ESMO GI 2025 Clinical and AI / ML Preview

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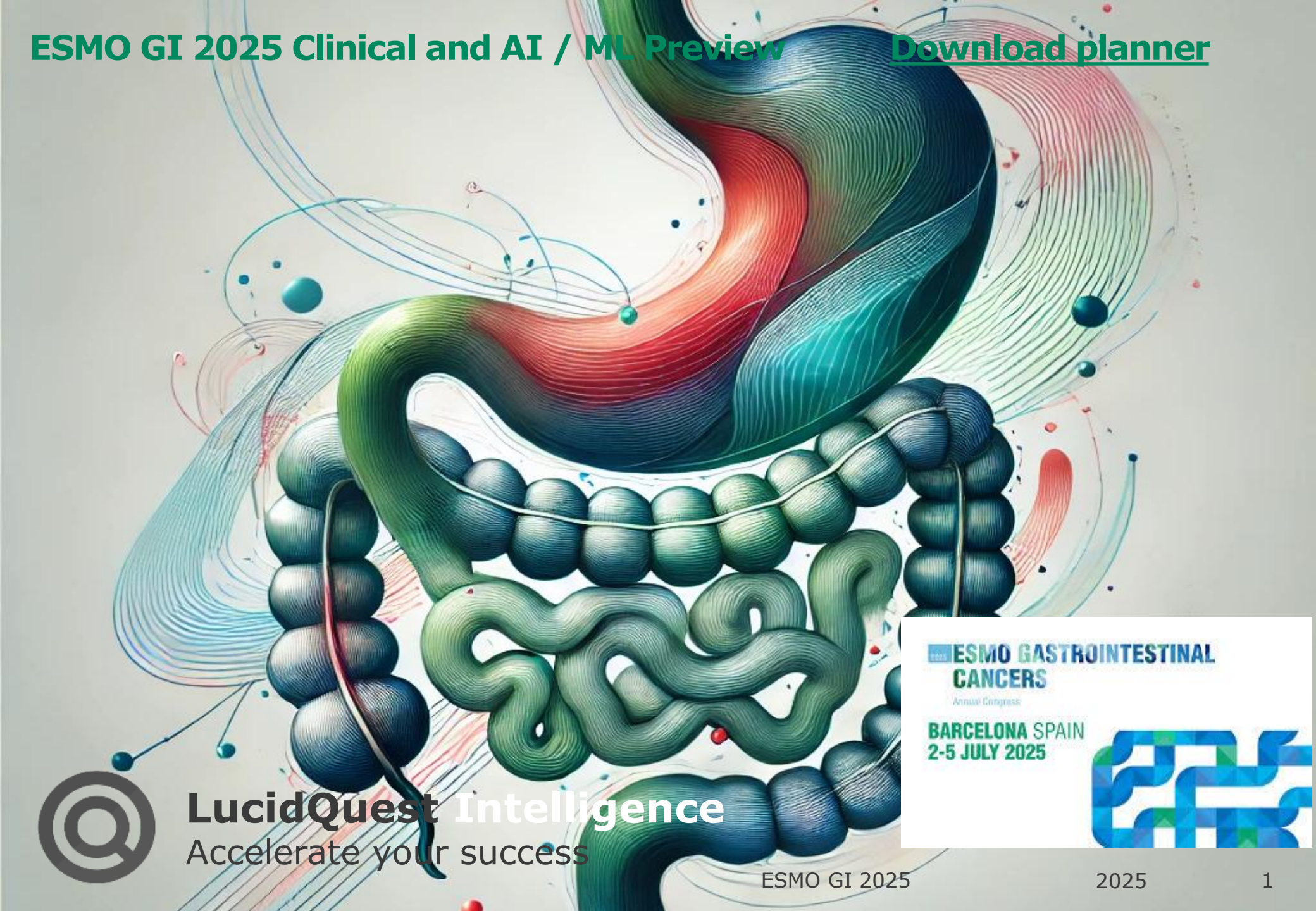

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ESMO GI 2025 – General Overview

- **Interdisciplinary Collaboration:** The conference will facilitate collaboration between oncologists, molecular biologists, and pharmacologists, fostering new synergies for developing GI cancer therapies
- **Regulatory Highlights:** ESMO GI 2025 will feature multiple pivotal regulatory updates, including new drug approvals and ongoing pivotal clinical trial results across various GI cancer types
- **Cutting-edge Technology Showcase:** Digital therapeutics, real-time biomarkers, and AI-driven patient monitoring systems will be integrated into discussions to push the boundaries of GI cancer care
- **Emerging Market Focus:** Studies and clinical trial data from emerging regions, such as Africa and Southeast Asia, enhance the global diversity of research will be featured
- **Patient-Centered Innovations:** Sessions will emphasize improving quality of life and treatment outcomes for patients with GI cancers, focusing on symptom management and survivorship care

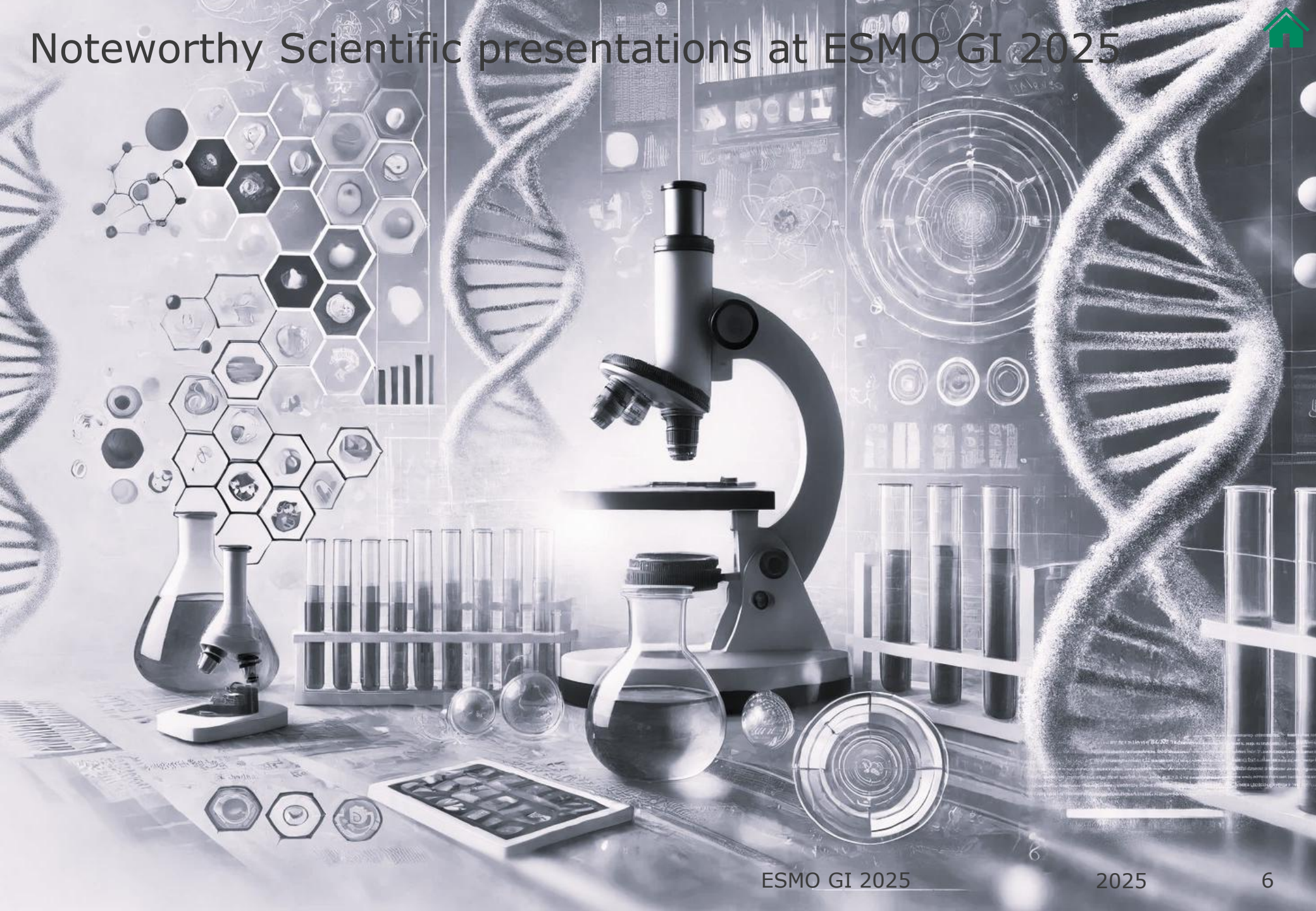
ESMO GI 2025 – Conference Themes (1/2)

- **Immunotherapy Progress:** Discussions on novel immune checkpoint inhibitors and combination therapies in the treatment of refractory GI cancers
- **Precision Oncology:** Insights into the latest advancements in molecular profiling and personalized treatment strategies in GI cancer
- **Targeted Therapy Development:** Presentations will cover new molecular targets and antibody-drug conjugates for treating advanced GI cancers
- **Advancements in Colorectal Cancer:** Updates on the use of immunotherapy and novel targeted therapies for both RAS/BRAF wild-type and MSI-high colorectal cancers
- **Early Detection & Screening:** Focus on advances in liquid biopsy and non-invasive screening technologies for detecting early-stage GI cancers
- **Combination Therapies with Radiation:** Presentations will focus on the combination of immunotherapy, targeted therapies, and radiation for advanced or refractory GI cancers

ESMO GI 2025 – Conference Themes (2/2)

- **Adjuvant & Neoadjuvant Therapy Approaches:** Key data on neoadjuvant and adjuvant therapies in improving patient outcomes in locally advanced GI cancers
- **Real-World Evidence:** Sessions will explore the role of real-world data in optimizing treatment decisions for advanced GI cancer patients
- **Clinical Trials and Biomarkers:** Exploration of ongoing clinical trials and how biomarkers are shaping therapeutic strategies in GI oncology
- **Tumor Microenvironment (TME) Modulation:** Discussions will focus on strategies to modify the TME to enhance immune response and improve the efficacy of both targeted therapies and immunotherapies in GI cancers
- **Minimal Residual Disease (MRD) Detection:** Emerging technologies for detecting MRD in GI cancer patients will be explored to predict relapse and guide therapeutic decisions post-treatment

Noteworthy Scientific presentations at ESMO GI 2025



Key Topics From Notable Presentations at ESMO GI 2025 (1/9)

- **Biliary Tract Cancer:** Sessions will highlight how combination therapies such as CisGem-pembrolizumab and Durvalumab-based regimens offer promising survival benefits for patients with advanced and metastatic biliary tract cancer, with manageable toxicity profiles

  - CisGem and Pembrolizumab in Advanced Biliary Tract Cancer: A phase II study on CisGem-pembrolizumab demonstrated a 61% 6-month progression-free survival (6mPFS) rate and 41% objective response rate (ORR), with higher CPS scores correlating with improved outcomes

  - FTD/TPI and Irinotecan in Cholangiocarcinoma: The TRITICC study showed promising second-line activity for FTD/TPI combined with irinotecan, with median PFS of 3.1 months and median OS of 74% at 6 months in patients with cholangiocarcinoma

  - Durvalumab and Chemotherapy in Metastatic BTC: A retrospective cohort study in Mexico found that chemotherapy plus Durvalumab improved overall survival (OS) to 11.2 months compared to chemotherapy alone (7.5 months), highlighting its efficacy in metastatic BTC

Key Topics From Notable Presentations at ESMO GI 2025 (2/9)

- **Esophageal Cancer:** Studies at ESMO GI 2025 will highlight promising treatment strategies for advanced ESCC, including immunotherapy combinations and radiotherapy for frail patients, showing potential for improved survival with manageable toxicities
  - Reactive Cutaneous Capillary RCCEP and Clinical Outcomes in ESCC: A pooled analysis from ESCORT and ESCORT-1st phase 3 trials showed that RCCEP, a common immune-related adverse event (irAE) with camrelizumab, correlates with better clinical outcomes, including improved OS and PFS in advanced ESCC
  - Cabozantinib and Atezolizumab in Recurrent/Metastatic ESCC: The combination of cabozantinib and atezolizumab in second-line treatment for R/M ESCC showed a moderate ORR of 29.1% and a DCR of 58.3%, with a median OS of 7 months, despite a high incidence of grade 3 adverse events
  - Radiotherapy in Elderly/Frail ESCC Patients: A study on radiation therapy (RT) alone for elderly or frail patients with stage II/III ESCC showed promising local control with an L-CR rate of 40%, while the median OS was 23.6 months, with manageable adverse effects like esophagitis and anorexia

Key Topics From Notable Presentations at ESMO GI 2025 (3/9)

- **Pancreatic Cancer:** The spotlight will be on Combination therapies, molecular profiling, and novel therapeutic targets are enhancing clinical outcomes in pancreatic cancer, offering new hope for improved survival and treatment efficacy
  - Combination Therapies and Targeted Approaches in mPDAC: Studies on CERT with gemcitabine/nab-paclitaxel, lixumistat with chemotherapy, and cabozantinib with atezolizumab showed promising improvements in PFS, ORR, and OS in metastatic PDAC patients
  - Biomarkers and Molecular Profiling in PDAC: The PANTHEIA study highlighted the prognostic value of the Systemic Inflammation Response Index (SIRI), while next-generation sequencing (NGS) identified targetable mutations in over 50% of patients, underscoring the role of biomarkers in treatment decisions
  - Emerging Therapeutic Targets and Mechanisms in PDAC: XPO1 inhibition with Eltanexor showed potential in modulating key signaling pathways, and CXCR4 inhibition in combination with immune checkpoint inhibitors improved T-cell-mediated cytotoxicity and reduced tumor size, offering new therapeutic possibilities for PDAC

Key Topics From Notable Presentations at ESMO GI 2025 (4/9)

- **Gastric Cancer:** The conference will highlight innovative combinations of immunotherapy and chemotherapy that are reshaping the treatment landscape for gastric cancer, with promising outcomes in advanced and resectable disease, highlighting the role of predictive biomarkers in optimizing therapeutic strategies
  - CT041 CAR-T Therapy and Biomarkers in Gastric Cancer: The CT041-CG4006 phase 1 trial explored biomarkers for predicting response to CT041 in gastric cancer, identifying GZMK+ Tpex cells as strong predictors of response and IQGAP3+ cells as markers of resistance
  - Nivolumab and Chemotherapy in Advanced Gastric Cancer: The INGA study demonstrated the real-world effectiveness of nivolumab combined with chemotherapy in advanced HER2-negative gastric and gastroesophageal junction (GC/GEJC) cancers, showing a median OS of 12.4 months and PFS of 6.6 months
  - Neoadjuvant and Perioperative Approaches in HER2-Positive and dMMR Gastric Cancer: Studies like NeoART and ZODIAC investigate the efficacy of novel combinations of immunotherapies with chemotherapy in resectable HER2-positive and dMMR gastric cancer, showing potential improvements in pCR and surgical outcomes

Key Topics From Notable Presentations at ESMO GI 2025 (5/9)

- **Rectal Cancer:** Experts will discuss combination strategies using immune checkpoint inhibitors like sintilimab and nivolumab, along with chemoradiation, which can show promising improvements in pCR rates for locally advanced rectal cancer, with manageable toxicity profiles

  - Sintilimab with SCRT and CAPOX in Locally Advanced Rectal Cancer (LARC): A phase II study demonstrated that SCRT combined with sintilimab and CAPOX significantly improved pathological complete response (pCR) in high-risk LARC patients, with a pCR of 59.2% compared to 32.7% for CAPOX alone

  - Nivolumab and Chemoradiation in LARC: The CA209-8M4 trial showed that adding nivolumab to total neoadjuvant therapy (TNT) with chemoradiation enhanced pCR rates, with 64% of patients achieving modified pCR (mpCR), and excellent long-term survival outcomes (92.2% disease-free survival)

  - Combination of Adebrelimab, SCRT, and CAPOX in pMMR LARC: A study evaluating Adebrelimab (PD-L1 inhibitor) with SCRT and CAPOX in mismatch repair-proficient (pMMR) LARC patients resulted in a pCR rate of 43.5% and a major pathological response (MPR) rate of 60.9%, with manageable toxicity

Key Topics From Notable Presentations at ESMO GI 2025 (6/9)

- **Gastroesophageal Cancer:** Sessions will highlight the data that will show combination therapies involving immune checkpoint inhibitors, such as Givastomig and nivolumab, are demonstrating strong efficacy and manageable safety in treating advanced gastroesophageal cancer, providing new hope for improving patient outcomes
  - Givastomig (Giva) in Combination with Nivolumab and mFOLFOX in 1L Gastric and Esophageal Cancer: The phase 1b trial of Giva, a bispecific antibody targeting CLDN18.2 and 4-1BB, combined with nivolumab and mFOLFOX, showed an 83% objective response rate (ORR) and promising safety profile in 1L metastatic gastroesophageal cancer (GEC)
  - Invikafusp in Anti-PD(L)1-Resistant GI Cancers: The START-001 trial revealed that invikafusp, a dual T-cell agonist, demonstrated 67% disease control in antigen-rich gastrointestinal cancers, particularly showing efficacy in TMB-H colorectal cancer, with partial responses in 22.2% of patients
  - Nivolumab Combinations in Advanced Gastric Cancer (GC): Trials like CheckMate 649 and INGA highlighted nivolumab-based combinations in advanced GC, showing a median overall survival (OS) of 12.4 months and improved quality of life (QoL) in patients with PD-L1 CPS ≥5

Key Topics From Notable Presentations at ESMO GI 2025 (7/9)

- **Colorectal Cancer (CRC):** Innovative approaches such as amivantamab rechallenge, CD47 inhibition, and PDTO-based personalized treatment, advancing the therapeutic landscape of metastatic colorectal cancer, offering promising options for EGFR inhibitor-resistant patients, will be discussed
  - Amivantamab Rechallenge in EGFRi-Resistant mCRC: The OrigAMI-1 trial demonstrated that amivantamab rechallenge in left-sided RAS/BRAF wild-type metastatic colorectal cancer (mCRC) showed improved progression-free survival (PFS) and overall survival (OS) in patients with a longer interval since prior EGFR inhibitor treatment
  - ONO-7913 in Combination with Nivolumab and Chemotherapy in mCRC: The phase 1 study of ONO-7913, a CD47 monoclonal antibody, combined with nivolumab and chemotherapy in RAS/BRAF wild-type mCRC, showed promising objective response rates (ORR) and PFS, with better efficacy in the left-sided cohort
  - PDTOs and Personalized Drug Screening in mCRC: The use of patient tumor-derived organoids (PDTOs) in mCRC demonstrated feasibility for personalized drug screening, leading to clinically beneficial outcomes in some patients, including progression-free survival beyond six months

