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CLINICAL Colorectal Cancer

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Jianwei Zhang, Meijin Huang, Yue Cai, Lei Wang, Jian Xiao, Ping Lan, Huabin Hu, Xiaojian Wu, Jiayu Ling, Junsheng Peng, Dianke Chen, Liang Kang, Yan Zhang, Donglin Ren, Hui Wang, Shuang Chen, Feng Lin, Jian Zheng, Zhiyang Zhou, Jianping Wang, Yanhong Deng
The efficacy of preoperative chemotherapy with mFOLFOXIRI (folinic acid, 5-fluorouracil, oxaliplatin, and irinotecan) in 106 enrolled patients with locally advanced rectal cancer in a phase II trial was explored. The endpoints included tumor downstaging to ypT₀₋₂N₀M₀, pathologic complete response rate, disease-free survival rate, and safety. The pathologic complete response and tumor downstaging rates were 20.4% and 42.7%, respectively. Neoadjuvant chemotherapy with mFOLFOXIRI and selective radiation did not compromise outcomes in locally advanced rectal cancer.
- 245 Relationship Between Tumor Response and Tumor-Related Symptoms in RAS Wild-Type Metastatic Colorectal Cancer: Retrospective Analyses From 3 Panitumumab Trials
Julien Taieb, Michael Geissler, Fernando Rivera, Meinolf Karthaus, Richard Wilson, Fotios Loupakis, Timothy Price, Michael Tracy, Peter Burdon, Marc Peeters
Tumor-related symptoms can affect treatment choices in metastatic colorectal cancer (mCRC). In the current study, 659 patients with RAS wild-type mCRC were retrospectively analyzed to evaluate the relationship between tumor shrinkage and the time to onset of tumor-related symptoms. Symptom onset was delayed in patients with earlier and greater tumor shrinkage. Therefore, treatments that facilitate cytoreduction may delay symptom development.
- 257 Clinical Outcomes of Small Bowel Adenocarcinoma
Mehmet Akce, Renjian Jiang, Katerina Zakka, Christina Wu, Olatunji B. Alese, Walid L. Shaib, Madhusmita Behera, Bassel F. El-Rayes
Small bowel adenocarcinomas (SBAs) are rare tumors. This study provides clinical outcomes of SBAs from the National Cancer Database. Adjuvant chemotherapy was associated with improved survival in stage II and III SBAs. Duodenal SBAs presented often with advanced stage disease, underwent surgery, adjuvant chemotherapy, and palliative chemotherapy less often, and had the worst survival. Jejunal SBAs had the best survival.

- 269 **Health-related Quality of Life in the Phase III LUME-Colon 1 Study: Comparison and Interpretation of Results From EORTC QLQ-C30 Analyses**
Heinz-Josef Lenz, Guillem Argiles, Takayuki Yoshino, Sara Lonardi, Alfredo Falcone, María Luisa Limón, Alberto Sobrero, Claudia Hastedt, Barbara Peil, Florian Voss, Ingolf Griebisch, Eric Van Cutsem
Based on European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) outputs from the LUME-Colon 1 study, we compared and discussed different statistical methods for evaluating health-related quality of life data in oncology clinical trials. The different analyses consistently showed that patients' overall global health status/quality of life status was not impaired by active treatment with nintedanib versus placebo, and that patients perceived some benefits with nintedanib compared with placebo.
- 280 **ACORN: Observational Study of Bevacizumab in Combination With First-Line Chemotherapy for Treatment of Metastatic Colorectal Cancer in the UK**
Shelize Khakoo, Ian Chau, Ian Pedley, Richard Ellis, Will Steward, Mark Harrison, Shobhit Baijal, Saad Tahir, Paul Ross, Sherif Raouf, Agnes Ograbek, David Cunningham, on behalf of the ACORN investigators
Real-world data from 714 patients who received bevacizumab with first-line chemotherapy were collected to understand why survival in metastatic colorectal cancer is worse in the United Kingdom than in other countries. Shorter total chemotherapy duration (8.1 months) and less frequent use of bevacizumab provided after disease progression (13.9% of patients) may have contributed to the poorer overall survival (17.8 months) observed in the UK.
- 292 **Overuse and Limited Benefit of Chemotherapy for Stage II Colon Cancer in Young Patients**
Richard T. Birkett, Elias Chamely, Seth J. Concors, Joshua I. Bleier, Cary B. Aarons, Skandan Shanmugan, Nicole M. Saur, Emily Carter Paulson
The benefit of adjuvant chemotherapy in stage II colon cancer is debated. A retrospective analysis of the National Cancer Database demonstrates more frequent use of chemotherapy in patients with both high- and normal-risk stage II colon cancer who are younger than 50 years compared with older patients. No survival benefit was found to be associated with adjuvant chemotherapy in either risk group.
- 301 **A Phase II Study of Capecitabine/Oxaliplatin With Concurrent Radiotherapy in Locally Advanced Squamous Cell Carcinoma of the Anal Canal**
Cathy Eng, Alexandre A. Jácome, Prajnan Das, George J. Chang, Miguel Rodriguez-Bigas, John M. Skibber, Robert A. Wolff, Wei Qiao, Yan Xing, Salil Sethi, Aki Ohinata, Christopher H. Crane
This was a single-arm phase II trial with locally advanced squamous cell carcinoma of the anal canal (SCCA) patients, to evaluate the feasibility of a more convenient therapeutic regimen composed of XELOX (capecitabine and oxaliplatin) concurrent with radiation therapy (XELOX-XRT). Complete response and Grade 3 toxicity rates occurred in 19 patients (100%) and in 2 patients (22% of the group with adjusted dose), respectively. XELOX-XRT might be an alternative therapeutic regimen for SCCA patients.

