Conclusions: Yttrium-90 radioembolisation for chemo-refractory colorectal liver metastases has an acceptable safety profile with a 50% estimated survival after 8.0 months. Pretreatment high bilirubin, alkaline phosphatase and tumour volume levels are associated with early death.

O03

Inhibition of Epithelial-Mesenchymal Transition (EMT): Treatment Option for Advanced Pancreatic Cancer

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Introduction: Epithelial-Mesenchymal Transition (EMT) has been shown to contribute significantly for the aggressiveness and chemo-resistance of several GI-cancers, including pancreatic cancer. The tumor microenvironment plays an important role in inducing EMT in tumor cells.

Aim: In the present study, we examined whether hypoxia and/or TGF-β1 can induce EMT in human PANC-1 cells and whether HIF inhibitor drugs can inhibit or reverse this EMT process.

Methods: PANC-1 cells were cultured under normoxic or hypoxic conditions (2% O2) for 48 hrs in the presence of TGF-β1 to induce EMT. To study EMT inhibition, cells were treated with a combination of hypoxia and/or TGF-β1 and different concentrations of 3 different HIF inhibitor drugs. Changes in cell morphology were captured using an inverted phase-contract microscope equipped with a digital camera. The expression of markers related to EMT was measured by quantitative PCR and Western blot analysis. Cell mobility was assessed using wound healing and invasion assay. Promoter region methylation status of the EMT related markers was tested by methylation-sensitive high-resolution melting (MS-HRM).

Results: We found that the morphology of the cells changed to spindle type and the number of cell-cell contacts was reduced in PANC-1 cell exposed to hypoxia and/or TGF-β1. Hypoxia alone had no significant effect on gene or protein expression of the EMT markers we investigated. qRT-PCR analysis showed, for TGF-β1 and TGF-β1 + hypoxia stimulated PANC-1 cells, that SPARC and the epithelial marker E-cadherin were downregulated and that SPOCK1, the transcription factor SNAI1 and the mesenchymal marker Vimentin were upregulated. Concomitantly, at the protein level E-cadherin expression was dowregulated and SNAI1 expression was upregulated. There was no noticeable change in VIM expression. Two HIF inhibitors could reverse the EMT in a dose dependent manner that we are now investigating in detail. We found that neither TGF-β1, hypoxia or HIF inhibitor drug treatment had effect on the promoter methylation signature of the EMT related markers under study.

Conclusions: These results show that we have developed an in vitro model for EMT. Using this model we are now studying in detail the molecular pathways involved in EMT induction and of its inhibition with the aim of identifying novel therapeutic strategies for advanced pancreatic cancer. *) A.B. is a recipient of a bursary from the Interfaculty Council for Development Co-operation (IRO, KUL).

O04

Lymph node ratio and surgical quality are strong prognostic factor of rectal cancer: results from a referral single-centre experience

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Introduction: Different prognostic factors of oncological outcome after rectal cancer treatment have been described. Circumferential resection margin and total mesorectal excision quality have been in the foreground but both tumour staging and particularly the nodal stage remain the mainstay. In order to compensate for the variation in total number of harvested node, lymph node ratio (LNR), adjusting the number of positive to the total number of nodes, has been advocated.

Aim: To assess the impact of LNR, compared to other predicting factors of rectal cancer outcome, particularly TME quality and circumferential resection margin, on the long-term oncological outcomes.

Methods: In the setting of a tertiary referral centre, consecutive patients operated for non-metastatic rectal cancer were extracted from a prospectively maintained database. A retrospective uni- and multivariable analysis was performed based on patient-, surgical- and tumour-related factors.

Results: Over the period between 1998 and 2013, 456 patients were operated for rectal adenocarcinoma. Patients with synchronous metastatic disease (n=99, 21.7%) were excluded, leaving 357 patients in this analysis. Overall, neoadjuvant radio(chemo)therapy was administered to 66.7% of the patients. A sphincter saving operation (SSO) was performed in 78.2% of the patients. The anastomotic fistula rate was 6.8% and there were two post-operative deaths (0.6%). The mean number of lymph nodes removed was 12.8 ± 8.78 per specimen and the mean number of positive nodes was 0.8 ± 1.97. The mean LNR was 0.74 ± 0.16. A lower lymph node yield was reached in patients who received neoadjuvant chemoradiotherapy (11.8 vs. 14.2, p = 0.014). On multivariable analysis age, surgical approach, TME quality, and the administration of chemoradiotherapy were independently associated with the total number of lymph nodes retrieved. The overall 5-year recurrence-free survival (ORFS) was 71.8% and the 5-year overall survival (OS) was 80.1%. Multivariable

analysis confirmed LNR, TME quality, absence of symptoms, peri-neural infiltration and age as independent prognostic factors of OS. LNR and extramural vascular infiltration were independently associated to ORFS. LNR reached the highest hazard ratios in both models. **Conclusions:** In our experience, LNR is the most prominent prognostic factor of OS and OR. The only "controllable variable" was the surgical quality, which is in line with the principles of optimal surgical management.

O05

Waist hip ratio better predicts oncological quality of resection and outcome after colon cancer surgery than body mass index

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