Key Topics From Notable Presentations at ESMO GI 2025 (8/9)

- **Hepatocellular Carcinoma (HCC) & Hepatobiliary:** Discussions will reinforce that combination therapies of immune checkpoint inhibitors like Atezolizumab and novel targeted agents, such as Irpagratinib can show promising results in both treatment-naïve and pre-treated HCC populations, advancing therapeutic options for this aggressive cancer
  - Irpagratinib + Atezolizumab for FGF19+ HCC: The phase 2 study demonstrated the promising efficacy of Irpagratinib combined with Atezolizumab in FGF19+ HCC patients, achieving an ORR of 51.7% and a median PFS of 7.0 months, supporting further development in both treatment-naïve and pre-treated settings
  - STRIDE Study for Unresectable HCC: The phase 3b SIERRA study assessed the safety and efficacy of STRIDE in a broader cohort of patients with unresectable HCC, including those with poor hepatic function and advanced vascular invasion. STRIDE showed manageable safety, with promising efficacy consistent with prior trials like HIMALAYA
  - Combination of Atezolizumab and Bevacizumab in uHCC: The AMETHISTA study confirmed the safety and efficacy of Atezolizumab combined with Bevacizumab as a first-line treatment for unresectable HCC (uHCC), with a median OS of 20.8 months and a median PFS of 8.8 months, demonstrating long-term survival benefits

Key Topics From Notable Presentations at ESMO GI 2025 (9/9)

- **Miscellaneous:** The studies underscore the potential of optimizing treatment approaches in GI cancers, whether through novel agents like BA3182 and Zongertinib or by adjusting ICI doses to improve accessibility and reduce costs
  - BA3182 as a Dual-Target Bispecific T-cell Engager: The phase 1 study on BA3182 demonstrated promising anti-tumor activity in treatment-refractory adenocarcinoma patients. Tumor reductions and prolonged progression-free intervals were observed, with manageable adverse events, warranting further investigation
  - Lower-Dose ICIs for Metastatic MSI-H/dMMR GI Cancers: The retrospective review highlighted that lower doses of immune checkpoint inhibitors (ICIs) in metastatic MSI-H/dMMR GI cancers were as effective as standard doses, with fewer immune-related adverse events, suggesting a potential cost-saving strategy
  - Zongertinib in HER2-Driven GI Tumors: Zongertinib, a HER2-targeting tyrosine kinase inhibitor, demonstrated a 17.2% ORR and 72.4% disease control rate in a phase Ia trial, showing promising clinical activity in HER2-driven GI cancers, including colorectal and gastric cancers

Focus of Key Industry Sponsored Sessions at ESMO GI 2025 (1/5)

- **BMS:**
  - Focus Areas: Advancements in GI Oncology
  - Discussions will cover the changing landscape in colorectal cancer (CRC), hepatocellular carcinoma (HCC), and pancreatic cancer treatment strategies
- **Revolution Medicines**:
  - Focus Areas: Evolving Treatment Strategies in Metastatic Pancreatic Adenocarcinoma
  - Sessions will focus on current and emerging therapeutic approaches, especially the role of RAS mutations in treatment response
- **AbbVie:**
  - Focus Areas: Targeting c-Met in Colorectal Cancer (CRC) & Beyond
  - The session will focus on the therapeutic implications of targeting c-Met in CRC and its potential applications beyond

Focus of Key Industry Sponsored Sessions at ESMO GI 2025 (2/5)

- **Pfizer:**
  - Focus Areas: Cancer Cachexia in Gastrointestinal Malignancies
  - Presentations will address the role of cancer cachexia in GI cancers and its impact on treatment outcomes and patient care
- **PeerVoice:**
  - Focus Areas: Shifting the Paradigm in Biliary Tract Cancers
  - Contemporary data and clinical decision-making in the management of biliary tract cancers will be highlighted
- **MSD**:
  - Focus Areas: Immuno-Oncology in First-Line Gastric Cancer
  - The session will highlight how biomarkers influence immune-oncology strategies in the treatment of first-line gastric cancer
- **GSK:**
  - Focus Areas: Role of Immuno-Oncology (IO) in dMMR/MSI-H CRC
  - Discussions will cover the role of IO, biomarker testing, and the multidisciplinary team (MDT) in managing locally advanced dMMR/MSI-H CRC

Focus of Key Industry Sponsored Sessions at ESMO GI 2025 (3/5)

- **AstraZeneca:**
  - Focus Areas: Hepatobiliary Cancer Management & Resectable Gastric Cancer (GC) / Gastroesophageal Junction Cancer (GEJC)
  - Presentations will examine current treatment approaches for hepatobiliary cancers and the evolving landscape for resectable GC/GEJC
- **Merck:**
  - Focus Areas: Advancements in mCRC Populations
  - Sessions will focus on expanding treatment options and advancing therapeutic strategies for key populations in metastatic colorectal cancer
- **Gilead:**
  - Focus Areas: Immunotherapy in Advanced Gastroesophageal Adenocarcinoma
  - Discussions will explore new directions in improving patient care with immunotherapy in advanced gastroesophageal adenocarcinoma

Focus of Key Industry Sponsored Sessions at ESMO GI 2025 (4/5)

- **Medscape Global Oncology:**
  - Focus Areas: BRAF-Mutated Metastatic Colorectal Cancer
  - Presentations will highlight real-world insights and the personalized impact of BRAF inhibitors in metastatic CRC treatment
- **Takeda:**
  - Focus Areas: Treatment Choice in Previously Treated mCRC
  - The session will provide a case-based, interactive discussion on treatment choices and factors influencing decisions in previously treated metastatic colorectal cancer
- **Incyte:**
  - Focus Areas: Rare GI Tumors
  - Presentations will explore the evolving treatment landscape and emerging therapies for rare gastrointestinal tumors

Focus of Key Industry Sponsored Sessions at ESMO GI 2025 (5/5)

- **Astellas:**
  - Focus Areas: Personalizing Treatment for Advanced G/GEJ Adenocarcinoma
  - Sessions will explore how to tailor targeted treatments for advanced gastroesophageal/gastroesophageal junction (G/GEJ) adenocarcinoma
- **Eisai:**
  - Focus Areas: Response Timing in 1L HCC Management
  - Presentations will focus on the critical timing of response in first-line hepatocellular carcinoma treatment and its impact on patient management
- **Servier**:
  - Focus Areas: Evolving Treatment Pathways in mCRC, Multidisciplinary Approach in Cholangiocarcinoma & Metastatic Pancreatic Cancer
  - Discussions will focus on new mCRC treatment pathways, multidisciplinary approaches for cholangiocarcinoma, and evolving patient care strategies for metastatic pancreatic cancer.

Notable Presentations At ESMO GI 2025

Notable Presentations At ESMO GI 2025
Biliary Tract Cancer (1/4)

Date	Title	Author	Summary
03 July 2025	First-line therapy (1L) of cisplatin/gemcitabine (CisGem) with pembrolizumab (pembro) in patients with advanced biliary tract cancer (aBTC): Open-label, single-arm phase II EORTC-1607-GITCG/ABC-09 intergroup study with translational research (TR)	Markus Moehler	• **Introduction:** CisGem is the standard first-line therapy for advanced biliary tract cancer (aBTC), with recent approvals for CisGem plus Durvalumab or Pembrolizumab. This study explores the efficacy of CisGem-pembrolizumab and correlates biomarkers with therapeutic outcomes. • **Methodology**: A prospective, multi-center phase II study enrolled therapy-naïve patients with advanced intrahepatic cholangiocarcinoma (iCCA), extrahepatic cholangiocarcinoma (eCCA), and gallbladder cancer (GBC). CisGem-pembrolizumab was administered until progression or unacceptable toxicity. Primary endpoint: 6-month progression-free survival (6mPFS). • **Results:** The 6mPFS rate was 61%. The objective response rate (ORR) was 41%, and the median PFS was 8.3 months. Higher CPS scores correlated with improved outcomes. • **Conclusions:** CisGem-pembrolizumab demonstrated promising efficacy, with manageable toxicity. Immune biomarkers, particularly CPS, correlated with therapeutic response.
03 July 2025	Results of an open-label, single-arm phase II trial investigating the efficacy and safety of trifluridine/tipiracil combined with irinotecan as a second-line therapy in patients with cholangiocarcinoma (TRITICC)	Christoph Roderburg	• **Introduction:** Cholangiocarcinoma (CCA) is an aggressive cancer with poor prognosis, and second-line treatment options are limited. The TRITICC study evaluated the combination of trifluridine/tipiracil (FTD/TPI) and irinotecan in patients who progressed after first-line therapy. • **Methodology**: TRITICC was a multicenter, open-label, phase IIA trial. Patients with advanced metastatic biliary tract cancer received FTD/TPI plus irinotecan. The primary endpoint was progression-free survival (PFS), and secondary endpoints included response rates and overall survival (OS). • **Results:** Median PFS was 3.1 months, with a 35% PFS rate at 4 months. Median OS was 74% at 6 months. Most common adverse events were neutropenia and GI symptoms. • **Conclusions:** FTD/TPI plus irinotecan showed promising second-line activity in CCA. Further trials, such as TRITICC-2, are warranted.

Notable Presentations At ESMO GI 2025
Biliary Tract Cancer (2/4)

Date	Title	Author	Summary
03 July 2025	Ivosidenib in pretreated Japanese (JPN) patients (pts) with mutant isocitrate dehydrogenase 1 (mIDH1) nonresectable/metastatic cholangiocarcinoma (n/mCCA): Phase II study results	Tomoyuki Satake	• **Introduction:** mIDH1 cholangiocarcinoma (CCA) is rare with poor prognosis. The ClarIDHy study demonstrated the benefit of ivosidenib (IVO) in patients with advanced mIDH1 CCA. This phase 2 study evaluates IVO's efficacy and safety in Japanese patients (JPN) with 2-3L mIDH1 CCA. • **Methodology**: JPN patients with advanced mIDH1 CCA received 500 mg IVO daily in 28-day cycles. Primary endpoint: 6-month progression-free survival (PFS) rate. • **Results:** The 6-month PFS rate was 25%, with median PFS of 2.7 months. IVO was well tolerated, with no new safety signals identified. Most common adverse events were prolonged QT and hematologic. • **Conclusions:** IVO demonstrated clinical benefit in JPN patients with mIDH1 CCA, showing comparable PFS to ClarIDHy. IVO was well tolerated with manageable side effects.
03 July 2025	Early safety and efficacy from the phase IIIb TOURMALINE study of durvalumab (D) in combination with gemcitabine (G)-based chemotherapy in advanced biliary tract cancer (aBTC)	Do-Youn Oh	• **Introduction:** The TOURMALINE phase 3b study evaluates D + G-based chemotherapy as first-line treatment for advanced biliary tract cancer (aBTC). Early safety and efficacy results are presented. • **Methodology**: Patients received D 1500 mg with investigator-selected G-based chemotherapy (with or without oxaliplatin, carboplatin, cisplatin, S-1, or nab-paclitaxel). The primary endpoint was the number of patients with Grade 3/4 adverse events (AEs) within 6 months. Safety and objective response rate (ORR) were evaluated by non-platinum vs platinum-based regimens. • **Results:** 121 patients were enrolled. Grade 3/4 AEs occurred in 45.5%, with ORRs of 21.5%. Platinum-based regimens showed higher ORRs (25.8%). • **Conclusions:** D + G-based chemotherapy showed manageable safety and promising efficacy, with platinum-based regimens showing the most favorable outcomes.

Notable Presentations At ESMO GI 2025
Biliary Tract Cancer (3/4)

Date	Title	Author	Summary
03 July 2025	Real-world efficacy and toxicity data of durvalumab plus chemotherapy compared with chemotherapy in patients with advanced biliary tract cancer: A retrospective cohort at the National Cancer Institute in Mexico	Lorena Lagarde Nube	• **Introduction:** Biliary tract cancer (BTC) is prevalent in Mexico, with most cases diagnosed at metastatic stages. While treatment access has improved, high costs remain a barrier. This study evaluates overall survival (OS) outcomes and treatment-related adverse effects in metastatic BTC patients at our institution. • **Methodology**: A retrospective cohort study was conducted on metastatic BTC patients receiving chemotherapy or chemotherapy plus Durvalumab. Clinical characteristics and treatment details were reviewed. OS was calculated using the Kaplan-Meier method. • **Results:** 116 patients were included. Median OS was 11.2 months with chemotherapy plus Durvalumab and 7.5 months with chemotherapy alone. No immune-related adverse events (irAEs) were reported. • **Conclusions:** Durvalumab plus chemotherapy showed similar OS to global reports, but high treatment costs limit access to advanced therapies. Identifying and managing toxicities is crucial for optimizing outcomes.
03 July 2025	Comprehensive genomic profiling and efficacy data in patients with advanced biliary tract cancer treated in first-line with chemo-immunotherapy combination: A real world experience	Valeria Nacca	• **Introduction:** Cisplatin, Gemcitabine, and Durvalumab significantly improve overall survival (OS) in locally advanced/metastatic biliary tract cancer (La/mBTC) compared with doublet chemotherapy. This study evaluates the efficacy and safety of this combination in a real-world setting. • **Methodology**: A retrospective, observational study was conducted on La/mBTC patients treated with Gemcitabine + Durvalumab, with or without Cisplatin. Comprehensive genomic profiling was performed. Primary endpoints included overall response rate (ORR), disease control rate (DCR), progression-free survival (PFS), and OS. • **Results:** The median PFS was 7.9 months, with a median OS of 14.7 months. The triplet therapy (TrTP) group had better outcomes (mPFS 8.5 months, mOS 16.1 months) compared to the Cisplatin-ineligible group (CiP), which had mPFS of 3.0 months and mOS of 4.6 months. • **Conclusions:** The combination of chemotherapy and Durvalumab demonstrated promising efficacy and manageable safety in La/mBTC, with outcomes correlated to genomic profiling.

Notable Presentations At ESMO GI 2025
Biliary Tract Cancer (4/4)

Date	Title	Author	Summary
03 July 2025	CD80 tumour-expression predicts benefits from capecitabine in the BILCAP phase III randomized adjuvant trial	Michela Rofei	• **Introduction:** The BILCAP trial demonstrated the benefit of adjuvant capecitabine in resected biliary tract cancers (BTC). This post-hoc analysis explores CD80 expression as a predictive biomarker for capecitabine efficacy. • **Methodology**: CD80 expression was assessed in central and invasion front tumor regions of resected BTC samples. The CD80-CIF score was calculated and correlated with relapse-free survival (RFS) and overall survival (OS) using Kaplan-Meier analysis. • **Results:** A CD80-CIF score ≤40 was associated with shorter RFS in the observation arm, and capecitabine significantly improved RFS and OS in patients with low CD80-CIF scores. Adjustments were made for intrahepatic cholangiocarcinoma (iCCA) patients. • **Conclusions:** CD80-CIF score ≤40 may be a potential predictive biomarker for capecitabine efficacy in BTC patients. The cutoff for iCCA may require further refinement.
03 July 2025	ADJUBIL: A phase II study of durvalumab and tremelimumab with or without capecitabine in ADJUvant BILiary tract cancer: The IKF/AIO-ADJUBIL trial	Thorsten O. Goetze	• **Introduction:** The ADJUBIL trial evaluates the combination of anti-PD-L1 antibody durvalumab and anti-CTLA-4 antibody tremelimumab with or without capecitabine in resectable biliary tract cancer (BTC) in the adjuvant setting. • **Methodology**: In this open-label, multicenter phase II trial, patients with resectable BTC were randomized to receive tremelimumab and durvalumab with or without capecitabine. The primary endpoint was recurrence-free survival at 12 months (RFS@12). • **Results:** 40 patients were enrolled. RFS@12 was 57.9% for durvalumab/tremelimumab without capecitabine, and 52.4% with capecitabine. No new safety signals were identified, but higher toxicity rates were observed in the combination group. • **Conclusions:** Durvalumab and tremelimumab without capecitabine showed superior outcomes with manageable toxicity compared to the combination with capecitabine.

Notable Presentations At ESMO GI 2025
Esophageal Cancer (1/3)

Date	Title	Author	Summary
03 July 2025	Reactive cutaneous capillary endothelial proliferation in esophageal squamous cell carcinoma patients treated with camrelizumab-based therapy: A pooled analysis of two phase III trials	Hui Yan Luo	• **Introduction:** Reactive cutaneous capillary endothelial proliferation (RCCEP) is a common immune-related adverse event (irAE) associated with camrelizumab in advanced esophageal squamous cell carcinoma (ESCC). This study evaluates RCCEP characteristics and its correlation with clinical outcomes. • **Methodology**: A pooled analysis was conducted using data from the ESCORT and ESCORT-1st phase 3 trials. RCCEP incidence, clinicopathological features, and survival outcomes were analyzed, with landmark analysis comparing patients with and without RCCEP. • **Results:** 420 of 526 patients developed RCCEP. Patients with RCCEP showed improved objective response rates, progression-free survival (7.1 vs 5.5 months), and overall survival (13.4 vs 7.1 months). • **Conclusions:** RCCEP is a manageable irAE that correlates with better clinical outcomes, suggesting it may serve as a biomarker for predicting treatment response and survival in advanced ESCC.
03 July 2025	A single-arm phase II study of cabozantinib and atezolizumab in patients with recurrent or metastatic esophageal squamous cell carcinoma (R/M ESCC) who failed platinum-based chemotherapy	Hung-Yang Kuo	• **Introduction:** This phase II study evaluates the combination of cabozantinib, a multikinase inhibitor, with atezolizumab, an anti-PD-L1 ICI, in patients with recurrent or metastatic (R/M) esophageal squamous cell carcinoma (ESCC) after progression from first-line platinum-based chemotherapy. • **Methodology**: 24 patients with histologically confirmed R/M ESCC were treated with cabozantinib and atezolizumab. The primary endpoint was objective response rate (ORR), with secondary endpoints including progression-free survival (PFS), overall survival (OS), and toxicity profile. • **Results:** The ORR was 29.1%, with a disease control rate of 58.3%. Median PFS was 2.2 months, and median OS was 7.0 months. 50% of patients experienced grade 3 or higher adverse events, with hypertension being most common. • **Conclusions:** Cabozantinib combined with atezolizumab showed moderate activity and an acceptable safety profile as second-line therapy for R/M ESCC.