Case Reports

- 307 **Efficacy of PD-1 Blockade in Refractory Microsatellite-Stable Colorectal Cancer With High Tumor Mutation Burden**
Jun Gong, Mandy D. Robertson, Edward Kim, Marwan Fakih, Alexa B. Schrock, Kit W. Tam, Bhuvaneshwari Burugapalli, Arta M. Monjazez, Andrew E. Hendifar, Megan Hitchins, Samuel J. Klempner, May Cho
- 310 **Safety Report of TAS-102 in a Patient With Reduced DPD Activity**
Elena Bolzacchini, Giovanna Luchena, Monica Giordano

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e309 KRAS Status as a Predictor of Chemotherapy Activity in Patients With Metastatic Colorectal Cancer

Nirit Yarom, Gillian Gresham, Nana Boame, Derek Jonker

This is a retrospective analysis of the effect of KRAS status on chemotherapy efficacy. Among those treated with capecitabine-based regimens, survival was longer for patients with KRAS wild-type status (hazard ratio, 0.47; 95% confidence interval, 0.23-0.95; $P < .0001$), when compared with those with mutant status. The median overall survival was 46.7 versus 32.6 months for patients with KRAS wild-type versus mutant status, respectively.

e316 Evaluation of a Fully Automated Idylla Test System for Microsatellite Instability in Colorectal Cancer

Xiang Li, Jin Xu, Lei Li, Xiaofeng Mu, Ye Wang, Xinmin Li

A fast and accurate test for microsatellite instability (MSI) is crucial in colorectal cancer prognosis and treatment. In this manuscript, we validated an automated Idylla MSI detection platform using 42 patient samples. The new Idylla MSI system provided accurate results in 2.5 hours. This automated tool greatly simplified the MSI detection process.

e324 Next Generation Sequencing Reveals Novel Mutations in Mismatch Repair Genes and Other Cancer Predisposition Genes in Asian Patients with Suspected Lynch Syndrome

Samuel G.W. Ow, Kar Tong Tan, Henry Yang, Hui-Ling Yap, Nur Sabrina Binte Sapari, Pei Yi Ong, Richie Soong, Soo-Chin Lee

The genetic spectrum of Asian patients with Lynch Syndrome (LS) is not well understood. This study from an Asian cancer center studied multigene panel testing in patients with clinically suspected LS and identified novel mutations in both LS and non-LS genes, pointing to alternative culprit cancer predisposition genes that may not have been suspected using traditional clinical criteria.

e335 Diagnostic Nodes of Patient Selection for Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy Among Colorectal Cancer Patients: A Swiss National Multicenter Survey

Thomas Steffen, Paul Martin Putora, Martin Hübner, Beat Gloor, Kuno Lehmann, Christoph Kettelhack, Michel Adamina, Ralph Peterli, Jan Schmidt, Frédéric Ris, Markus Glatzer

The management of patients with colorectal cancer (CRC) with peritoneal metastases is challenging, and the roles of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) are unclear and debated among experts. Experts from 9 centers in Switzerland provided their decision algorithms for CRS/HIPEC for patients with or at high risk for peritoneal metastases from CRC; we used these algorithms to identify consensus and discrepancies. Multiple decision criteria relevant to all participating centers were identified. The consensus treatment algorithm included a total of 5 decision criteria. Because patient selection for CRS/HIPEC remains difficult, uniform criteria, such as those in the consensus algorithm, for the term, "high risk" for peritoneal metastases and systemic metastases are helpful.

e343 Neutrophil-related Variables Have Different Prognostic Effect Based on Primary Tumor Location in Patients With Metastatic Colorectal Cancer Receiving Chemotherapy

Giuseppe Antonio Colloca, Antonella Venturino, Domenico Guarneri

In contrast with patients with other advanced tumors, the relationship among systemic inflammation-related variables and prognosis is controversial among patients with metastatic colorectal cancer. In this retrospective analysis of 145 patients with metastatic colorectal cancer, we found that neutrophil-related variables predicted overall survival for patients with left-sided tumors and not for those with a right-sided cancer.

