PERGAMON

European Journal of Cancer 38 (2002) S1–S2

European Journal of Cancer

www.ejconline.com

New paradigms in the treatment of breast and colorectal cancer—an introduction

S. Kaye*

Royal Marsden Hospital, Downs Road, Sutton, Surrey SM2 5PT, UK

Received 25 June 2001; received in revised form 26 November 2001; accepted 29 November 2001

Breast and colorectal cancer are two of the most common cancers in Europe and the cause of considerable morbidity and mortality. Over the past 20 years, the 5-year survival for patients with both tumour types has increased by 10–15%, largely due to improved and earlier diagnosis and the use of adjuvant therapy. Nevertheless, the 5-year survival rates for patients with breast and colorectal cancer are currently 70% and 45%, respectively, and many patients ultimately die from their diseases [1,2].

Considerable challenges remain in the treatment of primary and metastatic breast and colorectal cancer. There is a significant need for adjuvant therapies which offer enhanced efficacy, tolerability and convenience. In addition, the use of highly active chemotherapeutic agents such as taxanes earlier in the disease course or as adjuvant therapy has resulted in an increasing number of patients presenting with disease that is refractory to traditional chemotherapeutic agents. Therefore, new treatment options are required for metastatic disease. An ideal therapy in the metastatic setting would effectively reduce tumour-related symptoms while maintaining or improving patients' quality of life and, ultimately, enhance survival.

In recent years, several agents have been developed which specifically target tumour cells. One of the most

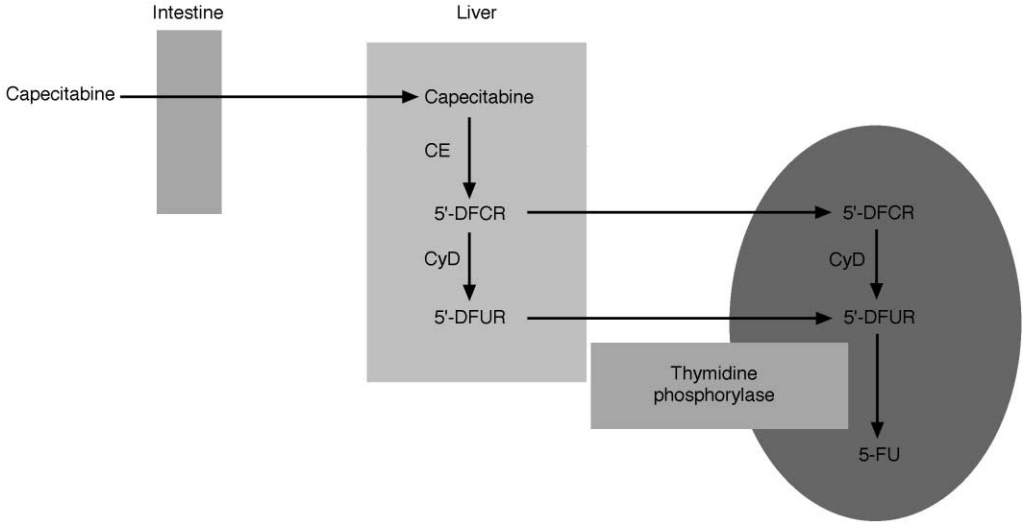

Fig. 1. Enzymatic activation of capecitabine. 5-FU, 5-fluorouracil; 5′-DFCR, 5′-deoxy-5-fluorocytidine; CE, carboxylesterase; CyD, cytidine deaminase; 5′-DFUR, 5′-deoxy-5-fluorouridine.

* Tel.: +44-208-661-3538; fax: +44-208-661-3541.
E-mail address: stan.kaye@rmh.nthames.nhs.uk (S. Kaye).

0959-8049/02/$ - see front matter
PII: S0959-8049(01)00418-X

promising of these is capecitabine, an oral fluoropyrimidine that was rationally designed to generate 5-fluorouracil (5-FU) preferentially in tumour tissue. For many years, 5-FU has been an important component of the standard treatment for a wide range of solid tumours. Owing to the unpredictable bioavailability of oral 5-FU, administration is usually intravenous (i.v.), either as a bolus or as protracted or continuous infusion. However, i.v. schedules are cumbersome to administer, inconvenient for the patient and labour-intensive for the medical staff. Oral capecitabine enables daily dosing, thus mimicking continuous infusion 5-FU, while sparing patients the discomfort and inconvenience associated with i.v. regimens. The unique mechanism of activation of capecitabine, which involves conversion to 5-FU by thymidine phosphorylase, results in higher concentrations of 5-FU in the tumour compared with normal tissue, thereby avoiding extensive systemic exposure and potentially improving tolerability and/or enhancing anti-tumour activity (Fig. 1).

This supplement contains detailed reviews of the rational development of capecitabine and clinical trial data that have established capecitabine as an effective and well tolerated treatment for patients with colorectal and breast cancer. The final article (Wilke) provides an overview of ongoing clinical trials investigating capecitabine either as a single agent in new treatment settings or as a component of combination regimens. The results of these trials should further expand the role of capecitabine in the treatment of solid tumour patients.

References

1. Black RJ, Bray F, Ferlay J, *et al*. Cancer incidence and mortality in the European Union: cancer registry data and estimates of national incidence for 1990. *Eur J Cancer* 1997, **33**, 1075–1107.
2. Richards MA, Stockton D, Babb P, Coleman MP. How many deaths have been avoided through improvements in cancer survival? *Br Med J* 2000, **320**, 895–898.