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Voting Begins for 2009–2010 ISGIO President

■ *Michael Choti, MD, MBA, Daniel G. Haller, MD, David H. Ilson, MD, PhD, and Alan P. Venook, MD, have been nominated as candidates for President of the International Society of Gastrointestinal Oncology, to serve during the 2009/2010 term.*

Each of the four candidates possesses the extensive knowledge and experience in gastrointestinal oncology and leadership roles in the field to lead the Society into 2010.

Current ISGIO members are eligible to vote in the election. Ballots have been sent via e-mail, and voting continues through July 31, 2009. To become an ISGIO member, with full voting privileges, please visit the ISGIO web site (www.ISGIO.org) for registration information.

Election results will be announced on October 1, 2009, during the annual ISGIO Gastrointestinal Oncology Conference, in Philadelphia, PA.

Biographic sketches of the candidates appear on page 4. More extensive biographies are available at www.ISGIO.org.

(continued on page 4)



Michael Choti, MD, MBA



Daniel Haller, MD



David H. Ilson, MD, PhD



Alan P. Venook, MD

ISGIO Mentoring Program Up and Running, Open to Applicants

■ *The International Society of Gastrointestinal Oncology's new mentoring program blog, "Pathways to Academic Success," is now open for membership application.*

In recognition of the acute need to prepare and support the next generation of gastrointestinal (GI) oncologists, ISGIO created this online interactive forum to open the lines of communication between junior oncologists and mentors. Several respected opinion leaders in the GI oncology arena are serving as mentors for the site. The primary goal is for the physicians to exchange ideas on nonclinical matters related to pursuing a career in GI oncology.

Current blog site topics cover several of the essential facets of building a successful career, including understanding cooperative groups, getting involved in key organizations, clinical trial participation and funding, working

with the pharmaceutical industry, obtaining grants, and writing and submitting papers to medical journals. Additional topics will be added in the future, such as balancing your medical practice and family life, and achieving success in a globalized oncology community.

Participating faculty for the current blogs include Jaffer Ajani, MD (M. D. Anderson Cancer Center, Houston, TX), Al B. Benson III, MD (Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago, IL), Daniel Haller, MD (Abramson Cancer Center at the University of Pennsylvania), Lisa Kachnic, MD (Boston Medical Center, Boston, MA)

(continued on page 3)

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News From ASCO 2009

Presentations Point to Potential New Standards

■ RESULTS OF SEVERAL studies with the potential to influence standard approaches for patients with certain gastrointestinal malignancies were presented at the 45th annual American Society of Clinical Oncology meeting, held in Orlando, Florida, from May 29 through June 2, 2009. Selected highlights are summarized below.

GEMCITABINE/CISPLATIN IMPROVES SURVIVAL OF ADVANCED BILIARY TRACT CANCER PATIENTS

Based on results of a large trial conducted in the United Kingdom in patients with advanced biliary tract cancer, the combination of cisplatin and gemcitabine may be the first standard treatment for this disease.

In the randomized, multicenter phase III UK ABC-02 trial, Valle et

al treated patients with inoperable, advanced, or metastatic disease with gemcitabine alone (n=204) or combined with cisplatin (n=206) (*Figure 2-1*). Patients were treated for up to 6 months. With a median follow-up of 6.1 months, a 3.5-month improvement in the primary end point of overall survival was noted for the gemcitabine/cisplatin patients (11.7 months) vs. the gemcitabine patients (8.2 months), and this was statistically significant ($P = .002$; hazard ratio [HR] 0.68; 95% confidence interval [CI] 0.53–0.86). Progression-free survival (PFS) was also improved in the combination therapy group (8.5 vs. 6.5 months, $P = .003$; HR 0.70; 95% CI 0.56–0.88).

Toxicity was similar in the two arms, according to the authors, (continued on page 2)

News From ASCO 2009 (cont'd from page 1)

with moderate neutropenia (mostly asymptomatic) as the most common adverse effect seen (23% with the combination vs. 18% with gemcitabine alone). [Valle et al, abstract 4503]

TOGA RESULTS SUPPORT TRASTUZUMAB USE IN HER2+ ADVANCED GASTRIC CANCER

In the randomized phase III ToGA trial, conducted in 24 centers in Europe, Australia, Asia, South and Central America, and South Africa, overall survival improved significantly when trastuzumab was added to chemotherapy for patients with HER2-positive metastatic gastric cancer.

