Submission from CancerBACUP to NICE Appraisal Committee on oxaliplatin and capecitabine for adjuvant colorectal cancer

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CancerBACUP welcomes the opportunity to contribute to the appraisal of oxaliplatin and capecitabine for the adjuvant treatment of colorectal cancer. As the leading specialist provider of independent information on all types of cancer, CancerBACUP has regular contact with people living with colorectal cancer and those caring for them.

CancerBACUP received nearly 5,000 enquiries last year from people affected by colorectal cancer.

CancerBACUP believes that everyone with cancer should be offered the most effective and appropriate treatment, based on the available evidence and the patient's own wishes and preferences. We believe that:

- Patients should have access to the most effective treatments appropriate to them as individuals;
- Patients should be able to choose – in partnership with their oncologist – the treatment that is likely to suit them best in terms of relative benefits and side-effects;
- The impact of treatments on patient's quality of life, as well as length of life, should be given full consideration by the Appraisal Committee.

We urge the Appraisal Committee to recommend that oxaliplatin and capecitabine should be available for the adjuvant treatment of patients with colorectal cancer.

Living with colorectal cancer

An estimated 30,909[1] new cases of colorectal cancer are diagnosed each year in England and Wales. In most people the cause of cancer of the large bowel is still unknown, but research is going on all the time to try to find the cause. Like most types of cancer, colorectal cancer is more common in older people and it is unusual for bowel cancer to be diagnosed in people under 50.

The symptoms of colorectal cancer may include any of the following:

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[1] CancerStats Monograph 2004, Cancer Research UK

1. blood in, or on, the stools (bowel motion). The blood may be bright red or dark in colour
2. a change in normal bowel habit (such as diarrhoea or constipation) for no obvious reason, lasting longer than six weeks
3. unexplained weight loss
4. pain in the abdomen or back passage
5. a feeling of not having emptied the bowel after a bowel motion

Sometimes the cancer can cause a blockage in the bowel. The symptoms of this are sickness, constipation, griping pain and a bloated feeling in the abdomen.

Knowing the extent of the cancer helps the doctors to decide on the most appropriate treatment. Often the exact stage of bowel cancer can only be known after it has been removed by surgery. Generally, cancer of the large bowel is divided into four stages. Doctors often use a staging system created by pathologist called Dukes to describe large bowel cancer.

The Dukes staging system

Dukes A – The cancer is contained within the bowel wall.

Dukes B – The cancer has spread through the muscle of the bowel wall, but the lymph nodes are not affected.

Dukes C – The cancer has spread to one or more of the lymph nodes close to the bowel. Lymph nodes are usually the first place the cancer spreads to.

Dukes D – The cancer has spread to another part of the body such as the liver or the lungs (secondary cancer).

Chemotherapy as a current treatment option for colorectal cancer

In the treatment of colorectal cancer, chemotherapy is mainly used after surgery – known as adjuvant treatment. The aim of adjuvant treatment is to get rid of any remaining cancer cells and reduce the chance of the cancer coming back in the future.

In this situation there are various benefits and risks to patients having chemotherapy. The chemotherapy can reduce the chance of the cancer coming back but can also sometimes cause side effects that may be unpleasant. If the chance of the cancer coming back is low, the chemotherapy may only slightly reduce the chance of the cancer returning. On the other hand, if the risk of the cancer coming back is high, the chemotherapy can greatly reduce the chance of the cancer returning.

Capecitabine

Capecitabine is an oral chemotherapy that is given as a treatment for some types of cancer, including advanced bowel cancer, breast cancer and ovarian cancer.

Oxaliplatin

Oxaliplatin is a chemotherapy agent that is given as a treatment for some types of cancer. It is most commonly used to treat cancer of the large bowel. Oxaliplatin is often given in combination with other chemotherapy drugs such as 5FU or capecitabine.

CancerBACUP argues strongly that NICE should recommend that capecitabine and oxaliplatin is available on the NHS for the treatment of patients with colorectal cancer in the adjuvant setting in accordance with their licences for the following reasons:

1. **Adjuvant capecitabine and oxaliplatin can extend survival for patients with adjuvant colorectal cancer**

Results from one trial of patients with early stage adjuvant colorectal cancer show that adjuvant treatment with oxaliplatin can lead to improved survival.

