Methods: We have collected 68 genetically characterized tumors: 5 SDHB, 1 SDHC, 4 SDHD, 10 RET, 12 VHL, 2 NF1, 3 familial cases without mutations and 31 sporadic tumors. The transcriptional profiles obtained using the ® Agilent gene expression microarrays platform (Whole Human Genome, 4x44k) were subsequently analyzed with the ©GEPAS bioinformatics package. Quantitative RT-PCR and immunohistochemical assays will be performed to validate the transcriptional profiling data on the same collection of tumours, as well as on an independent series of paraffin embedded tumours respectively.

Result and conclusion: Will be presented at the Meeting.

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POSTER SESSION

Survivorship research

622 Poster

Survival rate of gastric and esophageal cancers in Ardabil Province, North-West of Iran

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Background: Upper gastrointestinal cancer is the most common cancer in Ardabil Province, North-West of Iran, accounting for more than 50% of all cancer deaths in this area. We conducted this study to determine the present survival rate of patients with esophageal and gastric cancers before launching interventional studies. Methods: A prospective follow-up study of 420 biopsy-proven patients (127 females, mean age: 64) with upper gastrointestinal cancer (141 esophageal and 279 stomach cancers) who were initially diagnosed in Aras Clinic, the main gastrointestinal referral center of Ardabil Province, from 2000 through 2004, was performed with collection of data on demographics, tumor characteristics, pathologic stage, treatment methods, complications, survival time, etc. Data were gathered through direct interview with patients or their families in 303 cases and evaluation of death certificates in 55 patients. Follow-up was from cancer diagnosis until death, or immigration. Survival according to stage of disease, Lauren tumor type, tumor location, surgery, and adjuvant chemotherapy was analyzed, and results were compared with those of western series. Results: Sixty-two cases were lost to follow-up. The one- and five-year survival rates in the patients with upper gastrointestinal cancer in Ardabil Province were 40.5%, and 0.8%, respectively. In the univariate analysis, men had a slightly lower survival rate than women ($P = 0.21$) and patients with esophageal cancer had a longer survival rate compared to stomach cancer patients ($P = 0.15$). Patients who had undergone surgery ($P < 0.001$) and/or chemotherapy ($P < 0.001$) survived longer than those without such treatments. Tumor morphology, age at diagnosis, radiotherapy, alcohol, and opium consumption did not show any significant effects on the survival rate of patients. In multivariate analysis, only smoking was remained as an independent factor for stomach cancer ($P = 0.04$) while in esophageal cancer, surgery and grade of differentiation were significant predictors of survival. Conclusion: Survival rate of stomach and esophagus cancer cases in Ardabil is relatively low. Intervention for early detection and therapy is necessary to increase survival.

623 Poster

Cognitive performance (cp), informed consent (ic), and age among advanced cancer patients (acp)

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Introduction: Cognitive impairment (CI) among cancer patients has been well described and is believed to be due to various factors, e.g. age and chemotherapy. Prior research indicates that acp participating in phase I clinical trials inadequately understand many elements of IC, but the prevalence of CI has not been well described in this population.

Methods: Acp CP was evaluated using a neuropsychological battery designed to assess domains of decisional capacity: Memory (Hopkins Verbal Learning HVLT and Mini-Cognitive Assessment); Executive Functioning (Verbal Fluency and Trail-making A/B); Language (Boston Naming-short); Attention (Digit Span); Comprehension (Auditory Comprehension & WAIS comprehension). Semi-structured interviews also evaluated IC, and included the Hospital Anxiety and Depression Scale (HADS), BDI-II, and the FACT-COG.

Results: To date, a total of 180 acp enrolling in Phase I trials have been studied: median age: 58y (range: 23-83y); 69% male; 86% Caucasian; 73% > HS education. Only 25% of responding acp correctly identified the purpose of Phase I trials. Older acp (>age 55y) were less likely to correctly describe the research purpose of the trial (30% v. 71% $p=0.02$). Older acp had measurable deficits in CP: Boston (13 ± 1 v.14 ± 0.8, $p<0.0$); HVLT Total Recall (16 ± 6 v. 24 ± 5, $p<0.00$) and Discrimination Index (8.3 ± 3 v.11 ± 2, $p<0.00$); Digit Span (15 ± 5 v. 19 ± 2, $p<0.00$); Trail-making A (61 ± 28 v. 41 ± 22, $p<0.00$) & B (178 ± 90 v.109 ± 56, $p<0.00$). ACP who correctly identified the purpose of a Phase I had greater CP as assessed by memory tasks (38.1 ± 7.9 v. 33 ± 2.6, $p=0.04$) and greater attentional abilities (21.1 ± 4.3 v. 18.6 ± 2.3, $p=0.06$). ACP who recalled that palliative care/hospice was presented as an option experienced greater deficits in processing speed & mental flexibility (282 ± 104 v. 214 ± 97, $p=0.04$). Older acp tended to report more depressive symptoms (14 ± 11 v. 6 ± 5, $p<0.00$). Also, older acp had FACT-COG scores well below reported means for impact on quality of life (24 ± 7 v. 27 ± 10, $p=0.03$). Conclusions: Our data strongly indicate that there are clear associations between several measurable domains of CP and understanding of the elements of IC for early phase clinical trials especially among the elderly.