Van Cutsem et al tested 3,807 tumors for HER2 status, and 22.1% were considered positive. A total of 584 HER2-positive patients were randomized to treatment with six cycles of chemotherapy (5-fluorouracil or capecitabine and cisplatin) with or without trastuzumab. Trastuzumab therapy was continued until disease progressed. Results showed an increase in median survival from 11.1 months with chemotherapy alone to 13.5 months with the addition of trastuzumab, a statistically significant difference ($P = .0048$; HR 0.74; 95% CI 0.60–0.91). Overall response rate in the intent-to-treat population was also higher

in the trastuzumab group (47.3% vs. 34.5%, respectively, $P = .0017$).

The authors reported similar safety profiles in the two arms, and no difference in symptomatic congestive heart failure. More cases of asymptomatic decreases in left ventricular ejection fraction were seen in the trastuzumab group (4.6% vs. 1.1%) (Figure 2–2). [Van Cutsem et al, abstract LBA4509]

ADJUVANT BEVACIZUMAB IN STAGE II/III COLON CANCER: NSABP C-08 TRIAL RESULTS

Results of the phase III randomized National Surgical Adjuvant Breast and Bowel Project (NSABP) C-08 trial have shown no difference in disease-free survival (DFS) at 3 years for patients (N = 2,672) with stage II and III colon cancer treated in the adjuvant setting with modified FOLFOX6 (5-fluorouracil, leucovorin, oxaliplatin) with vs. without bevacizumab.

PHASE III STAR-1 TRIAL: PREOPERATIVE CHEMORADIOTHERAPY ± OXALIPLATIN FOR LOCALLY ADVANCED RECTAL CANCER

The addition of oxaliplatin to 5-fluorouracil-based preoperative chemoradiation did not improve local tumor response rates, but increased toxicity in patients with locally advanced rectal cancer, according to results of the Italian STAR-1 trial.

A total of 747 patients were randomized to receive 5-fluorouracil (225 mg/m²/d) with concomitant external beam radiotherapy (50.4 Gy in 28 fractions, arm A) or the same regimen plus weekly oxaliplatin (60 mg/m² x 6, arm B). Patients had surgery 6 to 8 weeks later. Pathologic tumor response data, a secondary end point of the trial, were similar in the two treatment groups (Table 2-2). Fewer abdominal metastases were detected at the time of

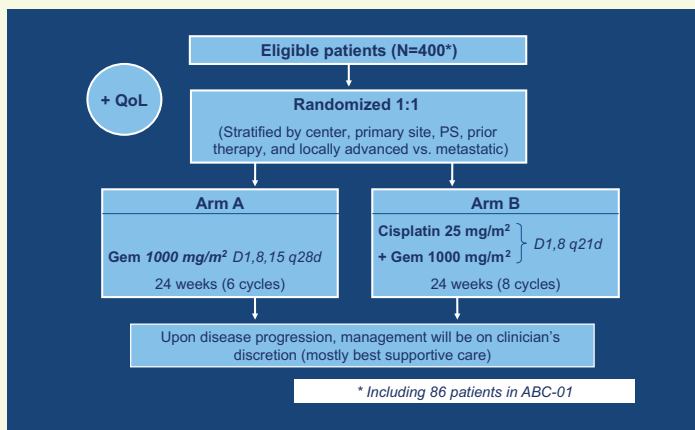


Figure 2-1. Study schema of ABC-02

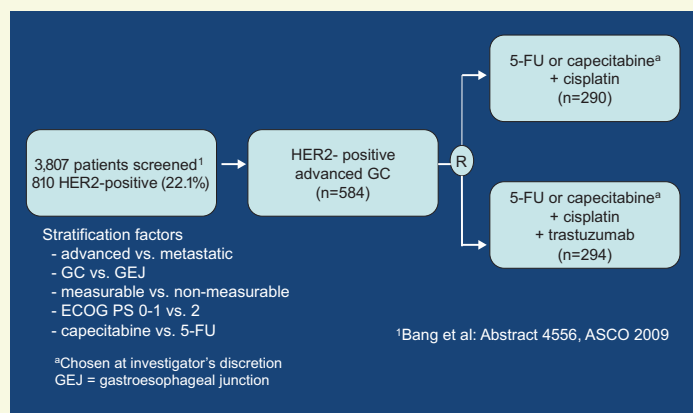


Figure 2-2. ToGA Trial Design. Phase III, randomized, open-label, international, multicenter study