Notable Presentations At ESMO GI 2025
Esophageal Cancer (2/3)

Date	Title	Author	Summary
03 July 2025	Efficacy and safety of radiation therapy alone in patients with stage II/III esophageal squamous cell carcinoma intolerant of chemotherapy and surgery: A multi-center retrospective study	Takako Yoshii	• **Introduction:** For stage II/III esophageal squamous cell carcinoma (ESCC), the standard of care is neoadjuvant therapy followed by surgery. However, in elderly or frail patients, radiation therapy (RT) alone is often used. This study evaluates the efficacy and safety of RT alone in treating stage II/III ESCC. • **Methodology**: A retrospective analysis was conducted on patients receiving RT alone (≥50Gy) from January 2014 to December 2023 at 12 Japanese institutions. Key outcomes included local complete response (L-CR), local progression-free survival (L-PFS), progression-free survival (PFS), overall survival (OS), and adverse events (AEs). • **Results:** 82 patients were included. The L-CR rate was 40% (with deemed CR) and 23% (without deemed CR). The median L-PFS, PFS, and OS were 12.3, 9.7, and 23.6 months, respectively. Common grade 3+ AEs were esophagitis (4%) and anorexia (4%). • **Conclusions:** RT alone provided good local control and was well tolerated in frail patients with stage II/III ESCC who could not tolerate chemotherapy or surgery.
03 July 2025	DKN-01 and atezolizumab as second or third-line therapy in advanced mismatch repair proficient (MMRp) oesophagogastric adenocarcinoma (OGA): WAKING trial	Anderley Gordon	• **Introduction:** This phase IIb study evaluates the combination of cabozantinib and atezolizumab in advanced esophageal squamous cell carcinoma (ESCC) after platinum-based chemotherapy. • **Methodology**: Patients received cabozantinib (600 mg) and atezolizumab (840 mg) bi-weekly. The primary endpoint was objective response rate (ORR), with secondary endpoints including PFS, OS, and toxicity. • **Results:** 42 patients were enrolled. ORR was 7.5%, with a disease control rate of 32.5%. Median PFS was 1.8 months, and OS was 5.9 months. Common grade 3 AEs included fatigue and anemia. • **Conclusions:** Cabozantinib and atezolizumab showed moderate efficacy with manageable toxicity.

Notable Presentations At ESMO GI 2025
Esophageal Cancer (3/3)

Date	Title	Author	Summary
03 July 2025	Tumour-free lymph node microarchitecture associates with tumour location-specific survival in oesophagogastric cancer: Results from the OE05 and ST03 trials	Elzbieta Budginaite	• **Introduction:** This pilot study explores the microarchitecture of lymph nodes (LNnegs) in oesophagogastric cancer (OGC) patients, specifically focusing on germinal center (GermC) formation and histiocyte accumulation as potential biomarkers for overall survival (OS). • **Methodology**: Post-chemotherapy adenocarcinoma resections from two OGC trials (OE05 and ST03) were analyzed. GermC count and histiocyte coverage in the largest LNneg were measured and patients stratified by primary tumour location (oesophageal, junctional, gastric). Associations with OS were analyzed using Kaplan–Meier curves. • **Results:** GermC count ≤3 in oesophageal patients and histiocyte coverage ≤23.2% in junctional patients were associated with poor OS. • **Conclusions:** GermC count and histiocyte coverage in LNnegs are prognostic in OGC, with variations depending on primary tumour location. Further investigation into these biomarkers is needed.
03 July 2025	Mismatch repair deficiency (MMRd) in esophagogastric adenocarcinoma (ADC) following chemotherapy for resectable disease: Correlation with survival and recurrence patterns from ST03 and OE05 trials	Panagiotis Ntellas	• **Introduction:** This study evaluates the role of MMR deficiency (MMRd) as a prognostic factor in esophagogastric adenocarcinoma (OGC) patients treated with chemotherapy and surgery in the OE05 and ST03 trials. • **Methodology**: Tumor samples from 1424 patients were analyzed for MMR status, and survival outcomes (overall survival, recurrence patterns) were assessed, including multivariate analysis. • **Results:** 5.6% of patients were MMRd. MMRd patients had improved overall survival (OS) with a 10-year OS of 50.01% compared to 26.0% for MMRp patients. Recurrence patterns differed, with MMRd patients more likely to experience local recurrence. • **Conclusions:** MMRd is an independent prognostic marker for improved survival and distinct recurrence patterns in OGC patients.

Notable Presentations At ESMO GI 2025
Pancreatic Cancer (1/7)

Date	Title	Author	Summary
02 July 2025	AGITG ASCEND study: Randomised, double-blind phase II study of certepetide (CERT) or placebo (PLA) added to gemcitabine plus nab-paclitaxel in patients with untreated metastatic pancreatic ductal adenocarcinoma (mPDAC): Cohort B progression-free survival (PFS) results	Andrew Dean	• **Introduction:** CERT (LSTA1/CEND-1) is a cyclic peptide enhancing drug penetration in tumors and stroma, potentially boosting anti-cancer efficacy. This phase 2 trial evaluates CERT's combination with gemcitabine/nab-paclitaxel in mPDAC. • **Methodology**: 63 mPDAC patients (ECOG 0-1) were randomized to receive gemcitabine/nab-paclitaxel with either CERT (3.2 mg/kg) or placebo (PLA) in cohort B. Primary outcome: 6-month PFS. Secondary outcomes: mPFS, OS, ORR, toxicity. • **Results:** 6-month PFS: CERT 60.8%, PLA 25%. mPFS: 7.5 vs. 4.7 months. ORR: CERT 45.2%, PLA 19%. Grade 3/4 adverse events were similar in both arms • **Conclusions:** CERT combined with GEM/NPC showed promising PFS and ORR improvements in mPDAC with manageable safety. Further studies are warranted.
03 July 2025	A phase Ib dose-escalation trial of gemcitabine and nab-paclitaxel in combination with lixumistat in patients with advanced pancreatic cancer (COMBAT-PC)	Shubham Pant	• **Introduction:** Lixumistat (IM156), targeting oxidative phosphorylation, was tested with gemcitabine and nanoparticle paclitaxel in metastatic PDAC. • **Methodology**: A phase 1b trial (NCT05497778) enrolled 17 patients to receive Lixumistat (400 mg or 800 mg daily) with standard chemotherapy. Efficacy and safety were assessed. • **Results:** No severe toxicities occurred. The recommended phase 2 dose (RP2D) was 400 mg. At this dose, ORR was 42%, DCR was 100%, median PFS was 7.34 months, and OS was 18 months. • **Conclusions:** Lixumistat with gemcitabine and nanoparticle paclitaxel shows promising safety and efficacy in metastatic PDAC.

Notable Presentations At ESMO GI 2025
Pancreatic Cancer (2/7)

Date	Title	Author	Summary
03 July 2025	Provisional results of immunotherapy combined with LSTA1 plus nab-paclitaxel and gemcitabine for locally advanced pancreatic ductal adenocarcinoma	Andrew Dean	• **Introduction:** Pancreatic ductal adenocarcinoma (PDAC) has a dense stroma that hinders drug penetration. LSTA-1, an iRGD peptide, enhances drug delivery by targeting tumor endothelial receptors, activating the CENDR pathway to facilitate immune cell penetration. • **Methodology**: Participants were divided into 3 cohorts: Cohort 1 (gemcitabine, nab-paclitaxel, placebo LSTA-1, placebo durvalumab), Cohort 2 (active LSTA-1), and Cohort 3 (active LSTA-1, durvalumab). Tumors were assessed using RECIST v1.1, and CA19-9 levels were measured. • **Results:** After 4 cycles, 13/20 had partial responses, 7 had stable disease, and 1 had a complete response. 16/20 had decreased CA19-9 levels, with 7 showing >90% reduction. • **Conclusions:** LSTA-1 with chemotherapy and durvalumab showed significant clinical responses and disease control in PDAC.
03 July 2025	Metastatic pancreatic adenocarcinoma: Real-world efficacy of first-line treatment	Mélanie Debiais	• **Introduction:** This study evaluates first-line chemotherapy outcomes for metastatic PDAC, comparing FOLFIRINOX (FFX) and Gemcitabine-Nabpaclitaxel (GN). • **Methodology**: A retrospective analysis of 1012 patients from 2010-2024, collecting clinical, radiological, and molecular data. • **Results:** FFX showed a higher ORR (41%) vs. GN (16%), with median OS of 14.5 months for FFX and 12.4 months for GN. • **Conclusions:** FFX improved clinical outcomes in metastatic PDAC, especially in patients with good performance status. Liver metastases were a negative prognostic factor.

Notable Presentations At ESMO GI 2025
Pancreatic Cancer (3/7)

Date	Title	Author	Summary
03 July 2025	Second-line nanoliposomal irinotecan plus fluorouracil (NIF) versus fluoropyrimidine-based chemotherapy plus oxaliplatin (OF) after gemcitabine plus nab-paclitaxel in patients with advanced pancreatic cancer patients: Efficacy comparison using real-world data evidence	Jesus Rodriguez Pascual	• **Introduction:** This study compares the overall survival (OS) between two treatment regimens for advanced pancreatic cancer (aPC) after first-line gemcitabine plus nab-paclitaxel: nanoliposomal irinotecan plus fluorouracil (NIF) and fluoropyrimidine-based chemotherapy plus oxaliplatin (OF). • **Methodology**: This study compares the overall survival (OS) between two treatment regimens for advanced pancreatic cancer (aPC) after first-line gemcitabine plus nab-paclitaxel: nanoliposomal irinotecan plus fluorouracil (NIF) and fluoropyrimidine-based chemotherapy plus oxaliplatin (OF). • **Results:** The median OS was 140 days for the NIF arm and 159 days for the OF arm. OS was superior in the OF arm (HR 1.149, p=0.002). • **Conclusions:** Fluoropyrimidine-based chemotherapy plus oxaliplatin (OF) demonstrated better survival than NIF in advanced pancreatic cancer.
03 July 2025	Molecular landscape of advanced pancreatic cancer: Results from NGS testing in real-world clinical practice	Mireia Busquets Godall	• **Introduction:** Understanding the molecular landscape of pancreatic cancer (PC) is crucial for identifying novel treatments. This study explores the utility of next-generation sequencing (NGS) in advanced PC, irrespective of KRAS status, to identify actionable mutations. • **Methodology**: A retrospective analysis of 111 patients with advanced PC who underwent NGS testing from Jan 2017 to Dec 2024 was performed. Data on clinical, histopathological, molecular, treatment, and follow-up were collected. • **Results:** NGS revealed targetable alterations in 56.8% of patients, including KRAS G12C, ATM, BRCA1/2, and ARID1A. Despite these findings, only one patient received targeted therapy. • **Conclusions:** NGS identifies targetable mutations in both KRAS mutant and wild-type PC, highlighting the need for broader use of NGS, though access to targeted therapies remains limited.

Notable Presentations At ESMO GI 2025
Pancreatic Cancer (4/7)

Date	Title	Author	Summary
03 July 2025	Prognostic significance of the systemic inflammation response index (SIRI) and nutritional status in metastatic pancreatic cancer: Results from the PANTHEIA–SEOM study	Carmen Guillen Ponce	• **Introduction:** Systemic inflammation, measured by the Systemic Inflammation Response Index (SIRI), is a key prognostic factor in metastatic pancreatic cancer (mPC). This study examines its relationship with chemotherapy response and nutritional status. • **Methodology**: PANTHEIA, an observational study across 28 Spanish hospitals, included 285 mPC patients. SIRI was categorized as low (L) or high (H), and clinical and nutritional data were collected. • **Results:** SIRI-H was associated with poorer overall survival (OS) and progression-free survival (PFS). mFOLFIRINOX showed superior outcomes compared to gemcitabine-based regimens. Nutritional status also impacted survival. • **Conclusions:** SIRI is a strong prognostic biomarker in mPC, and combining it with nutritional screening can enhance treatment strategies.
03 July 2025	Adjuvant chemotherapy of S-1 plus metformin versus S-1 for radical resection of pancreatic cancer: Multicenter randomized phase II trial	Masayuki Furukawa	• **Introduction:** Epidemiological data suggest metformin may reduce pancreatic cancer risk. This trial evaluates the combination of S-1 and metformin versus S-1 monotherapy for overall survival in patients with resected pancreatic cancer. • **Methodology**: Patients with stage I–II invasive pancreatic ductal carcinoma were randomized to receive either S-1 + metformin (group A) or S-1 alone (group B). The primary endpoint was 2-year overall survival (OS), and secondary endpoints included recurrence-free survival (RFS) and adverse events. • **Results:** 2-year OS rates were similar (66.7% for group A, 66.1% for group B), and median survival was also comparable. Toxicity was low in both groups. • **Conclusions:** Adding metformin to S-1 did not significantly improve survival outcomes in resected pancreatic cancer patients. The S-1 regimen demonstrated similar efficacy with better safety.

Notable Presentations At ESMO GI 2025
Pancreatic Cancer (5/7)

Date	Title	Author	Summary
03 July 2025	Perioperative and oncological outcomes of laparoscopic versus open pancreaticoduodenectomy: A meta-analysis of randomized controlled trials	Ashraf Abdelghany	• **Introduction:** Laparoscopic pancreaticoduodenectomy (LPD) is considered a minimally invasive alternative to open pancreaticoduodenectomy (OPD), but its efficacy and safety are still debated. This meta-analysis compares perioperative and oncological outcomes between LPD and OPD. • **Methodology**: A meta-analysis of randomized controlled trials (RCTs) comparing LPD and OPD was conducted. Outcomes assessed included operation time, blood loss, ICU and hospital stay, complications, and oncological results such as lymph node yield and R0 resection rates. • **Results:** LPD reduced blood loss, ICU stay, and hospital stay, with a longer operative time. No significant differences were found in complications, mortality, or oncological outcomes. • **Conclusions:** LPD offers significant perioperative benefits without compromising oncological outcomes. Further studies should focus on long-term survival and cost-effectiveness.
03 July 2025	AI-driven patient screening for clinical trials in pancreatic cancer: Integrating LLMs with tumor board meetings	Arthur Claessens	• **Introduction:** Screening for clinical trials is time-consuming and repetitive for clinicians, particularly in pancreatic cancer with its poor outcomes. Artificial intelligence (AI) offers an opportunity to improve screening efficiency and reproducibility. • **Methodology**: Patient records presented at tumor board meetings between 2018 and 2023 were reviewed. Eligibility for 12 candidate trials was assessed manually by two blinded oncologists (gold standard) and by three AI large language models (LLMs). • **Results:** Mistral-7b-Instruct v0.3 showed the highest sensitivity (92.6%) in trial eligibility screening, outperforming GPT-4.5 (82.3%) and Claude 3.7 Sonnet (81.7%). Specificities were similar across models • **Conclusions:** LLM-based screening is a promising tool for improving the quality and efficiency of clinical trial eligibility assessments in pancreatic cancer

Notable Presentations At ESMO GI 2025
Pancreatic Cancer (6/7)

Date	Title	Author	Summary
03 July 2025	GPCR1 as a selective target in pancreatic cancer: Preclinical efficacy and safety of first-in-class SKM104-MA-L2, a topoisomerase-based antibody-drug conjugate with high therapeutic index	Manel K. Merabet	• **Introduction:** GPCR1, a G-protein-coupled receptor, is highly expressed in PDAC, including HER2-low models, offering a potential ADC target. • **Methodology**: GPCR1 expression was assessed in PDAC samples. SKM104-MA-L2, an anti-GPCR1 ADC, was tested in PDAC models and cynomolgus monkeys for efficacy and safety. • **Results:** GPCR1 was expressed in >90% of PDAC samples. SKM104-MA-L2 showed strong cytotoxicity, outperforming ENHERTU, with near-complete tumor regression in vivo. No dose-limiting toxicity was observed in cynomolgus monkeys. • **Conclusions:** SKM104-MA-L2 is a promising ADC candidate for PDAC, showing strong efficacy and safety.
03 July 2025	Evaluating efficacy of Fc-enhanced CTLA-4 inhibitor botensilimab, bastilimab with or without CXCR4 inhibitor (BL-8040) in an orthotopic murine model	Jonathan W. Lee	• **Introduction:** Pancreatic adenocarcinoma (PDAC) is poorly immunogenic and resistant to conventional immunotherapies. Targeting the CXCR4-CXCL12 axis may improve tumor T-cell infiltration. This study evaluates the efficacy of combining CXCR4 inhibitor (CXCR4i) BL-8040 with CTLA-4 inhibitors Botensilimab (BOT) and Balstilimab (BAL) in a PDAC murine model. • **Methodology**: Orthotopic pancreatic cancer models were treated with BL-8040 and BOT/BAL. Tumor volume, metastasis, and immune cell infiltration were assessed using immunohistochemistry and flow cytometry. • **Results:** The combination of BOT/BAL with CXCR4i resulted in reduced tumor size, increased CD8+ T-cells expressing GranzymeB, and decreased CD4+ cells and F4-80+ macrophages. • **Conclusions:** BOT/BAL and CXCR4i treatment enhanced T-cell-mediated cytotoxicity and reduced tumor size, suggesting a potential therapeutic approach for PDAC.

Notable Presentations At ESMO GI 2025
Pancreatic Cancer (7/7)

Date	Title	Author	Summary
03 July 2025	Targeted inhibition of exportin-1 enhances anticancer efficacy and augments therapeutic outcomes in pancreatic ductal adenocarcinoma by modulation of LAMC2/KRAS/ERK1/2/AKT signaling network via hsa-miR-193b-3p	Aishwarya Singh	• **Introduction:** Pancreatic ductal adenocarcinoma (PDAC) has poor prognosis and limited therapies. Exportin-1 (XPO1) plays a key role in regulating tumor suppressor proteins and non-coding RNAs. This study investigates the potential of XPO1 inhibitors, particularly Eltanexor, in targeting LAMC2 in PDAC. • **Methodology**: In-silico analysis, Eltanexor treatment, and various assays (e.g., qRT-PCR, cell proliferation, apoptosis) were used to explore XPO1 inhibition's effect on PDAC. Eltanexor was combined with gemcitabine for therapeutic evaluation. • **Results:** XPO1 and LAMC2 overexpression correlated with poor survival. Eltanexor reduced PDAC cell proliferation, migration, and EMT. It restored miR-193b-3p, suppressing LAMC2 and KRAS, inhibiting ERK/AKT signaling. • **Conclusions:** XPO1 inhibition through Eltanexor modulates key signaling pathways and may offer a promising therapeutic approach in PDAC.
03 July 2025	Tumor-microenvironment-on-chip: A real-time window into immunotherapy efficacy under heterogeneity	Chiao-Min Lin	• **Introduction:** PDAC's heterogeneous tumor microenvironment (TME) complicates treatment responses. This study presents a TME-on-chip (TMoC) platform for region-specific analysis of therapeutic responses, focusing on immune cell infiltration. • **Methodology**: TMoC integrates 3D culture, dynamic perfusion, and physiological gradients for drug screening and immune cell monitoring. • **Results:** TMoC identified a novel epigenetic drug candidate from a compound library, validated in animal models, revealing immune-related mechanisms. • **Conclusions:** TMoC enables precise evaluation of therapeutic responses, enhancing drug screening and discovering new therapeutic mechanisms for further validation.

