

COLORECTAL CANCER SUMMARY 2010

Colorectal cancer is the third leading cause of cancer in the United States and the third most common cause of cancer death. Approximately 149,000 new diagnoses will be made this year and 50,000 will die of it. Incidence has slowly increased in this country and has evolved such that right-sided colon tumors have become more common. This may be in part due to sigmoidoscopies that are removing adenomas and other polyps on the left side of the colon more routinely. Five year overall survival has steadily improved over the last two decades for left-sided colon cancers. Survival rates are relatively stable for right-sided tumors.

More patients are receiving adjuvant 5FU and oxaliplatin based chemotherapy with stage II colon cancer following a detailed assessment of risk. This includes clinical, pathologic, and molecular risk factors. Two examples of the latter are high frequency microsatellite (in)stability testing and B-raf mutation analysis.

Stage III colon cancer patients will routinely receive 5FU and oxaliplatin based adjuvant therapy. Irinotecan failed to meet primary end points in multiple trials that were stopped in this decade, essentially ending further investigation for irinotecan adjuvantly and solidifying the use of oxaliplatin for curative intent disease.

Disappointingly, the addition of Avastin in adjuvant disease did not improve outcomes in 2009 and so is not recommended in stage III disease outside of a trial.

Molecular testing is guiding treatment in metastatic disease and at least assisting with prognosis in early stage disease; Oncotype assay has been validated in stage II disease and while it is prognostic, it is unfortunately not predictive of response to therapy.

In the metastatic setting K-ras testing and reflexive B-raf testing for now guides use of anti-EGFR therapies. ERCC-1 and TS testing have limitations and assay cut-off issues, coupled with the practicality that the drugs these two tests inform us about are among the few FDA approved therapies we have. Thus, clinical decision-making is not yet often easily informed by these latter two tests. Likewise, circulating tumor cell assays inform overall prognosis in metastatic disease but do not yet clearly guide subsequent therapy decisions.

In rectal cancers trimodality therapy is the foundational approach appropriate in most cases. The use of endorectal ultrasound and PET scanning in clinical staging has become more common but is not as reliably accurate as we would like. There are also inter-operator dependence issues with the ultrasound. European data presented in 2010 on new MRI techniques have demonstrated remarkable improvements in accuracy for determination of small perirectal lymph nodes that may harbor tumor and differentiation of larger lymph nodes that are reactive. We may find this could even supplant endorectal ultrasound in the future.

Two large phase 3 trials of locally advanced rectal cancer (T3, T4, and/or node positive) reported at ASCO 2009 disappointingly showed that the addition of oxaliplatin to 5FU or Xeloda based neoadjuvant combined modality therapy and/or adjuvant therapy did not improve any outcomes. Furthermore, toxicities were substantially worse in the oxaliplatin arms. Thus, oxaliplatin for locally advanced rectal cancer can only be recommended in the context of a clinical trial.

In summary, science is rapidly moving ahead of the clinical aspects of colorectal cancer treatment. Our hope therefore is that as numerous new treatment targets are

discovered and limitations of current therapy are predicted sooner that we will be able to see new agents come to clinical trials and ultimately cure more patients of these diseases.

Respectfully submitted,

DEREK A. HELTON, M.D., F.A.C.P.
SAN DIEGO CANCER CENTER
MARCH 01, 2010
DAH/gls t:0223