NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA100 Capecitabine and oxaliplatin in the adjuvant treatment of stage III (Duke's C) colon cancer

This guidance was issued in April 2006 with a review date of June 2009.

Recommendation

- A review of the guidance should be transferred to the static guidance list. That we consult on the proposal.

Consideration of options for recommendation:

Options	Comment
A review of the guidance should be planned into the appraisal work programme.	No new information
The decision to review the guidance should be deferred [to a specified date].	No new information
A review of the guidance should be combined with a review of a related technology and conducted at the scheduled time for the review of the related technology.	No related technology
A review of the guidance should be combined with a new appraisal that has recently been referred to the Institute.	No new appraisal
A review of the guidance should be incorporated into an on-going clinical guideline.	No new information to warrant being incorporated into a review
A review of the guidance should be updated into an on-going clinical guideline.	Updating the guidance is not appropriate within the ongoing clinical guideline on colorectal cancer, as the topic does not match the prioritisations set for the guideline.
A review of the guidance should be transferred to the 'static guidance list'.	**No new information means that the guidance can move to the static guidance list**

Original remit(s)

To appraise the cost and clinical effectiveness of the use of oxaliplatin, irinotecan and capecitabine as adjuvant therapy in colorectal cancer.

Current guidance

1.1 The following are recommended as options for the adjuvant treatment of patients with stage III (Dukes' C) colon cancer following surgery for the condition:

• capecitabine as monotherapy

• oxaliplatin in combination with 5-fluorouracil and folinic acid.

1.2 The choice of adjuvant treatment should be made jointly by the individual and the clinicians responsible for treatment. The decision should be made after an informed discussion between the clinicians and the patient; this discussion should take into account contraindications and the side-effect profile of the agent(s) and the method of administration as well as the clinical condition and preferences of the individual.

Relevant Institute work

- Improving outcomes in colorectal cancer (Cancer service guidance). Issued: June 2004
- Irinotecan, oxaliplatin and raltitrexed for advanced colorectal cancer (review of TA33) (Technology appraisal). Issued August 2005. The Institute was proposing a review of the guidance should be incorporated into an on-going clinical guideline, "Diagnosis and management of colorectal cancer", due July 2011.
- Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer (Technology appraisal). Issued: January 2008. Review date: May 2009
- Colorectal cancer (metastatic) - cetuximab (terminated technology appraisal). Issued: June 2008. NICE is unable to recommend the use in the NHS of cetuximab for the treatment of colorectal cancer following failure of oxaliplatin-containing chemotherapy because no evidence submission was received from the manufacturer or sponsor of the technology.
- Capecitabine and tegafur uracil for metastatic colorectal cancer (Technology appraisal). Issued: May 2003. Reviewed: April 2006 - static guidance
- Laparoscopic surgery for the treatment of colorectal cancer (Technology appraisal). Issued: August 2006. Review date: September 2009

- Irinotecan for the adjuvant treatment of colon cancer (Technology appraisal). Publication date: unknown. Irinotecan not currently licensed in the UK for this indication.
- Colorectal cancer (first line) - cetuximab (Technology appraisal). In progress. Expected date of issue: July 2009
- Diagnosis and management of colorectal cancer (Clinical guideline) In progress. Publication date: July 2011

On-going trials

Trial name and contact	Details
NCT00646607 FOLFOX-4 3months Versus 6 Months and Bevacizumab as Adjuvant Therapy for Patients With Stage II/III Colon Cancer (TOSCA)	A randomized trial investigating the role of FOLFOX-4 regimen duration (3 Versus 6 Months). Estimated completion date: March 2008
NCT00749450 Combination Chemotherapy After Surgery in Treating Patients With High-Risk Stage II or Stage III Colorectal Cancer	Patients are randomized (within 10 weeks after surgery and before or after receiving 12 weeks of chemotherapy) to 1 of 2 treatment arms. The treatment regimen that a patient receives (Oxaliplatin Modified DeGramont [OxMdG] or XELOX) is determined by the participating center. Estimated completion date: March 2014
NCT00268463 Oxaliplatin and Capecitabine With or Without an Hepatic Arterial Infusion With Floxuridine in Treating Patients Who Are Undergoing Surgery and/or Ablation for Liver Metastases Due to Colorectal Cancer	This randomized phase III trial is studying oxaliplatin, capecitabine, and an hepatic arterial infusion with floxuridine to see how well they work compared to oxaliplatin and capecitabine in treating patients who are undergoing surgery and/or ablation for liver metastases due to colorectal cancer. Estimated completion date: June 2008
NCT00427713 Capecitabine and Oxaliplatin or Standard Follow-Up Care in Treating Patients Who Have Undergone Surgery for Locally Advanced Rectal Cancer	This randomized phase III trial is studying capecitabine and oxaliplatin to see how well they work compared with standard follow-up care in treating patients who have undergone surgery for locally advanced rectal cancer. Estimated completion date: March 2008

New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline(R) In-Process and Embase. References from 2005 onwards were reviewed.

