Reviewer's report

Title: Systemic Chemotherapy for Treatment of Advanced Small Bowel Adenocarcinoma with Prognostic Factor Analysis: Retrospective study

Version: 1 Date: 23 January 2011

Reviewer: Christopher Jackson

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The authors report a retrospective review of 91 patients diagnosed and treated for small bowel adenocarcinoma at a single institution between Jan 1989 and Dec 2009. Case notes were reviewed and data extracted. Data was analysed for prognostic factors. The authors attempt to identify whether palliative chemotherapy can improve survival.

The strengths of this data set include that it has been conducted at a single institution with a single database, meaning that all patients at that institution should have been captured. This will minimise selection bias. (Selection bias according to referral pattern is difficult to avoid in any series). The inclusion of a group that did not receive any chemotherapy is also a considerable strength of this data, as most other series do not include an untreated control. Also of note is that 20 patients with good PS received no chemotherapy due to patient choice, which provides a highly informative comparator group.

The propensity score-based weighting is a standard statistical approach which attempts to adjust for confounding by incorporating additional variables. Its use is another strength of this data set. The authors also attempt to identify clinical factors that may impact on outcome, such as site of metastases (liver, lymph nodes), synchronous or metachronous presentation, and primary resection. These factors have not previously been utilised in most other reported case series, which further adds to the strength of this report.

Specific comments follow (major revisions):

1. Some data points require further explanation in the text. For example, although the average age at presentation is similar to other case series, there is a heavy male predominance in this data set (73.6% of cases, compared to 61% in MD Anderson series, 53% AGEO series, and 53% in SEER database). The proportion of duodenal cancers is also much higher than in other reports (78% in this data set compared to 55% in SEER and other data sets), and the number of cases included from the second decade is double that of the first. Whilst these factors may all simply reflect referral patterns and variation between series, they do require discussion in the text and raise a concern regarding selection bias.

2. The clinical investigations that patients underwent are not clearly explained. Did all patients receive full body CT scanning? Was laparotomy used? Were lungs included in a CT or was chest xray used? Were bone scans standard? This information is useful to know because although “bone metastases” is a variable...
that is considered, it is not clear that all patients undergo bone scan, or whether the variable under investigation is symptomatic bone metastases. Lung metastases are also considered as a variable but it is also unclear from the text whether all patients underwent lung CT, or if some patients simply had a CXR. Understanding more of these details will enable the reviewer to more accurately appreciate the validity of the data.

3. The authors report that OS (6.6 months) and response rates (11%) are similar to other series. However in the MD Anderson series of 217 patients, the OS of stage 4 patients was 11 months, and in the AGEO study OS was 15 months and RR was 26%. At first appearance these figures seem discordant and warrant further discussion. Could perhaps the greater number of patients with duodenal carcinoma be a factor, such as is described in the ACS review of the National Cancer Database?

4. Performance status is not borne out as a prognostic variable, and this is in contrast to the other major published reports. Detailed discussion of this is required.

In summary, the data set the authors report is potentially useful, particularly given the inclusion of an untreated cohort with good performance status. The statistical analysis is sophisticated, and the authors are to be commended for their efforts to control for as many variables as possible. However such analyses are always fraught by confounding variables that are not readily identifiable or measurable from the case notes (hence the need for randomised trials). Also, there are notable differences in patient characteristics from other data sets that require elaboration, and more information on techniques of patient evaluation is required.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests