gender and treatment (79 of the patients were treated with standard stupp protocol).
Conclusions: This is the first study assessing RKIP expression levels in GBMs. We conclude that, in contrast to other solid tumours, the percentage of RKIP negative GBM cases is low and that the absence of RKIP expression seems not to be associated with poor survival in GBMs patients.

79 Association of JAK-STAT pathway related genes with lymphoma risk

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Background: Non-Hodgkin Lymphoma (NHL) belong to the seventh most common cancer in Europe and constitute the tenth most commonly diagnosed cancer worldwide. Apart from risk factors such as certain infectious agents and immunodeficiency syndromes, genetic variants related to immunity have been associated with lymphomagenesis. Previous studies suggested an important role of the JAK-STAT signalling pathway in tumour development. Therefore, we explored genetic variants in the JAK-STAT pathway associated with lymphoma risk.
Material and Methods: In total, 1481 lymphoma cases and 1491 age, sex and study centre matched controls of the EpiLymph study, a multi-centre case-control study on the aetiology of lymphomas among adults in Europe, were genotyped for 1536 single nucleotide polymorphisms (SNPs) using GoldenGate BeadArray™ Technology (Illumina, San Diego, CA).
Association between selected SNPs and haplotypes of the JAK-STAT pathway and risk of Hodgkin lymphoma (HL), NHL and most frequent NHL subtypes were estimated by calculating Odds Ratios (OR), the corresponding 95% confidence intervals (CI) and p-values using unconditional logistic regression using SAS (version 9.2).
Results: Among 220 relevant JAK-STAT pathway SNPs, polymorphisms in several genes (*STAT3, STAT6, IFNG, BMF, STAT5A*) were significantly associated with lymphoma risk. Reduced risk for NHL overall and diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL) were seen in association with seven *STAT3* SNPs in high linkage disequilibrium and respective haplotypes. Variant rs4103200 conferred an about 20% reduced NHL risk (OR_{CG} 0.79, 95% CI 0.66–0.94, OR_{GG} of 0.78, 95% CI 0.66–0.91, ptrend = 0.002). Reduced risk in association with this variant was also evident for DLBCL and FL. A putatively functional variant in STAT6 previously associated with IgE levels (rs324011) was inversely associated with HL risk ($OR_{TC/CC}$: 0.61, 95% CI 0.45–0.82, p = 0.001).
Conclusion: Our results implicate a relevant role of the JAK-STAT signalling in the development of lymphoma. Furthermore, our data support previously found associations between genetic variants of STAT genes and immune phenotypes.

80 NAT2 gene polymorphisms and risk susceptibility to childhood acute leukemia

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Background: Maternal exposures to a variety of carcinogens, such as those found in cigarette smoke, diet, drugs and environment during pregnancy play a role in the etiology of childhood leukemia. These compounds are acetylated by NAT2 resulting in activation or detoxification of a variety of heterocyclic amine drugs and carcinogens. Individuals may be classified as rapid or slow acetylators according to the rates at which drugs are acetylated by NAT2. Epidemiological studies suggest that the *NAT2* acetylation polymorphisms may modify the risk of developing childhood acute leukemia. To identify the distribution of *NAT2* polymorphisms in Brazilian children and the effects of the polymorphisms on the development of childhood acute leukemia, we performed a case-control study.
Material and Methods: DNA samples from a total of 194 childhood acute leukemia cases and 285 age-matched controls were analyzed. The genotypes of polymorphisms were assessed by PCR-RFLP and the phenotypes of subjects were defined as fast- or slow-acetylators based on their genotypes. Unconditional logistic regression methods were used.
Results: Point mutations at positions 191 and 341 were more frequent in children with acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) than in control group (7.3% and 9.7% vs. 3.7%, respectively of 191 position; and 46.5% and 48.6% vs. 34.3%, respectively of 341 position). We found an association of *NAT2* slow-acetylation alleles and increased risk of ALL and AML (odds ratio [OR] = 2.29; 95% confidence interval [CI], 1.69–3.11; and OR = 2.80; 95% CI, 1.55–5.07; respectively), due to a high frequency of *NAT2*5A* allele within the leukemia group. On the other hand, because of the underrepresentation of *NAT2*4* and **12A* alleles in leukemia group, *NAT2* rapid-acetylation alleles were associated with a protection role of ALL and AML (OR = 0.44; 95% CI, 0.32–0.59; and OR = 0.36; 95% CI, 0.20–0.65; respectively).
Conclusions: In conclusion, ours findings suggest that *NAT2* slow-acetylation phenotype modifies the risk of ALL and AML development in Brazilian children.

