

PG 2.03**SPEAKER ABSTRACT****Lessons from PETACC3 in adjuvant treatment of colorectal cancer: today's impact**

A. Roth, *Hug, Oncosurgery Unit, Geneva, Switzerland*

TNM staging remains so far the only validated tool to determine which patient might benefit from adjuvant systemic therapy. Prognostic markers allowing to better select which patient operated on from colon cancer could benefit from additional treatment are still missing. The clinical trial in post-operative treatment of colon cancer PETACC 3 enrolled 3,278 patients and collected the pathological material of 1564 of them for the study of new molecular prognostic factors. In addition to the ability to validate some already known potential prognostic molecular markers, we performed new tests to insulate mutations of the genome of the tumor and to study their genomic expression. The integration of some of these markers into the TNM staging suggests that we might be able to define new subpopulations of patients with distinct prognosis which still need to be validated in independent cohorts of patients. The implications of these results in the light of other published gene expression signatures aimed at improving prognosis prediction of stage II and III colorectal cancer to better select patients more likely to benefit from adjuvant systemic therapy shall be discussed.

PG 2.04**SPEAKER ABSTRACT****Systemic treatment of CRC: Molecular profiles ready for clinical practice?**

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Colorectal cancer is very heterogeneous disease, possibly even different diseases hitting the same organ. This has huge implications for clinical practice and the development of anti cancer drugs in this disease. Only two biomarkers for colorectal cancer are currently sufficiently validated for the clinic. Efforts to find genetic patterns that distinguish between tumours with good or poor prognosis or between patients who do or don't responder to various therapies are proceeding slowly but steadily. We will discuss various approaches, using cell lines, mouse models, patient tumors, that can provide key information. Key examples will be discussed, such as the identification of response signatures to EGFR inhibitors in colon cancer, or understanding the role of oncogenic BRAF in this disease, to highlight both gains and gaps in our knowledge. We will also discuss how lack of knowledge hampers current drug development and the challenges faced by both pharma and academia in developing successful trials, balancing biomarker identification and validation in this disease.

Thursday, 22 March, 12:00–12:30

Keynote Lecture I**PG 3.01****SPEAKER ABSTRACT****Cancer stem cells: the new target**

R. Fodde, *Pathology, Erasmus MC, CA Rotterdam, Netherlands*

Cancer stem cells (CSCs) represent a subpopulation of tumour cells endowed with self-renewal and multi-lineage differentiation capacity but also with an innate resistance to cytotoxic agents, a feature likely to pose major clinical challenges towards the complete eradication of minimal residual disease in cancer patients. Operationally, CSCs are defined by their tumour-propagating ability when serially transplanted into immune-compromised mice and by their capacity to fully recapitulate the original heterogeneity of cell types observed in the primary lesions they are derived from. CSCs were first identified in hematopoietic malignancies and later in a broad spectrum of solid tumours including those of the breast, colon and brain. Notably, several CSCs' characteristics are relevant to metastasis, such as motility, invasiveness and, as mentioned above, resistance to DNA damage-induced apoptosis. Here, the relation between colon CSCs and metastasis formation will be discussed. Preliminary studies on cancer cell lines and patient-derived material suggest a rate-limiting role for stem-like cells in the processes of tumour cell dissemination and metastasis formation. However, additional studies are needed to deliver formal proof of their identity as cell of origin of recurrences at distant organ sites. Nevertheless, several studies have already provided pre-clinical evidence of the efficacy of novel therapies directed against disseminated CSCs.

Reference(s)

- Sampieri K, Fodde R. Cancer stem cells and metastasis. *Seminars in Cancer Biology*. 2012 in press.
 Roth S, Fodde R. Quiescent stem cells in intestinal homeostasis and cancer. *Cell Commun Adhes*. 2011;18:33–44.
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Fodde R, Brabletz T. Wnt/beta-catenin signaling in cancer stemness and malignant behavior. *Curr Opin Cell Biol*. 2007;19:150–8.

