

Extracapsular lymph node spread was strongly associated with poor overall survival ( $P < 0.001$ ) and disease free survival ( $P < 0.001$ ).

**Conclusion:** The results of this study seem to confirm the role of extracapsular spread as a negative prognostic factor of patients with gastric cancer, by means of statistical analysis. Our results suggest that extracapsular spread is more sensitive than the total number of metastatic lymph nodes to identify classes of patients with similar life expectancy.

In conclusion, randomized multicenter studies are needed in the future to confirm these preliminary results; possibly including extracapsular spread in a more complete and accurate staging system, in order to reduce differences between the groups, trying to find the best treatment option and identify the correct prognosis for patients with gastric cancer and to compare results worldwide.

#### 04 SCIENTIFIC POSTER ABSTRACT Effect of one year adjuvant imatinib on gastric stromal tumors

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**Goals:** Though recurrence is high, local excision is the preferred approach for dealing with gastric stromal tumors. Achieving negative margins is mandatory, sometimes requiring subtotal gastrectomy. Adjuvant imatinib is essential for advanced cases and prolonging survival.

**Methods:** The study included 12 patients (7 males, 5 females, median age 46 years) presenting with gastrointestinal stromal tumors (GISTs). The schedule was imatinib (400 mg/day) for 1 year after surgery, in adjuvant setting. Clinical and radiological evaluation was at 4 months of treatment.

**Results:** All patients had abdominal discomfort, while 50% had epigastric pain, and 10% had hematemeses, in the beginning of the treatment.

**Conclusion:** Imatinib has an acceptable safety profile and can be considered as an adjuvant and why not as a neoadjuvant therapy in GISTs. More clinical data are needed to confirm this hypothesis.

#### 05 SCIENTIFIC POSTER ABSTRACT Methylation of MLH1, MGMT, DAPK genes in the cancerous and adjacent non-cancerous stomach tissues

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**Goals:** To assess the profile of the expression of methylated genes in the cancerous tissue and adjacent non-cancerous stomach tissues.

**Methods:** Genetic analysis of the cancerous and non-cancerous tissues (assessed by pathologist) sampled 2 cm away from the edge of the tumor was accomplished. Samples were acquired from patients who underwent surgeries for gastric cancer in LUHS Oncology Institute during 2009–2011 and who agreed to participate in the study. DNA extraction was accomplished according to protocol using commercial set, DNA was converted according to instructions provided by manufacturer using bisulfite kit. Bisulfite DNA was amplified during methylation-specific PCR by using gene-specific primers for methylated and non-methylated alleles. PCR products were separated using agarose gel electrophoresis and were visualized in ultraviolet illuminator after staining with ethidium bromide. Statistical analysis was performed using SPSS software.

**Results:** Results of our research have shown that the methylation of MLH1 gene occurrence rate is 66.6% (24 from 36) in cancerous tissue, and 58.3% (21/36) in adjacent non-cancerous tissue; the rates of DAPK were 9.7% (3/31) and 29% (9/31) respectively, and for MGMT rates were 7.1% (2/28) and 10.7% (3/28) respectively. A strong relationship between the expressions of gene methylation in cancerous and adjacent non-cancerous tissue was determined ( $MLH1 \chi^2 = 4.6$ ;  $p = 0.031$ ), ( $MGMT \chi^2 = 17.9$ ;  $p < 0.0001$ ). No statistically significant relationship between the expressions of methylation of DAPK was found ( $\chi^2 = 2.28$ ;  $p = 0.131$ ).

**Conclusion:** A strong relationship between the expressions of gene methylation in cancerous and adjacent non-cancerous tissue was determined (MLH1, MGMT). No statistically significant relationship between the expressions of methylation of gene DAPK was found.

## Oesophageal Cancer

#### 06 SCIENTIFIC POSTER ABSTRACT Postoperative chemotherapy and disease-free survival in esophageal and gastric adenocarcinoma

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**Goals:** Perioperative chemotherapy is used in the management of esophageal and gastric adenocarcinoma. Randomized studies have shown that it improves disease-free and overall survival in comparison with surgery alone. However, because of toxicity, inconvenience, or surgical complications, many patients do not receive the postoperative part of treatment. We have previously reported the efficacy and safety data of a phase II trial of docetaxel/cisplatin/5-FU perioperative chemotherapy. The current study specifically examines the impact of postoperative chemotherapy on disease-free survival.

