SAN FRANCISCO, CA – Five important studies with an impact on patient care are among those presented at the 2014 Gastrointestinal Cancers Symposium, taking place January 16-18, 2014 at the Moscone West Building in San Francisco, CA. Two studies examine treatments for metastatic colorectal cancer; a third evaluates the effect of obesity and smoking on esophageal adenocarcinoma survival; and the final two focus on second-line treatments for cancers that progressed or were non-responsive after first-line treatment.

2014 Gastrointestinal Cancers Symposium News Planning Team
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Click here to view the disclosures for the News Planning Team.

Thursday, January 16, 2014 Presentations

Abstract #10:
Early adulthood body mass index, cumulative smoking, and esophageal adenocarcinoma survival.

General Poster Session A Anna Spreafico, MD, PhD
Thursday, January 16, 2014: 12:00 PM - 02:00 PM PST Princess Margaret Cancer Centre
Thursday, January 16, 2014: 05:30 PM - 07:00 PM PST Toronto, Canada
Moscone West Building, Level 1, West Hall

Authors: Anna Spreafico, Linda E. Coate, Xiaowei Shen, Rihong Zhai, Wei Xu, Zhen-Fei Chen, Zhuo Chen, Devalben Patel, Catherine Brown, Qin Kuang, Kevin Boyd, Matthew Kulke, Li Su,
Background: Little is known about the individual and combined effect of early-adulthood obesity and cumulative smoking on the survival of esophageal adenocarcinoma (EAC) patients.

Methods: We analyzed two independent cohorts of EAC patients: 235 patients from Toronto, Canada (TO, 2006-2011) and 329 patients from Boston, USA (BO, 1999-2004). Associations between early adulthood body mass index (EA-BMI) and smoking with overall survival (OS) were assessed using Cox proportional hazard models, adjusted for stage, treatment, and other relevant covariates.

Results: Median age (range) for TO dataset was 64(29-88) yrs; for BO dataset, 64(21-91) yrs. Males comprised 86% of TO and 89% of BO datasets. 90% of TO and 98% of BO patients were Caucasians. The Median (range) for packyears was 34 (0.2-118; TO) and 34 (0.2-212; BO). The Median (range) for EA-BMI was 24(15-44; TO) and 24(15-47; BO). Median BMI 1 yr prior to diagnosis was 25(16-43; TO) and 25(20-49; BO). 92% of TO and 88% of BO patients had ECOG 0 or 1. Disease stage distribution (early/locally-advanced/metastatic) was 11%/64%/25% (TO) and 30%/52%/18% (BO). For TO, the aHR for smoking was 1.03 (95%CI: 1.02-1.04; p=8E-08) per packyear, while for BO, smoking also independently conferred worse OS, with aHR of 1.007 (95%CI: 1.002-1.01; p=0.003) for each packyear increase. The aHRs for being underweight (EA-BMI<18.5), overweight (EA-BMI 25-30), and obese (EA-BMI>30) in early adulthood were 2.19 (95%CI: 1.0-4.6), 1.89 (95%CI:1.2-3.0), and 2.49 (95%CI:1.5-4.2), respectively for the TO dataset (global p=0.003 for EA-BMI). In BO, the corresponding values were 1.30 (95%CI: 0.8-2.2), 1.45 (95%CI: 1.0-2.5), and 2.39 (95%CI:1.5-3.8), respectively (global p=0.002). In contrast, BMI at one year prior to diagnosis had no association with OS in either study.
Conclusions: Elevated BMI in early adulthood and heavy cumulative smoking history are independently associated with increased mortality risk in two North American EAC populations. These survival differences may reflect comorbidity differences, biological differences or both, and offer insight into how key modifiable behaviors in prevention can also affect cancer prognoses. AS, LC, DCC and GL contributed equally.

Disclosures: Nothing to disclose.

Friday, January 17, 2014 Presentations

Abstract # 172:
EVOLVE-1: Phase 3 study of everolimus for advanced HCC that progressed during or after sorafenib.