Notable Presentations At ESMO GI 2025
Gastric Cancer (1/4)

Date	Title	Author	Summary
03 July 2025	Decoding the responsive and resistant features to the claudin18.2-specific CAR T cell CT041 in gastric cancer: An exploratory biomarker analysis of the phase I clinical trial	Haoxin Peng	• **Introduction:** CT041, a Claudin18.2-specific CAR-T therapy, shows promise in gastric cancer (GC), but the mechanisms of response and resistance are not well understood. This exploratory biomarker analysis of the phase 1 CT041-CG4006 trial investigates potential predictors of response and resistance to CT041. • **Methodology**: Baseline and dynamic samples were collected from primary tumors (PT), peripheral blood, and malignant ascites in 35 patients. Single-cell RNA sequencing, spatial transcriptomics, and multiplex immunofluorescence were employed for biomarker analysis. • **Results:** Higher infiltrates of GZMK+CD8+ T-lymphocytes, exhibiting a progenitor exhausted-like (Tpex) state, were identified in responders. GZMK+ Tpex infiltration was a strong predictor of response and correlated with improved prognosis. Resistance was linked to IQGAP3+ cancer cells, which hindered Tpex infiltration and created an immunosuppressive environment. • **Conclusions:** Pre-existing GZMK+ Tpex cells are key to predicting CT041 response, while IQGAP3+ cancer cells are implicated in resistance. These findings provide insights into optimizing CAR-T therapy for GC.
03 July 2025	Real-world (RW) evidence in gastric and esophageal cancer: First results of patients (pts) treated with nivolumab (NIVO) plus chemotherapy (chemo) from the noninterventional INGA study in Germany	Gertraud Stocker	• **Introduction:** Nivolumab (NIVO) combined with chemotherapy (CTX) is approved in the EU as first-line treatment for HER2-negative advanced gastric cancer (GC), gastroesophageal junction (GEJC), and esophageal adenocarcinoma (EAC) with PD-L1 CPS ≥5. The INGA study evaluates the real-world (RW) effectiveness, tolerability, and quality of life (QoL) of NIVO + CTX in these patients. • **Methodology**: Patients with HER2-negative, advanced GC/GEJC/EAC and PD-L1 CPS ≥5, who received NIVO + CTX, were enrolled in cohort 1. They were followed for up to 3 years, with assessments at multiple time points. The primary endpoint was overall survival (OS), and secondary endpoints included progression-free survival (PFS), safety, and QoL. • **Results:** 198 patients were enrolled in cohort 1. With a median follow-up of 6.3 months, median OS was 12.4 months, and median PFS was 6.6 months. Six- and twelve-month OS rates were 73% and 53%, respectively. The ORR was 64.7%, and grade 3/4 treatment-related adverse events occurred in 11% of patients. • **Conclusions:** 1L NIVO + CTX demonstrated effectiveness and safety in real-world patients with advanced GC/GEJC/EAC, aligning with CheckMate 649 results despite the cohort's older median age and ECOG PS ≥2.

Notable Presentations At ESMO GI 2025
Gastric Cancer (2/4)

Date	Title	Author	Summary
03 July 2025	Evaluation of efficacy of definitive chemo-radiation in inoperable carcinoma esophagus	Vamshi Krishna Muddu	• **Introduction:** Surgery for esophageal carcinoma offers better local control but does not improve survival. Neoadjuvant chemoradiation is preferred for surgically fit patients, while definitive chemoradiation (dCRT) provides long-term disease control for inoperable patients. • **Methodology**: A retrospective study analyzed 99 inoperable patients with squamous cell carcinoma or adenocarcinoma treated with dCRT between January 2019 and March 2025. • **Results:** The median overall survival was 31 months, with 2- and 3-year survival rates of 60% and 50%. Median progression-free survival was 22 months. Stage, concurrent chemotherapy, and performance status were significant predictors. • **Conclusions:** dCRT is a viable, well-tolerated treatment for inoperable patients, offering comparable survival to surgery.
03 July 2025	A randomised phase II study of zimberelimab ± domvanalimab immunotherapy in resectable mismatch repair deficient (dMMR) gastric and gastroesophageal junctional (G/GOJ) adenocarcinoma (ZODIAC)	Georgina A. Keogh	• **Introduction:** For resectable dMMR gastric/gastroesophageal junction (G/GOJ) adenocarcinomas, chemotherapy combined with surgery is standard, but outcomes are limited. Immunotherapy with anti-PD1 and anti-TIGIT may offer enhanced efficacy. The ZODIAC study evaluates perioperative immune checkpoint inhibition (ICI) in this patient group. • **Methodology**: ZODIAC is a UK multicenter, randomized phase II trial comparing anti-PD1 (zimberelimab) versus anti-PD1 + anti-TIGIT (domvanalimab). Primary endpoint is pathological complete response (pCR), with secondary endpoints including safety, surgical outcomes, and QoL. • **Results:** The study requires 25 patients per arm. Interim futility analysis is planned after 7 evaluable patients. Recruitment is ongoing. • **Conclusions:** ZODIAC aims to explore the efficacy of ICI combinations in resectable dMMR G/GOJ adenocarcinoma, with the potential for improved pCR rates and surgical outcomes.

Notable Presentations At ESMO GI 2025
Gastric Cancer (3/4)

Date	Title	Author	Summary
03 July 2025	UCCL-IKF-NeoART: An international phase Ib/II trial investigating trastuzumab-deruxtecan (T-DXd) combined with neoadjuvant chemotherapy (Ctx) for HER2-positive, resectable esophagogastric adenocarcinoma (EGA)	Gertraud Stocker	• **Introduction:** For resectable HER2-positive esophagogastric adenocarcinoma (EGA), perioperative chemotherapy has limited efficacy. T-DXd, a HER2-targeting antibody-drug conjugate, has shown promise in advanced stages. The NeoART study investigates T-DXd combined with neoadjuvant chemotherapy in resectable HER2-positive EGA. • **Methodology**: NeoART is a phase Ib/II, multicenter, open-label trial. Patients with resectable HER2+ EGA receive T-DXd combined with chemotherapy (5-FU/LV, with or without oxaliplatin). The primary endpoint is feasibility, defined as the proportion of patients completing treatment without dose-limiting toxicity. • **Results:** Feasibility rates will be tested in two cohorts. Secondary endpoints include safety, pathological complete response (pCR), and resection rates. • **Conclusions:** NeoART aims to assess the combination of T-DXd and chemotherapy for improving outcomes in resectable HER2+ EGA, offering a potential alternative to standard perioperative chemotherapy.
03 July 2025	The predictive role of neutrophil-to-lymphocyte ratio in patients with solid cancers treated with immune checkpoint inhibitors: A pooled analysis of seven clinical trials of the German AIO study group	Lena Dreikhausen	• **Introduction:** Immune checkpoint inhibition (ICI) is standard in many cancers, but only some patients respond. This study investigates the predictive value of the neutrophil-to-lymphocyte ratio (NLR) for ICI response, focusing on solid cancers. • **Methodology**: Data from seven prospective trials (head and neck, non-small cell lung, gastroesophageal, esophageal, renal cell, and urothelial cancers) were pooled. Logistic and Cox regression analyses identified predictors for immune-related adverse events (IRAE), response, and overall survival (OS). • **Results:** Low NLR (≤3) was associated with better OS (HR 0.4) and progression-free survival (PFS) (HR 0.55). Higher NLR correlated with lower response rates and disease control. • **Conclusions:** NLR is a strong predictor of ICI response and OS, although its clinical applicability is affected by overlapping factors.

Notable Presentations At ESMO GI 2025
Gastric Cancer (4/4)

Date	Title	Author	Summary
05 July 2025	Phase III randomized IRIGA trial of FOLFIRINOX versus mFOLFOX6 as first-line treatment for patients with HER2-negative gastric and gastroesophageal adenocarcinoma	Daria Gavrilova	• **Introduction:** Platinum/fluoropyrimidine doublets are standard first-line treatment for advanced HER2-negative gastric or gastroesophageal adenocarcinoma (G/GEA). This phase III trial compares FOLFIRINOX (a triplet regimen) with mFOLFOX6 to assess efficacy and safety. • **Methodology**: Patients were randomized 1:1 to FOLFIRINOX or mFOLFOX6. The primary endpoint was progression-free survival (PFS), with secondary endpoints including overall survival (OS), objective response rate (ORR), and toxicity. • **Results:** Median PFS was 7.2 months with FOLFIRINOX versus 6.8 months with mFOLFOX6. Median OS was 13.4 months vs. 13.2 months, respectively. FOLFIRINOX showed higher ORR but increased toxicity. • **Conclusions:** FOLFIRINOX did not significantly improve PFS or OS overall, but select subgroups may benefit, particularly those with oligometastatic disease.
05 July 2025	Recurrent patient-reported outcome (PRO)-based deterioration predicts overall survival (OS) in patients with advanced gastric adenocarcinoma with PD-L1 score of ≥5%: Results from the RATIONALE-305 trial	Markus Moehler	• **Introduction:** The RATIONALE-305 trial demonstrated that adding tislelizumab (T) to chemotherapy (C) improved overall survival (OS) in gastric cancer (GC) patients with PD-L1 ≥5%. This analysis evaluates whether patient-reported outcomes (PROs) provide prognostic insights into OS for these patients. • **Methodology**: Longitudinal PRO data from 475 patients in the PD-L1 ≥5% subgroup were analyzed using linear mixed and recurrent event Cox models to assess the relationship between PRO changes and risk of symptomatic deterioration (RS-D) events and OS. • **Results:** T+C improved quality of life (QoL) and upper GI symptoms. T+C reduced the risk of death significantly (HR 0.647–0.731), indicating a 27%-35% lower likelihood of death. • **Conclusions:** T+C improved PROs and reduced mortality, supporting the prognostic value of PROs in guiding treatment decisions for GC patients with PD-L1 ≥5%.

Notable Presentations At ESMO GI 2025
Rectal Cancer (1/3)

Date	Title	Author	Summary
04 July 2025	Short-course radiotherapy followed by sintilimab and CAPOX as total neoadjuvant treatment in locally advanced rectal cancer: A prospective, randomized controlled trial (SPRING-01)	Feng Tian	• **Introduction:** Short-course radiotherapy (SCRT) combined with chemotherapy improves pathological complete response (pCR) in locally advanced rectal cancer (LARC). This phase II study explores SCRT with or without sintilimab (PD-1 inhibitor) combined with CAPOX as a total neoadjuvant therapy (TNT) for LARC. • **Methodology**: Patients with high-risk LARC were randomized 1:1 to receive SCRT followed by CAPOX with or without sintilimab. The primary endpoint was pCR in the intention-to-treat population. • **Results:** 98 patients were randomized. pCR was higher in the SIN + CAPOX arm (59.2% vs. 32.7%, $p<0.05$). Postoperative complications were higher in the SIN + CAPOX arm (24.4% vs. 11.4%). Grade ≥3 adverse events occurred in 32.7% (SIN + CAPOX) and 34.7% (CAPOX). • **Conclusions:** SCRT with sintilimab and CAPOX significantly improves pCR in LARC, with acceptable safety, supporting its potential as an effective TNT strategy.
04 July 2025	Updated results and first biomarker analysis of a phase II trial combining nivolumab (nivo) and total neoadjuvant treatment (TNT) for locally advanced rectal cancer (LARC) (CA209-8M4)	Baruch Brenner	• **Introduction:** CA209-8M4 is a phase II trial evaluating the addition of nivolumab (nivo) to total neoadjuvant therapy (TNT) in locally advanced rectal cancer (LARC). The study uses a composite endpoint combining pathological complete response (pCR) and sustained clinical complete response (cCR). • **Methodology**: Patients with high-risk LARC received chemoradiation followed by chemoimmunotherapy (mFOLFOX6 + nivo). The primary endpoint was the modified pCR (mpCR) rate, combining pCR and sustained cCR. • **Results:** 29 patients were enrolled. 64% achieved mpCR. The 5-year disease-free survival was 92.2%, and overall survival was 96.6%. CPS positivity trended toward better mpCR rates (78% vs. 33%). • **Conclusions:** Adding nivo to TNT in LARC is safe and potentially enhances effectiveness, with encouraging mpCR rates. CPS positivity may predict response, warranting further investigation.

Notable Presentations At ESMO GI 2025
Rectal Cancer (2/3)

Date	Title	Author	Summary
04 July 2025	Adebrelimab combined with short-course radiotherapy and CAPOX as total neoadjuvant therapy for pMMR locally advanced rectal cancer: Interim results	Changqing Jing	• **Introduction:** Current total neoadjuvant therapy (TNT) for locally advanced rectal cancer (LARC) results in suboptimal pathological complete response (pCR) rates (25%-28%). This study evaluates the combination of Adebrelimab (PD-L1 inhibitor), short-course radiotherapy (SCRT), and CAPOX chemotherapy as TNT for mismatch repair-proficient (pMMR) LARC. • **Methodology**: Patients with high-risk pMMR LARC received SCRT, CAPOX, and Adebrelimab. The primary endpoint was pCR, and total mesorectal excision (TME) was performed after neoadjuvant therapy. • **Results:** 31 patients were enrolled, with 23 completing treatment. The pCR rate was 43.5%, and the MPR rate was 60.9%. Grade 3-4 adverse events occurred in 17.4%, but no surgery delays or deaths were reported. • **Conclusions:** Adebrelimab combined with SCRT and CAPOX significantly improved pCR rates in pMMR LARC with manageable toxicity, supporting its potential as an effective TNT strategy.
04 July 2025	Surgical outcomes post-total mesorectal excision in patients with locally advanced rectal cancer undergoing total neoadjuvant treatment with short-course radiotherapy followed by chemo-immunotherapy: Data from the phase II Averectal trial	Ali I. Shamseddine	• **Introduction:** TME is crucial for locally advanced rectal cancer (LARC), but associated with significant morbidity. This analysis evaluates surgical outcomes in the Averectal study combining SCRT, mFOLFOX-6, and avelumab. • **Methodology**: A phase II trial assessed the combination of SCRT, chemotherapy, and avelumab in MSS LARC, with TME performed 4-6 weeks post-treatment. AEs were graded using CTCAE and Clavien-Dindo. • **Results:** 40 patients underwent surgery; 91.3% experienced serious AEs. The pCR rate was 37.5%, and 3-year local recurrence was 2.5%. • **Conclusions:** Avelumab with SCRT and FOLFOX followed by TME showed manageable surgical toxicity, emphasizing the need for careful perioperative management.

Notable Presentations At ESMO GI 2025
Rectal Cancer (3/3)

Date	Title	Author	Summary
05 July 2025	Phase II study of short-course radiotherapy (SCRT) followed by consolidation chemotherapy with FOLFOXIRI as total neoadjuvant therapy (TNT) for locally advanced rectal cancer (LARC) patients (pts): The ShorTrip study	Beatrice Borelli	• **Introduction:** Short-course radiotherapy (SCRT) followed by triplet chemotherapy (FOLFOXIRI) has not been studied in locally advanced rectal cancer (LARC). This study evaluates its feasibility and activity as total neoadjuvant therapy (TNT). • **Methodology**: 64 patients with high-risk LARC received SCRT followed by 8 cycles of FOLFOXIRI. The primary endpoint was pathological complete response (pCR). The protocol was amended after high neutropenia rates were observed. • **Results:** 21 (33%) patients achieved pCR, and 44 (69%) achieved major pathological response (MPR). The majority of pCRs and MPRs occurred in patients receiving at least 5 cycles of FOLFOXIRI. Grade 3/4 toxicities included neutropenia and diarrhea. • **Conclusions:** SCRT followed by FOLFOX and FOLFOXIRI showed promising activity and a feasible safety profile, warranting further studies in the NOM scenario.

Notable Presentations At ESMO GI 2025
Gastroesophageal Cancer (1/4)

Date	Title	Author	Summary
02 July 2025	Preliminary safety and efficacy of givastomig, a novel claudin 18.2/4-1BB bispecific antibody, in combination with nivolumab and mFOLFOX in metastatic gastroesophageal carcinoma (mGEC)	Samuel J. Klempner	• **Introduction:** Givastomig (Giva), a bispecific antibody targeting CLDN18.2 and 4-1BB, was evaluated for safety and efficacy in patients with CLDN18.2+ gastric, esophageal, or gastroesophageal adenocarcinomas (GEC). • **Methodology**: An ongoing Phase 1b trial (NCT04900818) assessed Giva combined with nivolumab and mFOLFOX in 1L GEC. The primary endpoint was safety, with pharmacokinetics (PK) and pharmacodynamics (PD) secondary measures. • **Results:** Giva was well-tolerated, with no dose-limiting toxicities. Common treatment-related adverse events (TRAEs) included nausea, vomiting, and fatigue. Partial responses (PRs) were observed in 71% of patients, with disease control in all cases. The ORR in the selected dose expansion cohorts was 83%. • **Conclusions:** Giva, combined with nivolumab and mFOLFOX, shows promising efficacy and a manageable safety profile in 1L metastatic GEC. Dose expansion is ongoing.
02 July 2025	Phase I/II clinical investigation of invikafusp alfa, a first-in-class TCR-beta chain-targeted bispecific antibody, as monotherapy in patients with anti-PD(L)1-resistant, antigen-rich gastrointestinal (GI) cancers	Elena Elez Fernandez	• **Introduction:** Invikafusp, a selective dual T-cell agonist targeting Vβ6/Vβ10 T cells, is being evaluated in the START-001 Phase 1/2 trial for anti-PD(L)1-resistant, antigen-rich solid tumors, including gastrointestinal (GI) cancers. Based on Phase 1 results, invikafusp received Fast Track Designation from the US FDA for TMB-H colorectal cancer. • **Methodology**: Patients with antigen-rich GI tumors (TMB-H, MSI-H, or HPV-associated) were treated with invikafusp at 0.08 mg/kg or 0.12 mg/kg every two weeks (Q2W). • **Results:** Of 22 patients enrolled, 67% achieved disease control. Four patients (22.2%) had partial responses (PR), and six had stable disease (SD). The most common treatment-emergent adverse event (TEAE) was transient, grade 1-2 cytokine release syndrome (CRS). Dose-dependent increases in invikafusp serum concentrations were observed. • **Conclusions:** Invikafusp demonstrated clinically meaningful anti-tumor activity in various GI cancers, particularly colorectal cancer. Phase 2 expansion is ongoing to further assess its efficacy.