**Methods:** From May 2007 to September 2009, we enrolled 43 patients with operable adenocarcinoma of the esophagus or stomach on a phase II clinical trial. Patients were to receive 3 cycles of chemotherapy (docetaxel/cisplatin/5-FU) before and after surgical resection. We performed a retrospective analysis to compare disease-free survivals between Group A (at least 1 postop cycle given) and Group B (no postop chemotherapy given). The log-rank test was used for univariate analysis, and the Cox regression model for multivariate analysis. P value is double sided. Median follow-up is 808 days, disease-free survival calculated from time of surgery.

**Results:** Surgery was not performed in 2 subjects (disease progression in one, and withdrawal of consent, for the other). One patient was excluded from analysis as her tumor was a neuroendocrine tumor. Grade 3/4 toxicity was observed in 47% of patients before surgery. Of 40 patients, 29 received postoperative chemotherapy (3 cycles/2 cycles/1 cycle: 24/26/29), and 11 did not (personal preference 4, postoperative complications 2, other reasons 5). Only 56% of study subjects completed the 6 cycles of chemotherapy planned in the protocol. After a median follow-up of 808 days, the median survival of patients in Group B is 455 days, while it has not been reached in Group A ( $p = 0.076$ ). Similar results were found by multivariate analysis, after adjustment for radiological, pathologic and metabolic response to preoperative chemotherapy.

**Conclusion:** Previous episodes of severe toxicity and occurrence of surgical complications probably contribute to relatively low rates of chemotherapy completion in the postoperative period. The small number of patients in this trial and a retrospective analysis do not allow us to draw definitive conclusions about the impact of postoperative chemotherapy on the risk of recurrence in patients with esophageal and gastric adenocarcinoma treated with a perioperative chemotherapy protocol. However, our results show a strong trend in improvement of disease-free survival in favor of postoperative chemotherapy, suggesting that, outside of a clinical trial, this part of therapy should not be discarded.

## Colorectal Cancer

#### 07 SCIENTIFIC POSTER ABSTRACT Serum tryptase as a new biomarker in colorectal cancer patients

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**Goals:** Data from experimental tumour models suggest that mast cells (MCs) accumulate near tumour cells before the onset of angiogenesis and that they are required for the macroscopic expansion and metastatic spread of primary tumour cells. Tryptase is a serin protease stored in mast cell granules that plays a role in tumour angiogenesis. Mast cells (MCs) can release tryptase following c-Kit receptor activation. On the other hand colo-rectal cancer (CRC) is a well-established angiogenesis dependent tumour and anti-angiogenic based therapy is a standard treatment in metastatic CRC. This preliminary study aims to assess tryptase serum levels in 54 CRC patients before and after radical surgery resection.

**Methods:** In this study patients with stage B and C CRC (according to Astler and Coller staging system) were selected. Samples of blood were taken from CRC patients between 7 and 9 a.m. 1 day before and 1 day after

tumour surgical resection. Venous blood was dispensed into a tube for serum (Becton Dickinson Hemogard Vacutainer Systems, Plymouth, UK). Serum blood samples were centrifuged at 1,500g for 10 minutes and then aliquoted and frozen at  $-80^{\circ}\text{C}$ . Trypsase levels were measured using the UniCAP Trypsase Fluoroenzymeimmunoassay (Pharmacia, Uppsala, Sweden).

**Results:** Mean  $\pm$  s.d. trypsin level pre-tumour surgical resection was  $6.38 \pm 4.49 \mu\text{g/L}$ , and mean  $\pm$  s.d. trypsin level post tumour surgical resection was  $5.11 \pm 3.81 \mu\text{g/L}$ . A statistically significant difference between pre-tumour surgical resection and post-tumour surgical resection trypsin level concentrations was found:  $p=0.000$  by t-test. No correlation among trypsin levels and other important clinical-pathological features of patients were found.