In the bevacizumab treatment arm, bevacizumab (5 mg/kg q2wk) was administered concomitantly with FOLFOX6 for 6 months and as a single agent for an additional 6 months. With a median follow-up of 3 years, the hazard ratio for DFS, the primary end point, was 0.89 (95% CI 0.76 – 1.04, $P = .15$). The authors reported that interval data showed an initial benefit of bevacizumab that decreased over time (Table 2-1). [Wolmark et al, abstract LBA4]

surgery in the oxaliplatin-treated patients (0.5% vs. 3%, $P = .014$).

Overall rates of grade 3/4 toxicity were 8% with 5-fluorouracil-based chemoradiotherapy and 24% with oxaliplatin added to the regimen ($P < .0001$), and this was primarily diarrhea. Grade 2–3 neurotoxicity was also more common with oxaliplatin ($P < .0001$). In arms A and B, respectively, 96% and 90% of patients received >90% of the (continued on page 4)

Table 2-1. NSABP C-08 trial of adjuvant mFOLFOX6 ± bevacizumab in stage II and III colon cancer patients: Disease-free survival data.

	No. pts	No. events	3-yr DFS	P value	Year					
					1	1.5	2	2.5	3	
mFOLFOX6	1,338	312	75.5%		HR	0.60	0.74	0.81	0.85	0.87
mFOLFOX6 + bevacizumab	1,334	291	77.4%	.15	P value	.0004	.004	.02	.05	.08

Abbreviations: DFS = disease-free survival; HR = hazard ratio; mFOLFOX6 = modified FOLFOX6 (5-fluorouracil, leucovorin, oxaliplatin).

Table 2-2. Pathologic response with preoperative 5-fluorouracil-based chemoradiotherapy (arm A) vs. the same regimen plus oxaliplatin (arm B) in patients with locally advanced rectal cancer: STAR-1 Trial.

Pathologic stage	Arm A (n=379)	Arm B (n=368)	Total (N=747)	P value
	No. (%)	No. (%)	No. (%)	
T0N0	60 (16)	57 (15)	117 (16)	.982
T1-2N0	104 (27)	103 (28)	207 (28)	
N1-2	92 (24)	96 (26)	188 (25)	.568
M1	11 (3)	2 (0.5)	13 (2)	.014

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CanLiv: The Hepatobiliary Cancers Foundation Launched

■ A NEW FOUNDATION TO SUPPORT patients with hepatobiliary cancer — CanLiv The Hepatobiliary Cancers Foundation — was recently established, with a mission statement that reads, "Committed to advancing knowledge, education, research, and treatment of cancers of the bile ducts, gallbladder, and liver."

The CanLiv Foundation has launched its web site (www.CanLiv.org), which provides comprehensive information for patients affected by hepatobiliary cancers. The web site also provides information for physicians through the "Newsworthy" link.

This is a timely undertaking, because while hepatobiliary cancers are relatively rare in the US and Europe, the incidence has been increasing. Age-adjusted



incidence rates of hepatocellular carcinoma (HCC), which accounts for the vast majority of hepatobiliary cancers, tripled between 1975 and 2005 in the US, according to Surveillance, Epidemiology, and End Results (SEER) data.¹ One-year survival remains less than 50% overall.¹ In 2008 in the US, there were approximately 31,000 people diagnosed

with hepatobiliary cancers and almost 22,000 deaths,² underscoring the challenges that both patients and physicians face when dealing with these tumors.

