proteoglycans of ECM, as a selective carrier to CHS of (i) radioisotopes for a targeted *in vivo* imaging or (ii) cytotoxics for a targeted therapeutic approach.
Materials and Methods: (i) For diagnosis application, a radiotracer radiolabeled with ^{99m}Tc (^{99m}Tc-NTP 15-5) was designed and tested *in vivo* in an orthotopic swarm CHS model. (ii) For therapeutic application, a first conjugate, a quaternary ammonium derivative of melphalan (Mel-AQ), was synthesized and assessed *in vitro* (cytotoxic activity, cell cycle distribution) and *in vivo* in the orthotopic swarm CHS model (antitumour efficacy, toxicity). Since CHS is characterized by hypoxia, research was focused on the vectorization of hypoxia-activated prodrugs. Quaternary ammonium derivatives of phosphormidate mustards were synthesized and tested in vitro (^{31}P NMR studies of cleavage kinetics, *in vitro* cytotoxicity under normoxic and hypoxic culture conditions).
Results: For diagnosis, ^{99m}Tc-NTP 15-5 radiotracer highly accumulated in tumoral tissue at very early stage of pathology while no palpable nor measurable tumour could be assessed. Furthermore, tumoral uptake increased as pathology progressed over time. For therapy, CHS-bearing rats treated with Mel-AQ at 16 μmol/kg (q4d × 3 schedule from Day 8) showed a significant tumour growth inhibition (TGI of 69% at day 43) with associated side effects (in term of weight and heamatological parameters) being significantly reduced as compared to Melphalan. Considering phosphoramidate-AQ derivatives, an improvement of cytotoxic activity was observed in CHS cells under hypoxic culture conditions respectively to normoxic conditions.
Conclusions: These experimental results underlined the potential of the PG vectorization strategy developed in our lab, for a targeted management of CHS including: (i) the first and only radiopharmaceutical able to provide *in vivo* a specific diagnosis and staging of the tumoral pathology of cartilage and (ii) a promising targeted antineoplastic approach exploiting both the chondrogenic and hypoxic features of CHS.
Grants: INCa, CPER, Ligue contre le cancer, FRI/OSEO.

9436 POSTER

The Role of Ki-67 as a Prognostic Factor in Gastrointestinal Stromal Tumours

B. Belev[1], D. Vrbanec[1], J. Jakic-Razumovic[2]. [1]*Clinical Hospital Centre Zagreb, Department of Medical Oncology, Zagreb, Croatia;* [2]*Clinical Hospital Centre Zagreb, Department of Pathology, Zagreb, Croatia*

Background: The aim of the study was to determine useful prognostic factors of gastrointestinal stromal tumours (GISTs), for recurrence in local disease but also for overall survival.
Materials and Methods: We analysed 100 GIST patients by retreiving all mesenchymal tumours of the GI-tract from the files of the University Hospital Center Zagreb, retrospectively in the period from 1997–2007., with various primary localization and different stages of disease. All pathological samples were stained for c-KIT (developed on the routine basis in 2001, retrospectively stained specimens from 1997–2001), PDGFRα, further specimens were analysed by immunohistochemistry for expression of CD34, SMA, S100, Ki-67, as well as for parameters like tumour size, mitotic count, morphology, haemorrhage, necrosis and mucosal ulceration. Proliferating index counted by Ki-67 antibody was calculated as a number of positive nuclear reaction over 100 cells. The Cox's proportional hazard model was used in univariate and multivariate analyses, chi-squared test or Student's t-test was used for statistical comparisons of baseline characteristics. Survival rates were calculated by the Kaplan–Meier method, and statistical significance was determined by the log-rank test.
Results: There were 36 patients with localized disease, 29 had localized disease with recurrence and 35 had initially metastatic disease. In univariate analysis for recurrence of disease tumour size, mitotic rate, pattern of c-KIT staining, SMA positivity and Ki-67 showed to be significant prognostic factor, especially Ki-67 ($p < 0.0001$). In multivariate analysis only Ki-67 and SMA seems to be prognostically important ($p < 0.01$ and $p < 0.05$, respectively). It was found that cut-off level of Ki-67 on the level of 6% was significant for recurrence of initially localized disease. It was also found, in Cox regression analysis, statistically significant difference in overall survival (Cox F-test, $p = 0.04$) on the level of Ki-67 above vs below 6%. All other analysed parameters have not been found significant considering overall survival.
Conclusions: Beyond classic pathohistologic parameters, the level of Ki-67 seems to be important and taken into consideration when assesing recurrence risk in localized disease, maybe even more for adjuvant treatment. It is notable that the level of Ki-67 was consistent no matter of primary tumour localization, what was not the case with mitotic count.

9437 POSTER

Prognostic Factors in Patients With Cancer of Unknown Primary (CUP)

D. Petrakis[1], E. Voulgaris[1], G. Pentheroudakis[1], N. Pavlidis[1]. [1]*Ioannina University Hospital, Medical Oncology, Ioannina, Greece*

Introduction: CUP represents a heterogeneous population of patients with systemic malignancy and variable outcomes. Identification of clinical, pathologic and laboratory parameters with prognostic utility would contribute to better prognostication and individualised therapy.
Patients and Methods: We collected clinical, pathologic and laboratory data of 211 patients with CUP treated from 1995 until 2010 and analysed them for prognostic significance. The log-rank test was used for univariate analysis, and a Wald backwards Cox Regression model was applied for multivariate analysis.
Results: 211 patients (113 males, 98 females) of a median age of 69 (range 27−87) and performance status 0−1 in 54% harboured adenocarcinoma (112), squamous carcimona (16), neuroendocrine tumours (15) and undifferentiated/poorly differentiated carcinomas (80) of unknown primary. The clinicopathologic subgroup of the patients was Visceral CUP (122), Head Neck CUP (12), Axillary Nodal CUP (9), Neuroendocrine (10), Serous Peritoneal CUP (23) and Mucinous Peritoneal (12). 34% of patients had 2 or more comorbid conditions, while at diagnosis, anemia was seen in 22%, leukocytosis (>10000/mm^3) in 33%, lymphocytopenia (<1500 mm^3) in 47%, hypoalbuminemia in 16%, abnormal serum alkaline phosphatase in 32% and hyponatremia in 15% of patients. Platinum-based therapy was administered in 106, the rest receiving taxanes, fluoropyrimidines or vinca alkaloids without platinum. The objective response rate was 36.6%; patients achieved a median Progression-Free Survival of 4 months (95% CI 3.2−5.3) and a median Overall Survival of 9 months (95% CI 5−12). In univariate analysis, the following parameters exhibited significant prognostic utility.

Table 1. Univariate prognostic analysis

Parameter	Median Overall Survival	Logrank 2-sided P
PS 0−1 vs 2 or more	10 vs 7 months	0.01
Platinum-based therapy vs non-platinum	11 vs 7 months	0.009
Lymphopenia	7 vs 12 months	0.021

In multivariate analysis, administration of platinum-based therapy had a favourable impact on outcome (Relative Risk of death, RR 0.62, 95% CI 0.39−0.9, $p = 0.049$), while lymphopenia at diagnosis carried an unfavourable prognostic significance (RR 1.6, 95% CI 0.98−2.6, $p = 0.058$).
Conclusion: Host-related factors such as performance status and lymphopenia and therapy-related factors such as platinum treatment impact on the outcome of patients with CUP. A prognostic algorithm will be devised and validated upon expansion of the patient cohort.