Implementation

A submission from Implementation is attached at the end of this paper.

Equality and diversity issues: Andres Roman – technical analyst

No equality and diversity issues identified.

Appraisals comment: Andres Roman – technical analyst

Overall the evidence base for capecitabine and oxaliplatin for the adjuvant treatment of colon cancer has not significantly changed since guidance was published.

The original remit for capecitabine and oxalipaltin included irinotecan. However, irinotecan was excluded from the original guidance because at the time it was not licensed in the UK for this indication. This remains the situation for irinotecan.

Summary

The evidence available concerning capecitabine and oxaliplatin has not significantly changed, and the manufacturer of irinotecan is not pursuing a license for adjuvant therapy, it is recommended the guidance is transferred to the static list.

Information Specialist: Daniel Tuvey
Technical Lead: Andres Roman
Technical Adviser: Prashanth Kandaswamy
Implementation Analyst: Mariam Biby
Project Manager: Natalie Bemrose

GE paper sign off:

Nina Pinwill, Associate Director, CHTE
7 August 2009

NATIONAL INSTITUE FOR HEALTH AND CLINICAL EXCELLANCE

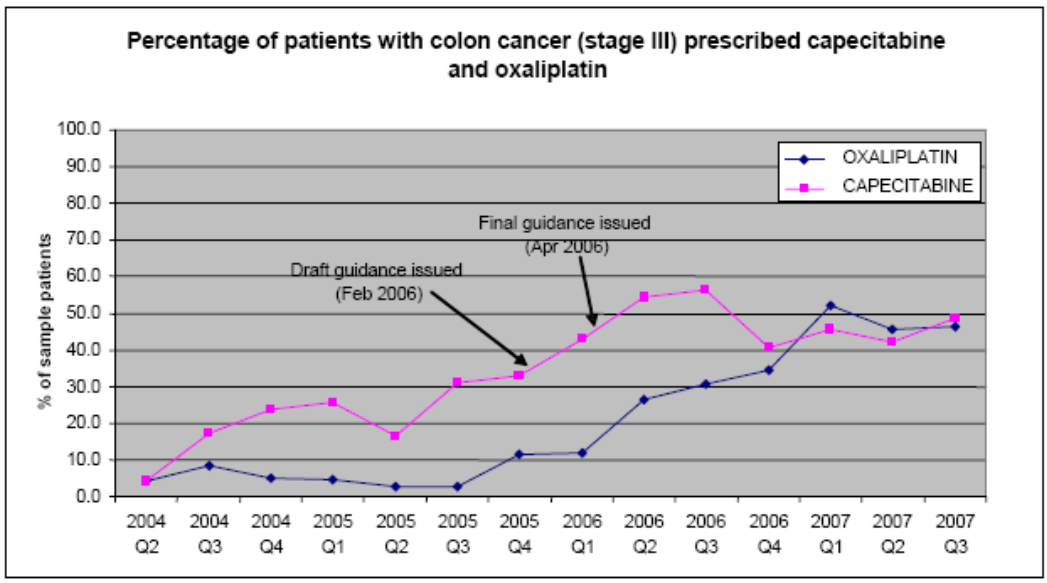
IMPLEMENTATION DIRECTORATE

Guidance Executive Review

Technology appraisal 100: Guidance on the use of capecitabine and oxaliplatin for the treatment of colon cancer (adjuvant)

1. NICE implementation uptake report: capecitabine and oxaliplatin for colon cancer

IMS Health completed an analysis of a sample of anonymised patient records data using the IMS Oncology Analyzer (IMS OA). In this analysis the number of patients in the sample varies each quarter but the average number included is 65.



The IMS OA links treatment to diagnosis enabling analysis beyond the scope of national prescribing costs. The above chart shows that the proportions of patients receiving oxaliplatin and capecitabine increased following the publication of draft NICE guidance in February 2006 and continued to increase following publication of the final guidance in April 2006. The proportions of patients receiving these drugs appears to have levelled off since the beginning of 2007 at between 40 and 50% but further data is needed to confirm this trend.

