"Timing and Deferral of Rectal Surgery Following a Continued Response to Pre-Operative Chemoradiotherapy"
RMT Ethics No. 2759

Date

Dear Dr,

Your patient has been enrolled onto a research trial at the Royal Marsden hospital. This trial tests the safety of avoiding surgery for those patients that are judged to have a complete response to neo-adjuvant therapy, using both clinical and radiological criteria.

All of the modern pre-operative Chemo-Radiotherapy trials for rectal cancer see a percentage of patients that achieve a complete response, ie that do not have any tumour found in the pathology specimen. This may account for up to 25% of patients. With such impressive rates of pathological complete response, there is increasing interest in the possibility of selecting those patients that will achieve complete response, and omitting surgery. The results from two trials have particularly inspired this trial.

Between November 2001 and August 2004, EXPERT (a phase II study of Oxaliplatin Capecitabine and pre-operative radiotherapy for patients with locally advanced and inoperable rectal cancer) study has recently completed its accrual of 77 patients at the Royal Marsden hospital. This trial delivered neo-adjuvant chemotherapy with 4 cycles of Oxaliplatin and Capecitabine prior to Chemo-Radiotherapy. 67 patients proceeded to appropriate surgery after an interval of 6 weeks with total mesorectal excision. The rate of pathological complete response, ie no tumour found at surgery, was 24% and minimal microscopic disease was found in a further 48%. Long-term results are awaited.

In a landmark study published in the Annals of Surgery in October 2004, Professor Angelita Habr-Gama at the University of Sao Paulo presented long-term results of a policy of omission of surgery for selected patients following neo-adjuvant Chemo-Radiotherapy with radiological and clinical evidence of complete response. 265 patients with distal resectable rectal tumours were treated with neo-Adjuvant Chemo-Radiotherapy from 1991 to 2002.Approximately 71 (26.8%) of patients were judged to have achieved complete response on clinical and radiological grounds. These patients did not have surgery. All other patients proceeded to surgery.

Median follow-up was 5-year overall and disease-free survival rates were 88% and 83% in the resection group and 100% and 92% in the Observation group respectively. 5-year overall and disease-free survival rates were 100% and 92% respectively. 10-year overall and disease-free survival rates were 97.7% and 84% respectively. Of 71 patients considered to be in stage 0 following Chemo-Radiotherapy, about 70% were T3, 10% T4, and only 20% radiologically staged as node positive.

Of 71 "stage 0" patients, only 2 suffered an endoluminal relapse, both of whom were successfully salvaged. 3 patients developed metastatic disease. Thus this data appears to show that once "stage 0" patients are diagnosed correctly, it is safe to omit surgery. A trial of omission of surgery will therefore allow those who would achieve a complete response to avoid the morbidity and mortality of surgery. Furthermore, patients who would otherwise have only minimal microscopic disease at surgery may have an opportunity to achieve complete response with time.

All patients will be followed up in clinic at regular intervals with CEA estimation at each clinic visit. Patients will be followed after completion of all treatment every 3 months for the first 2 years, every 6 months to 5 years, and then annually until 10 years have elapsed. An intensive schedule of MRI, CT and flexible Sigmoidoscopy follow-up has been formulated, such that any evidence of recurrence will be diagnosed and treated swiftly.

Please do not hesitate to contact me with any queries. A copy of the protocol is available on request.

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