SS07-02

## POSTOPERATIVE CTDNA IS ASSOCIATED WITH OUTCOMES AFTER CURATIVE-INTENT HEPATECTOMY: RESULTS FROM THE INTERCEPT PROGRAM

B. C. Fields[1], A. Haddad[1], Y. Wang[1], E. M. Arvide[1], D. E. Mrema[1], K. D. Alfaro-Munoz[2], R. J. Kell[2], V. K. Morris[2], A. N. Dasari[2], T. Konishi[3], Y. S. Chin[1], H. S. Tran Cao[1], C. -W. D. Tzeng[1], S. W. Kopetz[2], J. -N. Vauthey[1] and T. E. Newhook[1]

*[1]The University of Texas MD Anderson Cancer Center, Surgical Oncology, Houston, United States, [2]The University of Texas MD Anderson Cancer Center, GI Medical Oncology, Houston, United States, and [3]The University of Texas MD Anderson Cancer Center, Colon & Rectal Surgery, Houston, United States*

**Introduction:** Circulating tumor DNA (ctDNA) is a dynamic biomarker associated with minimal residual disease (MRD) and colorectal cancer-associated outcomes. We evaluated the impact of ctDNA detection after curative-intent hepatectomy for colorectal liver metastases (CLM) within a ctDNA surveillance initiative at a comprehensive cancer center.

**Method:** INTERCEPT is a prospective initiative to integrate plasma ctDNA testing into post-treatment colorectal cancer surveillance. ctDNA results were paired with clinicopathologic data from a prospective institutional database for CLM patients who underwent curative-intent hepatectomy+/-completion ablation from 12/2022-06/2024. MRD was defined as no suspicious or confirmed metastases on imaging in the setting of ctDNA positivity (ctDNA+; any detectable value ≤90 days of hepatectomy/ablation).

**Results:** 133 patients had available 90-day postoperative ctDNA results. 84% (111/133) received preoperative chemotherapy (median 4 [IQR 4-6]cycles). Surgical approach was primary-first in 87% (116/133), and combined primary/CLM resection in 13% (17/133); 4% (5/133) underwent completion ablation. Postoperatively, 23% (31/133) were ctDNA+, and 77%(102/133) were ctDNA-. A somatic mutation in ≥1 genes (*BRAF, KRAS, TP53, APC, PIK3C, SMAD4*) was identified in 92%(122/133). 36% (48/133) had a pathway-centric risk score of 3 (ctDNA+ 39%[12/31]; ctDNA- 35%[36/102]).

ctDNA+ was associated with a rectal primary (OR 5.6, 95%CI 1.8-17.8, p=0.004) and greatest CLM size ≥3cm (OR 4.3, 95%CI 1.6-11.4, p=0.004). Of ctDNA+ patients, 74%(23/31) had MRD for a median 60 (1-101)days until radiographic disease detection. 94%(29/31) of ctDNA+ patients received adjuvant therapy regardless of MRD status, and 63%(15/24) of patients with a follow-up test became ctDNA- with treatment after a median 3.6(3.0-5.3) months. Recurrence among ctDNA+ was 90%(28/31); 77%(24/31) had hepatic recurrence. The ctDNA- recurrence rate was 43%(44/102), with 80%(35/44) ≤1 year of hepatectomy. Compared to ctDNA- patients, ctDNA+ median recurrence-free survival (3.4 [2.3-4.6] months vs 21.3 [13.6-29.0], p<0.001) and hepatic disease-free survival (4.2 [1.1-7.2] months vs NR, p<0.001; respectively) were significantly lower (Fig 1).

**Conclusion:** Postoperative ctDNA testing for CLM is feasible and identifies patients with MRD and at risk of recurrence. Recurrence patterns are associated with postoperative ctDNA detection and may guide postoperative therapy and surveillance strategies.

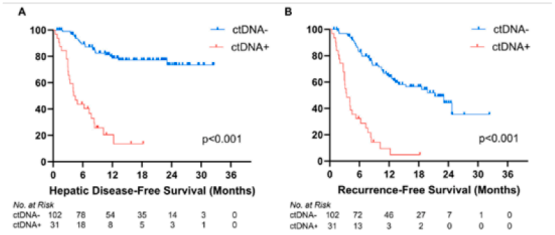


Figure 1 Kaplan-Meier survival analyses by postoperative ctDNA status within 90 days of curative-intent hepatectomy for colorectal liver metastases. **(A)** Hepatic disease-free survival and **(B)** recurrence-free survival. Log-rank *p*-values.