Notable Presentations At ESMO GI 2025
Gastroesophageal Cancer (2/4)

Date	Title	Author	Summary
03 July 2025	High amphiregulin (AREG) plasma levels are associated with shorter survival in patients with advanced gastric cancer but are not predictive for response to cetuximab in combination with first-line chemotherapy in the global EXPAND phase III trial	Benjamin Kobitzsch	• **Introduction:** In the EXPAND phase III trial, Cetuximab, an EGFR antibody, did not show clinical benefit when added to first-line chemotherapy in advanced gastric cancer. Amphiregulin (AREG), an EGFR ligand, is associated with poor prognosis in other cancers, but its role in gastric cancer is unclear. This study explores AREG's potential as a prognostic biomarker in advanced gastric cancer. • **Methodology**: AREG plasma levels were measured in 534 patients before treatment and in 454 patients after 12 weeks. The impact of baseline and post-treatment AREG levels on progression-free survival (PFS) and overall survival (OS) was analyzed using Log-Rank and Cox regression models. • **Results:** Higher baseline AREG levels were associated with shorter PFS (4.3 vs. 6.1 months, $p<0.001$) and OS (8.4 vs. 11.8 months, $p<0.001$), regardless of treatment. However, changes in AREG levels after 12 weeks did not predict response to Cetuximab or survival outcomes. • **Conclusions:** High baseline AREG levels are a negative prognostic factor in advanced gastric cancer. However, AREG levels do not predict the response to Cetuximab treatment.
03 July 2025	Immune composition-based efficacy assessment of first-line immune-chemotherapy combinations in gastroesophageal cancer: Subgroup analysis of the phase II IKF-AIO-STO-0417 / moonlight trial	Michael Masetti	• **Introduction:** The AIO-STO-0417 trial evaluated FOLFOX plus nivolumab and ipilimumab, FLOT with nivolumab, and FOLFOX alone in advanced gastroesophageal adenocarcinoma (GEA). This study examines the prognostic value of the neutrophil-to-lymphocyte (NLR) and monocyte-to-lymphocyte (MLR) ratios in patients receiving 1st-line therapy. • **Methodology**: 262 patients were grouped by baseline NLR and MLR levels. Treatment response was assessed by RECISTv1.1, and survival was analyzed using Kaplan-Meier and Cox models. • **Results:** Low NLR and MLR correlated with improved overall survival across treatment arms, especially in patients receiving FLOT + ICI (Arm A2). • **Conclusions:** NLR and MLR are valuable biomarkers for guiding treatment in GEA patients.

Notable Presentations At ESMO GI 2025
Gastroesophageal Cancer (3/4)

Date	Title	Author	Summary
03 July 2025	The shifting global landscape of interventional clinical trials in gastric and gastroesophageal cancers: A ClinicalTrials.gov analysis	Amalya Sargsyan	• **Introduction:** Global shifts in research infrastructure and drug development necessitate an analysis of the gastric and gastroesophageal cancer (GC/GEJ) clinical trial landscape to guide future efforts. This study examines trends in GC/GEJ drug trials across phases, locations, funding, and endpoints. • **Methodology**: From 5937 GC/GEJ studies identified on ClinicalTrials.gov, 3121 interventional drug trials were analyzed after excluding observational and non-interventional studies. Data on phase, location, funding, status, and primary endpoints were collected. • **Results:** Research is concentrated in early/mid-phases, with China leading in trial volume, surpassing the US. Surrogate endpoints like ORR and PFS dominate in Phase 2, while OS is more common in Phase 3, especially in China. High early-phase trial discontinuation (12.6%) remains a significant issue. • **Conclusions:** The GC/GEJ clinical trial ecosystem has shifted, with Asia, particularly China, leading the way. Surrogate endpoints dominate, but China is making strides in late-phase OS studies. High early-phase attrition rates remain a critical challenge.
03 July 2025	Comparative efficacy and safety of tislelizumab (TIS) vs other anti–PD-1 treatments in first-line (1L) gastric or gastroesophageal junction cancer (GC/GEJC): A network meta-analysis (NMA)	Maria Alsina Maqueda	• **Introduction:** Anti–PD-1 therapies like nivolumab (NIV) and pembrolizumab (PEM) combined with chemotherapy (CT) have improved outcomes in unresectable GC/GEJC. Tislelizumab (TIS) with CT has been approved for 1L treatment in PD-L1-positive cases. This study compares the efficacy and safety of TIS+CT to NIV+CT and PEM+CT using network meta-analysis (NMA). • **Methodology**: Bayesian fixed-effect NMAs were conducted with data from five trials, evaluating progression-free survival (PFS), overall survival (OS), and grade ≥3 treatment-related adverse events (TRAEs). Subgroup analyses were performed by PD-L1 status. • **Results:** TIS+CT showed similar efficacy to NIV+CT and PEM+CT for OS and PFS. TIS+CT had fewer grade ≥3 TRAEs compared to NIV+CT and numerically fewer than PEM+CT. • **Conclusions:** TIS+CT is as effective as NIV+CT and PEM+CT with a similar or better safety profile in 1L GC/GEJC treatment.

Notable Presentations At ESMO GI 2025
Gastroesophageal Cancer (4/4)

Date	Title	Author	Summary
03 July 2025	Chemotherapy (SOX) plus tisleizumab in gastric cancer patients with liver metastasis: The first report from a multi-center phase II study	Muxing Kang	• **Introduction:** Gastric cancer (GC) with liver metastasis (LM) presents a grim prognosis. Chemotherapy combined with PD-1 inhibitors like Tisleizumab has shown promise in improving outcomes for these patients. This study evaluates the efficacy and safety of Tisleizumab combined with chemotherapy (SOX regimen) in patients with synchronous GC-LM. • **Methodology**: In this multicenter, prospective phase 2 trial, adult patients with GC-LM received chemotherapy (SOX) plus Tisleizumab for 6-8 cycles, followed by maintenance therapy for up to 2 years or until disease progression. • **Results:** 18 patients were enrolled, with an overall response rate (ORR) of 77.78% and disease control rate (DCR) of 88.89%. The median progression-free survival (PFS) and overall survival (OS) were 18.00 and 23.00 months, respectively. Patients who underwent conversion surgery (CS) showed significantly better outcomes (OS: 30 months vs. 20 months, P=0.011). • **Conclusions:** Chemotherapy plus Tisleizumab improves treatment efficiency and prognosis in GC-LM patients, with conversion surgery offering additional survival benefits.
03 July 2025	Safety and efficacy of nivolumab plus chemotherapy in patients with advanced gastric cancer with ascites: A multi-center retrospective study in Japan	Misa Onishi	• **Introduction:** This retrospective study evaluates the safety and efficacy of first-line nivolumab plus chemotherapy (Nivo-CT) in advanced gastric cancer (AGC) patients with varying degrees of ascites. While the CheckMate 649 study demonstrated efficacy in AGC without ascites, data on patients with ascites are limited. • **Methodology**: 271 patients with AGC were stratified by ascites severity (none, mild, moderate, massive) and treated with Nivo-CT. Efficacy was assessed through progression-free survival (PFS), overall survival (OS), objective response rate (ORR), and disease control rate (DCR), while safety was evaluated through immune-related adverse events (irAEs). • **Results:** Ascites severity correlated with poorer prognosis. The median PFS and OS decreased with increasing ascites severity, with PFS ranging from 8.8 months in non-ascitic patients to 3.6 months in those with massive ascites. Grade ≥3 irAEs occurred in 26.8%-41.2% of patients with ascites. • **Conclusions:** Nivo-CT remains feasible for AGC patients with ascites, including those with massive ascites, despite poorer prognosis in these patients

Notable Presentations At ESMO GI 2025
Colorectal Cancer (CRC) (1/11)

Date	Title	Author	Summary
02 July 2025	Rechallenge with amivantamab, an EGFR-MET bispecific antibody, after disease progression on prior EGFR inhibitor in left-sided RAS/BRAF wild-type metastatic colorectal cancer: Updated results from OrigAMI-1	Dirk Arnold	• **Introduction:** This study investigates the efficacy of amivantamab, an EGFR-MET bispecific antibody, in rechallenging patients with left-sided RAS/BRAF wild-type metastatic colorectal cancer (mCRC) after progression on EGFR inhibitors (EGFRi). Previous data suggests that resistance mutations to EGFRi decay at a rate of 4.4 months • **Methodology**: The OrigAMI-1 trial (NCT05379595) examined amivantamab monotherapy in patients with mCRC after 2-3 prior lines of treatment. Patients were categorized into two subgroups based on the time interval since EGFRi treatment, assessed by RECIST v1.1 • **Results:** Of 54 patients, those who had a longer interval (≥8.8 months) between EGFRi and amivantamab showed higher objective response rates (32% vs 7%), longer progression-free survival (7.0 vs 2.8 months), and a trend toward better overall survival (16.1 vs 10.4 months) • **Conclusions:** Amivantamab rechallenge is promising, with significantly better outcomes for patients rechallenged after a longer gap post-EGFRi therapy. This supports amivantamab's potential as a viable option for EGFRi-resistant mCRC
04 July 2025	Phase I study of magrolimab (ONO-7913) and nivolumab (ONO-4538, NIV) in combination with FOLFOX and bevacizumab (Bev) or cetuximab (Cet) as first-line treatment in patients with unresectable advanced or recurrent colorectal cancer (CRC)	Kensei Yamaguchi	• **Introduction:** This phase 1 study evaluates the safety and efficacy of ONO-7913 in combination with NIV and chemotherapy (FOLFOX + Bev or Cet) in patients with RAS/BRAF wild-type metastatic colorectal cancer (mCRC) • **Methodology**:The study involved two cohorts: Cohort 1 (RAS mutation/BRAF wild-type) and Cohort 2 (left-sided RAS/BRAF wild-type). Patients were administered ONO-7913 alongside standard treatments, with primary endpoints of safety and secondary endpoints of efficacy • **Results:** A total of 32 patients were treated. No dose-limiting toxicities were observed. Cohort 1 showed an ORR of 62.5%, with median progression-free survival (PFS) of 11.1 months. Cohort 2 had a higher ORR of 78.1%, with median PFS of 14.8 months • **Conclusions:** ONO-7913 demonstrated an acceptable safety profile and promising efficacy, particularly in Cohort 2, supporting its potential as a therapeutic option for mCRC

Notable Presentations At ESMO GI 2025
Colorectal Cancer (CRC) (2/11)

Date	Title	Author	Summary
04 July 2025	NALIRIFOX plus targeted therapy as first-line treatment for metastatic colorectal cancer: A phase I study	Haojie Zhou	• **Introduction:** FOLFOXIRI with targeted therapies is a recommended regimen for metastatic colorectal cancer (mCRC) patients, particularly those suitable for intensive treatment or conversion surgery. However, the combination of irinotecan liposome, oxaliplatin, and fluorouracil (NALIRIFOX) has not been explored in mCRC • **Methodology**: This phase I study used a 3+3 dose-escalation design to determine the maximum tolerated dose (MTD) of irinotecan liposome in the NALIRIFOX regimen. Patients received fixed doses of oxaliplatin, fluorouracil, and bevacizumab, with irinotecan liposome starting at 60mg/m2. In phase Ib, the MTD was confirmed, and efficacy was assessed • **Results:** The MTD of irinotecan liposome was 50mg/m2. The most common treatment-related adverse events included diarrhea (53.9%), nausea (40.8%), and anemia (36.8%). The objective response rate (ORR) was 82.5%, with a 100% disease control rate (DCR) and 12.3% R0 resection rate • **Conclusions:** Irinotecan liposome at 50mg/m2 in the NALIRIFOX regimen demonstrates manageable safety and promising efficacy as a first-line treatment for mCRC
04 July 2025	ORGANOTREAT-01: A pioneer phase I/II multicenter trial of organoid-driven precision medicine for refractory colorectal cancer	Fanny Jaulin	• **Introduction:** This study evaluates the use of PDTOs to guide treatment decisions in metastatic colorectal cancer (mCRC), with a focus on demonstrating the feasibility of generating personalized therapies based on ex vivo drug testing • **Methodology**: In this phase I/II multicenter trial, mCRC patients underwent core biopsies to generate PDTOs, which were then screened with a 25-drug panel. A tumor board analyzed the results to recommend personalized treatments. The primary objective was to generate PDTOs for over 50% of patients within 10 weeks • **Results:** Out of 61 enrolled patients, 74.1% had successful PDTO generation within the timeline. Personalized treatment was administered to 21 patients, with 4 showing clear clinical benefits, achieving progression-free survival beyond 6 months • **Conclusions:** This study demonstrates the feasibility of PDTO-based drug screening in clinical workflows, with promising clinical signals observed in mCRC patients. These results support expanding this approach to other cancer types, including pancreatic cancer

Notable Presentations At ESMO GI 2025
Colorectal Cancer (CRC) (3/11)

Date	Title	Author	Summary
04 July 2025	Integrating tissue (TBx) and liquid biopsy (LBx) comprehensive genomic profiling to predict efficacy of anti-EGFR therapies in metastatic colorectal cancer (mCRC): Findings from the CAPRI-2 GOIM study	Eleonora Cioli	• **Introduction:** The CAPRI-2 GOIM study evaluates the integration of tumor biopsy (TBx) and liquid biopsy (LBx) comprehensive genomic profiling (CGP) to predict the efficacy of FOLFIRI plus cetuximab in RAS/BRAFV600E wild-type metastatic colorectal cancer (mCRC) • **Methodology**: Patients underwent TBx and LBx before starting treatment. Molecular profiles were analyzed using the FoundationOne CDx assay, and response rates and progression-free survival (PFS) were correlated with the genomic findings. The study aimed to compare the efficacy of TBx and LBx profiles in predicting treatment outcomes • **Results:** Of 156 evaluable patients, those with molecular profiles selected by TBx and LBx showed significantly higher objective response rates (79.6% vs 44.2%) and mPFS (12.4 months vs 7.4 months) than those with mutated profiles. Concordant cases had lower ORR and mPFS compared to discordant cases • **Conclusions:** Integrating TBx and LBx CGP can provide a more comprehensive molecular landscape for mCRC, improving patient selection. LBx alone is effective in cases with high ctDNA tumor fraction, while TBx adds valuable data for cases with low tumor fraction
04 July 2025	Comprehensive genomic profiling to guide personalized targeted and immunotherapy in gastrointestinal tumors: Subgroup analysis of the ROME trial	Chiara Cremolini	• **Introduction:** The ROME study (NCT04591431) evaluates tailored therapy (TT) guided by comprehensive genomic profiling (CGP) vs. standard care (SoC) in advanced solid tumors, focusing on a gastrointestinal (GI) subgroup after one or two prior therapies • **Methodology**: Genomic alterations were identified using tissue and blood CGP. Patients with targetable alterations were randomized to TT or SoC. Primary endpoint: objective response rate (ORR); secondary: progression-free survival (PFS) and overall survival (OS) • **Results:** Of 869 screened GI patients, 186 were randomized. TT showed higher ORR (20.0% vs. 10.5%) and significantly improved PFS (median 4.2 vs. 2.8 months, HR 0.55, $p<0.001$). In colorectal cancer, TT improved PFS (median 5.4 vs. 2.8 months, HR 0.53, $p=0.026$). TT also showed better outcomes for patients with HER2 alterations • **Conclusions:** CGP-guided TT offers significant benefits over SoC for GI cancer patients, identifying targeted therapies not routinely available. Further studies are needed to refine TMB and disease-specific thresholds

Notable Presentations At ESMO GI 2025
Colorectal Cancer (CRC) (4/11)

Date	Title	Author	Summary
04 July 2025	Plasmatic biomarkers of BRAF inhibitor combination therapy for BRAF-mutated metastatic colorectal cancer: Insights from the BEETS trial (JACCRO CC-18)	Chiaki Inagaki	• **Introduction:** This study evaluates the efficacy and safety of BRAF inhibitor combinations in second- or third-line treatment • **Methodology**: The trial employed whole-exome sequencing (WES) and mRNA sequencing on cell-free DNA and tumor-educated platelet RNA (TEP-seq) from plasma samples. The analysis aimed to correlate biomarkers with responders (R) and non-responders (NR) to treatment • **Results:** Of 203 patients, 189 had complete genomic data. Plasmatic BRAF mutations were present in 43%, with BRAF+ patients showing larger tumor volumes and more liver/lymph node metastases. BRAF+ patients had shorter progression-free survival (PFS) and overall survival (OS). TTx patients with elevated immune gene signatures, especially those linked to neutrophil aggregation, showed poorer responses • **Conclusions:** Plasmatic BRAF mutations are a prognostic marker for BRAF-mutated mCRC. Elevated immune-related gene signatures may impact TTx outcomes, highlighting the potential for tailored therapy in this population
04 July 2025	Clinical outcomes of modified (m)-FOLFOXIRI plus cetuximab versus bevacizumab by metastasis status in RAS/BRAF wild-type and left-sided metastatic colorectal cancer: The DEEPER trial (JACCRO CC-13)	Yu Sunakawa	• **Introduction:** This study explores the impact of metastasis status on treatment outcomes, particularly in patients with liver-limited disease (LLD) • **Methodology**: A post-hoc analysis was performed to evaluate resection rates and survival in patients with left-sided RAS/BRAF wild-type tumors. Patients were treated with m-FOLFOXIRI plus Cet or Bev, and outcomes were compared based on metastasis status • **Results:** Among 359 patients, Cet treatment improved median progression-free survival (PFS) and overall survival (OS) compared to Bev in non-LLD patients, especially in those without resection. In LLD patients, there were no significant differences between the two treatments in terms of resection rates or OS • **Conclusions:** m-FOLFOXIRI plus Cet significantly improves survival in non-LLD patients compared to Bev, regardless of resection status. This highlights the potential benefit of Cet as part of first-line therapy for mCR

Notable Presentations At ESMO GI 2025
Colorectal Cancer (CRC) (5/11)