General Poster Session B Andrew X. Zhu, MD, PhD
Friday, January 17, 2014: 12:00 PM - 02:00 PM Massachusetts General Hospital Cancer Center
Friday, January 17, 2014: 05:30 PM - 07:00 PM PST Boston, MA
Moscone West Building, Level 1, West Hall

Authors: Andrew X. Zhu, Masatoshi Kudo, Eric Assenat, Stéphane Cattan, Yoon-Koo Kang, Ho Yeong Lim, Ronnie Tung Ping Poon, Jean-Frédéric Blanc, Arndt Vogel, Chao-Long Chen, Etienne Dorval, Markus Peck-Radosavljevic, Armando Santoro, Bruno Daniele, Junji Furuse, Annette Jappe, Kevin Perraud, Ozlem Anak, Dalila B. Sellami, Li-Tzong Chen; Massachusetts General Hospital Cancer Center, Boston, MA; Kinki University School of Medicine, Department of Gastroenterology and Hepatology, Osaka, Japan; Institut du Cancer de Montpellier Val d'aurelle, Montpellier, France; University Nord De France, Lille, France; Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; Department of Surgery, The University of Hong Kong, Hong Kong, China; Hôpital Saint-André, Bordeaux, France; Medical School Hannover, Hannover, Germany; Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan; CHRU de Tours, Tours, France; Medical University of Vienna, Vienna, Austria; Humanitas Cancer Center, Istituto Clinico Humanitas, Rozzano, Italy; G. Rummo Hospital, Benevento, Italy; Department of Internal Medicine, Medical Oncology, Kyorin University School of Medicine, Tokyo, Japan; Novartis Pharma AG, Basel, Switzerland; Novartis Pharmaceuticals Corporation, East Hanover, NJ; National Institute of Cancer Research, National Health Research Institutes, Tainan, Taiwan

Track: General Poster Session B: Cancers of the Pancreas, Small Bowel, and Hepatobiliary
Background: No effective treatment options exist for advanced HCC following sorafenib failure. Preliminary data suggest everolimus may provide benefit after sorafenib. EVOLVE-1 (NCT01035229) assessed the efficacy and safety of everolimus for advanced HCC after sorafenib failure.

Methods: Pts aged ≥18 y with BCLC stage B or C HCC and Child-Pugh A liver function whose disease progressed during or after sorafenib or who were sorafenib intolerant were randomized 2:1 to everolimus 7.5 mg/d or placebo. All pts received best supportive care. Randomization was stratified by region (Asia v rest of world) and macrovascular invasion (yes v no). Study drug was given continuously until disease progression or intolerable toxicity. CT/MRI was performed every 6 wk. Primary endpoint was OS. Secondary endpoints were TTP, disease control rate (DCR; percentage of pts with best overall response of CR, PR, or SD per RECIST 1.0), and safety. Final analysis was performed when 454 deaths occurred.

Results: 546 pts from 18 countries enrolled from Apr 2010 to Mar 2012 (everolimus = 362, placebo = 184). Baseline characteristics were balanced between arms; median age was 66.0 y, 84.8% of pts were male, 86.3% had BCLC stage C disease, 16.7% were from Asia, 32.8% had macrovascular invasion, and 74.0% had extrahepatic disease. Prior sorafenib was discontinued for disease progression in 80.8% of pts and intolerance in 19.0%. Median OS was 7.56 mo with everolimus and 7.33 mo with placebo (HR 1.05; 95% CI 0.86-1.27; \(P = .675\)). Median TTP was 2.96 mo and 2.60 mo, respectively (HR 0.93; 95% CI 0.75-1.15). DCR was 56.1% and 45.1%, respectively (\(P = .010\)). The most common grade 3/4 AEs with everolimus (v placebo) were anemia (7.8% v 3.3%), asthenia (7.8% v 5.5%), decreased appetite (6.1% v 0.5%), and hepatitis B viral load increase or reappearance (6.1% v 4.4%). No pts experienced HCV flare. HBV reactivation was experienced by 39 pts (29 everolimus, 10 placebo); all cases were asymptomatic, but 3 everolimus recipients discontinued therapy.

Conclusions: Everolimus did not improve OS in pts with advanced HCC whose disease progressed on or after sorafenib or who were sorafenib intolerant. The safety profile was consistent with that previously observed with everolimus.