SS07-03

## SURGERY FOR CHRONIC PANCREATITIS ACROSS EUROPE (ESCOPA): PROSPECTIVE INTERNATIONAL MULTICENTER STUDY

C. Leseman[1,2], C. van Veldhuisen[1,2], M. Besselink[1,2], O. Belyaev[3], F. Berrevoet[4], S. Bouwense[5], K. Conlon[6], S. Dokmak[7], M. Falconi[8], A. Ibrahimli[9], J. Izbicki[10], A. Kokkola[11], S. Mieog[12], G. Nappo[13,14], H. Plaudis[15], G. Roeyen[16], C. van Eijck[17], H. van Santvoort[18,19], A. Waage[20] and Dutch Pancreatitis Study Group

*[1]Amsterdam UMC, Surgery, Amsterdam, Netherlands, [2]Amsterdam Gastroenterology Endocrinology Metabolism Amsterdam, NL, Amsterdam, Netherlands, [3]St. Josef-Hospital, University, Ruhr-Universität, Bochum, Germany, [4]University Hospital Ghent, Ghent, Belgium, [5]Maastricht UMC+, Maastricht, Netherlands, [6]Trinity College Dublin, Dublin, Ireland, [7]Hopital Beaujon, Paris, France, [8]San Raffaele Hospital, Milan, Italy, [9]Liv Bona Dea Hospital, Baku, Azerbaijan, [10]University Hospital Hamburg Eppendorf, Hamburg, Germany, [11]Helsinki University Hospital and University of Helsinki, Helsinki, Finland, [12]Leiden University Medical Center, Leiden, Netherlands, [13]Humanitas University, Milan, Italy, [14]Humanitas Clinical and Research Center, Milan, Italy, [15]Riga East Clinical University Hospital, Riga, Latvia, [16]Antwerp University Hospital and University of Antwerp, Antwerp, Belgium, [17]Erasmus MC Cancer Institute, Rotterdam, Netherlands, [18]St Antonius Hospital, Nieuwegein, Netherlands, [19]University Medical Center Utrecht, Utrechtnet, Netherlands, and [20]Oslo University Hospital, Rikshospitalet, Oslo, Norway*

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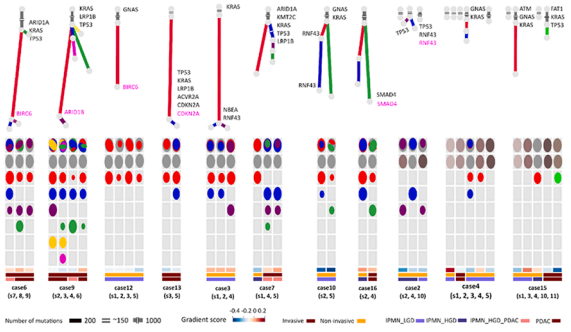
**Background:** Although randomized trials have shown the superiority of surgery over endoscopy for symptomatic chronic pancreatitis (CP), most patients are only referred for surgery as 'last resort'. Therefore, large international studies quantifying the impact of surgery for CP are needed but such studies are lacking. This study aimed to evaluate the use and outcome of surgery for CP across Europe.
**Method:** In this prospective multicentre study, consecutive patients undergoing surgery for symptomatic CP were included from 22 centres in 13 countries (June 2021 - November 2022). The primary endpoint in patients with pain as indication was Izbicki pain score at 6 months, with 'complete pain relief' defined as Izbicki score $\leq$10 and 'partial pain relief' as >10 but a >50% reduction from baseline. Quality of life was assessed using PANQOLI and SF-12 surveys. Predictors of complete pain relief were analyzed using multivariable analysis.
**Results:** Overall, 207 patients underwent surgery for symptomatic CP: 51 drainage procedures (24.6%), 61 duodenum-preserving head resections (29.5%), and 95 formal pancreatic resections (45.9%). Preoperatively, 48.8% (n=101) used opioids and 51.2% (n=106) had endoscopic treatment. Postoperatively, major morbidity occurred in 14% (n=29) and 90-day mortality in 1.4% (n=3). Among 113 patients operated for pain, the median Izbicki score decreased from 61.3 (IQR 49.1-84.9) at baseline to 19.0 (IQR 0.0-33.5) at 6 months ($p<0.001$). Pain relief was achieved in 72.6% (n=82) of patients (43 complete, 39 partial), with 90.3% reporting reduced pain. Both the PANQOLI and SF-12 PCS scores improved ($p<0.001$). A multivariable analysis showed that longer duration of symptoms (OR 0.947 [0.897-1.000], p = 0.045) and 'opioids prior to surgery' (OR 3.161 [1.036-9.643], p = 0.043) were associated with less pain relief after 6 months.
**Conclusion:** This prospective pan-European study found low morbidity and mortality rates, good pain relief, and improved quality of life following surgery for chronic pancreatitis and confirmed the need for earlier patient referral.

