P-149 Integrative analysis of the genomic and transcriptomic landscape identifies novel key genes as a therapeutic target in bile duct cancer

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Background: Bile duct cancer (BDC) is a malignancy thought to be derived from cholangiocytes, the epithelial cells lining the biliary tree. BDC is a highly aggressive tumour whose incidence has been increasing worldwide over the past two decades, now accounting for 10–15% of all hepato-biliary malignancies. Advanced BDC has a devastating prognosis, with a median survival of less than 24 months. The mechanisms underlying cholangiocyte malignant transformation and BDC progression is still not completely understood. Genomic profiling can offer a clearer understanding of their carcinogenesis, classification and treatment strategy. We performed large-scale genome sequencing analyses on BTCs to identify novel key-genes driving BDC and drug resistance. The long-term goals of this program are to understand the pathogenesis of BDC and develop new therapies for its treatment.

Methods: We analyzed 100 BTC (Age: 50% >65y; Sex: 40% M, 60% F; Type: 30% iCCA, 30% dCCA; TNM: 11% I, 40% II, 43% III, 7% IV) samples from Modena Cohort, 40 by whole-exome sequencing (WES), 80 by RNA sequencing (RNAseq), and a further 30 samples by SmallRNA sequencing. We identified somatic alterations, transcriptomic and epigenetic profiles of tumours and stromal area of each sample, and searched for driver genes in BTCs. By using a bio-informatic pipeline, we integrated somatic mutation patterns and epigenetic features defined at the spatial level to identify novel target genes in the tumour microenvironment. Functional studies in 2D and 3D culturing models were conducted to investigate candidate genes linked to BDC progression.

Results: A total of 3392 and 6315 DEGs (Differentially expressed genes) were respectively observed in BDC comparing tumour (T), normal (N) and stromal (ST) areas with the criterion of false discovery rate < 0.05. In top-ranked differentially regulated gene sets, we identified primary cilium-associated genes (PC). OFD1, CNGB1, AURKA, CENPF, STIL, STK39, RAB23 and OSR1 were found based on the criteria of fold change > 2.5 and $P < 0.01$. We started also to clarify at molecular level the role of PC in BDC pathogenesis and progression. A therapeutic approach targeting OFD1 in BDC cells was also investigated.

Conclusions: We performed large-scale genome sequencing analysis of 100 BTC samples from Italian populations. Among top-ranked dis-regulated gene sets we identified ciliary-associated genes. Loss of PC is frequently observed in BDC, suggesting that the absence of this organelle may promote tumorigenesis through aberrant signal transduction and the inability to exit the cell cycle. We investigated the molecular mechanisms underlying the cilia loss and test whether may be potential therapeutic target. These findings could be useful to establish treatment and diagnostic strategies for BTCs based on genetic information. The proposed research is relevant to public health because understanding and manipulating asymmetric ciliary signaling in cancer cells and cells of the tumour microenvironment can potentially improve understanding of cancer pathogenesis, and application of anti-cancer therapies.

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P-150 Insights into the gastric and oesophageal cancer patient experience: Results of a pan-European patient survey

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Background: Oesophageal and gastric cancers result in approximately 186 000 new cases and 170 000 deaths per year in Europe. Both of these cancer types cause considerable difficulties to patients; however, information and support that available for patients with oesophageal and gastric cancers and their caregivers is scarce. The aim of this study was to gain insight on areas that can be improved in Europe in terms of care and support for patients with oesophageal or gastric cancer. For this, we have conducted a survey to capture the patient experience throughout all phases of the patient pathway.

Methods: Patients with either gastric or oesophageal cancer living in Europe were eligible to participate. Patients completed the survey either online or through a paper version given to them by their healthcare team. Taking part in the survey implied that participants consented to it. The survey responses were anonymised, and no patient organisation or clinicians received monetary compensation to promote and/or conduct the survey. The survey run from January 2018–December 2020; it was produced in English and translated into 11 languages.

Results: In total, 544 respondents (272 men and 254 women) from 16 European countries participated in the survey. Participants were divided into six groups from Italy (n=117), Latvia (n=87), Poland (n=103), Spain (n=119), the United Kingdom (n=69) and "other European countries" (n=49). The majority of participants (55%) were 51–70 years old. Most of the participants were patients with gastric cancer (68%); 22% had oesophageal cancer, while 10% did not specify. The three most frequent symptoms patients experienced prior to diagnosis were indigestion/gastric discomfort, gastric pain and trouble swallowing. Although 59% of respondents were very satisfied or quite satisfied with the time it took to receive a cancer diagnosis, 36% were not very satisfied with this time. Importantly, 14% of patients were very dissatisfied with the time to diagnosis. In addition, 41% of respondents were initially misdiagnosed with another condition such as irritable bowel syndrome, bloating, jaundice or excessive fatigue. Approximately 40% of patients responded that either their treatment was not discussed by a multidisciplinary team or they were not aware if this discussion took place. Overall, the three most demanded areas for improvement patients called out for were the presence of a nutritionist/dietitian (58%), the presence of a psychologist (45%) and talking to other patients (42%). When asked if their family members had received adequate emotional support, 35% strongly disagreed, while only 8% of respondents strongly agreed with this statement.

Conclusions: Our survey reveals some important gaps in the gastric/oesophageal patient journey that call for more prompt and accurate diagnosis; better communication between the patient and the multidisciplinary team; and an expansion in the support services to include key elements that are overlooked in the patient journey such as nutritional support for patients and emotional support – for both patients and caregivers. A collaborative approach between different stakeholders, including health professionals and patient organisations, helps in recognising areas of improvement and providing additional needed support.

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P-151 The prognostic value of TCF1+CD8+T cell in primary small cell carcinoma of the esophagus

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Background: TCF1+CD8+T cells are reported to exhibit stem-like properties with the ability to self-renew and differentiate into terminal effector T cells (TCF1-CD8+T cells) to enhance anti-tumor response. Previous studies indicated that TCF1+CD8+TILs are related to response to immunotherapy. However, their role in predicting prognosis remains unclear. Here, we investigated the prognostic value of TCF1+CD8+T cells in patients with primary small cell carcinoma of the esophagus (PSCCE).

Methods: The tumor tissues from 79 patients with PSCCE were analyzed by multiple immunofluorescence staining. The optimal cut-off value and corresponding sensitivities and specificities were determined by time-dependent receiver-operating characteristic (ROC) curves. The percentage of indicators in all tumor cells were used to define expression levels. The Kaplan–Meier method and Cox proportional hazards model were used to analyze survival distributions.

Results: High TCF1+CD8+T cells infiltration has longer OS than low infiltration (31 vs 17 months, p=0.009, HR=0.506). TCF1+CD8/ CD8 ratio > 21% showed superior OS than ≤21% (31 vs 16 months, $p < 0.001$, HR=0.394). In patients with high CD8+T infiltration, high ratio shows better OS (32 vs 19 months, P=0.042, HR=0.511).

Conclusions: We identified intratumoral stem-like T cells (TCF1+CD8+T) abundance in PSCCE. High infiltration of TCF1+CD8+T cell is related to better clinical outcomes. TCF1+CD8/CD8 ratio is a strong and independent prognostic predictor.

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