e349 A Pilot Study of the PD-1 Targeting Agent AMP-224 Used With Low-Dose Cyclophosphamide and Stereotactic Body Radiation Therapy in Patients With Metastatic Colorectal Cancer

Charalampos S. Floudas, Gagandeep Brar, Donna Mabry-Hrones, Austin G. Duffy, Bradford Wood, Elliot Levy, Venkatesh Krishnasamy, Suzanne Fioravanti, Cecilia M. Bonilla, Melissa Walker, Maria Pia Morelli, David E. Kleiner, Seth M. Steinberg, William D. Figg, Tim F. Greten, Changqing Xie

This study aimed to investigate the benefit of combining immunotherapy (AMP-224) with radiation for patients with metastatic colorectal cancer. Fifteen patients were enrolled. No objective response was observed although 3 patients (20%) had stable disease. A signal of immune modulation was noted.

- e361 Comparative Oncologic Outcomes of Upper Third Rectal Cancers: A Meta-analysis**
Cillian Clancy, Michael Flanagan, Franco Marinello, Brian D. O'Neill, Deborah McNamara, John P. Burke
The role for neoadjuvant radiation in upper rectal cancer remains unclear. A meta-analysis of studies comparing outcomes following resection of upper third and distal rectal cancers was performed. The data suggests that upper rectal cancer has reduced local and distant recurrence despite similar disease stage and margin positivity. Upper rectal tumors should be considered a distinct entity to mid and lower rectal tumors.
- e368 Comment on De Felice et al, "Intensified Neoadjuvant Chemoradiotherapy for Locally Advanced Rectal Cancer in Elderly Patients: Toxicity, Disease Control, and Survival Outcomes"**
Guler Yavas, Cagdas Yavas
- e370 Angiogenic and Antiangiogenic VEGFA Splice Variants in Colorectal Cancer: Prospective Retrospective Cohort Study in Patients Treated With Irinotecan-Based Chemotherapy and Bevacizumab**
George Pentheroudakis, Leonidas Mavroeidis, Kyriaki Papadopoulou, Georgia-Angeliki Koliou, Christina Bamia, Kyriakos Chatzopoulos, Epaminontas Samantas, Davide Mauri, Ioannis Efstratiou, Dimitrios Pectasides, Thomas Makatsoris, Dimitrios Bafaloukos, Pavlos Papakostas, George Papatsibas, Iliada Bombolaki, Sofia Chrisafi, Helen P. Kourea, Kalliopi Petraki, Georgia Kafiri, George Fountzilias, Vassiliki Kotoula
We investigated the predictive and prognostic significance of tumoral messenger RNA levels of vascular endothelial growth factor A (VEGFA) splice variants in metastatic colorectal cancer (mCRC) patients treated with bevacizumab. VEGFA145b had negative predictive significance predominantly in those patients with right-sided primary tumors. All VEGFAxxx variants were negative prognosticators for patients with right-sided mCRC, whereas VEGFA165b was of favorable prognostic significance in patients with left-sided tumors.
- e385 Effect of Body Mass Index on 5-FU-Based Chemotherapy Toxicity and Efficacy Among Patients With Metastatic Colorectal Cancer; A Pooled Analysis of 5 Randomized Trials**
Omar Abdel-Rahman
We conducted a pooled analysis of 5 clinical trials to assess the effect of baseline body mass index (BMI) on the toxicity and efficacy of systemic chemotherapy among patients with metastatic colorectal cancer (CRC). Lower BMI was associated with a higher risk of hematological toxicities (anemia and neutropenia) whereas higher BMI was associated with a higher risk of nausea, vomiting, and peripheral neuropathy, and seemed to be associated with better overall survival among patients with metastatic CRC.
- e394 Validated Nomogram Predicting 6-Month Survival in Pancreatic Cancer Patients Receiving First-Line 5-Fluorouracil, Oxaliplatin, and Irinotecan**
Lorenzo Fornaro, Francesco Leone, Angélique Vienot, Andrea Casadei-Gardini, Caterina Vivaldi, Astrid Lièvre, Pasquale Lombardi, Emmanuele De Luca, Dewi Vernerey, Elisa Sperti, Gianna Musettini, Maria Antonietta Satolli, Julien Edeline, Rosella Spadi, Cindy Neuzillet, Alfredo Falcone, Giulia Pasquini, Mario Clerico, Alessandro Passardi, Paola Buscaglia, Aurélie Meurisse, Massimo Aglietta, Clémence Brac, Enrico Vasile, Francesco Montagnani
FOLFIRINOX (leucovorin, 5-fluorouracil, irinotecan, and oxaliplatin) is an accepted standard in metastatic and locally advanced pancreatic cancer (PC), but long-term prognosis is still poor. Indeed, no criteria reliably identify patients with limited, if any, chances of long-term benefit. We therefore developed and externally validated a prognostic nomogram predicting the risk of early death in PC patients treated with first-line triplet chemotherapy.