# Chinese American Hematologist Oncologist Network (CAHON)


**Timely News and Information Updates for Members**

**Volume 2, Issue 1**

**January 30 , 2011**

**Highlights:**



**鴻運當頭，財源廣達旺運年, 吉祥高照、招財進寶輕鬆來**

**祝愿兔年好!**

Dear CAHON Members and Friends:

May we wish you the best luck in the Year of Rabbit! As Chinese, we certainly feel the real New Year starts with our tradition. As Chinese professionals in hematology and oncology, we hope that the New Year brings us more advancements and prosperity for our network or organization. More we work together, more we contribute to our community. We'd happy to share with you few important developments in GI Oncology in this issue. We hope you find the information useful and we welcome your comments and feedback.


## Updates from the 2011 Gastrointestional Cancer Symposium

# Circulating free DNA (cfDNA): Detect Genetic Mutations in Metastatic/Advanced Colorectal Cancer

A prospective study from UK showed a minimally invasive way for detecting mutations in advanced colorectal cancer patients. 26 consented patients provided DNA from matched archival formalin fixed paraffin-embedded (FFPE) tumor and plasma. Samples had ~200 described gene mutations genotyped using Sequenom MassARRAY (OncoCarta Panel). *KRAS*, *BRAF* and *PIK3CA* mutations were detected in 8 (31%), 3 (12%) and 3 (12%) tumor specimens. 100% concordance for KRAS status was observed between multiple FFPE biopsies from the same patient and analysis by Amplification Refractory Mutation System (ARMS)-Scorpion PCR. Concordance between matched FFPE and cfDNA was 88% for *KRAS* and 100% for *BRAF* mutations. No mutations were detected in patients with wildtype *KRAS* or *BRAF* tumor genotypes in cfDNA analysis confirming the high specificity. The data indicated that cfDNA appears representative of tumor DNA and may be used for the prospective selection of cancer patients for treatment with targeted therapeutics.

J Clin Oncol 29: 2011 (suppl 4; abstr 356)

# Everolimus for Treatment of Neuroendocrine Tumors

In the past several years, biological therapy including octreotide and sunitinibhas been demonstrated to be active in neuroendocrine tumors (NET). However, there is still an unmet need for effective treatments of NET. In the 2011 GI Cancers Symposium, two large phase III studies updated the efficacy of everolimus, a mTOR inhibitor, in the disease.

RADIANT 3, a randomized, double-blind, placebo-controlled study approved the benefit of everolimus over best supportive care in the patients with pNET after failure of prior systemic chemotherapy (50% had octreotide treatment previously). Patients with advanced low- or intermediate-grade pNET were randomly assigned to everolimus 10 mg/d orally + best supportive care (BSC; n = 207) or placebo + BSC (n = 203). The median PFS was 11.0 months in the everolims arm vs. 4.6 months in the placebo arm (HR = 0.35; 95% CI: 0.27-0.45; $p < 0.0001$. Estimated 18-month PFS is 34% for everolimus (95% CI: 26-43) vs 9% (95% CI: 4-16) for placebo.

RADIANT 2 trial is a randomized, double-blind, study as well. 429 patients with well or moderately differentiated advanced NET and history of carcinoid symptoms were randomized to everolimus (10 mg/day) + octreotide LAR (30 mg IM q 28 days) (n = 216) or placebo + octreotide LAR (n = 213). Crossover from placebo + octreotide arm to open-label everolimus arm was allowed at disease progression. Median PFS (95% CI) from central review was 16.4 months in the everolimus + octreotide arm vs. 11.3 months in the placebo + octreotice arm, associated with a 23% reduction in risk of progression. (HR = 0.77; 95% CI: 0.59-1.00, p=0.026). Interesting thing is that the mPFS from investigator's review was different 12.0 months vs. 8.6 months, HR =0.78; 95% CI 0.62-0.98, p= 0.018.

Most frequent drug-related adverse events reported were stomatitis, rash, diarrhea, fatigue, and infections.

***Comments: Whether an improvement in PFS in the disease represent clinical benefit remains to be discussed or defined.***

## Cetuximab Benefits at Adjuvant Setting in Stage III Colon Cancer When Combined with FOLFIRI ? Data of N0147

Irinotecan (CPT-11) has been demonstrated to be active against metastatic colorectal cancer, either used alone or in combination with 5-fluorouracil (5FU)/leucovorin (LV). However, there have been no benefit shown in adjuvant use based on 3 large Phase III studies (either IFL or FOLFIRI) when compared with 5-FU/LV (CALGB 89803 [J Clin Oncol. 25:3456, 2007], PETACC-3 [J Clin Oncol. 27:3117, 2009], and Accord02 [Ann Oncol. 20:674, 2009]. Cetuximab (Cmab), a monoclonal antibody inhibits EGFR, was only effective in patients with mCRC positive for wild type KRAS (wtKRAS). The FOLFIRI +/- cetuximab arms were discontinued from the phase III N0147 after a short period time because of the above rationale. The data from these relative small groups were reported 2011 GI Cancers Symposium. 156 patients (111 in the FOLFIRI arm, 45 in the FOLFIRI + Cmab) were enrolled; median follow-up on 81 patients in FOLFIRI arm was 60.3 months and on 41 patients in FOLFIRI + Cmab was 58.2 months. wtKRAS (vs mt) status was associated with improved DFS (HR=0.6 [95% CI 0.4-1.1], p = 0.09) and OS (HR 0.7 [95% CI 0.4-1.5], p = 0.38). The addition of Cmab improved DFS and OS in the overall group and within wtKRAS pts. Grade greater than III non-hematologic adverse effects were significantly increased in the Cmab arm (46% vs. 64%, p = 0.05). The result showed that adjuvant FOLFIRI resulted in a 3-year DFS lower than that expected for FOLFOX. Trends for improved DFS and OS with the addition of Cmab were observed in patients with resected stage III colon cancer patients, regardless of KRAS status. The mechanism remains unknown at present. It is possible that a synergistic effect of combining FOLFIRI with cetuximab differs from that of the combination FOLFOX with cetuximab.

