

# GI Oncology

Colloquium



## OncoAlert Colloquium 2026

### GI Cancer Day

February 4, 2026

Moderators: *Dr. Gilberto Morgan | Dr. Joseph McCollom, DO*

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#### Editorial Note

Due to unforeseen circumstances, Dr. Cathy Eng was unable to record her scheduled presentation on colorectal and anal cancer. Her presentation will be made available in the coming weeks, at which point it will replace the introductory CRC overview segment. The colloquium organisers apologised for the inconvenience and thanked participants for their flexibility.

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### Session 1: Colorectal and Anal Cancer – Year in Review

Overview presented by: Dr. Joseph McCollom, DO (Moderator)

In the absence of Dr. Eng's pre-recorded presentation, Dr. McCollom provided an expert overview of the major developments in colorectal and anal cancer in 2025–2026, covering screening trends, biomarker-guided therapy, adjuvant strategies, and immunotherapy.

#### Colorectal Cancer Incidence and Early-Onset Disease

**Dr. Joseph McCollom** [Moderator]

Colorectal cancer (CRC) incidence continues to rise in adults under 50, sharpening the focus on early screening, lifestyle risk factors, and symptom awareness. The data regarding GLP-1 receptor agonists and CRC risk are mixed: some retrospective studies show increased incidence, others are neutral. Overall, given the improvements seen in obesity-related malignancies and the potential for all-cause mortality reduction through improved cardiovascular risk profiles, these agents are viewed favourably – but prospective cancer prevention data are needed before broad recommendations can be made outside of already approved settings.

#### BREAKWATER Trial – BRAF V600E-Mutant Metastatic CRC

**Dr. Joseph McCollom** [Moderator]

The BREAKWATER trial demonstrated that adding targeted therapy (encorafenib + cetuximab) to chemotherapy in BRAF V600E-mutant metastatic colorectal cancer significantly improved response rates, with deeper and faster tumour shrinkage compared

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with chemotherapy alone. These findings signal a potential new first-line standard for this aggressive CRC subtype, and the combination has been established as the first-line approach for BRAF V600E-mutant metastatic CRC.

### **CheckMate-8HW – MSI-H/dMMR Metastatic CRC**

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The CheckMate-8HW trial was highlighted as supporting dual checkpoint blockade (nivolumab + ipilimumab) as an upfront strategy for MSI-H/dMMR metastatic CRC, adding to the immunotherapy-first evidence base in this biomarker-selected population.

### **DYNAMIC Trial – ctDNA-Guided Adjuvant Therapy in Stage II Colon Cancer**

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**Dr. Joseph McCollom** *[Moderator]*

The DYNAMIC trial evaluated whether circulating tumour DNA (ctDNA) could guide adjuvant therapy decisions in stage II colon cancer. A ctDNA-guided approach safely reduced chemotherapy use without compromising recurrence-free survival. This study has helped establish ctDNA as a practical tool for risk-adapted, personalised colon cancer care.

### **ALASCCA Trial – Aspirin Chemoprevention in Lynch Syndrome**

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**Dr. Joseph McCollom** *[Moderator]*

The ALASCCA trial tested low-dose aspirin to prevent colorectal cancer in people with Lynch syndrome, using a biomarker-guided approach. Aspirin significantly reduced CRC incidence in carriers with elevated urinary PGE-M, identifying a responsive high-risk subgroup. This supports a precision chemoprevention approach – matching aspirin use to biological risk rather than treating all Lynch syndrome carriers identically. In 2025, the NCCN guidelines integrated this recommendation for Stage II and Stage III patients. Next-generation sequencing (NGS) is utilised to assess PIK3CA mutations in this adjuvant setting.

### **PLATO/ACT4 and Anal Cancer**

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In anal cancer, the PLATO/ACT4 trial confirmed that radiotherapy de-escalation is safe, and retifanlimab plus chemotherapy is now established as first-line therapy for advanced disease.

### **CHALLENGE Trial – Structured Exercise After Adjuvant Chemotherapy**

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**Dr. Joseph McCollom** *[Moderator]*

The CHALLENGE trial (NCT00819208) was a phase III randomised study testing a 3-year structured exercise programme versus health education materials alone in patients with high-risk stage II or stage III colon cancer after adjuvant chemotherapy. It showed significantly improved disease-free survival (5-year DFS 80% vs 74%; HR 0.72) and consistent overall survival benefits with exercise. Published in NEJM 2025, it provides the first level-1 evidence that structured exercise reduces recurrence and mortality – outcomes comparable to adjuvant chemotherapy, and without its side effects.