Melanie B. Thomas, MD (Hollings Cancer Center, Charleston, SC), and Andrew X. Zhu, MD, PhD (Massachusetts General Hospital Cancer Center, Boston, MA) head up CanLiv as President and Vice President, respectively. ❖

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Melanie B. Thomas, MD

SAVE THE DATE



The 6th Annual Meeting of
The International Society of Gastrointestinal Oncology

GASTROINTESTINAL ONCOLOGY CONFERENCE

2009

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The Sheraton Philadelphia City Center, Philadelphia, PA

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CALL FOR ABSTRACTS AND EDUCATIONAL GRANTS

Abstract Submission Requirements

ISGIO invites all participants to submit abstracts describing original work to the 2009 Conference Organizing Committee.

Abstracts must be written in English and begin with a concise **Title** followed by a list of all **Authors** and their respective **Affiliations**. The body of the abstract should not exceed 500 words and must contain the following labeled sections:

- **Background**, including a statement of the hypothesis or research question;
- **Methods**, an explanation of the study design and experimental methods used;
- **Results**, a summary of the major findings; and
- **Conclusions**, a summary of the overall findings and implications of the results

Educational Grants

Young investigators and fellows are eligible for up to a \$750 educational grant to attend the conference. Meeting materials and registration fees are complimentary with the grant.

To qualify for the educational grant, you must submit a request in writing to the 2009 Conference Organizing Committee, along with one of the following two items: (1) A **data-driven abstract** on clinical or basic science regarding GI cancer (2) A **letter** from the **Chief of Division of Medicine** (or comparable position) stating that you have been working on a GI research project.

E-mail all **materials** and **contact information** (full name, affiliation, mailing address, phone, fax and e-mail address) no later than midnight **August 31, 2009**, to rae.bretana@isgio.org. Approved authors will be notified by **September 4, 2009**.

ISGIO Mentoring Program (cont'd from page 1)

MA), and John Marshall, MD (Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC).

By facilitating active communication between mentors and members, ISGIO also hopes to help the next generation of GI oncology experts build leadership skills and establish relationships with their local and global colleagues. Such

networks will contribute not only to the individual oncologist's success but to the future outlook of the GI oncology field as well.

Participation in this blog site is limited to registered blog members. An application form is available by clicking on the "Mentor Program" tab on the ISGIO web site (www.ISGIO.org). ❖

PROGRAM DESCRIPTION

The 2009 Gastrointestinal Oncology Conference, the official meeting of the International Society of Gastrointestinal Oncology, will provide an educational forum for presenting and discussing the latest advances in the broad field of GI cancer research, as well as critical issues relevant to the care of persons with GI cancer.

The conference will feature distinguished speakers covering a broad spectrum of topics ranging from basic science to clinical therapeutics. Presenters and discussants will explore current issues and debate controversial topics. Case presentations will be given by the faculty and the audience will participate by an interactive audience response system to stimulate discussion on diagnosis and management. This program should be of interest to professionals actively engaged clinically or scientifically in all facets of GI cancer research and care.

PRELIMINARY SCIENTIFIC PROGRAM

Session 1: Esophageal Cancer

- Increasing Importance of Esophageal Cancer: Epidemiology and Combined-Modality Approaches
- Esophagus Sparing Strategies in Patients with Esophageal Cancer
- Case Presentation 1: Locally Advanced Esophageal Cancer
- Case Presentation 2: EMR Before or After Radiation
- Case Presentation 3: Barrett's Dysplasia Treated With an Ablative Approach

Session 2: Pancreatic Cancer

- Metastatic Pancreatic Cancer: How to Select the Best Treatment Options
- Neuroendocrine Tumors of the Pancreas: An Update
- Case Presentation 1: Metastatic Second-Line Therapy
- Case Presentation 2: Locally Advanced (Radiotherapy vs. Chemotherapy)

Session 3: Advanced Colorectal Cancer

- Treatment of Incurable Metastatic CRC
- Curable Metastatic Colorectal Cancer
- Case Presentation 1: First-Line Advanced
- Case Presentation 2: Metastatic but Potentially Curable
- Case Presentation 3: Second-Line and Third-Line

Session 4: Hepatobiliary Cancer

- Case Presentation 1: Localized Hepatocellular Carcinoma: Resection, Ablation, or Transplantation?
- Case Presentation 2: Patient Who Had a Bile Duct Cancer
- Case Presentation 3: Patient Treated with TACE, but Where Are the Data

Session 5: Emerging Science

- Keynote Presentation: Oncogenes and Cancer
- Cancer Stem Cells: Cancer Initiation, Therapy Resistance, and Metastases
- Signaling Pathways of Survival – What Can They Teach Us?