J Clin Oncol 29: 2011 (suppl 4; abstr 363)

| | Overall (n = 156) | | | wtKRAS (n = 99) | | |
|---|---|---|---|---|---|---|
| | FOLFIRI | FOLFIRI +Cmab | HR (95% CI) | FOLFIRI | FOLFIRI +Cmab | HR (95% CI) |
| **N** | 111 | 45 | - | 72 | 27 | - |
| **3-yr DFS** | 65% | 80% | 0.6 (0.3-1.1) p=0.09 | 67% | 88% | 0.4 (0.1-1.0) p=0.05) |
| **3-yr OS** | 83% | 90% | 0.4 (0.1-1.0) p=0.04 | 83% | 92% | 0.3 (0.1-1.3) p=0.08 |

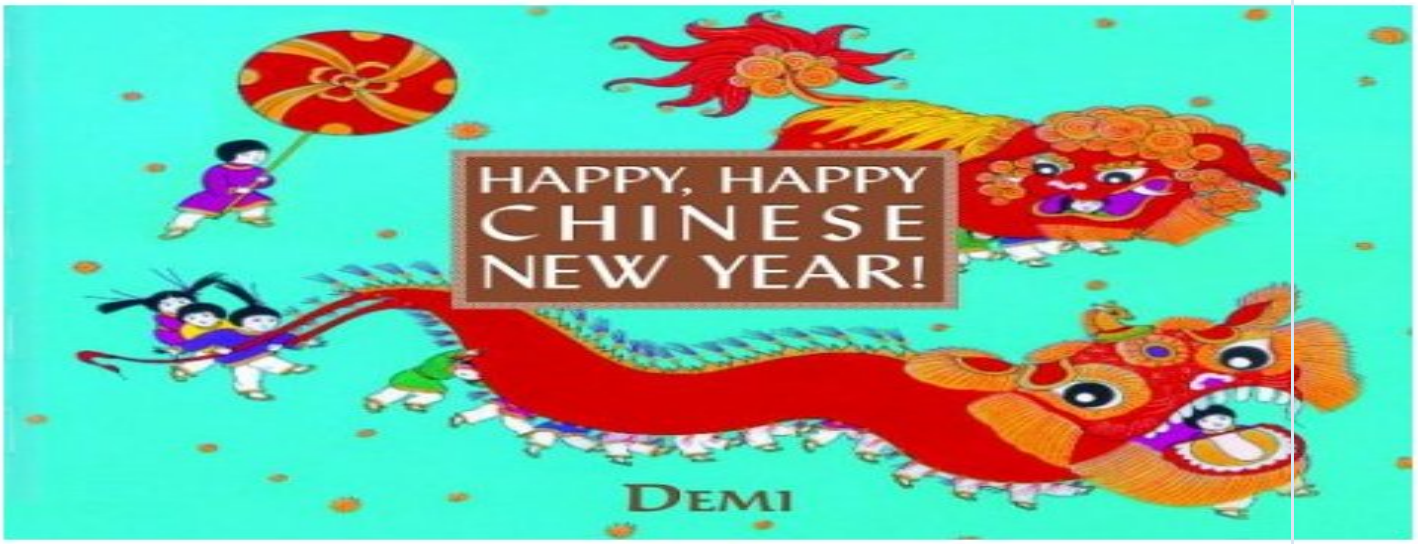
## Timely News and Information Updates

E-mail Addresses:
tianhong.li@ucdmc.ucdavis.edu
janice.lu@stonybrook.edu
ningy@mail.nih.gov
Weijing.Sun@uphs.upenn.edu

**We are on Web: http://www.cahon.org/**

## CAHON's MISSION

CAHON, founded by Chinese American Hematologists and Oncologists in 2005, is dedicated to fostering communication amongst Chinese-American medical professionals for delivering high-quality health care to patients with neoplastic and hematological diseases, and to promoting medical information exchange between the United States and China in the field of hematology and oncology. CAHON strives to serve as a vital bridge between American and Chinese Hematology-Oncology communities in the levels of academia, industry, government regulation, and private practice.




*We'd like to have more volunteers to help fulfill our mission and develop in the future. We are specially interested in any motivated member or their kid (at college or high school) who has strong knowledge and skills on managing websites to maintain and update our website(www.cahon.org). Periodic complimentary pay for the service provided will be negotiable and available. Please contact our website improvement team members.*

*We also welcome your super ideas on how we could improve or what else would be appropriate to add or modify. Together, we advance and will have more opportunities to magnify the value of life.*

### CAHON Management Team:

**President: Weijing Sun, MD**
**VP: Yang-Min Ning, MD, PhD**
**Treasurer: Jeff Ye, MD**
**Chair, Membership: Tina Li, MD, PhD**
**Director, Education and Communication: Janice Lu, MD**
**Director, Clinic Practice Coordination: Zili He, MD**
**Director, Relationship and General management: Jingzhou Hou, MD**