Results from the MOSAIC trial, a study in 2246 patients with stage II or stage III colon cancer, showed that the addition of oxaliplatin to adjuvant therapy with fluoracil and folinic acid (FOLFOX4 regimen) is associated with a significantly greater disease free survival at three years (78 percent vs 73 percent). This equates to a 23 percent reduction in the risk of disease recurrence after surgery was seen with FOLFOX4 compared with fluorouracil/folinic acid in the MOSAIC trial.[2]

In the subgroups of patients with stage III disease, the 3-year disease-free survival rate was 72 percent with FOLFOX4 and 65 percent with fluorouracil/folinic acid.[3]

The overall survival at 3 years was 88 percent with FOLFOX4 and 87 percent with fluorouracil/folinic acid.[4] Five-year results are likely to clarify the impact of oxaliplatin on overall survival.[5]

Recent data from a large, international, randomised trial confirm that capecitabine is at least as effective as IV 5-FU/LV in the adjuvant treatment of patients with resected stage III colon cancer.[6]

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[2] Susan J Keam, Christopher J Dunn and David P Figgitt. Drugs 2005: 65 (1): 89-96
[3] Andre T, Boni C, Mounedji-Boudiaf L, et al. Oxaliplatin, fluouracil and leucovorin as adjuvant treatment for colon cancer. N Engl J Med 2004 Jun 3; 350 (23): 2343-51
[4] Oxaliplatin: summary of product characteristics. Paris: Sanofi- Synthelabo, 2004 Sep 13
[5] Susan J Keam, Christopher J Dunn and David P Figgitt. Drugs 2005: 65 (1): 89-96

2. Capecitabine and oxaliplatin are well-tolerated in patients with colorectal cancer

Capecitabine has a favourable safety profile compared with 5-FU/LV. Overall, fewer treatment-related adverse events occur with capecitabine than with 5-FU/LV. Patients receiving capecitabine experienced significantly less diarrhoea, nausea and vomiting, stomatitis and alopecia compared with those receiving 5-FU/LV. Hand-foot syndrome was more frequent with capecitabine that with 5-FU/LV.[7]

Oxaliplatin was generally well tolerated in the MOSAIC trial. The most common reported side effect was peripheral sensory neuropathy. Apart from peripheral neuropathy, neutropenia, diarrhoea and vomiting were the most common adverse side effects reported with FOLFOX4. [8]

3. Capecitabine can significantly improve quality of life

Patients given capecitabine report a significantly higher improvement in quality of life. Capecitabine gave high concentration of 5-FU to the tumour site, thereby limiting the side effects and other complications associated with intravenous 5-FU.[9] Because capecitabine is orally administered, it is possible to intervene promptly with dose interruption/reduction to resolve adverse events without impacting on efficacy. As an oral drug, capecitabine is preferred to many patients as it can be conveniently taken at home.[10]

Other points for consideration by the Appraisal Committee

Patients receiving oral chemotherapy such as capecitabine will need access to nursing support and care to ensure concordance and safety.

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[6] Eric Van Cutsem, Chris Verslype and Sabine Tejpar. Seminars in Oncology Feb 2005, vol 32, no. 1, p 43-51

[7] Cassidy J, Twelves C, Van Cutsem E, et al: First-line oral capecitabine therapy in metastatic colorectal cancer: A favourable safety profile compared with intravenous 5-fluouracil/leucovin. Ann Oncol 13: 566-575, 2002

[8] Susan J Keam, Christopher J Dunn and David P Figgitt. Drugs 2005: 65 (1): 89-96

[9] Ishitsuka, H,. 2000. Capecitabine: preclinical pharmacology studies. Investigational New Drugs 18 (4), 343-354.

[10] Borner, Mm., Schoffski, P., de Wit, R., et al., 2002a. Patient preference and pharmacokinetics of oral modulated UFT versus intravenous fluorouracil and leucovorin: a randomised crossover trial in advanced colorectal cancer. European Journal of Cancer 38, 349-358.

Declaration of interest

CancerBACUP has received sponsorship from Sanofi Aventis, the manufacturer of oxaliplatin, and Roche, the manufacturer of capecitabine, for several publications and projects.

Joanne Rule
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