD risk groups ($p = 0.0001$). In a stratified log rank test combining BFM risk groups and MRD groups, blasts on day 15 are not predictive for EFS ($p = 0.28$).

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### Monitoring and functional characterization of rare tumor cells in the haematopoietic system

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The detection and quantification of rare tumor cells in the bone marrow (BM) or peripheral blood (PB) is becoming of particular significance for the treatment of cancer patients. Moreover, exact genetic and functional data of the infiltrating tumor cells can further help to better understand the biology of the infiltrating cells and thus help to refine the anti-tumor therapy in individual patients. A fully automated scanning system was adapted, to enable a sequential demonstration of tumor specific immunological and molecular cytogenetic investigations at a single tumor cell level. 200 BM samples from 60 pediatric cancer patients were analyzed sequentially using a tumor specific antigen and by demonstrating the tumor typical genetic aberration. The proliferative capacity of tumor cells was assessed by a simultaneous detection of the tumor specific antigen and the proliferation marker Ki67. Automatic analysis of 29 BM samples revealed Ki67 antigen expression in up to 78% of the tumor cells in the BM of newly diagnosed patients. A similar percentage of Ki67 positive cells was found in patients undergoing cytotoxic treatment. Automatic search and sequential genetic and immunological characterization of tumor cells prove to be a powerful diagnostic tool in clinical oncology and allow new insights in the biological nature of rare tumor cells circulating in the haematopoietic system.

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### Cutaneoes and subcutaneous Ewing's sarcoma – A relatively indolent disease

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To analyze the outcomes of extraosseous Ewing's Sarcoma (ES) in a primary cutaneous or subcutaneous site.

Between July 1985 and March 1997, 14 patients with cutaneous or subcutaneous ES were treated.

13 had definitive surgical resections and 1 had biopsy of the mass at the time of referral. All patients received chemotherapy. Twelve patients on ES-87 and ES-92 protocols received radiation (36 Gy) to the operative bed