**Conclusion:** This is the first report that analyzes the possible significance of serum trypsin levels changes in CRC patients who underwent radical surgical resection. Trypsin is one of the most powerful angiogenic mediators released by mast cells and it may be angiogenic via several mechanisms. On the other hand CRC is a well established angiogenesis dependent tumour. Our results demonstrated higher serum trypsin levels CRC patients suggesting the release of trypsin from CRC tissue. As expected, after radical surgical resection, serum trypsin levels had decreased. We suggest that trypsin may play a role as a new circulating biomarker of response to radical surgery in CRC patients.

#### 08 SCIENTIFIC POSTER ABSTRACT Colorectal cancer in elderly patients: A single-center experience

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**Goals:** As more people live longer, the incidence of cancer in elderly patients (pts) is expected to rise. The cancer treatment is beneficial for elderly pts in adjuvant and palliative setting. However, elderly pts with cancer have been underrepresented in clinical trials and there is little literature on this pts group. Our goal is to present our own experience in the treatment of elderly pts with colorectal cancer (CRC).

**Methods:** Since January 2005, all pts  $\geq 75$  years with new diagnosed CRC were enrolled and evaluated. Patients were followed for progression free survival (PFS) and overall survival (OS).

**Results:** 28 pts  $>75$  years (range 75–84) with a diagnosis of CRC stage I–IV were recorded till May 2010. 17 (60.7%) and 11 (39.2%) out of these pts were men and women. Stage II has been diagnosed in 12 pts (42.8%), stage III in 7 pts (25%) and stage IV in 9 pts (32%). 28.5% (8 pts) had a tumor located in the rectum and 71.4% (20 pts) had colon cancer. All pts (100%) had chemotherapy as adjuvant (67.8%) or palliative settings (32.1%).

**Conclusion:** Although elderly pts often have comorbidities and poor performance status, age alone should not determine treatment options and person's eligibility the treatment.

#### 09 SCIENTIFIC POSTER ABSTRACT The intra-tumor stroma microenvironment as a strong prognosticator for colon cancer

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**Goals:** There is need to identify patients who benefit from additional treatment. Adjuvant chemotherapy after resection for primary colon cancer reduces the risk of death by approx. 5% in stage II colon cancer and about 15–20% in stage III. Adjuvant treatment has to be evaluated for each stage separately also taking into account tumor features. We previously have found that the stroma-tissue surrounding the cancer cells plays an important role in the tumor behavior and has been reported as a strong independent prognostic parameter. Patients with a high stroma percentage within the primary tumor have a poorer prognosis. Validation of this parameter was proven for stage II and III colon cancer and has also been tested in a cohort of patients from the VICTOR trial. Furthermore we found the stroma percentage within the lymph nodes as a factor for further refinement of patient-outcome.

**Methods:** Tissue samples from patients participating in the VICTOR trial were analyzed for their tumor-stroma percentage, consisting of 5  $\mu\text{m}$  Haematoxylin and Eosin (H&E) stained sections from the most invasive part of the primary tumor. Stroma-high ( $>50\%$  stroma) and stroma-low ( $\leq 50\%$  stroma) groups were evaluated with respect to survival time. Lymph nodes from stage III patients were analyzed for their stroma percentage.

**Results:** Our earlier results were validated in the VICTOR trial (OS  $p < 0.0001$ , HR = 1.96; DFS  $p < 0.0001$ , HR = 2.15) (5-year OS 69.0% vs 83.4% and DFS 58.6% vs 77.3%) for stroma-high versus stroma-low patients, with stroma-high patients having a worse prognosis. The stroma percentage evaluated in lymph

nodes can identify colon stage III patients with good prognosis who might not need adjuvant chemotherapy.

**Conclusion:** This study confirms the intra-tumor stroma ratio as a prognostic factor of colon cancer in an independent patient series. Patients with a high intra-tumor stroma percentage have a poorer prognosis. Further refinement for stage III patients can be performed analyzing stroma formation in the lymph nodes. This parameter could be a valuable and low cost addition to current high-risk parameters such as TNM-status and MSI status used in routine pathology reporting.