81 Catumaxomab: a causal therapy for malignant ascites

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Background: Malignant ascites is a typical complication of several epithelial tumours due to the spread of malignant cells into the peritoneal cavity and is associated with a poor prognosis. Catumaxomab (Removab®, anti EpCAM x anti-CD3) is the first approved causal therapy for malignant ascites. The safety and efficacy data reported here are from the international pivotal trial (NCT00836654).
Material and Methods: The trial was a two-arm, randomized (2:1) open-label, phase II/III study. Patients (pts) received either paracentesis plus catumaxomab or paracentesis alone (control). Following randomisation, pts were stratified into groups with ovarian and non-ovarian cancer. Catumaxomab treatment consisted of 4 i.p. infusions of 10, 20, 50, and 150 μg on day 0, 3, 7, and 10. The primary endpoint was puncture-free survival, defined as time to first therapeutic puncture or death, whichever occurred first. Main secondary endpoints were time to next therapeutic puncture, and overall survival (OS).
Results: Overall, 258 pts (129 ovarian and 129 non-ovarian cancer pts) were randomized. Statistical significant improvement was demonstrated for the catumaxomab group for both median puncture-free survival ($p < 0.0001$, 46 days versus 11 days for control), as well as time to first need of therapeutic puncture with 77 versus 11 days in the control group, ($p < 0.0001$). The study was neither designed nor powered for overall survival, however the pooled analysis showed a positive trend for catumaxomab, and statistical significant OS was shown in the gastric cancer subgroup. The benefit of catumaxomab was confirmed independent of the primary tumour or prognostic factors like number of previous chemotherapies or presence of distant metastases. Catumaxomab was well tolerated with more than 80% of the pts receiving all four infusions. The observed safety profile was expected due to the mode of action and consisted of cytokine release related symptoms like pyrexia, nausea or vomiting. The side effects were generally mild to moderate and fully reversible.
Conclusions: Catumaxomab treatment resulted in a clear clinical benefit in patients with symptomatic malignant ascites. Based on these results catumaxomab (Removab®) was granted approval in the European Union April 2009 for the treatment of malignant ascites in patients with EpCAM-positive cancer.

82 PET and MRI determination of the effects of Sunitinib on hypoxia and vasculature on a rat brain tumour model

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Background: The use of anti-angiogenic treatments has proven highly efficient for solid tumour including brain tumours [1,2]. However, it has also been shown that these treatments led, paradoxically and at least transiently, to a normalization of the vasculature instead of its disappearance [3]. Although the normalization process should result in more functional vasculature associated with a decrease in tumour hypoxia, until now, no direct proof has been brought in vivo for a correlation between hypoxia and vasculature following an anti-angiogenic treatment. Consequently, the aim of the present study was to analyse, using MRI and PET imaging, the effects of an anti-angiogenic treatment (Sunitinib) on tumour growth, vasculature and hypoxia.
Methods: A rat brain tumour model has been used after inoculation of C6 glioma cells in Wistar rats (5.10^4 cells/3μl). Rat received Sunitinib orally from Day 17 to Day 24 daily (20 mg/Kg) and underwent MRI and PET imaging on Day 17 and 24. MRI was performed on a 7 teslas magnet (Bruker) using (i) T2w RARE imaging; (ii) T2 maps; (iii) T2* maps; (iv) ADC maps and (v) T1w imaging. T2 and T2* maps were performed prior and after an intravenous injection of Sinerem (200 μmol/kg; Guerbet SA) to compute CBV and VSI maps [4]. Hypoxia detection was performed using a microPET imaging (Inveon, Siemens) 120–150min after injection of ^{18}F-FMISO (600 μCi/rat).