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Thursday, 22 March, 14:00–15:30

Session III. Improving Treatment of Pancreatic Cancer**PG 4.01****SPEAKER ABSTRACT****Neoadjuvant approaches to pancreatic cancer**

M. Lesurtel¹, B. Pestalozzi², P. Clavien¹. ¹*Visceral & Transplantation Surgery, University Hospital of Zurich, Zurich, Switzerland*, ²*Oncology, University Hospital Zurich, Zurich, Switzerland*

Despite major improvements in the perioperative outcome of pancreas surgery, the prognosis of pancreatic cancer after curative resection remains poor. Adjuvant chemotherapy increases disease-free and overall survival, but this treatment cannot be offered to 20% to 40% of patients due to the surgical morbidity. In contrast, neoadjuvant therapy has a substantial impact in several gastro-intestinal malignancies and has many theoretical advantages over adjuvant treatment in patients with pancreatic cancer. Neoadjuvant treatment has been proposed to have greater benefits on well oxygenated, non-devascularized tissue, with improved delivery of chemotherapeutic agents. It may be better tolerated, allowing for greater completion rates and may also reduce any delay in therapy, and could potentially downstage unresectable tumors. However, no phase III trials are available examining this approach in pancreatic cancer. Only prospective phase II trials using neoadjuvant treatment (chemotherapy or radio-chemotherapy) for resectable, borderline resectable and unresectable pancreatic cancer are available. Based on these studies, neoadjuvant treatment seems to have some activity in patients with borderline/unresectable pancreatic cancer. Nearly one third of tumors initially deemed marginal for operative intervention could be resected after treatment. In case of initially resectable pancreatic tumors, it is not clear whether patients may benefit from neoadjuvant therapy. In a recent phase II trial we have shown that neoadjuvant Gemcitabine-Oxaliplatin is safe and effective, and has resulted in a median survival of 26.5 months. Moreover, it improved the nutritional status of patients with pancreatic cancer. We have therefore initiated a multicenter prospective randomized phase III trial (NEOPAC) to explore the efficacy of neoadjuvant chemotherapy in patients with pancreatic cancer. Patients with resectable, cytologically proven, adenocarcinoma of the pancreatic head are eligible for this study. An infiltration of the superior mesenteric vein >180° or major visceral arteries are considered exclusion criteria. Eligible patients are randomized to surgery followed by adjuvant gemcitabine (1000 mg/m²) for 6 months or neoadjuvant chemotherapy followed by surgery and the same adjuvant treatment. Neoadjuvant chemotherapy (gemcitabine 1000 mg/m², oxaliplatin 100 mg/m²) is given four times every two weeks. The staging as well as the restaging protocol after neoadjuvant chemotherapy includes computed tomography (or PET-CT if available) of chest and abdomen and diagnostic laparoscopy. The primary study endpoint is progression-free survival. According to the sample size calculation, 155 patients need to be randomized to each treatment arm. Disease recurrence will be documented by scheduled computed tomography scans 9, 12, 15, 21 and thereafter every 6 months until disease progression. For quality control, circumferential resection margins are marked intraoperatively, and representative histological sections will be centrally reviewed by a dedicated pathologist. The NEOPAC study will determine the efficacy of neoadjuvant chemotherapy in pancreatic cancer for the first time and offers a unique potential for translational research. Furthermore, this trial will provide the unbiased overall survival of all patients undergoing surgery for resectable cancer of the pancreatic head (clinicalTrials.gov NCT01314027).

Reference(s)

- Heinrich S, Pestalozzi B, Lesurtel M, Berrevoet F, Laurent, Delpero JR et al. Adjuvant gemcitabine versus NEOadjuvant gemcitabine/oxaliplatin plus adjuvant gemcitabine in resectable pancreatic cancer: a randomized multicenter phase III study (NEOPAC study). *BMC Cancer*. 2011, 10(11):346.

PG 4.02**SPEAKER ABSTRACT****Pancreatic surgery: Beyond the traditional limits**

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Pancreatic cancer is the fourth leading cause of death in male and female in the western world. Pancreatic surgery with complete resection of the tumor is the only curative approach for pancreatic cancer at this time. In more than 85% pancreatic tumors are of ductal origin but cystic tumors such as