624 Poster

The effect of cabbage juices on the activity and expression of GST isozymes in HepG2 cells

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There is a very convincing epidemiological evidence that a diet high in cruciferous vegetables protects against tumorigenesis in many tissues, including the colon. A substantial part of this protective effect has been ascribed to the induction of detoxifying enzymes especially glutathione S-transferase (GST). GSTs are superfamily of enzymes which catalyze the conjugation of some electrophilic compounds with glutathione. Based on the structural, physicochemical, enzymatic and immunological properties the cytosolic GSTs are divided into four classes: alpha, mu, pi and theta. The induction of GST was closely correlated to reduction in the number of chemically induced tumours in humans or human cells. The human hepatoma cell line HepG2 retains many of the xenobiotic metabolizing enzymes found in normal hepatocytes, including an inducible GST. The predominant isoform of GST that is induced by xenobiotics in this cell line is GST alpha.

Our previous in vivo studies demonstrated the modulation of GST isozymes expression by cabbage and sauerkraut juice in rat liver and kidney. To get a more complete view about the mechanism of anticarcinogenic properties of cabbage, in this study the total activity of GST and expression of GSTs alpha, mu, pi and theta by Western blot in hepatoma cell line HepG2 were analyzed. HepG2 cells were incubated with cabbage juices obtained from vegetables cultivated in industrial and ecological farms for 3, 6 and 24 hours.

Administration of the all cabbage juices for 3, 6 and 24 hours significantly enhanced activity of GST in HepG2 cells. Changes in the expression of GST isozymes in HepG2 cells were dependent on time of treatment. In HepG2 the constitutive expression of the all tested GST isozymes was detected. However, the expression of GST in HepG2 was lower than in rat liver. Western blot analysis showed that the all cabbage juices increased the expression of GST class alpha (by 30%) and to lesser extent the GST class mu at all time points of exposure, but did not affect the GST theta and pi.

The results of this study indicate that cabbage juices are effective inducers of human GST in agreement with previous studies on GST in animals. Modulation of the total activity and expression of GST isozymes may be responsible for their biological activity and chemoprotective properties of cabbage.

625 Poster

A psychoeducation group for patients at the end of primary treatment for cancer - preliminary results

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Background: End of treatment has been shown to be a very difficult time for patients, as they often feel vulnerable with less frequent contact with the health service, anxious about disease recurrence and under stress

regarding “picking up the pieces” of their life before cancer. (eg, Ganz et al. 2004, Cimprich et al, 2005).

Various different studies have examined ways of making the progression from the end of adjuvant treatment easier for patients. Psycho-educational groups have been proposed as an effective method of easing the transition.

Methods: A literature review identified the topics that patients describe as difficult to cope with, effective formats of intervention and the predictors of distress at the end of treatment. A focus group was conducted with a sample of patients who had finished active trreatment in the previous year. The focus group was structured by the findings of the literature review, but participants were also able to comment freely on their own experiences.

The results of this were compiled with the evidence base and a six session group programme was developed. Each week would consist of a psycho-educational slot covering a different topic, with guest speakers, followed by a therapeutic session. The topics highlighted by the literature and the focus group included diet and exercise, relaxation, managing emotions, family relationships, returning to work and preparation for ongoing symptoms.

The group was evaluated using the Hospital Anxiety and Depression Scale and the Mental Adjustment to Cancer Scale, administered pre and post group. This would be followed up at six months post group to assess whether improvements were maintained.

Participants were also asked to feedback their own feelings about the effect of the group.

Results: The overall usefulness of the group was rated on a Likert Scale of 0 = not useful, to 10 = extremely useful. The average rating from the group was 8.4 (n=23) indicating members had subjectively found it very beneficial.

The group was shown to be beneficial in all areas of assessment pre and post, including anxiety, depression and mental adjustment (n=23). (Up to date data will be presented)

Conclusion: Preliminary results are encouraging and suggest that patients find a combination of psychoeducation and psychotherapeutic support to be beneficial at this point in their cancer journey. Results will become more robust as further data is collected but it is hypothesised that the improvements in mood and mental adjustment will be sustained.