Session 6: Adjuvant Colon Cancer

- Biomarker Signatures That Predict Benefit From Therapy
- Case Presentation 1: Stage II
- Case Presentation 2: Stage III
- Case Presentation 3: Stage IVa After Primary Surgery for Previously Untreated Synchronous Liver Metastases

Session 7: Gastric Cancer

- Molecular Biology: East and West
- Localized Gastric Cancer: East and West – Which Is the Best Approach?
- Gastric Cancer Surgery: East and West
- Case Presentation 1: Preoperative Therapy
- Case Presentation 2: Metastatic First-Line
- Case Presentation 3: Chemoradiation as Adjuvant Therapy
- Advanced Gastric Cancer: An Update

Session 8: Rectal Cancer

- Prognostic Factors of Rectal and Anal Cancer Outcomes
- Current Approaches to Localized Rectal Cancer – T1 T2 Approaches and the Trans-Anal Approach
- Case Presentation 1: Preoperative Chemoradiation
- Case Presentation 2: Postoperative Chemoradiation
- Case Presentation 3: Radiation Is Not Necessary in This Case

Voting Begins for 2009–2010 ISGIO President (cont'd from page 1)



Alan P. Venook, MD: Dr. Venook is Professor of Clinical Medicine at the University of California in San Francisco (UCSF), CA, where he leads the GI oncology clinical program. He is a nationally recognized expert in colorectal and liver cancers. Currently, Dr. Venook is Chairman of the National Cancer Institute's Hepatobiliary Task Force and he serves on the National Comprehensive Cancer Network (NCCN) Hepatobiliary Cancers Guidelines panel and the Colorectal Cancer Guidelines panel. He is also Chair of the Committee on Human Research and Director of the RKS (Regulatory Knowledge and Support) Program, UCSF Clinical and Translational Science Institute. Dr. Venook is co-principal investigator of the Cancer and Leukemia Group B 80405 trial, an Intergroup study for patients with metastatic colorectal cancer.



Michael A. Choti, MD, MBA: Dr. Choti is the Jacob C. Handelsman Professor of Surgery and Oncology, and Vice Chair of the Department of Surgery at Johns Hopkins School of Medicine in Baltimore, MD. He is also director of the Johns Hopkins Colorectal Center. Dr. Choti serves on the American College of Surgeons' Commission on Cancer and on the Colorectal Cancer and Neuroendocrine Tumor Panels for the National Cancer Coalition Network. Research interests include robotics and computer assistance to treat cancer surgically using minimally invasive image-guided approaches, molecular genetics and biomarkers in GI cancer, and clinical trials and outcomes research in hepatobiliary, pancreatic, and other GI malignancies. Dr. Choti has mentored many trainees and investigators, and directs the Surgical Oncology Fellowship training program at Johns Hopkins.



Daniel G. Haller, MD: Dr. Haller is Professor of Medicine, Department of Medicine, at the Abramson Cancer Center at the University of Pennsylvania, and Attending Physician at the Hospital of the University of Pennsylvania in Philadelphia, PA. He is considered one of the most prominent GI oncologists both nationally and internationally. Dr. Haller currently co-chairs the US National Cancer Institute GI Intergroup and has served as the GI Committee Chair for the Eastern Cooperative Oncology Group. He is on the International Advisory Board of the INCa (the French National Cancer Institute) and is a Fellow of the American College of Physicians. He has been an active member of the American Society of Clinical Oncology, American Association for Cancer Research, and European Society for Medical Oncology. Since 2001, Dr. Haller has served as Editor-in-Chief of the Journal of Clinical Oncology.