Disclosures: Andrew X. Zhu, MD, PhD, consultant or advisory role with Eisai, Daiichi Sankyo and Sanofi, research funding from Onyx, ImClone Systems, Novartis, Bayer, Lilly; Masatoshi Kudo, MD, PhD, consultant or advisory role with Novartis; Eric Assenat, MD, Phd, consultant or advisory role with Novartis; Yoon-Koo Kang, MD, PhD, consultant or advisory role with Novartis, Sanofi, Roche, and Bayer, research funding from Novartis, Sanofi, Roche and Bayer; Ronnie Tung Ping Poon, MBBS, MS, PhD, FRCS, FACS, FHKCS, FHKAM consultant or advisory role with Novartis;
Markus Peck-Radosavljevic consultant or advisory role with Bayer Schering Pharma, Boehringer Ingelheim, ArQule, and Daiichi Sankyo, honoraria from Bayer Schering Pharma, Abbott Laboratories, Novartis and Lilly, research funding from Bayer Schering Pharma; Bruno Daniele, MD, PhD consultant or advisory role with Bayer and Daiichi Sankyo, honoraria from Novartis, Bayer and Daiichi Sankyo; Junji Furuse, MD, PhD, honoraria from Novartis; Annette Jappe, employment/leadership position with Novartis, stock ownership in Novartis; Kevin Perraud, employment/leadership position with Novartis; Ozlem Anak, MD, employment/leadership position with Novartis, stock ownership in Novartis; Dalila B. Sellami, MD, employment/leadership position with Novartis, stock ownership in Novartis; Li-Tzong Chen, MD, PhD, honoraria from Novartis, research funding from Novartis.

Abstract # 207:
*Long-term results of salvage endoscopic treatment for patients with local failure after chemoradiotherapy for esophageal squamous cell carcinoma.*

General Poster Session B Ken Hatogai, MD
Friday, January 17, 2014: 12:00 PM - 02:00 PM National Cancer Center Hospital East
Friday, January 17, 2014: 05:30 PM - 07:00 PM PST Kashiwanoha, Japan
Moscone West Building, Level 1, West Hall

Authors: Ken Hatogai, Tomonori Yano, Takashi Kojima, Masakatsu Onozawa, Toshihiko Doi, Kazuhiro Kaneko, Atsushi Ohtsu; National Cancer Center Hospital East, Kashiwa, Japan

Track: General Poster Session B: Cancers of the Pancreas, Small Bowel, and Hepatobiliary Tract - Translational Research

Background: Local failure is a major problem after chemoradiotherapy (CRT) in patients with esophageal squamous cell carcinoma (ESCC), and salvage surgery presents high morbidity and mortality rates. We have introduced photodynamic therapy (PDT) and endoscopic resection (ER) for local failures to develop a less invasive salvage treatment. The aim of this retrospective study was to clarify the long-term outcome of salvage endoscopic treatments (SET).

Methods: Between 1998 and 2008, 716 patients with ESCC were treated with definitive CRT in our institution. There were 314 patients with incomplete response and 103 with local recurrence after achieving complete response (CR) once. The indication criteria of SET were as follows: 1) absence of lymph node and distant metastasis and 2) local failures limited within T2. ER was performed for local failures limited to T1b (SM1), and PDT was performed for lesions invading T1b (SM2) or T2, in patients who could not tolerate or who refused surgery. We assessed overall survival (OS), relapse-free survival (RFS), and also prognostic factors. This study was approved
Results: A total of 164 patients with local failure underwent SET (ER: 58, PDT: 106). The characteristics before CRT were as follows: T1/2/3/4, 44/25/75/20; N0/1, 85/79; stage I/II/III/IV, 35/59/57/13; and those of before SET were as follows: T1/2, 126/38; residue/recurrence, 76/88. ER achieved curative resection in 51 (87.9%), and PDT achieved CR in 61 (57.5%) patients. With a median follow up period of 73 months, the OS and RFS rates at 5 years from SET were 38.6% (95% CI 31.0–46.2) and 28.1% (95% CI 21.0–35.2). Multivariate analysis revealed 2 preferable prognostic factors in common for OS and RFS, N0 before CRT (OS HR: 0.47 [95% CI 0.32–0.69], RFS HR: 0.61 [95% CI 0.43–0.87]) and a period from initiation of CRT to SET longer than 6 months (OS HR: 0.57 [95% CI 0.39–0.84], RFS HR: 0.67 [0.47–0.95]). After 5 years of follow up, 58 patients (35.4%) were alive without any metastasis under esophagus preservation.