## Session 2: Gastric and Gastroesophageal Junction (GEJ) Cancer

Presenter: Dr. Nicholas Hornstein

### MATTERHORN Trial – Perioperative Durvalumab + FLOT

**Dr. Joseph McCollom** [Moderator]

The MATTERHORN trial tested perioperative durvalumab + FLOT versus placebo + FLOT in resectable gastric and GEJ cancer. It improved event-free survival and pathological complete response rates, with an overall survival benefit, leading to FDA approval in 2025. While a difficult regimen for fit patients, it has demonstrated improved outcomes in a very challenging disease setting.

### DESTINY-Gastric04 – T-DXd in HER2+ Gastric/GEJ Cancer

**Dr. Joseph McCollom** [Moderator]

The DESTINY-Gastric04 trial is a phase 3 randomised study comparing second-line trastuzumab deruxtecan (T-DXd/Enhertu) versus ramucirumab plus paclitaxel in HER2-positive metastatic gastric/GEJ cancer after trastuzumab progression. It showed significantly longer overall survival (median 14.7 vs. 11.4 months) with improved PFS and ORR with T-DXd, establishing it as the superior option in this setting (NEJM 2025). Key toxicities include nausea and ILD, requiring vigilant monitoring.

### HERIZON-GEA-01 – Zanidatamab in HER2+ Advanced GEA

**Dr. Joseph McCollom** [Moderator]

The HERIZON-GEA-01 trial is a phase 3 randomised study evaluating zanidatamab – a bispecific HER2 antibody – plus chemotherapy ± tislelizumab versus trastuzumab plus chemotherapy as first-line treatment for HER2-positive advanced/metastatic gastroesophageal adenocarcinoma (GEA). Both zanidatamab-based arms significantly improved PFS versus trastuzumab plus chemotherapy. The triplet (zanidatamab + chemotherapy + tislelizumab) achieved a median OS of 26.4 months (HR 0.72), while zanidatamab + chemotherapy achieved 24.4 months (trend vs. control), compared with trastuzumab + chemotherapy at 19.2 months. The triplet met its primary endpoint for both PFS and OS benefit, supporting zanidatamab – particularly with PD-1 blockade – as a potential new first-line standard for HER2-positive advanced GEA.

**Dr. Joseph McCollom** [Moderator]

A key toxicity consideration with zanidatamab regimens is diarrhoea, occurring in more than 50% of patients. Prevention with loperamide (Imodium) is recommended, escalating to diphenoxylate/atropine (Lomotil) for refractory cases. Proactive palliative care integration can assist with symptom management.



## Session 3: Pancreatic Cancer

Presenter: Dr. Grainne O'Kane

### PREOPANC-2 – Neoadjuvant Strategies in Resectable/Borderline Resectable PDAC

**Dr. Joseph McCollom** [Moderator]

The PREOPANC-2 trial was a phase 3 randomised study comparing neoadjuvant FOLFIRINOX (8 cycles) followed by surgery versus neoadjuvant gemcitabine-based chemoradiotherapy followed by surgery and adjuvant gemcitabine in resectable and borderline resectable pancreatic cancer. It showed no difference in median overall survival (21.9 vs. 21.3 months; HR 0.88) or resection rates between arms. Both regimens are viable neoadjuvant options, and the debate about which to choose should shift away from trial evidence and instead focus on tailoring toxicity profiles to individual patient preferences and comorbidities.

### CA19.9 and Endpoints Discussion

**Dr. Grainne O'Kane** [Presenter]

EFS using CA19.9 failure as an endpoint is a new and potentially important way of thinking about trial design in PDAC, but it needs further validation before broad adoption.

**Dr. Ben Westphalen** [Participant]

CA19.9 failure is not really feasible as a universal endpoint. Some patients do not produce CA19.9 at all; others have very low secretion. In clinical practice, I have never acted on CA19.9 alone and have seen meandering values without patients relapsing. ctDNA in localised disease currently has low sensitivity, but the question of whether ctDNA can be harnessed more specifically in the future is very relevant.

