

# Widening choices for patients with colon cancer

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**T**HE X-ACT AND TREE TRIALS provide important clinical information on therapeutic options for patients with stage III and IV colon cancer.

## Superior survival benefit

It is clear from the results of the X-ACT trial that not only is capecitabine (Xeloda) an alternative to 5-fluorouracil in the adjuvant therapy of colon cancer, but it is, in fact, superior by most objective criteria and also offers safety and convenience advantages. It is important to remember that although this trial was designed to demonstrate equivalence between oral capecitabine and intravenous 5-FU plus leucovorin (Mayo Clinic regimen), capecitabine actually showed a statistically superior benefit for relapse-free survival and a strong statistical trend toward increased overall survival.

The TREE trials provide comparative results for several regimens utilized in the treatment of metastatic colon cancer. The modified FOLFOX6 regimen is attractive due to the decreased number of required clinic visits, and the bFOL regimen eliminates the need for infusional 5-

FU, creating greater convenience for the patient. The CapeOx regimen takes advantage of the oral (as opposed to intravenous) administration of capecitabine in combination with oxaliplatin (Eloxatin), greatly simplifying the dosing of this combination. Now that bevacizumab (Avastin) has become the standard of care due to its survival advantage in metastatic colon cancer, TREE-2 provides information on the efficacy of adding bevacizumab to these three regimens.

Although these trials are small, the trends clearly favor prolonged exposure of a thymidylate synthase inhibitor via either the modified FOLFOX6 regimen or CapeOx. The advantages in overall response rate were seen in both the TREE-1 and TREE-2 trials, suggesting that CapeOx should be an appropriate substitution if intravenous infusion of 5-FU is not suitable for an individual patient.

## Comparative toxicity

The comparative toxicity profiles enable oncologists to discuss with their patients which regimen might be more appropriate for their particular situation. Although the incidence of diarrhea is similar among all three regimens, neutropenia is more fre-

quent with the modified FOLFOX6 regimen, and hand-foot syndrome is more commonly observed with the CapeOx regimen. Neurotoxicity is also slightly more frequent with CapeOx, due to the increased dose of oxaliplatin in the every-3-week schedule. The addition of bevacizumab, as expected, increased the incidence of hypertension in TREE-2 but resulted in no substantial worsening of other toxicities.

## Summary

These clinical trials provide useful comparative information to both the oncologist and the cancer patient with regard to the toxicities and efficacy of these greatly different chemotherapeutic regimens. Clearly, the convenience of oral capecitabine is also supported by the improved clinical results obtained with this drug in the X-ACT trial. The TREE trials indicate that prolonged exposure to a thymidylate synthase inhibitor offers a relative advantage over bolus administration and that bevacizumab can be safely added to these therapeutic combinations.

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