Conclusions: SET demonstrated a favorable outcome in an analysis of a large number of patients with local failure after definitive CRT for ESCC.

Disclosures: Nothing to disclose.

Saturday, January 18, 2014 Presentations

Abstract # 386:
Regular aspirin (ASA) use and survival in patients with PIK3CA-mutated metastatic colorectal cancer (CRC).

Oral Abstract Session Nishi Kothari, MD
Saturday, January 18, 2014: 02:00 – 02:12 PM PST H. Lee Moffit Cancer Center & Research Institute
Moscone West Building, Level 2, Ballroom Tampa, FL

Authors: Nishi Kothari, Richard D. Kim, Peter Gibbs, Timothy Joseph Yeatman, Michael J. Schell, Jayesh Desai, Jeanne Tie, Lara Rachel Lipton, Robert N. Jorissen, Hui-Li Wong, Oliver Sieber, Fiona Day, Ian Faragher, Ian Jones, Ben Tran; H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; Royal Melbourne Hospital and Western Hospital and BioGrid Australia, Melbourne, Australia; The Royal Melbourne Hospital, Melbourne, Australia; Royal Melbourne Hospital, Parkville, Australia; Royal Melbourne Hospital, Melbourne, Australia; Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia; Western Hospital, Footscray, Australia; Royal Melbourne Health, Melbourne, Australia
Track: Oral Abstract Session: Cancers of the Colon and Rectum (eQ&A) - Multidisciplinary Treatment

Background: Recent data has demonstrated that regular ASA use improves overall and cancer-specific survival in the subset of CRC patients harboring PIK3CA mutations. However, as this series only analyzed 15 PIK3CA mutant CRC patients with metastatic disease at diagnosis, it remains uncertain whether the survival benefit associated with regular ASA use extends to patients with metastatic disease. We combined data from two large academic institutions to explore the association between regular ASA use and survival in metastatic CRC.

Methods: Patients with PIK3CA mutated CRC were identified at Moffitt Cancer Center (MCC) in Tampa, FL and Royal Melbourne Hospital (RMH) in Australia. Prospective clinicopathological data (including age, sex, site of disease) and survival data were available. At MCC, PIK3CA mutations were identified by exome sequencing using an Illumina Next Generation Sequencing platform with 50-100X coverage. At RMH, Sanger sequencing was used to identify PIK3CA mutations. Survival analyses were conducted using Cox regression.

Results: We identified 187 CRC patients who harbored a PIK3CA mutation. Median age was 72 years and median follow up was 48 months. 49 (26%) patients used ASA regularly. 47 (25%) patients had metastatic disease at diagnosis. In univariate analyses, regular ASA use was not associated with improved overall survival (HR 0.87, p = 0.60), although there was a trend towards improved cancer-specific survival (HR 0.48, p = 0.06). In patients with stage-II or stage-III disease, regular ASA use did not improve overall, cancer-specific or recurrence-free survival. However, in stage-IV patients, regular ASA use was significantly associated with improved overall (HR 0.35, p = 0.04) and cancer-specific (HR 0.28, p = 0.02) survival in a univariate analysis.

Conclusions: Our study demonstrates that in patients with metastatic CRC harboring a PIK3CA mutation, regular ASA use is associated with a significant overall and cancer-specific survival advantage. However, we were not able to confirm the survival advantage across all stages. To our knowledge, our study is the largest to examine ASA use in PIK3CA mutated CRC.

Disclosures: Nothing to disclose.

Abstract # 524:
SoMore trial: Early metabolic response assessment of a sorafenib (SOR) and capecitabine (CAP) combination in chemorefractory metastatic colorectal cancer (mCRC).