#### 10 SCIENTIFIC POSTER ABSTRACT Capecitabine based adjuvant therapy for stage III colon cancer – single institution experience

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**Goals:** There is a general consensus that adjuvant treatment prolongs survival in patients with stage III colon cancer and it is accepted as standard of care for this stage. Different regimens of 5 fluorouracil (5 FU) with leucovorin (LV) were utilized. Oral fluoropyrimidine, capecitabine is an effective alternative to intravenous 5-FU/LV, which has been the foundation of adjuvant treatment for patients with colon stage III cancer for 40 years. Combination of oxaliplatin and capecitabine was shown to be superior to bolus 5 FU/LV in terms of disease free survival as adjuvant therapy for stage III colon cancer. The aim of this retrospective, single institution study was to report the safety results comparing combination regimen of oxaliplatin plus capecitabine with capecitabine as monotherapy used in the adjuvant setting for stage III colon carcinoma.

**Methods:** 42 consecutively treated patients with histologically confirmed stage III colon carcinoma received postoperative adjuvant therapy with oxaliplatin plus capecitabine (XELOX regimen) or capecitabine monotherapy. XELOX regimen consisted of oxaliplatin 130  $\text{mg/m}^2$  on day 1 and capecitabine 1000  $\text{mg/m}^2$  twice daily for 14 days. Therapy with capecitabine was given according to the standard schedule (1250  $\text{mg/m}^2$  twice daily for 14 days). Both regimens were repeated every 3 weeks for 8 cycles.

**Results:** 23 patients (pts) received therapy with capecitabine and 19 pts received oxaliplatin plus capecitabine. Most treatment related adverse events (AEs) in both groups were grade I–II. Grade III AEs manifested as hand foot syndrome and diarrhoea occurred in 3 pts (13%) in monotherapy group and in 4 (21%) pts receiving XELOX regimen who had diarrhoea, nausea and vomiting, and pharyngo-laryngeal dysesthesia. As expected pts who were treated with XELOX regimen showed neurosensory toxicity and higher rate of hematologic toxicity. Diarrhoea and hand foot syndrome as capecitabine-related toxicity occurred at similar rates in both treatment groups. Dose reduction was necessary in 10 patients (52.6%) receiving XELOX and in 4 (17.4%) of patients treated with capecitabine. Median dose intensity of oxaliplatin was 89.4%. Median dose intensity of capecitabine was 89.1% in XELOX compared with 93.4% for monotherapy treatment. After a median follow-up period of 23 months, disease relapse was diagnosed in 3 pts (13%) treated with capecitabine and in 2 pts (10.5%) who received XELOX. At the time of analysis one pts from the capecitabine monotherapy group has died.

**Conclusion:** There were no major differences in the safety profile due to addition of oxaliplatin to capecitabine. Considering the superiority of regimens with oxaliplatin in the adjuvant treatment of colon carcinoma and the advances of oral treatment with capecitabine, XELOX regimen is convenient treatment option for patients with stage III disease.

#### 11 SCIENTIFIC POSTER ABSTRACT Use of IHC and DISH of EGFR to evaluate efficacy of anti-EGFR drugs in KRAS-WT patients with mCRC

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**Goals:** KRAS mutation status is a strong predictive factor for anti-EGFR monoclonal drugs in metastatic colorectal cancer (mCRC). In the BOND trial, objective response rates of cetuximab in irinotecan-refractory mCRC were not significantly different based on the intensity of EGFR staining by immunohistochemistry (IHC). However KRAS mutation status was not evaluated in this trial. We evaluated the efficacy of anti-EGFR drugs by combined use of IHC and dual color in situ hybridization (DISH) of EGFR in KRAS-WT patients with mCRC.

**Methods:** Between August 2008 and July 2011, We analyzed 120 patients who received chemotherapy containing anti-EGFR drugs retrospectively. Eligible criteria were as follows: Adenocarcinoma, KRAS-WT, at least 1 previous regimen of the fluoropyrimidine-containing standard chemotherapy, ECOG PS score 0–2.

**Results:** 94 of 120 patients received chemotherapy containing cetuximab. 18 patients (19%) with strong intensity (IHC 3+) of EGFR staining by IHC had better response rate (38.8% vs. 21.1%) and significant improvement of