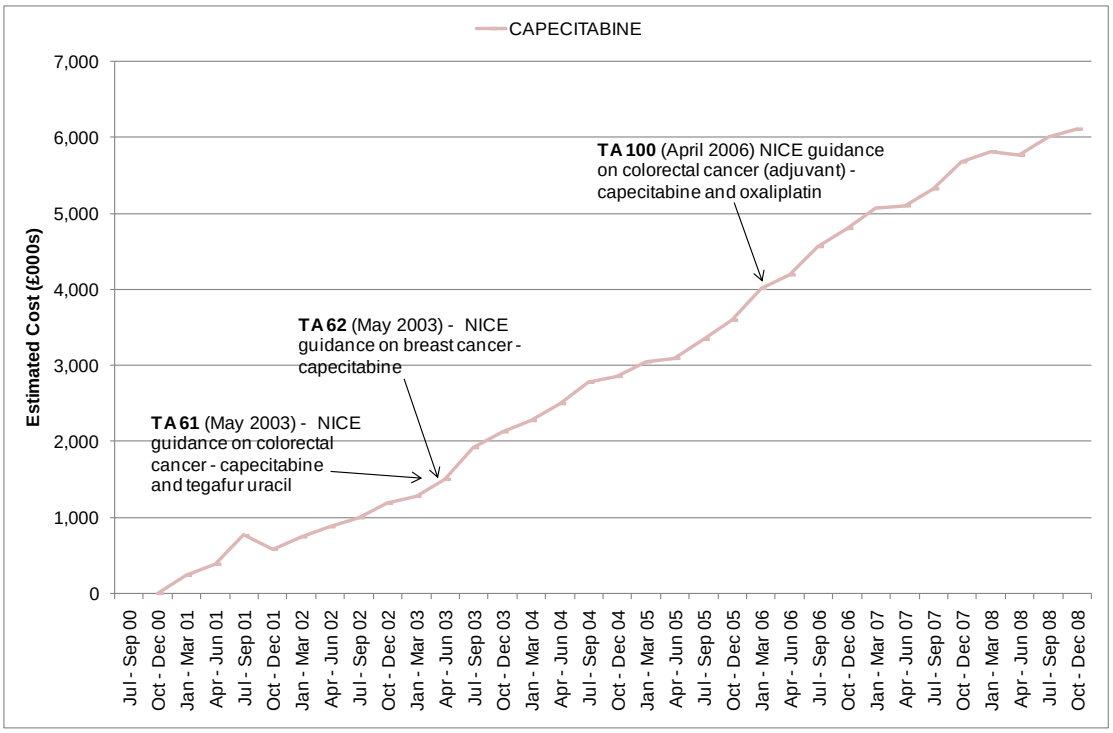
The IMS OA also allows analysis of specific drug regimens in use. The specific drug regimens in use in the year to June 2007 demonstrate both compliance and variation with

the NICE guidance recommendations. Data show that in line with predictions made in the NICE costing report, 23% of patients were prescribed oxaliplatin with 5-fluorouracil, although folinic acid was only added in half of these cases (12%). Capecitabine was prescribed for 45% of patients in total. This was slightly less than the suggested 60% but the small sample size may account for some of this difference. Importantly, 16% of patients received both capecitabine and oxaliplatin.