626 Poster

Modulation of PKC delta and epsilon distribution by plant phenols in mouse epidermis

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Protein kinase C (PKC) is thought to be a major intracellular receptor for the mouse skin tumor promoter 12-O-tetradecanoylphorbol-13-acetate (TPA). PKC is a serine-threonine-specific kinase and represents a family of at least 11 isozymes, which can be divided into three main groups: the Ca+2-dependent or conventional PKCs (alpha, beta and gamma), the Ca+2-independent or novel PKCs (delta, epsilon and ni) and atypical PKCs (zeta). The diversity of PKC isoforms and their central role in many signaling pathways makes them important targets for potential chemopreventive agents. Our previous studies showed that three structurally diverse phenolic acids: protocatechuic acid, chlorogenic acid and tannic acid and trihydroxystilbene – resveratrol, altered the TPA-stimulated distribution and activity of PKC alpha, beta, gamma and zeta in mouse epidermis. Their effect on other PKC isozymes: delta and epsilon, might be of interest since transgenic mice with over-expressed PKC delta showed resistance to tumor promotion by TPA, while over-expression of PKC epsilon caused a reduction in the pappiloma burden, although enhanced carcinoma formation. Better understanding of different epidermal expression of PKC isoform patterns and substrate proteins is needed to explain their opposing effects on skin carcinogenesis and its modulation by plant phenols.

Thus, the aim of current study was the evaluation of the effect of plant phenols on TPA-stimulated PKC delta and epsilon distribution. Phenolic acids and resveratrol were applied topically at the dose of 16 micromoles 15 minutes before a single application of 3.4 nmoles of TPA in acetone. Control mice were treated with acetone only. Forty eight hours after TPA treatment animals were sacrificed and the cytosolic and particulate fractions were isolated. The distribution of PKC isozymes was determined by Western blot analysis.

TPA treatment resulted in the translocation of both estimated PKC isozymes from cytosolic to particulate fractions. All tested phenolic compounds affected the TPA-induced PKC isozymes translocation. The observed effects, however, were depended on the phenol structure and to a certain extent were isozyme specific. Protocatechuic acid and chlorogenic acid significantly inhibited the TPA stimulated translocation of PKC delta. For PKC epsilon the similar effect was observed after treatment with chlorogenic acid, tannic acid and resveratrol.

The results of the present study may point out the significant role of PKC isozymes in the promotion of mouse skin tumorogenesis by TPA and suggest that antipromotional activity of plant phenols may result from the modulation of PKC isozymes distribution, including PKC delta and epsilon.

627 Poster

Immunohistochemical study of intratumoral microvessels in resected non-small cell lung carcinomas, N-status, pTNM-stage and survival period of the patients

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Goal: Study of intratumoral microvessels in resected non-small cell lung carcinomas (NSCLC), N-status, pTNM-stage and survival period.

Material and method: Resected material from 54 patients radically operated for NSCLC is observed. 21 cases concern N0-status, 33-N1,2 – status. 48 cases concern I, II and IIIA, and 6-IIIB and IV pTNM stage. The number of intratumoral microvessels (NITMV) is determined through application of CD31. There is an account of high (NITMV=>75), and a low (NITMV<75) degree of vascularisation. Intratumoral vessel invasion is determined. Statistical methods: t-test, chi-square, survival according to Kaplan-Meier, logistic regression analyses.

Results: The average survival period in low vascularisation is 1731 days, and in high vascularisation – 1158 days (a 573 days difference, p=1067). NITMV has statistically significant influence on the N-status: chi-square-p=0.041, logistic regression analyses – p=0.045. A significant dependency between the average NITMV and pTNM stage (p=0.029) has been proven. In vessel invasion (in 27.4% of the cases) the survival period is shorter with 478 days. In 28 cases (54.9%) intratumoral vessels immediately bordering tumor cells are observed, while in 5 NSCLC there are intratumoral vessels, in part of whose walls endothelial cells are not found.

Conclusion: NITMV has a statistically significant influence on the N-status. The survival period is longer in NSCLC with low vascularisation.

POSTER SESSION

Tumour immunology

628 Poster

Regulatory T cells are recruited and activated within primary breast tumors with an adverse clinical outcome

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Background: Breast Cancer (breast adenocarcinoma) is the most common cause of cancer in women in developed countries and the second leading cause of cancer death in women. Clearance of primary breast tumors by immune mechanisms is rare despite the fact that some of them contains T cells infiltrates. Regulatory T cells (Treg) are increased in peripheral blood of patients with breast cancer and present in tumor environment. In this work we assessed the role of Treg in breast tumor progression.

Materials and methods: Immunohistochemical analysis of Foxp3 expression by TMA and ex-vivo analysis of Tumor-infiltrating Treg (Ti-Treg) were performed on patients suffering from primary breast carcinoma.

Results: Immunohistochemical analysis of Foxp3 expression in primary human breast tumors showed that the presence of Ti-Treg within the tumor bed had no influence on tumor progression in opposition to Ti-Treg within lymphoid infiltrates that was predictive of relapse and death, in particular in ER+ patients. Moreover, our ex-vivo analyses demonstrated that these tumors are highly infiltrated by $CD4^+CD25^{high}CD127^{low}Foxp3^+$ Ti-Treg that suppress the functions of conventional T cells (Tconv). Ti-Treg are selectively recruited through CCR4 or CCR7 as suggested by their down-regulation at cell-surface and the presence of their ligands in tumor environment. Furthermore, Ki67 and Hoechst 33342 stainings demonstrated their local expansion. Importantly, in contrast to Ti-Tconv and circulating Treg, Ti-Treg expressed high levels of GITR, ICOS, HLA-DR,