Colorectal Cancer Research
Week Ending July 25th, 2008

DRUGS

1. **Safety & Efficacy of Oxaliplatin & Fluoropyrimidine Regimens With or Without Avastin as First-Line Treatment of mCRC: Results of the TREE Study** (Jul 20/08)

   The safety and efficacy of 3 oxaliplatin and fluoropyrimidine regimens, with (TREE 2) or without avastin (TREE 1), as first line treatment for mcrc were evaluated. Patients with no prior treatment for advanced disease were randomly assigned to receive

   - FOLFOX 6 (bolus and infusion fluorouracil [FU] and leucovorin [LV] with oxaliplatin)
   - bFOL (bolus FU and low dose LV with oxaliplatin, or
   - CapeOx (capecitabine with oxaliplatin)

   The study was later modified such that subsequent patients were randomized to the same regimens plus avastin (TREE 2). The investigators concluded that the addition of avastin to oxaliplatin and fluoropyrimidine regimens is well tolerated as first line treatment of mcrc and does not markedly change overall toxicity. CapeOx tolerability and efficacy is improved with reduced dose capecitabine. First line oxaliplatin and fluoropyrimidine based therapy plus avastin resulted in a median overall survival of approximately 2 years.

   Hochster, Howard, et al., Safety and Efficacy of Oxaliplatin and fluoropyrimidine Regimens with or without bevacizumab as first line treatment of metastatic colorectal cancer: Results of the TREE Study. Journal of Clinical Oncology Vol 26, No 21(July 20), 2008: pp. 3523-3529

2. **YM Biosciences Compares Data on Nimotuzumab To Cetuximab and Panitumumab** (Jul 21/08)

   YM Biosciences is an oncology company, situated in Mississauga, Ontario, and it has announced its results in respect of its humanized monoclonal antibody that targets the epidermal growth factor receptor (EGFR) compared to two other EGFR targeting drugs cetuximab and panitumumab. The data described the unique binding properties of nimotuzumab to EGFR that allows the antibody drug to be effective against cancers such as colorectal cancer without causing the severe side effects of other EGFR targeting drugs. Currently, there is an ongoing 59 patient phase II study in colorectal cancer of nimotuzumab with irinotecan which confirms the low level of interaction between nimotuzumab and normal tissue with less than a quarter of the patients exhibiting skin toxicity and in all of whom it was both mild and transitory. The data also describes the mechanism through which nimotuzumab distinguishes between normal cells, binding preferentially to cancer cells over-expressing EGFR, whereas the currently approved anti-EGFR antibodies, Cetuximab and panitumumab, bind to all tissues expressing EGFR.
   www.newswire.ca/en/releases/archive/July2008/21/c6361.html
   Clinical trial Information may be found at:
   http://www.clinicaltrials.gov/ct2/show/NCT00493857?term=nimotuzumab&rank=1

3. **Xelox, Folfox, Folfiri in mCRC: Physician Choice Based on Toxicity Profiles [Gastrointestinal Cancers Symposium]** (Jul 10/08)

Large amounts of data were reported from the Gastrointestinal Cancers Symposium, a meeting cosponsored by the American Society of Clinical Oncology (ASCO) which indicated that

- **Xelox** and **Folfox** regimens have equivalent efficacy in mcrc
- Additionally, a randomized phase II trial found that **Cetuximab** plus **Folfox** appears similar to **Cetuximab** plus **Folfiri**
- **5FU** and **Capecitabine** are interchangeable, though the toxicity patterns are a bit different with the two of them which is quite useful, because with some patients neutropenic sepsis may wish to be avoided; whereas in others diarrhea may wish to be avoided. Hence, a clinician would choose the regimen on the basis of clinical need for the patient in question

Although these concepts have been reported previously, the current analyses are very important for making the optimal choice of chemo regimen, said Heinz-Josep Lenz, MD , Professor of Medicine at the Keck School of Medicine at the University for Southern California and Associate Director of Clinical Research at the USC/Norris Comprehensive Cancer Center.

Oncology Times: Volume 30 (13) 10 July 2008 p 48

4. **Switching From 5FU to Xeloda Can Cause Significant Side Effects** (Jul 24/08)

An immediate switch from 5FU to Xeloda (capecitabine) for stage III colon cancer caused so much toxicity that a trial designed to test patient preferences for treatment had to be stopped. Patients in the *PACT* trial who switched after 6 weeks from weekly 5FU with leucovorin to oral capecitabine experienced excessive side effects. The trial was designed to determine which approach to treatment patients liked best. Patients either started with 5FU and switched to Xeloda or vice versa. And then patients would choose the treatment they preferred. However, the trial was halted after 40 of a planned 74 patients were enrolled because of the high toxicity in the first group who made the 5FU to Xeloda switch because of side effects such as diarrhea, hand-foot syndrome and lethargy. Researchers do not know the reason that the sequence of 5Fu with leucovorin and Xeloda made such a startling difference in side effects, but they think that leucovorin (folic acid) may be at the bottom of the mystery. It is possible that leucovorin allows folate to build up in cells and contributes to more serious side effects when Xeloda is begun. The team headed by Dr. Ivo M Hennig, concluded:
"In chemotherapy-naïve patients, capecitabine produced more toxicity than FU/LV, but at levels in line with previously reported data. However, treatment with capecitabine after FU/LV caused markedly increased toxicity, indicating a sequence-specific interaction. The mechanism has not been determined, but interaction with intracellularly retained folate after FU/LV therapy is a possibility. Oncologists need to be aware of this risk if considering crossing patients over from FU/LV to capecitabine-based regimens".

Hennig et al., Journal of Clinical Oncology, Volume 26, Number 20, July 10, 2008

NUTRITION

5. **Consumption of trans-Fatty acid and Its Association with Colorectal Adenomas** (Jul 25/08)

Researchers investigated the association between colorectal adenomas/cancers and trans-fatty acid consumption by utilizing data from a cross sectional study of 622 patients who underwent complete colonoscopy between 2001 and 2002 at the University of North Carolina Hospitals. Patients were interviewed about demographic, lifestyle, and dietary factors thought to be related to colorectal cancer. Those in the highest quartile had an increased prevalence of colorectal adenomas. The results of the study suggest that consumption of high amounts of trans-fatty acid may increase the risk of colorectal cancer, and they provide additional support to recommendations to limit trans-fatty acid consumption.

Vinikoor, Lisa, et al., Consumption of trans-fatty acid and Its Association with Colorectal Adenomas, American Journal of Epidemiology, 2008; 168(3): 289-297