## SS07-04
## CLONAL EVOLUTIONARY ANALYSIS REVEALS PATTERNS OF MALIGNANT TRANSFORMATION OF INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS (IPMN) OF THE PANCREAS

A. Pea[1,2]
[1]*University of Verona, Verona, Italy, and* [2]*University of Glasgow, Glasgow, United Kingdom*

**Introduction:** Intraductal papillary mucinous neoplasms (IPMNs) are precursors to pancreatic ductal adenocarcinoma (PDAC), a lethal cancer due to late detection and rapid progression. Previous exome and target sequencing studies have shown distinct mutations in the same genes, suggesting independent evolutionary pathways within the same lesion. This study aims to perform a comprehensive whole-genome, including copy number (CNVs) and structural (SVs) variants, and transcriptomic analysis of IPMNs to understand the molecular evolutionary patterns that underlie IPMN heterogeneity and progressions to invasive carcinoma.
**Design:** We conducted multi-region whole-genome and -transcriptome sequencing on multiple samples from 11 surgically resected IPMN. Phylogenetic trees were constructed to trace the clonal evolution during IPMN progression. Mutational signatures and SVs were identified and integrated with subclonal architecture, histological features and transcriptomic profiles to understand the molecular dynamics of IPMN progression.
**Results:** Two distinct evolutionary trajectories were identified: one driven by a single ancestral clone and another involving multiple independent ancestral clones, potentially affecting PDAC onset. No shared CNVs or SVs were identified among independent clones, even in high-grade lesions within the same IPMN. Structural variants contribute significantly in clonal progression, contributing to new subclones emergence. Distinct gene expression profiles and immune landscape variations were observed, correlating with the different stages of IPMN progression.
**Conclusion:** This study reveals the complex genomic dynamics of IPMN clonal progression, highlighting the role of structural variations and underscoring the need to refine early detection and treatment strategies.



## SS07-05
## NOVEL BIOLOGICAL AND RADIOLOGICAL MARKERS FOR PREDICTING MALIGNANT PROGRESSION IN IPMN: A PROSPECTIVE STUDY

P. R. Camisa[1], D. Palumbo[2], B. Ferrara[3], G. Belfiori[4], F. Aleotti[4], M. Schiavo Lena[5], L. Valeria[3], L. Cerri[4], F. Di Salvo[4], F. De Cobelli[6], C. Doglioni[7], M. Falconi[1], L. Piemonti[3] and S. Crippa[1]
[1]*Vita Salute San Raffaele University, Division of Pancreatic Surgery and Transplantation, Pancreas Translational and Clinical Research Center, Milano, Italy,* [2]*IRCCS San Rafaele Scientifc Institute, Department of Radiology, Milan, Italy,* [3]*Vita Salute San Raffaele University, Diabetes Research Institute, Milano, Italy,* [4]*IRCCS San Rafaele Scientifc Institute, Division of Pancreatic Surgery and Transplantation, Pancreas Translational and Clinical Research Center, Milano, Italy,* [5]*IRCCS San Rafaele Scientifc Institute, Department of Pathology, Milano, Italy,* [6]*Vita Salute San Raffaele University, Department of Radiology, Milan, Italy, and* [7]*Vita Salute San Raffaele University, Department of Pathology, Milano, Italy*