**Dr. Grainne O'Kane** [Presenter]

Agreed. OS must remain the true endpoint for phase 3 trials in pancreatic cancer.

### Emerging KRAS Targeting and Molecular Subtypes in PDAC

**Dr. Grainne O'Kane** [Presenter]

There is now real evidence for distinct molecular subtypes in pancreatic cancer – DNA-based and RNA-based subtypes – and as we better characterise these, clinical trials may be able to stratify or select patients upfront accordingly. In-vivo data suggest that the basal-like subtype may respond to RAS inhibitors, which will be hugely significant. Combinations will be key, and chemotherapy is unlikely to disappear from the picture. Targeting KRAS is finally here and is a genuine game changer for patients.

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### Dr. Ben Westphalen *[Participant]*

The therapeutic landscape is becoming more complex. Many PDACs carry both RAS mutations and MTAP deletions. A realistic future sequencing strategy could look like: allele-specific KRAS inhibitor plus chemotherapy in first line; followed by a broader RAS inhibitor plus a PRMT5 inhibitor in second line; followed by pan-RAS inhibition plus ICI in later lines. This is not an unrealistic scenario.

### Dr. Ben Westphalen *[Participant]*

The most interesting question for me is how RAS inhibitors can sensitise tumours to immunotherapy. Mutant RAS drives an immunosuppressive tumour microenvironment through IL-6, IL-8, and other immune effectors. If RAS signalling can be dampened, this immunosuppressive component may be attenuated as well – opening the door to meaningful ICI activity in a disease that has been largely refractory to checkpoint blockade. Looking further ahead, 'electronic biomarkers' may support clinical decision-making in this increasingly complex space.

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## Session 4: Emerging Molecular Targets in GI Oncology

Presenter: Dr. Ben Westphalen

Dr. Westphalen presented a forward-looking review of the rapidly expanding portfolio of molecular targets across GI malignancies, many of which were considered undiscoverable or untargetable only a decade ago.

### Key Discussion Points

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#### Dr. Joseph McCollom *[Moderator]*

The breadth of targets in GI oncology that were undiscovered or thought untargetable just decades ago are now showing shining promise. Can you discuss any targets that may augment or discourage the use of ICI for GI malignancies?

#### Dr. Ben Westphalen *[Presenter]*

For me, the most interesting question is how RAS inhibitors can sensitise tumours to ICI. Mutant RAS drives an immunosuppressive tumour microenvironment through IL-6, IL-8, and other immune effectors – and dampening RAS signalling may attenuate this immunosuppressive phenotype. Strategic sequencing of KRAS-targeted agents with immunotherapy in RAS-mutant and MTAP-deleted tumours represents a plausible and exciting future treatment paradigm. We would love to see more trials paving the way to approvals for KRAS inhibition across GI cancers.

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### Session 5: Radiotherapy in GI Oncology

Presenter: Dr. Nina Sanford, Radiation Oncologist, UT Southwestern Medical Center, Dallas, TX  
Dr. Sanford provided a focused update on the role of radiotherapy across GI malignancies, with particular attention to the ongoing relevance of chemoradiotherapy in the modern multimodal era.

#### Key Discussion Points

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##### Dr. Joseph McCollom *[Moderator]*

There remain patients who are not fit enough for FLOT-based perioperative systemic therapy, or who have localised disease that may truly benefit from chemoradiotherapy even in our modern era. Other patients may have contraindications to systemic therapy – such as uncontrolled rheumatological disease or severe baseline neuropathy – for whom chemoRT, especially in localised disease with favourable histological features, remains an important and appropriate option.

##### Dr. Erman Akkus *[Participant]*

Very few centres are using FOLFIRINOX in total neoadjuvant therapy (TNT) protocols in practice – it tends to be reserved for selected cases only. The JANUS trial results will be very interesting to see.

##### Dr. Joseph McCollom *[Moderator]*

JANUS may determine the optimal order of neoadjuvant therapy as well as the role of ctDNA in patient stratification. We were a JANUS site, and I appreciate the focus on late curve separation and the tracking of quality of life outcomes.