Date	Title	Author	Summary
04 July 2025	AntiEGFR-based maintenance versus stop&go strategy in patients with left-sided, non MSI, RAS/BRAF wild type (wt) metastatic colorectal cancer (mCRC): Individual patient data (IPD) pooled analysis of randomized clinical trials (RCTs)	ALESSANDRA RAIMONDI	• **Introduction:** The DEEPER trial (JACCRO CC-13) compared the efficacy of induction therapy with FOLFOX/FOLFIRI plus anti-EGFR, followed by maintenance strategies (stop&go vs. anti-EGFR + FUFA) in this patient group • **Methodology**: An individual patient data (IPD) meta-analysis of four phase 2 RCTs was conducted, including 378 patients treated with anti-EGFR+FUFA, anti-EGFR, or a treatment break. Primary endpoint: overall survival (OS); secondary endpoints: progression-free survival (PFS) and time to failure of strategy (TTFS) • **Results:** OS was similar across stop&go and maintenance strategies. PFS was superior with maintenance therapy (anti-EGFR + FUFA) compared to stop&go. TTFS favored stop&go, especially in patients without resection. In non-LLD patients, the stop&go regimen showed longer OS, particularly in those with no resection • **Conclusions:** Both stop&go and maintenance strategies are valid options for patients treated with anti-EGFR-based therapies. The choice should consider patient characteristics, treatment response, and tolerability. Further phase 3 studies are needed to compare these strategies
04 July 2025	Trifluridine/tipiracil plus bevacizumab (TTB) versus regorafenib (R) in refractory advanced colorectal cancer patients: A real-word evidence efficacy study	Jesus Rodriguez Pascual	• **Introduction:** Trifluridine/tipiracil plus bevacizumab (TTB) and regorafenib (R) both extend overall survival (OS) in refractory advanced colorectal cancer (aCRC), but no direct comparative studies have been conducted. This study compares OS between TTB and R using real-world dat • **Methodology**: The TriNetX Global Collaborative Network was used to analyze retrospective data from 1483 aCRC patients across 59 healthcare organizations. Propensity Score Matching (PSM) was employed to balance cohorts by age, gender, and race/ethnicity. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated to compare O • **Results:** 442 patients received TTB, and 1041 received R. TTB-treated patients had a significantly better OS than those treated with R (median OS 255 days vs. 197 days, HR 0.784, 95% CI 0.675-0.910) • **Conclusions:** Based on real-world data, TTB plus bevacizumab is associated with better overall survival than regorafenib in refractory advanced colorectal cancer

Notable Presentations At ESMO GI 2025
Colorectal Cancer (CRC) (6/11)

Date	Title	Author	Summary
04 July 2025	Pooled safety analysis of trifluridine/tipiracil (FTD/TPI) plus bevacizumab (BEV) for metastatic colorectal cancer (mCRC) using individual patient data (IPD) from five clinical trials	Kentaro Yamazaki	• **Introduction:** This pooled analysis examines the clinical outcomes and safety of FTD/TPI plus BEV across different treatment lines • **Methodology**: The analysis included individual patient data (IPD) from four clinical trials: C-TASK FORCE, TAS-CC3, TRUSTY, and KSCC1602. Patients were categorized into 1st/2nd-line and late-line treatment groups, with safety and efficacy assessed based on treatment line and patient background • **Results:** A total of 292 patients received FTD/TPI plus BEV. Thrombocytopenia, nausea, and proteinuria were more common in the late-line group. Female patients, especially in late-line treatment, had higher rates of nausea, vomiting, anorexia, and fatigue • **Conclusions:** FTD/TPI plus BEV is effective across treatment lines, but more supportive care may be necessary for females, especially in late-line treatment, due to the higher incidence of certain AEs
04 July 2025	BETTER study: An open-label, single-arm trial of tislelizumab, bevacizumab, TAS102, and SBRT as third-line therapy for MSS/pMMR metastatic colorectal cancer	Qun Zhang	• **Introduction:** This study investigates a novel combination therapy to enhance the efficacy of third-line treatment for MSS/pMMR mCRC patients • **Methodology**: The therapy combines stereotactic body radiation therapy (SBRT) with tislelizumab (200 mg), bevacizumab (7.5 mg/kg), and TAS102. SBRT targets metastatic lesions, followed by consolidation therapy every 21 days. Primary endpoints were progression-free survival (PFS) and objective response rate (ORR), with secondary endpoints of overall survival (OS), disease control rate (DCR), and safety • **Results:** Of 16 evaluable patients, 25% achieved partial response (PR), 62.5% stable disease (SD), and 12.5% progressive disease (PD). The ORR was 25%, and DCR was 87.5%. Median PFS was 7.5 months, with a 6-month PFS rate of 58.4% and 12-month PFS rate of 22.3%. Grade 3+ AEs occurred in 6.25% of patient • **Conclusions:** The quadruple therapy combination shows promising efficacy and safety in third-line treatment for MSS/pMMR mCRC, supporting further clinical investigation

Notable Presentations At ESMO GI 2025
Colorectal Cancer (CRC) (7/11)

Date	Title	Author	Summary
04 July 2025	Age cut-off for oxaliplatin efficacy in stage II/III colorectal cancer	Sanghee Kang	• **Introduction:** his study investigates the optimal age threshold for survival benefit from adding oxaliplatin to fluoropyrimidine-based chemotherapy • **Methodology**: A population-based retrospective study was conducted using data from Korea's Health Insurance Review and Assessment Service. Patients who underwent curative resection for stage II/III colorectal cancer between 2014 and 2016 were included. The primary outcome was overall survival, assessed via Cox regression and propensity score matching • **Results:** Among 8,561 patients, oxaliplatin showed no survival benefit in stage II cancer at any age threshold. In stage III, oxaliplatin significantly improved survival up to age 70 (5-year OS: 84.8% vs. 78.1%, P=0.003). No benefit was observed in patients older than 70. Oxaliplatin use led to higher treatment discontinuation in patients >70 (aOR 1.53, P=0.002) • **Conclusions:** Oxaliplatin improves survival in stage III colorectal cancer patients ≤70 but not in older patients or those with stage II disease. Tailored treatment strategies are needed for older patients due to higher discontinuation rates
04 July 2025	Efficacy of pembrolizumab and feasibility of organ preservation in non-metastatic, unresectable dMMR CRC	Lauren Van den Dungen	• **Introduction:** The PUMA study aimed to evaluate the efficacy of pembrolizumab (pembro) and the feasibility of organ preservation in this patient population • **Methodology**: Patients with non-metastatic dMMR CRC requiring multivisceral surgery or induction treatment were treated with pembrolizumab (200 mg every 3 weeks for up to 2 years). Primary endpoints were the radiographic objective response rate (ORR) of at least 60%, with secondary endpoints including clinical complete response (cCR) and pathologic response • **Results:** 25 patients were treated, with 80% ORR in the 20 patients with measurable disease. 68% underwent surgery, and 32% opted for organ preservation. 48% had a combined cCR/pCR rate. Of the surgery group, 65% had major pathologic response (MPR), including 35% with pCR. One patient had recurrence, and one died from a second primary tumor • **Conclusions:** Neoadjuvant pembrolizumab resulted in significant cCR/pCR rates and successful organ preservation in selected patients with unresectable dMMR CRC, suggesting the need for further investigation into this treatment approach

Notable Presentations At ESMO GI 2025
Colorectal Cancer (CRC) (8/11)

Date	Title	Author	Summary
04 July 2025	Results of colorectal cancer screening in the Republic of Kazakhstan over 14 years (2011-2024)	Abay Jumanov	• **Introduction:** Colorectal cancer (CRC) incidence in Kazakhstan has been increasing, aligning with global trends. CRC screening was introduced in 2011 to address the rising incidence. This study evaluates the outcomes of CRC screening in Kazakhstan from 2011 to 2024 • **Methodology**: From 2011 to 2024, 13,200,497 men and women aged 50-70 were screened, representing approximately 65% of the target population. The screening program utilized fecal occult blood testing (FOBT) to identify positive cases • **Results:** Over the 14-year period, 202,847 positive FOBT results were identified, with 4,896 CRC cases detected. The percentage of stage I cases increased significantly from 7.0% in 2011 to 41.4% in 2023. The average detection rate was 0.037%, with CRC moving from 5th to 2nd in the structure of oncopathology • **Conclusions:** The introduction of CRC screening in Kazakhstan has improved early detection, reduced mortality, and altered the epidemiological landscape, despite organizational challenges. The program's benefits are evident, especially in increasing the detection of early-stage CRC cases
04 July 2025	Efficacy and safety of triple-therapy with bevacizumab, oxaliplatin, with irinotecan for metastatic colorectal cancer failed with previous fluorouracil-centered treatment	Lu Han	• **Introduction:** This study aims to analyze the effectiveness of BOI therapy for metastatic CRC patients • **Methodology**: A retrospective study was conducted on 35 metastatic CRC patients treated with BOI therapy from July 2019 to December 2023. Patients had received at least one prior combination therapy with two anti-cancer drugs. The main outcomes assessed were overall survival (OS), progression-free survival (PFS), and objective response rate (ORR) • **Results:** The median OS was 340 days, and the median PFS was 139 days. The ORR was 22.9%, and the disease control rate was 54.3%. Following progression, 57.1% of patients switched to novel treatments. The most common adverse events included leukaemia (26%), abnormal liver function (25.7%), and thrombocytopenia (22.9%) • **Conclusions:** BOI therapy is effective and safe for treating metastatic CRC patients who are resistant to prior fluorouracil-based therapy. The treatment provides a reasonable survival benefit with manageable adverse effects

Notable Presentations At ESMO GI 2025
Colorectal Cancer (CRC) (9/11)

Date	Title	Author	Summary
04 July 2025	MIRACLE3: Phase II study of ivonescimab plus radiotherapy and chemotherapy as first-line treatment in MSS colorectal cancer patients with unresectable liver/lung metastases	Xinxiang Li	• **Introduction:** The MIRACLE-3 study evaluates combining radiotherapy with chemotherapy and Ivonescimab (PD-1/VEGF dual antibody) in first-line treatment for MSS unresectable mCRC • **Methodology**: MIRACLE-3 is a phase 2, single-arm study enrolling patients aged 18-75 with untreated or post-adjuvant chemotherapy MSS mCRC. Patients receive Ivonescimab plus CapeOX, followed by short-course radiotherapy. Primary endpoint: progression-free survival (PFS); secondary endpoints include objective response rate (ORR), overall survival (OS), disease control rate (DCR), and immunotherapy-related toxicity • **Results:** 36 patients will be enrolled, aiming to detect a median PFS improvement from 9 to 15 months. Correlative studies will assess genomic, ctDNA, and immune biomarkers • **Conclusions:** MIRACLE-3 will evaluate if combining radiotherapy, chemotherapy, and Ivonescimab improves outcomes in MSS unresectable mCRC, with full accrual expected by late 2025
04 July 2025	Liquid biopsy-guided selection for anti-EGFR re-treatment in RAS/BRAF wild-type (wt) chemorefractory metastatic colorectal cancer patients (mCRC pts): Results from the phase II randomized PARERE trial	Paolo Ciracì	• **Introduction:** The PARERE study (NCT04787341) investigates the optimal sequencing of panitumumab (pani) and regorafenib (rego) in chemorefractory RAS and BRAF wild-type (wt) metastatic colorectal cancer (mCRC) patients who previously benefited from first-line anti-EGFR therapy and received at least one subsequent line of anti-EGFR-free treatment • **Methodology**: Patients were screened using the Oncomine Colon cfDNA assay, and those without RAS or BRAF V600E mutations in circulating tumor DNA (ctDNA) were randomized to receive pani followed by rego or the reverse sequence. The primary endpoint was overall survival (OS), with secondary endpoints including objective response rate (ORR), progression-free survival (PFS), and disease control rate (DCR) • **Results:** Of 428 patients screened, 213 ctDNA-wt patients were randomized. Treatment with pani followed by rego showed significantly higher ORR (16% vs. 2%) and DCR (59% vs. 32%) and longer PFS compared to the reverse sequence. A longer time interval from the last anti-EGFR treatment was associated with better PFS in the pani group • **Conclusions:** ctDNA-guided treatment selection identified patients who benefit from re-treatment with anti-EGFR in the chemorefractory setting, supporting the use of pani followed by rego in RAS and BRAF wt mCRC patients

Notable Presentations At ESMO GI 2025
Colorectal Cancer (CRC) (10/11)

Date	Title	Author	Summary
05 July 2025	Panitumumab (P) + FOLFIRINOX or mFOLFOX6 in unresectable metastatic colorectal cancer (mCRC) patients (pts) with RAS/BRAF wild-type (WT) tumor status from circulating DNA (cirDNA): Final results of the randomised phase II PANIRINOX-UCGI28 study	Thibault Mazard	• **Introduction:** Results for liver-limited (str 1) and non-liver-limited (str 2) cases are reported • **Methodology**: Patients were randomized to Arm A or B. Primary endpoint: CR rate (RECIST 1.1). Secondary endpoints: PFS, OS, and adverse events • **Results:** Between 10/2017 and 08/2023, 152 patients were randomized. CR rates: 27.3% (Arm A, str 1) vs 23.5% (Arm B), and 7.7% (Arm A, str 2) vs 7.4% (Arm B). ORR: 90.9% (Arm A, str 1) vs 91.2% (Arm B) and 75.4% (Arm A, str 2) vs 77.8% (Arm B). Median PFS: 10.7 months (Arm A, str 1) vs 11.2 months (Arm B) and 9.1 months (Arm A, str 2) vs 9.0 months (Arm B). Grade ≥3 adverse events: diarrhea (34.2% vs 11.9%), neuropathy (18.8% vs 19.4% • **Conclusions:** PANIRINOX showed high response rates but met the primary endpoint only in non-liver-limited cases. Intensified chemotherapy with anti-EGFR isn't supported for first-line chemorefractory RAS/BRAF wild-type mCRC, and further evaluation is needed for low mutation frequency patients
05 July 2025	Tumor immune microenvironment and survival outcome following preoperative chemoradiotherapy in locally advanced rectal cancer: Results from the STAR-01 study cohort	Francesca Negri	• **Introduction:** In this study, how immune cell distribution in locally advanced rectal cancer (LARC) patients was explored , before and after preoperative chemoradiotherapy (CRT), correlates with patient outcomes • **Methodology**: 413 samples (110 paired pre- and post-treatment) from 303 patients in the STAR-01 trial (fluorouracil-based CRT with/without oxaliplatin) was analysed. Tumor-infiltrating lymphocytes (TILs) were quantified and subtyped. We correlated immune cell composition with overall survival (OS) and event-free survival (EFS) outcomes • **Results:** Pre-treatment CD20+ cell counts were associated with better EFS (70.8% vs 59.6%, P = 0.051). Post-treatment, moderate-high TIL scores, low CD4/CD8 ratio, and CD20+ cell counts were significantly associated with improved EFS and OS. Survival analyses adjusted for treatment confirmed the independent predictive role of these marker • **Conclusions:** Post-CRT immune profiling of the TME offers valuable prognostic insights for LARC patients, supporting its use for risk stratification and personalized treatment

Notable Presentations At ESMO GI 2025
Colorectal Cancer (CRC) (11/11)

Date	Title	Author	Summary
05 July 2025	A phase II study of olaparib in patients (pts) with advanced biliary tract cancer (aBTC) with aberrant homologous recombinant repair (HRR) mutations	Daniel Ahn	• **Introduction:** This study tested the efficacy of olaparib in patients with HRR-associated mutations in advanced BTC (aBTC) • **Methodology**: A single-arm Phase II trial (NCT04042831) enrolled patients with HRR-associated mutations after prior chemotherapy. Patients received olaparib 300mg twice daily until progression. Primary endpoint: progression-free survival (PFS) rate at the first scan. Secondary endpoints: overall survival (OS), objective response rate (ORR), and duration of response (DOR • **Results:** 31 patients enrolled, median age 67 years, with a median of 2 prior treatments. 22/30 patients (73.3%) were progression-free at the first scan. Median OS was 11.2 months, and PFS was 16.7 weeks. One complete response and one partial response were observed. Grade 3/4 treatment-related adverse events (TRAEs) occurred in 21.9%, with hematologic TRAEs in 18.8% • **Conclusions:** Olaparib demonstrated efficacy in HRR-deficient aBTC, achieving the primary endpoint of PFS. Treatment was well tolerated, and PARP inhibitors represent a potential therapy for this subgroup. Further studies on combination strategies are warranted

Notable Presentations At ESMO GI 2025
Hepatocellular Carcinoma (HCC) (1/3)

Date	Title	Author	Summary
02 July 2025	Irpagratinib (ABSK-011) plus atezolizumab in first-line (1L) and immune checkpoint inhibitors (ICIs) treated advanced hepatocellular carcinoma (HCC) with FGF19 overexpression (+): Updated results of the phase II ABSK-011-201 study	Qi Cheng	• **Introduction:** This study reports updated phase 2 results with more patients at the recommended dose • **Methodology**: Patients with FGF19+ HCC, ECOG PS ≤1, BCLC stage B/C, and Child-Pugh 5-7, received 220 mg BID Irpagratinib plus 1200 mg Q3W Atezolizumab. Tumor assessments were done every 6 weeks per RECIST v1.1 • **Results:** As of Nov 19, 2024, 33 patients were enrolled (15 1L, 18 pre-treated), including 16 with prior ICI therapies. The overall response rate (ORR) was 51.7%, with ORRs of 50.0% (1L) and 52.9% (pre-treated). Median PFS was 7.0 months with a 9-month PFS rate of 40.6%. Common adverse events included ALT increase (75.8%) and diarrhea (51.5%) • **Conclusions:** Irpagratinib plus Atezolizumab showed promising activity in both 1L and ICI-treated FGF19+ HCC. This combination warrants further development in treatment-naïve and ICI-pretreated settings
02 July 2025	Safety results from the phase IIIb SIERRA study of durvalumab (D) and tremelimumab (T) as first-line (1L) treatment (tx) for hepatocellular carcinoma (HCC) participants (pts) with a poor prognosis	Stephen L. Chan	• **Introduction:** The phase 3b SIERRA study (NCT05883644) investigates the safety and efficacy of STRIDE (Single T Regular Interval D) as 1L treatment for a broader population, including those with Child-Pugh (CP) B7/B8, ECOG PS 2, or chronic main trunk portal vein thrombosis (Vp4) • **Methodology**: Patients received D 1500 mg + T 300 mg on Day 1, followed by D 1500 mg every 4 weeks. The primary endpoints were Grade 3/4 adverse events (AEs) within 6 months and objective response rate (ORR). Safety data are presented after ~60 patients were followed for ≥6 months (data cutoff: 27 September 2024) • **Results:** 98 patients were treated, with 35 having CP B7/B8, 44 with ECOG PS 2, and 19 with Vp4. The median age was 70, with 87% male. Grade 3/4 PRAEs occurred in 19.4% of patients. Any AE was reported in 90.8%, with 65.3% reporting PRAEs. Serious AEs occurred in 32.7%, and immune-mediated AEs were reported in 25.5% • **Conclusions:** STRIDE had manageable safety and was consistent with the HIMALAYA study, even in patients with worse hepatic function, poorer ECOG PS, or more advanced vascular invasion. Further studies are warranted

Notable Presentations At ESMO GI 2025
Hepatocellular Carcinoma (HCC) (2/3)