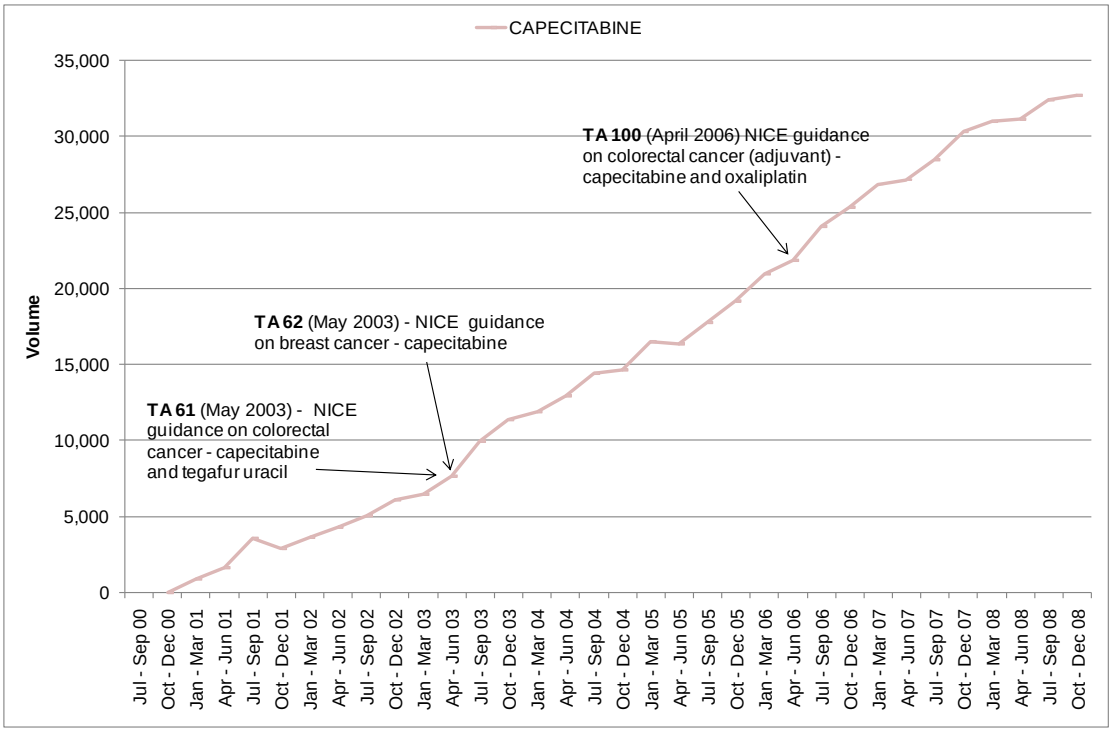
2. National Prescribing Data

Data showing trends in prescribing costs and volume are presented below. Unfortunately this data does not link to diagnosis or stage of cancer so needs to be treated cautiously in relation to the specific recommendations of the guidance. Additionally, the HPAI database measures volume in packs and a drug may be available in different pack sizes and pack sizes can vary between medicines. Estimated costs are also calculated by IMS using the drug tariff and other standard price lists. Many hospitals receive discounts from suppliers and this is not reflected in the estimated cost.