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### Session 6: Upper GI Surgical Oncology

Presenter: Dr. Herrera (European Society of Surgical Oncology)

#### Key Discussion Points

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##### Dr. Joseph McCollom *[Moderator]*

Dr. Herrera's approach exemplifies treating the whole person, not just the cancer. The focus on less morbid surgery for early-stage disease with favourable prognostic factors – without compromising outcomes – is exactly the direction the field should be heading.

The role of prehabilitation emerged as a significant theme. Evidence is accumulating that even short-course prehabilitation programmes improve surgical and oncological outcomes in patients anticipating major cancer surgery, and this aligns with the broader lifestyle data discussed throughout the day.

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**Dr. Joseph McCollom** *[Moderator]*

The major changes I have observed in surgical oncology that stand out most include: the rise of non-operative management in rectal cancer, robotic approaches improving surgical recovery, prehabilitation before major cancer surgery, and the re-emergence of liver-directed therapy options for patients with isolated liver metastatic disease – including hepatic arterial infusion (HAI) pump therapy and techniques such as Histiosonics. Effective neoadjuvant treatment is enabling smaller, less morbid operations across GEJ/gastric and rectal cancer, but patient selection remains critical. Non-operative management requires close surveillance, and early local relapses are predictive of distant disease and mortality – surgery still has an essential role for many patients, particularly those with primary refractory disease or those unlikely to maintain follow-up.

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## Session 7: Lower GI Surgical Oncology

Presenter: Dr. Inama (European Society of Surgical Oncology)

### Key Discussion Points

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**Dr. Joseph McCollom** *[Moderator]*

Dr. Inama's focus on multidisciplinary team discussions is exactly right. Surgical, medical, radiation, palliative, and interventional oncology all have a role, and coordinated multidisciplinary care is the best care for patients – it is the only way to decide how to proceed in complex GI malignancy cases.

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## Session 8: Resource-Limited Settings and Global Access in GI Oncology

Presenter: Dr. Erman Akkus, Ankara, Turkey

### Key Discussion Points

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**Dr. Joseph McCollom** *[Moderator]*

Dr. Akkus's approach – examining subgroup populations that derive maximal benefit in order to argue for the distribution of limited resources to the patients most likely to benefit – is a clinically and ethically sound framework for resource-limited settings. His emphasis on the ALASCCA trial and the updated NCCN recommendations is timely: NGS large panels are increasingly used to identify PIK3CA mutations and other biomarkers in this adjuvant context, though access to such testing is not universal worldwide. The Italian study discussed presents interesting EFS data, and while EFS as a primary endpoint has

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limitations, it may be a reasonable surrogate in resource-constrained settings where longer follow-up is operationally difficult.

**Dr. Joseph McCollom** *[Moderator]*

An excellent and nuanced summary of the approach to GI malignancies with worldwide perspectives on delivering high-quality oncology care in the context of limited resources.

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## Session 9: The Patient Perspective

Presenter: Ms. Allison Rosen, Patient Advocate Faculty

### Key Themes

**Ms. Allison Rosen** *[Patient Advocate]*

Quality of life is paramount when considering treatment options. Issues such as sexual health often go unaddressed during initial treatment conversations – this is an area where oncology must do better. Patients deserve to have these discussions proactively, not retrospectively. It is an honour to provide the patient advocate voice and perspective in this forum.

**The OncoAlert Network** *[Moderator]*

Sexual health is something that often goes unspoken when treatment is first discussed. This must change. Allison Rosen brings a fierce, vital perspective to this faculty, and the patient advocate voice is an essential part of how we continue to improve oncology care.

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## Faculty

Moderators: Dr. Gilberto Morgan | Dr. Joseph McCollom, DO (@realbowtiedoc)

Presenters: Dr. Nicholas Hornstein (Gastric/GEJ) · Dr. Grainne O'Kane (Pancreatic Cancer) · Dr. Ben Westphalen (Molecular Targets) · Dr. Nina Sanford (Radiation Oncology, UT Southwestern) · Dr. Herrera (Upper GI Surgery, ESSO) · Dr. Inama (Lower GI Surgery, ESSO) · Dr. Erman Akkus (Global Access, Ankara)

Patient Advocate: Ms. Allison Rosen

**Special Note:** Dr. Cathy Eng's presentation on CRC and Anal Cancer will be available in the coming weeks.