Date	Title	Author	Summary
04 July 2025	Tegavivint, a downstream Wnt/ß-catenin inhibitor: Interim results from a phase I/II trial in advanced hepatocellular carcinoma (aHCC)	Daneng Li	• **Introduction:** Tegavivint is an inhibitor of TBL1, blocking the Wnt/β-catenin pathway and degrading nuclear β-catenin. This study evaluates tegavivint in aHCC patients with mutations in the HRR pathway (NCT05797805) • **Methodology**: This phase 1/2 trial used a 3+3 dose escalation design. Eligible patients had aHCC, received prior treatment, and had mutations in APC, AXIN1, or CTNNB1. Primary endpoint: safety, secondary: preliminary efficacy and PK/PD • **Results:** 28 patients enrolled; median age 67, 15 had AXIN1 or CTNNB1 mutations. Doses of 3, 5, and 6.5 mg/kg were safe, with no grade ≥4 adverse events. The only grade 3 adverse event was hyperbilirubinemia. In patients with β-catenin mutations, the disease control rate was 88%, with 2 partial responses, compared to 45% in wild-type patients. 50% of mutation-positive patients remained on treatment for >6 months • **Conclusions:** Tegavivint is tolerable and shows promising efficacy, especially in patients with β-catenin mutations
04 July 2025	Atezolizumab plus bevacizumab as first-line therapy in unresectable HCC: Final analysis from phase IIIb AMETHISTA study	Lorenza Rimassa	• **Introduction:** The phase IIIb AMETHISTA study (NCT05883644) was conducted in Italy to assess its safety and efficacy in a broader cohort. This report presents the final analysis as of August 2024 • **Methodology**: Patients with uHCC and no prior systemic therapy received atezolizumab (1200 mg) plus bevacizumab (1500 mg) every 3 weeks. The primary endpoint was the incidence of grade 3-5 bleeding. Secondary endpoints included overall survival (OS), progression-free survival (PFS), ORR, DOR, TTP, and PPS • **Results:**152 patients were enrolled, with a median follow-up of 18.5 months. Grade 3-5 bleeding occurred in 13.4%. Median OS was 20.8 months, with a 36-month OS rate of 29.2%. Median PFS was 8.8 months, and ORR was 28.3%. The median DOR was 17.4 months, and median TTP was 11.2 months. Patients with progression at target lesions had longer OS (26.4 months vs. 18.8 months). Patients discontinuing due to progression had a median OS of 22.1 months • **Conclusions:** The AMETHISTA study confirmed the safety and efficacy of atezolizumab plus bevacizumab in uHCC. The combination showed promising outcomes with insights into factors influencing treatment results

Notable Presentations At ESMO GI 2025
Hepatocellular Carcinoma (HCC) (3/3)

Date	Title	Author	Summary
04 July 2025	ATHECA: Final safety and efficacy analysis of a phase IIIb study of atezolizumab + bevacizumab in Spanish patients with unresectable HCC	Maria Elisa Reig Monzon	• **Introduction:** The phase 3b AMETHISTA study (NCT05883644) evaluated the safety and efficacy of this regimen in an Italian cohort. This report presents the final analysis with a median follow-up of 29.2 months • **Methodology**: Patients with uHCC and no prior systemic therapy received ATZ+BEV until progression or unacceptable toxicity. The primary endpoint was the incidence of grade 3–5 bleeding. Secondary endpoints included overall survival (OS), progression-free survival (PFS), overall response rate (ORR), duration of response (DOR), and post-progression survival (PPS). • **Results:** 152 patients were enrolled, with a median follow-up of 29.2 months. The incidence of grade 3–5 bleeding was 13.4%. Median OS was 20.8 months (36-month OS rate: 29.2%), with a median PFS of 8.8 months. ORR was 28.3%. Patients with progression at target lesions had a longer median OS (26.4 months). Discontinuing due to progression resulted in a median OS of 22.1 months • **Conclusions:** The AMETHISTA study confirmed the safety and efficacy of ATZ+BEV in uHCC. The combination provided promising outcomes and insights into factors influencing treatment results
04 July 2025	Real-world experience of immune checkpoint inhibitors in Hepatocellular carcinoma from India: Efficacy and liver related toxicity	Namratha Udupa M S	• **Introduction:** HCC etiology is shifting from viral to non-viral causes like ALD and MASLD. ICIs have significantly impacted HCC treatment • **Methodology**: This retrospective multicenter study analyzed 71 HCC patients treated with ICIs between October 2018 and March 2025. ICIs used were Nivolumab, Nivolumab plus Ipilimumab, Atezolizumab plus Bevacizumab, and Durvalumab. Demographic data, liver function, and liver-related toxicity, including portal hypertension-related upper GI bleed and viral reactivation, were assessed. Survival outcomes (OS and PFS) were calculated • **Results:** 58 (81.6%) males, median age 68 years. Comorbidities: hypertension (87.3%), diabetes (77.4%), dyslipidemia (64.7%), obesity (90%). MASLD-related HCC (50%) was most common, with ALD (22.5%) and viral-related HCC (8.4%). Liver-related toxicities included IMH (21.1%), GI bleed (16.9%), and viral reactivation (1.6%). Median OS was 16 months, PFS was 15.5 months • **Conclusions:** HCC screening should extend to non-cirrhotic NAFLD. Lifestyle changes and chemoprevention are key in preventing NASH-related HCC. Differentiating ICI-induced hepatitis from autoimmune hepatitis is challenging

Notable Presentations At ESMO GI 2025
Hepatocellular Carcinoma (HCC) & Hepatobiliary (1/3)

Date	Title	Author	Summary
04 July 2025	Transarterial chemoembolization (TACE) with or without anti-PD1/PD-L1 systemic therapy in unresectable hepatocellular carcinoma: A meta-analysis of randomized clinical trials	Henrique J. Kim	• **Introduction:** This systematic review and meta-analysis aimed to evaluate the safety and efficacy of combining TACE with immunotherapy in this patient population • **Methodology**: A systematic search was conducted on March 24, 2025, across multiple databases for randomized clinical trials (RCTs) evaluating TACE with or without anti-PD1/PD-L1 therapies in unresectable HCC. Primary outcomes assessed were objective response rate (ORR), progression-free survival (PFS), and safety • **Results:** Three RCTs (CAP-ACE, EMERALD-1, LEAP-012) with 1,296 patients were included. TACE plus immunotherapy reduced the risk of disease progression or death by 41% (HR 0.59, p=0.007). Combination therapy also showed a higher ORR (OR 2.31, p=0.0006) and disease control rate (OR 2.0, p=0.03). However, higher rates of treatment discontinuation (OR 5.22, p < 0.00001) and serious adverse events (OR 4.62, p=0.0004) were noted • **Conclusions:** TACE combined with immunotherapy demonstrates significant efficacy for unresectable HCC, though further studies with extended follow-up are needed to assess long-term benefits and safety
04 July 2025	Final analysis of a randomized, double blind, phase II study of sorafenib with or without YIV-906 in patients with advanced HCC	Ghassan K. Abou-Alfa	• **Introduction:** Preclinical studies suggest that YIV-906 modulates the tumor microenvironment, enhances immunity, and reduces GI inflammation and non-hematological toxicities • **Methodology**: A phase II, double-blinded, placebo-controlled study combined YIV-906 with sorafenib (SORA) in advanced, naïve HCC patients (NCT04000737). The primary endpoint was PFS, with secondary endpoints including TTP, ORR, DCR, OS, QoL, and safety. Patients were stratified by metastatic status and ECOG. Translational studies included pharmacokinetics and biomarker analysis • **Results:** Out of 107 screened, 60 received at least one dose. The YIV-906 arm (N=41) had a median PFS of 4.1 months vs. 2.3 months in the placebo arm (HR=0.50, p=0.063). Median OS was 14.3 months vs. 7.5 months (HR=0.92, p=0.81). Among those completing ≥2 cycles (N=49), the YIV-906 arm showed a median PFS of 5.6 months vs. 2.3 months (HR=0.31, p=0.004). No new safety signals were identified • **Conclusions:** Despite early closure, the trial met its statistical requirements, supporting further studies of YIV-906 in HCC

Notable Presentations At ESMO GI 2025
Hepatocellular Carcinoma (HCC) & Hepatobiliary (2/3)

Date	Title	Author	Summary
04 July 2025	Dose escalation STRATegy of regorafenib in Advanced HepatoCellular Carcinoma: Phase II STRATA-HCC trial	Leonardo G. Fonseca	• **Introduction:** This trial evaluates the safety and activity of an escalated regorafenib dosing schedule to alleviate toxicities • **Methodology**: STRATA-HCC is a phase II, single-arm study of previously treated HCC patients with Child-Pugh A-B7 and PS 0-1. Regorafenib started at 80 mg/day with weekly increases of 40 mg, reaching 160 mg/day if no significant drug-related AEs occurred in cycles 1-2. The primary endpoint was the proportion of patients completing cycle 4 without progression or intolerance • **Results:** Twenty-five patients were enrolled (median age 64, 80% with viral etiology, 80% with prior locoregional therapies). Eight (32%) had prior immunotherapy, and 20% had received ≥2 systemic treatments. The primary endpoint was met, with 72% completing 4 cycles. The maximum tolerated dose (MTD) was 120 mg/day in 52% and 80 mg/day in 44%. Common grade ≥2 AEs were fatigue (20%), hand-foot skin reaction (12%), and hypertension (12%). The median OS was 9.9 months, with a 1-year survival rate of 66.9% for second-line regorafenib treatment. Disease control was achieved in 88% • **Conclusions:** The dose-escalation strategy of regorafenib provided treatment benefits with a favorable safety profile, offering an alternative approach after 1st-line therapy
04 July 2025	A phase II, non-randomized, single-arm, translational study of cabozantinib for patients with hepatocellular carcinoma (HCC) refractory to first-line treatment (the IKF-t018 AURORA trial)	Arndt Vogel	• **Introduction:** This trial evaluates the safety and efficacy of cabozantinib after any first-line therapy other than sorafenib • **Methodology**: This phase II, open-label, single-arm trial included patients with unresectable HCC, Child-Pugh A-B7, and PS 0-1. Cabozantinib was administered at 60 mg/day with dose escalation if tolerated. The primary endpoint was the proportion of patients completing cycle 4 without progression or intolerance. Secondary endpoints included OS, PFS, ORR, DCR, and toxicity • **Results:** Twenty-two patients were enrolled (median age 71 years, 80% viral etiology). The primary endpoint was met, with 72% completing 4 cycles. Median OS was 12.94 months, and PFS was 2.96 months. Only one patient (4.5%) had a partial response. TRAEs of grade ≥3 occurred in 31.8% of patients. Dose modifications occurred in 6 patients due to AEs. ECOG and Child-Pugh scores worsened in 59.1% and 63.6% of patients, respectively • **Conclusions:** Cabozantinib demonstrated comparable outcomes to sorafenib in second-line HCC therapy, suggesting its potential after ICI-based first-line treatments

Notable Presentations At ESMO GI 2025
Hepatocellular Carcinoma (HCC) & Hepatobiliary (3/3)

Date	Title	Author	Summary
04 July 2025	Safety and response to neoadjuvant lenvatinib for poor-prognosis BCLC A hepatocellular carcinoma treated by percutaneous ablation in a curative intent: Preliminary analysis of the French LENVABLA multicentre phase II trial (NCT05113186)	Pierre Nahon	• **Introduction:** A phenotype of aggressive BCLC A HCC with high rates of local recurrences is well-established. Adding Lenvatinib, a multikinase inhibitor, to percutaneous ablation (PA) as neo- and adjuvant therapy may improve tumor control • **Methodology**: BCLC A HCC patients (specific tumor criteria) received 21-day neoadjuvant Lenvatinib before PA, followed by 3-month adjuvant phase. Response assessed via tumor size, AFP drop, and biopsy necrosis. Primary endpoint: 1-year local recurrence-free survival • **Results:** 31 patients (mean age 69); 47 nodules (mean 26 mm). 90% started Lenvatinib at 12 mg; 22% discontinued. No grade 3/4 SAEs. Radiological response in 4 nodules; 3/21 showed pathological response. AFP response in 25.8%. PA completed in all, 93% on schedule • **Conclusions:** Neoadjuvant Lenvatinib is feasible for poor-prognosis BCLC A HCC patients and does not delay curative-intent ablation. A neoadjuvant response is observed in 63% of patients
04 July 2025	Real-world efficacy and safety of anlotinib in hepatocellular carcinoma previously treated with immune checkpoint inhibitors	Changzhen Shang	• **Introduction:** This study investigates anlotinib's efficacy and safety in HCC patients previously treated with ICIs • **Methodology**: Data from HCC patients who received ICIs and not local treatments were collected from six Chinese hospitals between Jan 2018 and May 2024. Patients were divided into two groups: one treated with anlotinib and the other with non-anti-angiogenic treatments. Propensity score matching (PSM) was used for age, gender, BCLC stage, and prior treatment lines • **Results:** 210 patients (median age 52.0 years, 84.3% male, 75.7% BCLC-C) were enrolled. After 1:1 PSM, 77 patients were in each group, with 87% continuing ICIs. Median PFS was significantly longer in the anlotinib group (6.8 months vs 5.0 months; HR 0.65, P=0.038). The 1-year PFS rates were 46.8% for anlotinib vs 39.0% for other treatments. ORR and DCR were similar: ORR 6.5% vs 7.8% (P=0.754) and DCR 45.5% vs 39.0% (P=0.415). Common adverse events in the anlotinib group included allergy (6.5%), gastrointestinal events (5.2%), and hand-foot syndrome (4.9%) • **Conclusions:** This real-world analysis shows that anlotinib significantly improves survival in HCC patients previously treated with ICIs

Notable Presentations At ESMO GI 2025
Miscellaneous (1/4)

Date	Title	Author	Summary
03 July 2025	Preliminary results from a first-in-human phase I study of a dual-conditionally binding EpCAM x CD3 bispecific T-cell engager, BA3182, in pts with treatment refractory metastatic adenocarcinoma	Alexander Starodub	• **Introduction:** BA3182 is a dual-conditionally binding bispecific T-cell engager targeting EpCAM and CD3, designed to selectively bind to tumor cells and improve anti-tumor activity with minimal healthy tissue damage. • **Methodology**: This phase 1 study evaluates the safety and efficacy of BA3182 in patients with treatment-refractory adenocarcinoma, assessing outcomes such as tumor reduction, adverse events, and pharmacokinetics. • **Results:** Preliminary data from 25 patients showed partial tumor reductions and prolonged progression-free intervals, with manageable adverse events. Dose escalation is ongoing. • **Conclusions:** BA3182 demonstrates promising anti-tumor activity and tolerability, with further investigation at higher doses in progress.
03 July 2025	Uncharted territory: Efficacy and safety of lower dose intensity immunotherapy in mismatch-repair-deficient and microsatellite instability-high gastrointestinal cancers: Real world data	Ali I. Shamseddine	• **Introduction:** Immune checkpoint inhibitors (ICIs) have shown significant efficacy in treating metastatic MSI-H/dMMR GI malignancies, but their high cost limits accessibility, particularly in low-income settings. Early studies suggest that lower doses might provide similar outcomes at a reduced cost. • **Methodology**: This retrospective review evaluates the efficacy of ICIs at reduced doses or extended intervals in metastatic MSI-H/dMMR GI cancers at the American University of Beirut Medical Center (2018-2024), focusing on overall survival (OS), progression-free survival (PFS), response rate (ORR), and immune-related adverse events (irAEs). • **Results:** 29 patients were reviewed, with no significant difference in OS, PFS, ORR, or clinical benefit between those receiving <75% or ≥75% of the recommended ICI dose. Four patients experienced irAEs, all in the ≥75% dose group. • **Conclusions:** Lower doses of ICI are effective and safe in treating metastatic MSI-H/dMMR GI malignancies. Prospective trials are needed to validate these findings.

Notable Presentations At ESMO GI 2025
Miscellaneous (2/4)

Date	Title	Author	Summary
03 July 2025	Zongertinib in HER2-altered gastrointestinal cancers: Preclinical activity and clinical findings from a phase Ia study	Kiyotaka Yoh	• **Introduction:** Zongertinib, a HER2-targeting tyrosine kinase inhibitor, demonstrated preclinical tumor inhibition in GI cancer models. This study presents its clinical efficacy and safety in patients with HER2-driven GI tumors in a Phase Ia trial. • **Methodology**: A Phase Ia, open-label, dose-escalation study (NCT04886804) evaluated zongertinib in 121 patients with advanced solid tumors, focusing on GI cancers. The primary endpoint was objective response rate (ORR), and secondary endpoints included progression-free survival (PFS), overall survival (OS), and adverse events. • **Results:** Zongertinib was well tolerated, showing a 17.2% ORR and a disease control rate of 72.4%. Common treatment-related adverse events included diarrhea and fatigue, with manageable toxicity. • **Conclusions:** Zongertinib demonstrates promising clinical activity and safety in HER2-driven GI cancers, warranting further investigation.
03 July 2025	Young-onset gastrointestinal cancer patients enrolled in phase I clinical trials: The experience from Gustave Roussy Cancer Center	Irene Gonzalez Caraballo	• **Introduction:** The increasing prevalence of gastrointestinal (GI) cancers in patients under 50 underscores the importance of investigating novel treatments. This study evaluates early-onset GI cancer patients enrolled in phase I clinical trials from 2010 to 2022. • **Methodology**: A retrospective review was conducted on 263 patients with early-onset GI cancer enrolled in phase I trials. Patients were categorized into two groups: Group 1 (2010-2015) and Group 2 (2016-2022). • **Results:** The median overall survival (mOS) was longest in colon cancer (43.19 months) and shortest in pancreatic cancer (22.8 months). Group 1 showed better mOS than Group 2, though no significant differences were observed after phase I trial inclusion. • **Conclusions:** Early-onset GI cancer remains a growing issue, highlighting the need for continued clinical trials targeting this population.

Notable Presentations At ESMO GI 2025
Miscellaneous (3/4)

Date	Title	Author	Summary
03 July 2025	Prevalence of malnutrition and its impact on hospitalized gastrointestinal cancer patients: Screening results conducted at admission to the oncology inpatient unit	Maria M. Pereira	• **Introduction:** Malnutrition is common in oncology patients, particularly those with gastrointestinal (GI) cancers, and correlates with worse clinical outcomes. This study assesses the impact of nutritional risk on outcomes in GI cancer inpatients. • **Methodology**: A retrospective study of 88 GI cancer patients was conducted, using the Nutritional Risk Screening tool (NRS-2002) to assess nutritional risk at admission. Clinical outcomes were analyzed using various statistical methods. • **Results:** 43.2% of patients had nutritional risk. While at-risk patients received more nutritional interventions, no significant effect was observed on complications or survival. • **Conclusions:** Nutritional risk is prevalent, but further prospective studies are needed to assess the clinical impact of early nutritional intervention.
03 July 2025	Real-world efficacy of anlotinib in bevacizumab-treated gastrointestinal cancers	Jinzhang Chen	• **Introduction:** Anlotinib, a multi-targeted anti-angiogenic agent, may reverse bevacizumab resistance in gastrointestinal cancers. This real-world study investigates anlotinib's efficacy in patients with hepatocellular and colon cancers previously treated with bevacizumab. • **Methodology**: Data from 256 patients with gastrointestinal cancers (123 hepatocellular, 133 colon) treated with bevacizumab were analyzed. Patients received either anlotinib (monotherapy or combination) or other treatments, with progression-free survival (PFS) compared using propensity score matching. • **Results:** No statistical differences in PFS or disease control rate (DCR) were found. However, a trend toward improved PFS was observed with anlotinib in both cancer types. • **Conclusions:** Anlotinib may offer potential benefits in bevacizumab-treated hepatocellular and colon cancer patients, warranting further investigation.