General Poster Session C Amélie Deleporte, MD
Saturday, January 18, 2014: 07:00 AM – 07:55 AM PST Institut Jules Bordet
Saturday, January 18, 2014: 12:00 – 02:00 PM PST Brussels, Belgium
Moscone West Building, Level 2, Ballroom

Authors: Amélie Deleporte, Alain Hendlisz, Camilo Garcia, Thierry Delaunoit, Raphael Maréchal, Marc Peeters, Stephane Holbrechts, Marc Van Den Eynde, Ghislain Houbiers, Bertrand Filleul, Jean-Luc Van Laethem, Christian Diego Rolfo, Marie Diaz, Renaud Lhommel, Gauthier Demolin, Michel Moreau, Lieveke Ameye, Marianne Paesmans, Martine J. Piccart-Gebhart, Patrick Flamen; Institut Jules Bordet, Brussells, Belgium; INDC Entité Jolimontoise, Haine-St-Paul, Belgium; Hôpital Universitaire Erasme, Brussels, Belgium; UZ Antwerpen, Edegem, Belgium; Centre Hospitalier Universitaire Ambroise Paré, Mons, Belgium; Saint-Luc University Hospital, Brussels, Belgium; St. Joseph's Community Health Centre, Liège, Belgium; Universitair Ziekenhuis Antwer, Senior Staff Member Oncology, Antwer, Belgium; Department of Nuclear Medicine, St-Luc Hospital, Catholic University of Louvain, Brussels, Belgium; Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium; Institut Jules Bordet, Université Libre de Bruxelles and Breast International Group, Brussels, Belgium

Track: General Poster Session C: Cancers of the Colon and Rectum - Multidisciplinary Treatment

Background: The SOR-CAP combination has shown clinical activity in several phase I-II trials involving metastatic breast cancer and mCRC patients (pts). SoMore aims to substantiate the combination’s effects in mCRC refractory to all medications and the predictive value of early metabolic response (MR) on survival.

Methods: SoMore (EUDRACT 2010-023695-91) has 2 coprimary objectives: 1) to demonstrate an overall survival (OS) rate at 6 months (mths) > 30%, and 2) to compare OS between pts with and without MR. CAP was given at 1700 mg/m²/day (D), 2 weeks out of 3. SOR was administered at 600mg/D for the first cycle, then at 800mg/D until progression or unacceptable toxicity. FDG-PET-CT was performed at baseline and before the 2nd cycle. MR analysis was centralized and blinded for the investigators.

Results: From February to October 2011, 92 eligible pts were prospectively recruited in 6 Belgian centers: M/F: 54%/46%; ECOG PS 0/1: 55%/45%; median age: 61. A median of 5 treatment cycles were given (0-28+). Grade 3-4 toxic reactions were reported in 61.2%, mainly fatigue (18%), hand-foot skin reaction (14%) and diarrhea (11%), but no toxic death. 6.9% of the pts stopped therapy due to toxicity. 6 mths OS was 71% (95% CI: 61%-79%), significantly >30% (p<0.001). 47% of the 79 pts evaluable for metabolic assessment showed homogeneous MR (HMR) of all metastatic lesions, 32% mixed MR and 21% homogeneous non-MR. Hazard ratio for HMR was 0.34 (95% CI, 0.21 to 0.56) p-value <0.001 for PFS and
0.59 (95% CI, 0.37 to 0.96) p-value 0.03 for OS.

**Conclusions:** These data suggest robust efficacy for the SOR-CAP combination in heavily pretreated mCRC, associated with high but manageable toxicity. Early MR assessment, by detecting unresponsive lesions within the whole body tumoral load, is able to capture the pts’ likelihood of benefit, opening the path to personalized medicine.

<table>
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<tr>
<th>Disclosures</th>
<th>All pts (92)</th>
<th>MR (37)</th>
<th>Non-MR (42)</th>
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<td>About ASCO:</td>
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<tr>
<td>mOS</td>
<td>8.15 (95% CI: 6.77-10.45)</td>
<td>9.9 (95% CI, 7.6 to 16.3)</td>
<td>6.6 (95% CI, 4.8 to 8.3)</td>
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<td>mPFS</td>
<td>4.27 (95% CI: 3.48-4.83)</td>
<td>5.0 (95% CI, 4.0 to 8.9)</td>
<td>2.3 (95% CI, 1.4 to 3.1)</td>
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