David H. Ilson, MD, PhD: Dr. Ilson is Attending Physician and Member at Memorial Sloan-Kettering Cancer Center (MSKCC), and Associate Professor of Medicine at Weill-Cornell Medical College in New York, NY. He sits on the GI committees of the Cancer and Leukemia Group B, the Radiation Therapy Oncology Group, and the Upper GI Cancer Guidelines Committee of the National Comprehensive Cancer Network (NCCN). Dr. Ilson is also chairman of the Intergroup Esophageal and Gastric Cancer Task Force Committee. His research interests are in the area of upper GI cancers, with a focus on esophageal cancer. Dr. Ilson has conducted research to evaluate new agents in advanced disease and novel agents in combined-modality therapy programs in locally advanced disease. ♦

News From ASCO 2009 (cont'd from page 2)

Table 4-1. Prognostic impact of MSI – Univariate

HR MSI H (95% CI)		5-FU (n= 625)	5-FU/iri (n= 608)	Both arms
Stage II (n = 391)	RFS	0.228 (0.05–0.955) P = .043	0.296 (0.091–0.968) P = .044	0.265 (0.107–0.661) P = .0044
	OS	0.18 (0.02–1.34) P = .095	0.143 (0.02–1.06) P = .057	0.159 (0.039–0.659) P = .011
Stage III (n = 842)	RFS	0.596 (0.344–1.03) P = .064	0.815 (0.478–1.39) P = .45	0.693 (0.473–1.02) P = .06
	OS	0.515 (0.261–1.02) P = .055	0.939 (0.515–1.71) P = .84	0.699 (0.446–1.09) P = .12
Both stages (P values are stage corrected)	RFS	0.501 (0.300–0.837) P = .0083	0.642 (0.394–1.05) P = .076	0.569 (0.400–0.811) P = .0018
	OS	0.437 (0.229–0.833) P = .012	0.676 (0.380–1.20) P = .18	0.548 (0.357–0.842) P = .006

planned radiotherapy, and 96% of patients in both arms were able to have surgery.

The authors noted that the lower M+ rate in the oxaliplatin group suggests an effect on distant micrometastases. Longer follow-up is needed to determine treatment effects on overall survival, the primary study end point. [Aschele et al, abstract 4008]

PROGNOSTIC VALUE OF MICROSATELLITE INSTABILITY IN STAGE II/III COLON CANCER

Patients with microsatellite-unstable (MSI-H) tumors have been shown to have better prognosis than those with microsatellite-stable (MSS) tumors. Tejpar et al investigated the incidence of microsatellite instability (MSI-H) in patients with stage II/III colon cancer enrolled in the large, randomized phase III PETACC-

3 trial, and the effects of MSI-H status on patient prognosis and treatment response.

Previous data from PETACC-3 demonstrated no difference in 5-year disease-free survival for stage III patients treated with 5-FU/leucovorin vs. 5-FU/leucovorin plus irinotecan (the primary study end point).

In this analysis, examination of paraffin tissue blocks from available patients revealed MSI-H status in 22% of 395 stage II patients and in 12% of 859 stage III patients, a statistically significant difference ($P < .0001$). MSI-H was defined as instability in ≥ 3 markers out of the 10 markers included in the National Cancer Institute extended panel.

MSI-H status was statistically significantly prognostic for both relapse-free survival and overall survival for the stage II/III patients combined; when the groups were analyzed separately, however, the

prognostic value was strongly significant in the stage II group but marginal in the stage III patients (Table 4-1); the authors noted, however, that subgroup analysis was limited by multiple testing and sample size.

The strong prognostic effect of MSI-H status in the combined stage II/III patients and the stage II cohort was retained in those treated with 5-FU/leucovorin, with 5-year relapse-free survival rates of 83% vs. 66% in the MSI-H vs. MSS groups, respectively ($P = .0077$).

While previous reports have shown conflicting data regarding the potential predictive role of MSI-H for 5-FU treatment in colon cancer patients,¹⁻⁴ this study did not examine this issue, as all of the patients were treated with 5-FU with or without irinotecan. However, the potential predictive effects of MSI status for response to irinotecan therapy were analyzed; results showed no influence of MSI status on irinotecan treatment response in both stage II and stage III patients. This is in contrast to a previous report in which MSI-H was predictive for response to irinotecan therapy.⁵ [Tejpar et al, abstract 4001] ♦

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