Notable Presentations At ESMO GI 2025
Miscellaneous (4/4)

Date	Title	Author	Summary
03 July 2025	Evaluating the efficacy of atorvastatin in mitigating radiotherapy-induced gastrointestinal toxicity: A randomized controlled trial	Mohammadreza Elhaie	• **Introduction:** Radiotherapy for pelvic malignancies often causes gastrointestinal toxicity. This study evaluates the protective effects of atorvastatin against acute gastrointestinal toxicity in patients undergoing pelvic radiotherapy. • **Methodology**: In a randomized, double-blind, placebo-controlled trial, 64 patients were assigned to atorvastatin (40 mg daily) or placebo for 3 months. Acute gastrointestinal toxicity was measured by changes in Inflammatory Bowel Disease Questionnaire-Bowel Subset (IBDQ-B) scores. • **Results:** No significant differences were observed in IBDQ-B scores or the incidence of symptoms like diarrhea and abdominal pain between atorvastatin and placebo groups. • **Conclusions:** Atorvastatin did not reduce acute gastrointestinal toxicity compared to placebo. Further research is needed to explore statins' radioprotective potential.

Key Industry Supported Sessions Information

ESMO GI 2025 Key Industry Supported Sessions Information (1/3)

Date	Sponsor	Title
2 July 2025	BMS	Advancing GI oncology: Changing landscape in CRC, HCC, and pancreatic cancer
2 July 2025	Revolution Medicines	Evolving treatment strategies in metastatic pancreatic adenocarcinoma: Current and emerging therapeutic approaches and the role of RAS
2 July 2025	PeerVoice	Shifting the paradigm in biliary tract cancers: Contemporary data and decision-making
2 July 2025	AbbVie	Solving the mystery of targeting c-met in colorectal cancer (CRC) and beyond
2 July 2025	Astellas	Characterising advanced G/GEJ adenocarcinoma: How can we personalise targeted treatment?
2 July 2025	Pfizer	Cancer cachexia in gastrointestinal malignancies
2 July 2025	Servier	Navigating through the evolving treatment pathways in mCRC: Insights and practical implications

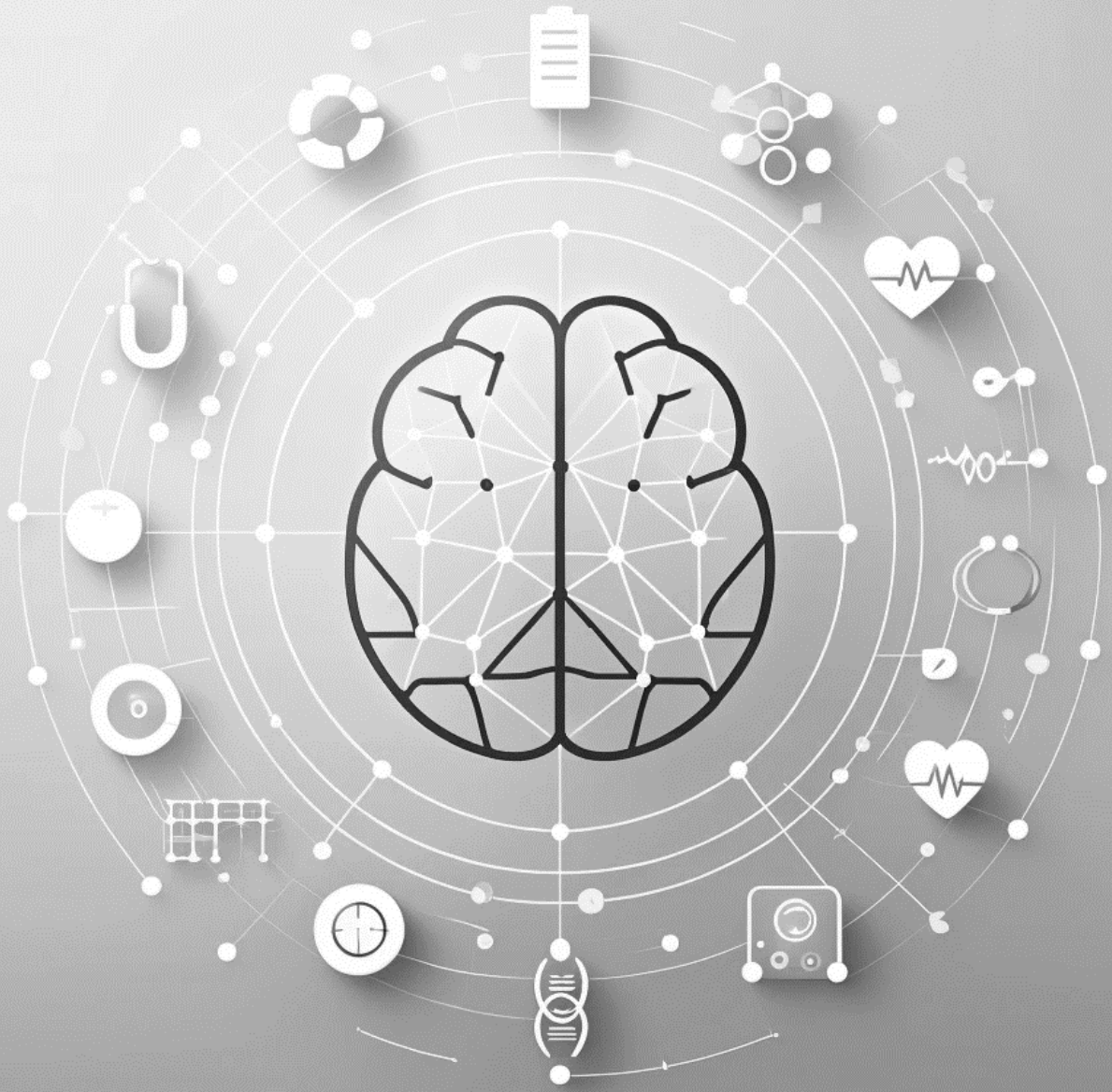
ESMO GI 2025 Key Industry Supported Sessions Information (2/3)

Date	Sponsor	Title
3 July 2025	MSD	Optimizing immune-oncology strategies in first-line gastric cancer: From biomarkers to therapeutic impact
3 July 2025	AstraZeneca	Examining current approaches and future prospects for the management of hepatobiliary cancers
3 July 2025	Merck	Expanding treatment horizons: Advancements in key mCRC populations
3 July 2025	Servier	A multidisciplinary approach in cholangiocarcinoma: From clinical evidence to improved patient outcomes
3 July 2025	Gilead	Improving patient care in advanced gastroesophageal adenocarcinoma: New directions with immunotherapy
3 July 2025	Eisai	Why and when does response matter in 1L HCC management?
4 July 2025	Servier	Metastatic pancreatic cancer: Towards a change in patient care?

ESMO GI 2025 Key Industry Supported Sessions Information (3/3)

Date	Sponsor	Title
4 July 2025	AstraZeneca	Evolving treatment landscape for resectable GC / GEJC
4 July 2025	Medscape Global Oncology	BRAF-mutated metastatic colorectal cancer: Real-world insights, personalized impact
4 July 2025	Takeda	Treatment choice and influencing factors in previously treated mCRC: A case-based interactive discussion
4 July 2025	Incyte	Rare GI tumours: Transformations in the treatment landscape
4 July 2025	GSK	What is the role of IO, biomarker testing and the MDT in locally advanced dMMR/MSI-H CRC?

Noteworthy AI / ML presentations at ESMO GI 2025



Themes from key AI / ML presentations at ESMO GI 2025 (1/3)

- **AI/ML models are revolutionizing cancer diagnostics and prognostics by enhancing prediction accuracy, improving treatment strategies, and offering scalable solutions, particularly in GI cancers like gastric, colorectal, and pancreatic cancers will be the focused theme of the ESMO GI 2025 conference**
- Check out the key AI / ML themes at ESMO GI 2025 below:

- **Muscle Mass and Inflammation in Metastatic Pancreatic Cancer:**
  - AI-based CT imaging and SIRI levels were used to predict treatment toxicity and survival in 50 patients from the PANTHEIA-SEOM study, showing that higher muscle mass and lower SIRI correlated with better outcomes
- **Deep Learning in Gastric Cancer Segmentation:**
  - In a study on gastric cancer, deep learning (DL) methods achieved a 95.8% accuracy rate for CT segmentation, outperforming manual methods and showing strong predictive performance (AUC = 0.873–0.937) for progressive disease
- **Long-term Survival Prediction in Gastric Cancer:**
  - A study of 806 gastric cancer patients found that neural networks, along with statistical methods, identified key survival factors, with a 5-year survival rate of 58.6% and adjuvant chemotherapy improved survival outcomes (67.5% vs. 56.9%)

Themes from key AI / ML presentations at ESMO GI 2025 (2/3)

- **AI-Assisted Endoscopy in Upper GI Cancers:**
  - A meta-analysis demonstrated that AI-assisted endoscopy (AIE) significantly reduced blind spots and missed lesions in upper GI examinations, achieving 99% sensitivity and specificity, and an AUC of 0.99
- **Deep Learning for Immune Infiltrates in Colon Cancer:**
  - A deep learning model analyzing CD3 tumor slides predicted better 5-year disease-free survival (DFS) in colon cancer patients, with a hazard ratio of 2.2, highlighting its potential for predicting outcomes across multicenter cohorts
- **Deep Learning for MSI/MMR Prediction in Colorectal Cancer:**
  - A deep learning model trained on 2,270 primary CRC specimens achieved an AUROC of 94.4% for predicting microsatellite instability (MSI) and mismatch repair (MMR) status, offering a rapid, scalable diagnostic tool for CRC
- **AI Models in Hepatocellular Carcinoma (HCC) Diagnosis:**
  - A systematic review showed that cell-free DNA (cfDNA) combined with AI models achieved 87% sensitivity and 89% specificity for HCC detection, demonstrating promising diagnostic performance with an AUC of 0.87

Themes from key AI / ML presentations at ESMO GI 2025 (3/3)

- **Machine Learning in Recurrence Prediction for Rectal Cancer:**
  - Machine learning models, particularly XGBoost, outperformed traditional TNM staging in predicting recurrence after curative rectal cancer treatment, with 79.6% accuracy and an AUC of 0.705, improving clinical follow-up decisions

Noteworthy AI / ML presentations at ESMO GI 2025 (Detailed Summary)

Notable Presentations At ESMO GI 2025
AI / ML (1/4)

Date	Title	Author	Summary
03 July 2025	Impact of the systemic inflammation index (SIRI) and artificial intelligence(AI)-based muscle mass (FocusedON® software) on chemotherapy toxicity and prognosis in metastatic pancreatic cancer: A proof-of-concept from the PANTHEIA-Spanish Society of Medical Oncology (SEOM) study group	Vilma E. Pacheco-Barcia	• **Introduction**: Muscle mass is a potential prognostic marker in oncology. This analysis explores the impact of muscle mass and systemic inflammation (SIRI) in metastatic pancreatic cancer (mPC). • **Methodology**: Fifty patients from the PANTHEIA-SEOM study were analyzed for muscle mass using AI-based CT image assessment and SIRI levels. Clinical outcomes, including treatment toxicity and overall survival (OS), were evaluated. • **Results:** Patients with higher muscle mass had improved OS. mFOLFIRINOX showed higher muscle mass and lower SIRI compared to gemcitabine-based regimens. High SIRI and low muscle mass were linked to worse OS. • **Conclusions:** AI-based muscle mass assessment and SIRI play critical roles in treatment toxicity and prognosis, suggesting their utility in optimizing therapeutic decision-making in mPC.
03 July 2025	Deep learning-based CT segmentation methods for radiomics in pembrolizumab-treated gastric cancer	TAEWON HAN	• **Introduction**: Accurate CT segmentation is vital for radiomics in gastric cancer. Manual segmentation is time-consuming, while deep learning (DL) methods may improve efficiency. This study compares DL and manual segmentation methods to predict progressive disease (PD) in patients with unresectable gastric cancer (uGC) receiving immunotherapy. • **Methodology**: Three segmentation methods were compared: automated DL segmentation, manual segmentation by a radiology resident, and manual segmentation by a non-radiologist with expert review. Radiomics features were analyzed to predict PD using logistic regression models. Model performance was assessed using receiver operating characteristic curves. • **Results:** DL segmentation showed the highest overlap (DSC = 0.901) and strong predictive performance (AUC = 0.873–0.937). Accuracy was highest for DL (95.8%). • **Conclusions:** DL-based automated segmentation offers comparable predictive performance to manual methods, with advantages in efficiency and reproducibility.

Notable Presentations At ESMO GI 2025
AI / ML (2/4)

Date	Title	Author	Summary
03 July 2025	Gastric cancer: Artificial intelligence, synergetics, complex system analysis, biometrics and modeling of alive supersystems for best management	Oleg Kshivets	• **Introduction**: Gastric cancer (GC) presents a global challenge. This study analyzed overall life span (LS) and 5-year survival (5YS) rates of patients (GCP) after radical surgery for GC (T1-4N0-2M0). • **Methodology**: Data from 806 GCP were analyzed, covering a period from 1975 to 2025. Various statistical methods (Cox, clustering, neural networks) were used to identify significant factors affecting survival. • **Results:** The 5YS was 58.6%, with 52.5% surviving 10 years and 40.2% surviving 20 years. Adjuvant chemotherapy (AT) significantly improved 5YS (67.5% vs. 56.9%, p=0.047). Factors influencing 5YS included tumor stage, cell ratios, blood cell factors, surgery type, and AT. • **Conclusions:** 5YS after surgery for GC depends on multiple factors, including early cancer stage, cell dynamics, and surgery quality. Early detection, skilled surgery, and AT for high-risk patients are key to improving outcomes.
03 July 2025	Artificial intelligence in action: A meta-analysis of AI-assisted endoscopy for upper GI cancers	Ashraf Abdelghany	• **Introduction**: Upper gastrointestinal (GI) cancers are often diagnosed at advanced stages due to limitations in early detection. AI-assisted endoscopy (AIE) has emerged as a promising tool to enhance diagnostic performance in endoscopic imaging. • **Methodology**: A systematic review and meta-analysis were conducted, evaluating studies on the diagnostic performance of AIE. Outcomes included blind spots, miss rates, neoplasm detection rates, inspection time, and biopsy rates. Diagnostic accuracy (sensitivity, specificity, AUC) was also assessed. • **Results:** AIE significantly reduced blind spots (MD = -3.44) and miss rates (RR = 0.29). It showed excellent diagnostic accuracy with 99% sensitivity and specificity, and AUC of 0.99. • **Conclusions:** AIE enhances lesion detection in upper GI examinations, offering great potential for cancer screening and early detection in clinical practice.

Notable Presentations At ESMO GI 2025
AI / ML (3/4)

Date	Title	Author	Summary
04 July 2025	Deep learning-based automated prognostic stratification through analysis of invasive margin T-cell infiltrates in localized colon cancer	Francois Ghiringhelli	• **Introduction**: T-cell immune infiltrates are prognostic markers in colon cancer. This study explored whether deep learning (DL) analysis of CD3 tumor slides could predict survival outcomes across multicenter cohorts. • **Methodology**: Data from three cohorts were used. Tumor slides stained with anti-CD3 monoclonal antibody were analyzed using a VGG19-based model to segment tumor zones. CD3+ density was quantified and used to predict 5-year disease-free survival (DFS) with a DL score. • **Results:** DLHigh patients had better DFS in all cohorts (HR = 2.2, p<0.001). The DL score, based on immune margin features, was associated with higher CD3 density and better DFS. • **Conclusions:** DL-based analysis of CD3 infiltrates can predict patient outcomes and may be integrated into clinical workflows.
04 July 2025	Deep learning can predict MSI/MMR status from primary and metastatic colorectal tissue slides	Foivos Ntelemis	• **Introduction**: This study evaluates the effectiveness of a deep learning (DL) model in predicting microsatellite instability (MSI) and mismatch repair (MMR) status in colorectal cancer (CRC) using H&E-stained slides. • **Methodology**: Data from 2,270 primary CRC specimens were used to train the model. The model was validated on 488 primary CRC and 507 metastatic CRC specimens, assessing the area under the receiver operating characteristic curve (AUROC). • **Results:** The model achieved AUROCs of 94.4% for primary CRC and 91.4% for metastatic CRC, demonstrating high accuracy in MSI/MMR prediction. • **Conclusions:** DL effectively predicts MSI/MMR status, offering a rapid and scalable alternative to traditional testing

Notable Presentations At ESMO GI 2025
AI / ML (4/4)

Date	Title	Author	Summary
04 July 2025	Cell-free DNA (cfDNA) biomarkers and AI models for early detection of liver cancer: A systematic review and meta-analysis	Minh H. Le	• **Introduction**: Hepatocellular carcinoma (HCC) is a major global health issue. This review evaluates the potential of cell-free DNA (cfDNA) and AI models in diagnosing and managing HCC. • **Methodology**: A systematic review and meta-analysis, adhering to PRISMA-DTA guidelines, analyzed studies comparing cfDNA in HCC detection versus healthy/non-HCC controls. • **Results:** Pooled sensitivity for cfDNA detection was 87%, with specificity at 89%. The area under the curve (AUC) was 0.87, indicating good diagnostic performance. • **Conclusions:** cfDNA shows promise as a screening marker for HCC. However, further validation through additional studies is required.
04 July 2025	Machine learning-based prediction of recurrence after curative treatment for rectal cancer: A multi-model analysis from a tertiary cancer centre	UmaSankar Tantravahi	• **Introduction**: Predicting recurrence after curative rectal cancer treatment is difficult, especially for those with initially metastatic disease. This study evaluates if machine learning (ML) models can improve recurrence prediction over traditional TNM staging. • **Methodology**: The dataset from 902 patients was split for training and testing. Four ML models (LR, SVM, RF, XGBoost) were trained using clinical, imaging, and pathological data. Accuracy was compared to models using only TNM variables. • **Results:** XGBoost outperformed other models with 79.6% accuracy and an AUC of 0.705, while TNM-based models showed significantly lower performance. • **Conclusions:** ML models, especially XGBoost, can improve recurrence prediction, offering better risk stratification and clinical follow-up insights.

Strategic Insights and Strategy Development is our focus