Estimated Cost

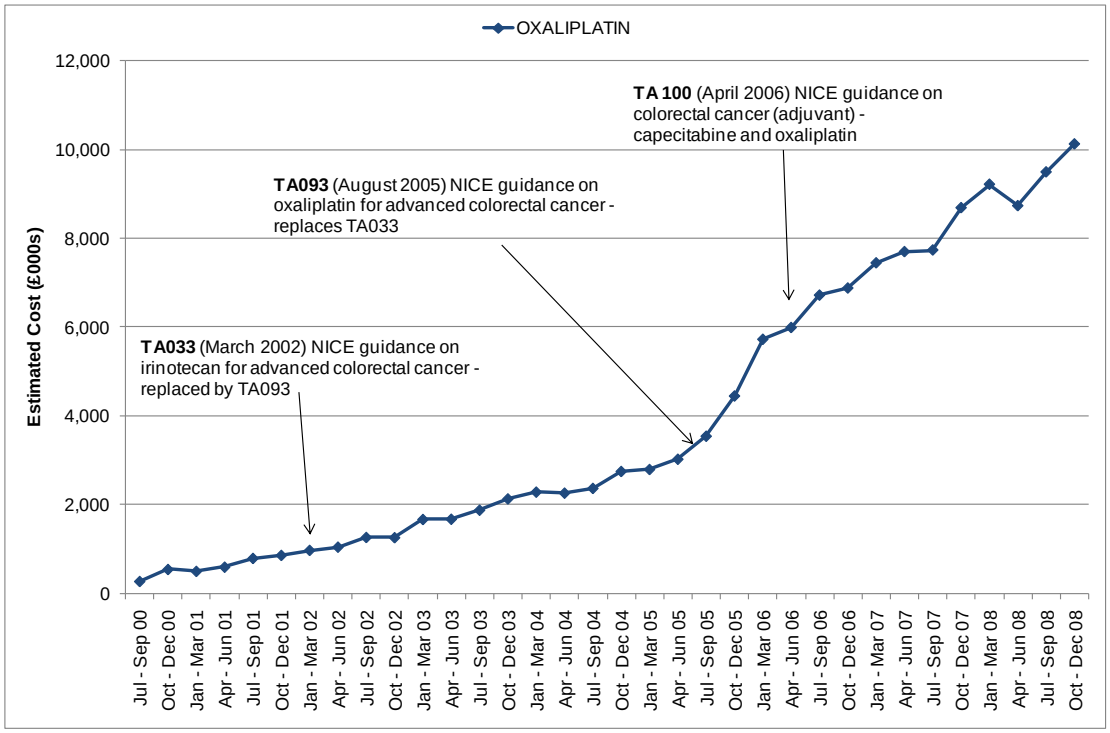


Volume

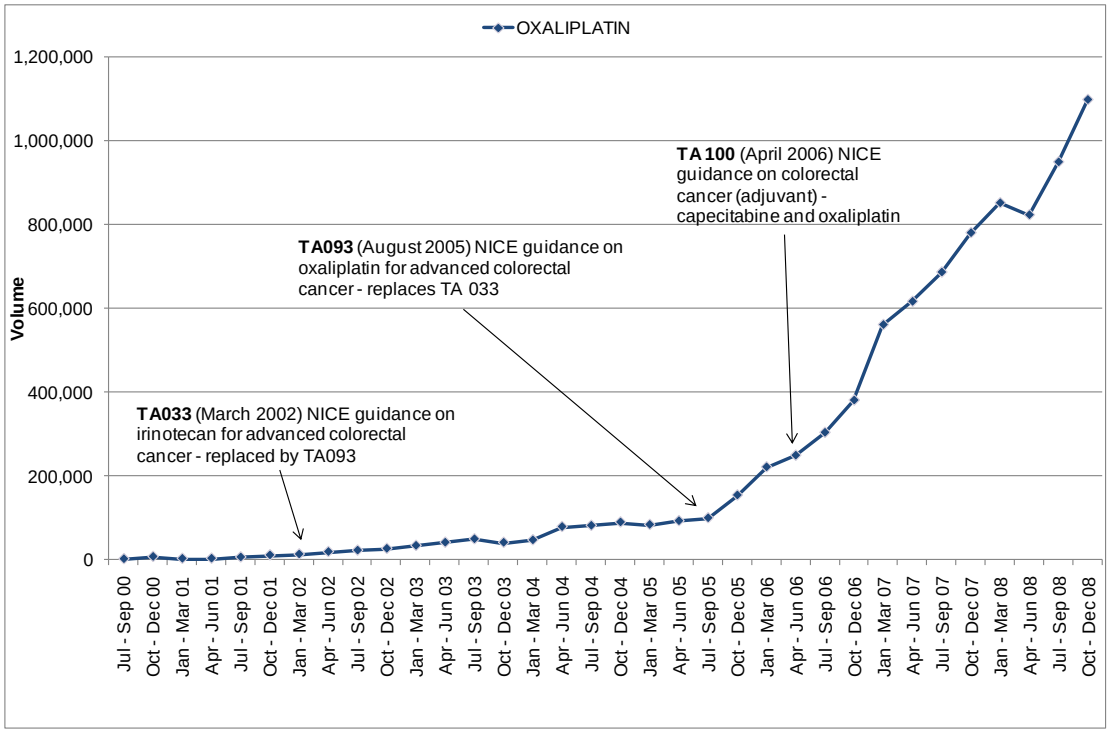


IMS Health: Hospital Pharmacy Audit.

Estimated Cost



Volume



IMS Health: Hospital Pharmacy Audit.

3. External literature

Richard M (2006) "Usage of cancer drugs approved by NICE: Report of Review undertaken by the National Cancer Director" Department of Health: London

The 2006 report shows: (i) a continued increase in uptake of cancer drugs following a positive NICE appraisal, (ii) a reduction in the variation in usage of all 15 NICE-approved drugs since a 2003 analysis. Variations in usage between cancer networks were wider for some NICE-approved drugs than others. The X-fold variation in usage over the first half of 2005 for Capecitabine (Xeloda) was 3.3, and 3.0 for Oxaliplatin (Eloxatin), a reduction in variation of 9% and 19% respectively since the second half of 2003.

4. References

- Capecitabine and oxaliplatin for colon cancer - uptake report http://www.nice.org.uk/media/543/99/UptakeReportTA100CapecitabineOxaliplatin.pdf
- Richard M (2006) "Usage of cancer drugs approved by NICE: Report of Review undertaken by the National Cancer Director" Department of Health: London